

**62nd Annual Academic Day
29 August 2018**

**62^{ste} Akademiese Jaardag
29 Augustus 2018**

ABSTRACTS / ABSTRAKTE

ABSTRACTS / ABSTRAKTE

Theme 1 - Health Systems Strengthening / Tema 1 – Gesondheidsisteme

Versterking

Abstracts / Abstrakte

p3

Theme 2 - Infectious Diseases / Tema 2 - Infeksiesiektes

Abstracts / Abstrakte

p20

Theme 3 - Mental Health and Neurosciences / Tema 3 – Geestesgesondheid en Neurowetenskappe

Abstracts / Abstrakte

p65

Theme 4 - Non-communicable Diseases / Tema 4 – Nie-oordraagbare Siektes

Abstracts / Abstrakte

p92

Theme 5 - Maternal and Child Health / Tema 5 – Moeder- en Kind Gesondheid

Abstracts / Abstrakte

p117

Theme 6 – Perioperative Sciences / Tema 6 – Perioperatiewe Wetenskappe

Abstracts / Abstrakte

p141

Theme 7 - Violence, Injuries, Trauma and Rehabilitation / Tema 7 – Geweld, Beserings, Trauma en Rehabilitasie

Abstracts / Abstrakte

p154

**The contents of this section are published as received /
Die inhoud van hierdie afdeling is gepubliseer soos dit ontvang is**

Theme 1 / Tema 1

***Health Systems Strengthening/
Gesondheidsisteme Versterking***

ORAL PRESENTATIONS / REFERATE

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

Burden and profile of spinal pathology at a major tertiary hospital in the Western Cape, South Africa

Sanesh Miseer (Division of Orthopaedic Surgery, Department of of Surgical Sciences, Faculty of Medicine and Health Sciences, Tygerberg)

Background Spinal pathology in the Western Cape is managed at three tertiary level hospitals. The Tygerberg Hospital Orthopaedic Spinal Unit is responsible for the management of spinal pathology in the hospital's catchment area. However, the Unit's overall burden of disease and resource use is unclear. **Aim** The first aim was to investigate the overall burden and clinical profile of spinal pathology presenting to Spine Unit over a one-year period. The second aim was to determine resource use associated with spine pathology admissions. **Methods** Overall burden was investigated by performing a retrospective review of all patients admitted to the Spine Unit between 2016-2017. Demographic and clinical data was collected and patients were assigned to one of five spinal pathology sub-groups. Resource use was determined by length of hospital stay, waiting times and advanced imaging and theatre usage. **Results** Overall burden was comprised of 349 individual patients and 376 admissions, including readmissions. Trauma (51%) and infection (24%) accounted for the majority of admitted pathology. Motor vehicle accidents (MVA's) were the primary mechanism of injury accounting for 48% of spine trauma. Tuberculosis (TB) was the causative organism in 87% of spinal infections with 44% HIV co-infection. Hospital resource use was considerable with 92% of spine patients requiring advanced imaging, a median operating time of 3h 36min and a median hospital stay of 19 days. Infection and malignancy sub-groups had the longest waiting times for advanced imaging and theatre with a median wait of 14-16 days, accounting for approximately 62% of the typical total hospital stay. **Conclusions** The Spine Unit experienced a substantial patient burden requiring significant hospital resources. Reduced in-patient waiting times and upskilling of orthopaedic services at secondary hospitals represent key areas for health system strengthening. However, multi-sectoral strategies are required to effectively address our high burden of preventable spinal pathology.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Effectiveness of Physiotherapy versus Standard Medical Care on Pain, Disability, Kinesiophobia and Pain Catastrophization in Adult Patients with Non-Specific Acute Low Back Pain: A Systematic Review and Meta-analysis

Carla Maritz (Stellenbosch University), Chane' van Straaten (Stellenbosch University), Courtney-Jade Nel (Stellenbosch University), Linzette Morris (supervisor) (Stellenbosch University), Lizaan Johannes (Stellenbosch University), Petro Rossouw (Stellenbosch University), Tine' Kitshoff (Stellenbosch University)*

Objective The objective of this systematic review is to identify and evaluate the best available evidence for improving pain, disability, fear-avoidance behaviour and pain catastrophization in individuals experiencing non-specific acute LBP. **Methods and Analysis** A comprehensive search strategy was conducted within the following seven databases: Cochrane Library, EBSCO Cinahl, EBSCO SportDiscus, PEDro, Pubmed, Science Direct and Scopus. No date limit was applied. The PEDro score was used for methodological appraisal and the National Health and Medical Research Council (NHMRC) Evidence Hierarchy for determining the strength of the evidence. Three reviewer pairs evaluated the relevant articles according to the inclusion criteria and extract relevant data. Ethics approval was not required due to the nature of the study design. **Results** A total of nine articles were included. Total sample size consisted of 993 participants, 508 in the physiotherapy group and 486 in the standard medical care group. The mean age in the studies ranged from 33.3 to 41.4 years. Both male and female participants were included. The study reported on the effect of physiotherapy to standard medical care. In the short term period the meta-analysis showed that physiotherapy was significantly more effective in reducing pain than standard medical care [95% CI, -0.90 to -0.12, p=0.01]. When measuring disability, the

meta-analysis found no significant difference but did favour physiotherapy at all time-intervals. For the other two outcomes, no significant findings were found. Conclusion The results obtained in this review found no significant difference between physiotherapy versus standard medical care. However, in general physiotherapy was favoured in the outcomes measured. It is therefore recommended, that within the short-term period, patients should seek physiotherapy treatment opposed to standard medical care, in order to prevent chronicity and therefore prevent the need for mid to long term intervention.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

Factors associated with non-attendance of scheduled occupational and physiotherapy outpatient follow-up appointments at the Western Cape Rehabilitation Centre (WCRC)

Andrea Boon (Stellenbosch University), Lize Eloff (Stellenbosch University), Megan Carelse (Stellenbosch University), Michaela Stewart (Stellenbosch University), Minal Zaidi (Stellenbosch University), Zani Naud  (Stellenbosch University)

Introduction: Occupational therapists and physiotherapists use follow-up appointments, to continue and monitor the effectiveness and outcome of therapy intervention. Patients with physical impairments are assisted by therapists to prevent and manage secondary complications and to maintain their functionality. Attendance of follow-up appointments are essential in the treatment process, as non-attendance has negative implications for both the patient and healthcare facility. Objectives: The objectives of this research were to 1) provide a description of the characteristic factors of attending and non-attending patients with scheduled occupational therapy and physiotherapy appointments at outpatient clinics at the Western Cape Rehabilitation Centre and 2) to determine the association between non-attendance and identified covariates. Methodology: A retrospective, cross-sectional study of all outpatients with a scheduled appointment between January 2017 and December 2017 at Western Cape Rehabilitation Centre was conducted in which a period census was used to sample patients (n =837). Descriptive statistics was used to report the research results and additionally, logistic regression was employed to determine the adjusted odds ratio for the association between non-attendances and identified characteristic factors. Ethical clearance was obtained from the Undergraduate Research Ethics committee at Stellenbosch University prior to data collection. Results and conclusion: The current study provides useful insights into the factors associated with non-attendance of outpatients to scheduled occupational therapy and physiotherapy appointments at the Western Cape Rehabilitation Centre and contributes to limited research on the topic in a South African context. Factors that had a significant association with non-attendance included hospital classification, diagnostic category and impairment according to ICD 10 coding. Further studies are needed to determine the reasons for non-attendance at institutions such as Western Cape Rehabilitation Centre which will assist the institutions in implementing solutions to reduce high rates of non-attendance.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Lost to follow-up: Challenges to conducting orthopaedic research in South Africa

De la Rey Badenhorst (Tygerberg orthopaedic department), Elsab  Britz (Tygerberg orthopaedic department), Mariliza Burger (Tygerberg orthopaedics research department), Nando Ferreira (Tygerberg orthopaedic department)

Loss-to-follow-up presents a major concern for treating physicians and researchers. The aim of this study was to describe potential factors contributing to the loss-to-follow-up experienced in orthopaedic patients attending the sole public orthopaedic service provider within the Northern Cape Province in South Africa. Patients who underwent ankle fracture surgery at Kimberly Provincial hospital were included in this study. Demographic information of all patients that were admitted for ankle fracture surgery between January 2012 and July 2013 were captured and reviewed. (ECUFS NR 50/2012) Two-hundred-and-sixty-eight patients (male: n=112 (42%); female: n=156 (58%)) were included in this study between January 2012 and July 2013 after admission to Kimberly Provincial Hospital for surgical intervention. The mean age was 42.3 \pm 13.8 (95% CI 40.6 $\hat{=}$ 43.9, n=266) years and the mean BMI

was 28.0 $\hat{\pm}$ 6.5 (95% CI 27.2 $\hat{\pm}$ 28.8, n=251) with the BMI of females being 30.2 $\hat{\pm}$ 6.1 (95% CI 29.3 $\hat{\pm}$ 31.2, n=152) compared to the 24.6 $\hat{\pm}$ 5.7 (95% CI 23.4 $\hat{\pm}$ 25.7, n=99) of male patients. Excluding the local patients residing in Kimberly (n=77) within 5km travel distance, the mean travel distance increased to 460km, ranging from 10 $\hat{\pm}$ 910km. Significant associations between the number of follow-up visits attended and i) travel distance (IRR 0.999 (95% CI 0.999 $\hat{\pm}$ 1.000), p=0.030), ii) BMI (IRR 0.980 (95% CI 0.966 $\hat{\pm}$ 0.994), p=0.004) and iii) HIV status (IRR 0.841 (95% CI 0.725 $\hat{\pm}$ 0.975), p=0.022) were observed. Research in the South African setting is hindered by loss to follow up in the public setting. Increased travel distance, financial constraints and lifestyle habits contribute to the complexities of follow-up. A future, multi-center approach could potentially provide an improved strategy in protocol planning to accommodate for these factors to improve our patient follow-up and related research quality.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Developing an innovative pre-vocational school to work programme at a special school in Cloetesville, Stellenbosch

Zelda Coetzee (Division Occupational Therapy)

The Occupational Therapy Division began partnering with Dorothea Special School in 2012. The school is registered as a school for Learners with Special Needs (LSEN), moderate levels of intellectual developmental disorders (IDD). The main aim was to train undergraduate occupational therapy students clinically at this practice site. Staffing included an occupational therapist on site with a learner-therapist ratio of 1: >800 = 0,125 per 1 learner. As a result of this statistic, few individual OT sessions are provided while a programmatic approach is utilized. When we arrived, the OT had created training structures such as Electives and community work placements. These served to offer training opportunities to the learners during the last two years of secondary education/training. As the SU lecturer, I was in a position to develop the existing school- to- work transition structures. My presentation will describe the process and future plans of this programme, set up in partnership of Stellenbosch University and Dorothea Special School. The existing and envisioned school- to- work transitional programme has the potential for strengthening educational-economic and social systems by preparing the learner earlier for employment and therefore, circumventing the poverty cycle.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

Understanding community mobility in older adults within the Cape Town Metropole using an occupational lens.

Courtney Hickson (Stellenbosch University), Ermen Venter (Stellenbosch University), Rene Potgieter (Stellenbosch University), Samantha Sephton (Stellenbosch University), Talita Stapelberg (Stellenbosch University)

Background: Aging world populations cast a spotlight on older adults' occupational participation. To encourage occupational participation in older adults, occupational therapists need to have a clear understanding of the ways older adults access out-of-home occupations. Purpose: This research project aims to identify and establish the meaning of out-of-home occupations of older adults in the Cape Town Metropole, the ways in which these occupations are accessed and the correlation of community mobility with self-reported health. Methods: Face-to-face interviews were conducted using a structured interview form in a cross-sectional research design with a convenience sample of a population of 40 older adults in the Cape Town Metropole. The sample included urban, healthy, independent living, upper-middle income individuals 65 years and older without known physical or cognitive impairments, residing in Oasis Retirement Resort. Results: The demographic make-up of the sample (N=40) consisted of majority of participants being English speaking (n=37), female (n=27) and widowed (n=23). Most of the participants (n=32) were active drivers, and self-driving was the mode of community mobility most frequently used. The second most used mode of community mobility was being a car passenger (n=38). Walking as a mode of community mobility was used by the majority of participants (n=33). The out-of-home places which signified the most meaning for the majority of the

sample were the community garden, restaurant, coffee shop or bar, friends and family members' houses, the doctor and dentist's office, the hairdresser, salon or barbershop and the pharmacy. Conclusion: As occupational beings, older adults benefit from, and have an occupational right to access their valued occupations. Occupational therapists facilitate participation in these occupations; one way in which this may be achieved, is by ensuring suitable community mobility options.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

A Framework for Effective Decentralised training in the health professions

Athol Kent (Stellenbosch University), Ian Couper (Stellenbosch University), Julia Blitz (Stellenbosch University), Marietjie De Villiers (Stellenbosch University), Susan Van Schalkwyk (Stellenbosch University)

Background Training institutions are being challenged to increase the number of graduates in the health professions. This has implications for available space on the clinical training platform. Decentralising training has proven workforce, health service, and academic advantages. Stellenbosch University Collaborative Capacity Enhancement through Engagement with Districts (SUCCEED) has developed a framework for effective decentralised training in the health professions which can serve as a basis for implementing and sustaining such training initiatives. Summary of work Various data sources were utilised in the development of the framework namely a scoping review of the literature on decentralised training, a national expert panel workshop, two multi-professional national workshops, a Delphi survey, and two separate processes of interpretive synthesis. Summary of results A transformative vision for decentralised training was formulated. At the centre of the composite framework, relationships bind together role players in training institutions, health services, regulatory bodies, and community. A series of enabling factors for each of five key components (leadership and governance, curriculum, students, training environment, communities) provides a practical approach to effective decentralised training for the role players. Five overarching principles that are needed to guide such training include shared vision, responsive adaptability, continuity, social accountability, and integration. A cascade approach guides the buy-in of relevant stakeholders. Discussion and Conclusions South Africa is committed to the policy of universal access to healthcare, requiring consistency in health professions training across disciplines, institutions, and regions. The framework provides an approach to decentralised training that encourages optimum consistency in universal access without overly constraining local decision-making and action. A matrix of enabling factors assisting implementation, and recommendations as to how the framework can be used to derive localised contextualised plans, is provided.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

INITIAL IMPLEMENTATION OF AN INTEGRATED E-PORTFOLIO TO FACILITATE TRANSFORMATIVE LEARNING AND ENHANCE QUALITY TEACHING IN A PREDOMINANTLY DISTANCE LEARNING POSTGRADUATE PROGRAMME

Mariette Volschenk (Centre for Health Professions Education, Faculty of Medicine and Health Sciences, Stellenbosch University)

Introduction: During a recent curricular revision of the MPhil in Health Professions Education Programme, the Centre for Health Professions Education at Stellenbosch University's Faculty of Medicine and Health Sciences decided to incorporate electronic portfolios (e-Portfolios) as a means to support transformative learning in this predominantly distance learning programme. Drawing on the powerful connection between quality teaching and the beliefs, values and professional ethics of educators, this integrated e-Portfolio module aims to facilitate the longitudinal development of students' personal teaching philosophies through engagement with multisource feedback, regular critical reflection, and professional development plans. Summative assessment comprises a reflective narrative about the impact of students' learning experiences on their teaching philosophy and longitudinal development as health professions educators, with reference to self-selected evidence showcased in their e-Portfolios. The module team regularly interacts with students on the e-Portfolio platform and provides scaffolding prompts and formative feedback to support the development of

metacognitive reflection and self-directed learning skills. Method: Action research methodology is employed to support the ongoing systematic inquiry, implementation, evaluation and improvement of this module, which is in its 3rd year of implementation. Discussion: This paper examines the initial implementation and further development of the e-Portfolio module and offers a critical reflection on how the various facets of the e-Portfolio learning process support students' interactions with their developing teaching philosophies and contribute to their development as educational scholars and leaders in the field of Health Professions Education.

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

Reflecting on the evolution of the Faculty of Medicine and Health Sciences Rural Clinical School

Jana Muller (Ukwanda Centre for Rural Health)

Introduction In reflection on the 100 years of the successful establishment of Stellenbosch University it is important to reflect on some of the Faculty of Medicine and Health Sciences (FMHS) achievements. In 2009 the FMHS and Stellenbosch University's HOPE project envisaged a university-wide rural platform, with the rural clinical school (RCS) being a significant component of that, growing into a truly sustainable rural development project with a dedicated focus on the issues that affect all aspects of human security in rural areas. In 2011 the Faculty opened the doors of the RCS to clinical training on a rural platform in the Cape Winelands and Overberg regions. This opportunity has resulted in 722 final year students experiencing the unique RCS environment over 6 years. **Methodology** In writing a comprehensive report regarding "The RCS Story", an explorative inquiry into the history of the Ukwanda CRH and the development of the RCS, spanning 17 years, was done. An inductive analysis of individual and focus group interviews with faculty role players involved in the development of the RCS was conducted using Atal Ti. The participants of the study were identified using a network analysis and represented faculty management, academic programmes and student coordinators. **Results** Major effort, time and resources were committed by the faculty to developing the vision of the RCS, which also involved extended engagement with multiple internal and external partners and stakeholders. A complex array of physical, academic and political barriers and facilitators in the success of the RCS will be presented. **Conclusion** The RCS was established successfully in 2011 and is considered a flagship of the Faculty, however understanding the facilitators and barriers in making this possible and ensuring sustainability is necessary for future planning.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

The use of embodied, enacted, and inscribed knowledge to enhance policy development and implementation: A case study of a mental health policy consultation process in South Africa

Debbie Marais (Research Development & Support Division, Faculty of Medicine & Health Sciences, Stellenbosch University)

Background: Policymakers who develop mental health policies must balance a number of competing demands, including calls for policies to be evidence based, calls for public participation in policymaking, and a complex burden of disease profile and requisite health system responses. In South Africa, public participation in policymaking is taken as a given, without problematising how such processes should be conducted. Developing policies that can be universally (nationally) applied whilst simultaneously addressing the idiosyncratic and contextual particularities associated with mental ill health at individual and local levels adds to this complexity. **Aim:** This study aimed to understand the intersection of knowledge and policy in the context of mental health system challenges in South Africa by tracing the movement of three knowledge forms – embodied, enacted and inscribed – through a policy consultation process. **Method:** A case study methodology was adopted and focused on the mental health policy consultation process that took place in South Africa. Data included mental health policy documents, reports and audio recordings from policy consultation summits, and key informant interviews. Thematic framework and thematic content analyses were conducted using the embodied-

enacted-inscribed analytical framework. Results: No substantive changes were made to the policy following the consultation summits, suggesting that the process had minimal impact on policy. There did not appear to be systematic processes for facilitating and capturing knowledge inputs, or for transferring these inputs through increasing levels of summarisation during the consultation process. One consequence of this was that much of contextual detail of participants' embodied knowledge was not followed through into policy outputs. Conclusion: This study draws attention to the unique challenges in reconciling the contextual detail of embodied knowledge with the abstract, inscribed knowledge of policy, highlighting the importance of designing participatory processes that enable optimal use of knowledge inputs in and beyond these enacted spaces.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

Using the Jefferson Scale for Empathy for undergraduate medical students: a cross sectional study

E Archer (University of Stellenbosch), I Meyer (University of Stellenbosch), R Turner (University of Stellenbosch)

Patient-centred medical care and the development of a caring relationship between doctors and patient have been shown to, not only improve health outcomes and reduces costs, but also to increase doctor satisfaction. A critical component in the development and maintenance of this relationship is empathy. Following a scoping review of educational interventions to enhance empathy, a variety of experiential interventions were incorporated into the medical curriculum, as part of the clinical skills module. The widely used Jefferson Scale for Empathy (JSE-S) was used to determine the baseline empathy levels of a student group before the interventions in the curriculum were implemented. The JSE-S comprises a 20-item Likert score questionnaire and has been widely used around the world and been found to be reliable and a valid measure of healthcare provider empathy. Reports of the use of the JSE-S with medical students within the South African context are limited. Two hundred and six (n=206) of the 287 3rd-year medical students were conveniently sampled and completed the questionnaire as a baseline measurement of empathy. Statistical analysis revealed females have a significantly higher score than males (p=.019) and those aged 25 years or older a significantly higher score than those under 22 year olds (p=.003). The Cronbach alpha scale reliability coefficient was 0.81, which indicates good reliability of the scale, however when individual items were evaluated used a Graded Item Response model there were 3 items which were found to have a discriminatory difference. The descriptive statistics are similar to most of the reports for medical students in the US and other parts of the world. The JSE-S seems to be a valid tool in our context and can therefore be recommended for use. The findings of this study may encourage researchers to use the Scale for measuring empathy in undergraduate medical students.

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

DETERMINING ADEQUACY OF NUTRITION SUPPORT IN TYGERBERG HOSPITAL

Janicke Visser (Stellenbosch University), Karla Lutzeler (Stellenbosch University), Renee Blaauw (Stellenbosch University)

Inadequate nutrition support (NS) practices are regarded as one of the main contributing factors to the high prevalence of hospital malnutrition. This study aimed to evaluate how enteral nutrition (EN) and oral nutrition supplement (ONS) prescriptions compared to delivery and to identify factors affecting this process. The latter included patient perceptions and knowledge and attitudes of nursing staff regarding NS. Patients receiving NS during February-March 2018 in Tygerberg Hospital were prospectively assessed over a maximum of 14 days. Nursing staff completed a self-administered questionnaire. A percentage difference between prescribed and received NS of between 90-110% was regarded as optimal NS. Acceptable knowledge was set at 80% a priori. Of the 143 patients receiving EN, the majority did not meet optimal NS targets: 64.1% for energy and 62.8% for protein. Significant differences regarding NS handling were noted between wards (p=0.02), diagnostic categories (p=0.04) and genders (p=0.04). Sixty-two patients received ONS (average 400ml/day; median 5 days). Many

patients did not know the purpose of the ONS prescribed (49%), nor the prescribed volume that they needed to consume (42%). On average, 52% of the prescribed product was received and 57% of the received product was consumed. A significant correlation was found between advancing age and percentage product consumed ($r=0.27$, $p=0.03$). Only three nurses (1.5%) obtained >80% knowledge score, with an average score of $51.8 \pm 12.8\%$. Improved knowledge was associated with a higher qualification ($p=0.01$) and longer working experience ($p<0.01$). Although 59% of nurses indicated no prior formal training on NS, 86% indicated that they would like to receive further information. Just over 60% of EN patients did not receive adequate NS and about a half of ONS patients received and consumed their ONS according to prescription. Knowledge of nursing staff on practical aspects of NS needs to be improved as a matter of urgency.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

Determinants of serum 25-hydroxyvitamin D levels in healthy young adults living in the Western Cape, South Africa

J Visser (Division of Human Nutrition, Stellenbosch University), K Knight (Division of Human Nutrition, Stellenbosch University), L Philips (Division of Human Nutrition, Stellenbosch University), M Wallace (Cancer Association of South Africa (CANSA)), R Blaauw (Division of Human Nutrition, Stellenbosch University), W Visser (Division of Dermatology, Stellenbosch University)

Rationale: The prevalence of vitamin D deficiency is fast emerging as a global pandemic. In South Africa few studies have been conducted to determine the vitamin D status of the healthy population. **Methods:** This cross-sectional phase of a larger study investigated vitamin D status of healthy, undergraduate students (20.41 ± 2.29 years old) at Stellenbosch University. Data collected included serum 25(OH)D (Institute of Medicine interpretation), anthropometry, dietary vitamin D intake (food-frequency questionnaire), skin tone (Fitzpatrick Skin Type Classification), and skin reflectometry (to measure dermal melanin content). Summary statistics, analysis of variance and non-parametric methods were used. **Results:** Results of the 242 students indicated a mean serum 25(OH)D of 63.80 ± 41.35 ng/ml and a high prevalence of vitamin D sufficiency (90%). Significantly more females experienced suboptimal vitamin D levels than males (18 vs. 5%; $p<0.01$). Participants with lighter skin tones had higher levels of 25(OH)D than those with darker skin tones ($\chi^2=24.02$; $p=0.02$). The majority (60.74%) had normal BMIs, although the relationship between BMI and serum 25(OH)D was not significant (Spearman's $r=-0.11$; $p=0.09$). Total mean dietary vitamin D intake was 7.99 ± 13.81 mcg, with 87.2% consuming inadequate intake (<15mcg). The relationship between total vitamin D intake and serum 25(OH)D was significant (Spearman $r=0.14$; $p=0.003$). Sun exposure and lifestyle factors had no effect on serum 25(OH)D levels. **Conclusion:** A low prevalence of vitamin D deficiency was found among healthy young adults, despite low dietary vitamin D intakes. Significant relationships were found between serum 25(OH)D and gender, skin tone and vitamin D intake. Further studies need to be conducted, especially in high-risk groups, before results are applied to the greater South African public.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

Adaptation and validation of a vaccine hesitancy measuring tool in South Africa

Elizabeth O. Oduwole (1. Division of Health Systems and Public Health, Department of Global Health, Faculty of Medicine and Health Sciences, S), Professor Charles S. Wiysonge (3. Cochrane South Africa, South Africa Medical Research Council), Professor Hassan Mahomed (2. Metro District Health Services, Western Cape Government)

INTRODUCTION: Vaccine hesitancy, which is defined as the delay in acceptance or refusal of vaccination despite the availability of vaccination services is an emerging global problem. It contributes to low and suboptimal vaccine coverage and can lead to intermittent outbreaks of vaccine-preventable diseases. The paucity of research and the lack of validated tools to measure vaccine hesitancy in South Africa is of concern. **AIM:** To adapt and validate a survey tool to investigate vaccine hesitancy in South Africa. **OBJECTIVES:** To (1) conduct an overview of reviews on vaccine hesitancy; (2) conduct a

comprehensive review of current tools to measure vaccine hesitancy; and (3) modify and validate the Vaccine Hesitancy Scale (endorsed in 2015 by the WHO Strategic Advisory Group of Experts on Immunisation), in South Africa. **METHODOLOGY:** This study will consist of two phases, a synthesis of existing research and a primary study. The first phase (evidence synthesis phase) will involve (a) an overview of existing systematic reviews on vaccine hesitancy; and (b) a scoping review of existing vaccine hesitancy measurement tools, irrespective of where they have been developed or validated. The second phase will utilize iterative testing methodology to adapt and validate the Vaccine Hesitancy Scale among a population of parents of children aged one year and under in the Western Cape Province of South Africa; drawn from the three strata of geographical dwelling areas as described by Statistics South Africa. The estimated total sample size for the study will be greater than 500 participants. **ANTICIPATED RESULTS AND PUBLIC HEALTH SIGNIFICANCE:** The two reviews and the validation study will contribute immensely to the existing body of knowledge on vaccine hesitancy both on the local and global scale. The validated tool will be valuable in reducing the knowledge deficit in addressing vaccine hesitancy in South Africa and similar settings.

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

THE EFFECT OF AN INTERACTIVE ELECTRONIC STORYBOOK ON VOCABULARY IN GRADE 1 XHOSA SPEAKING CHILDREN

Dr Daleen Klop (Division Speech, Language and Hearing Therapy, Stellenbosch University), Dr Febe deWet (Human Language Technology Research Group, Meraka Institute Council for Scientific and Industrial Research), Dr Laurette Marais (Human Language Technology Research Group, Meraka Institute), Ms Amanda Msindwana (Division Speech, Language and Hearing Therapy, Stellenbosch University)

Background: The first World Development Report (2018) claims that education is in a "learning crisis" and that reading literacy is at the heart of this learning crisis. Reading is a foundation used to measure academic performance and vocabulary is a precursor to reading. Children traditionally learn new word meanings by reading and listening to a printed book. There is a dearth of suitable literacy intervention tools and programmes in local languages, as a limitation to education, clinical services and research. The Electronic books (e-book) implemented on a tablet with audio narration provides support to the written text. The study investigated the efficacy of an interactive e-book, to facilitate vocabulary learning in Grade 1 Xhosa-speaking children. Objectives: The purpose was to measure if an e-book intervention without adult instructional input, developed for Xhosa speaking children could facilitate the acquisition and retention of new words at different levels of lexical representation. Method: Sixty-five Xhosa speaking Grade 1 learners participated in a randomised pre-test/post-test between-subjects design. The experimental group received the e-book intervention and was compared to a control group, before the control group received delayed intervention. Follow-up testing was performed to measure retention of the new vocabulary after 8 weeks. Mixed model repeated ANOVAs were used to determine differences between the participants in the experimental and control groups. Results: The short-term e-book intervention facilitated not only fast-mapping of new words, but enabled participants to develop more robust lexical representations of the newly acquired words. Follow-up assessment showed retention of newly acquired word knowledge. Conclusion: Electronic books with audio narration, can be utilised to provide vocabulary training to young children at risk for academic failure. These findings are particularly relevant for South African environments where there is limited parental support and educational resources to promote vocabulary learning in young children

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

Understanding Xhosa traditional healers' experience of receiving the calling: Illness, conflict, and belonging

ASJ van der Watt (Stellenbosch University), Irene Mbanga (Stellenbosch University), Jibril Abdulmalik (University of Ibadan), Priscilla Dass_Brailsford (The Chicago School of Professional Psychology), Sarah Biederman (University Medical Center Hamburg-Eppendorf), Soraya Seedat (Stellenbosch University)

Objectives: Traditional healers (THs) form an important component of the healthcare system in sub-Saharan Africa, thus understanding their training, experiences of becoming healers, and their perceived role/s in society is critical. This study aims to explore the meaning and experiences of becoming traditional healers in Xhosa communities and the self-defined identities of THs in their communities. Method: Semi-structured interviews (Phase 1; n = 50) and in-depth phenomenological interviews (Phase 2; n = 4) were conducted with Xhosa THs. In-depth phenomenological interviews were analysed using Giorgi's descriptive pre-transcendental Husserlian phenomenological analysis. Results: Half of all THs (n = 25) stated that they knew they had to become healers because they became ill at the time and received treatment; 90% indicated they had dreams and revelations. The experience of becoming a TH can be summarised using three units of significance: (i) the gift of healing as an illness; (ii) the experience of conflict; and (iii) the experience of belonging. Conclusion: These findings highlight the long and challenging process of becoming THs. Collaborations of medical practitioners with THs and with trainees may alleviate the burden on South Africa's scarce healthcare resources. Lastly, further research and culturally appropriate psychoeducation is needed to equip trainee THs and their family members with the necessary skills and knowledge to support each other through a difficult process.

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

Health Leadership and Management: A key Element of Health Improvement and System Performance

Kerrin Begg (Stellenbosch University), Lilian Dudley (Stellenbosch University), Michele Pappin (Stellenbosch University)

Background: Strong leadership and management competencies are essential in well-functioning health systems, and fundamental to any quality improvement strategy or initiative. There is clear evidence that health quality initiatives fail to realise desired outcomes without strong consistent leadership and management across the health system. Where there are perceived weaknesses in leadership in the health system, strategic interventions can improve capacity to ensure implementation and build commitment together with improving management and leadership competency to strengthen accountability. Methods: Leadership and management competencies were assessed in self-report surveys, routine data was assessed to review facility performance in HIV and TB service delivery and health outcomes, and assessments were done of quality improvement efforts in 2017 across three sub-districts in rural Eastern Cape. Tools used included the Leadership Competency Framework (LCF), the Institute for Healthcare Improvement (IHI) project progress scoring tool, an adapted QI Proposal Assessment Tool (QIPAT-7), the QI Knowledge Application Tool – Revised (QIKAT-R) and routine health information from DHIS and Tier.net. Results: Self-report scores for the LCF and IHI Project Progress tools were artificially high, as most facilities were failing to achieve targets, performing poorly on routine data metrics and had ongoing operational management and supply-chain challenges. Clinical governance needed support as aspects such as clinical protocols were observed to be inconsistently implemented and clinical meetings to discuss patient management were not routine, all affecting the quality of care delivered. Conclusion: Assessment of management and leadership competencies are essential to support the delivery of high quality of care and are fundamental to any quality improvement effort. 360 degree and other objective assessments are needed as insight by managers can be enthusiastically subjective. Insight and self-awareness are necessary to inform management and leadership capacity development programmes to strengthen individual and team leadership skills to enhance quality of care and improvement efforts.

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Global emergency care clinical practice guidelines: A landscape analysis

Ben de Waal (Department of Emergency Medical Sciences, Cape Peninsula University of Technology.), Jennifer Pigoga (Division of Emergency Medicine, University of Cape Town.), Lee Wallis (Division of Emergency Medicine, University of Cape Town. Division of Emergency Medicine, Stellenbosch University.), Michael McCaul (Centre for Evidence-based Health Care, Division of Epidemiology and

Biostatistics, Stellenbosch University.), Mike Clarke (Centre for Public Health, Queen's University Belfast, Northern Ireland), Peter Hodgkinson (Division of Emergency Medicine, University of Cape Town.), Stevan Bruijns (Yeovil District Hospital NHS Foundation Trust), Taryn Young (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University. Cochrane Sou)

Background: Adaptive guideline development methods, as opposed to de novo (new) guideline development, is dependent on access to existing high-quality up-to-date clinical practice guidelines (CPGs). Objectives: We described the characteristics and quality of CPGs relevant to prehospital care worldwide in order to strengthen guideline development in low-resource settings for emergency care. Methods: We conducted a descriptive study of a database of International CPGs relevant to emergency care produced by the African Federation for Emergency Medicine (AFEM) CPG project in 2016. Guideline quality was assessed with the AGREE II tool, independently and in duplicate. End-user documents such as protocols, care pathways and algorithms were excluded. Data were imported, managed and analysed in STATA 14 and R. Results & Discussion: In total, 276 guidelines were included. Less than 2% of CPGs originated from low- and middle income-countries (LMICs), only 15% (n=38) of guidelines were prehospital specific, and there were no CPGs directly applicable to prehospital care in LMICs. Most guidelines used de novo methods (58%, n=150), were produced by professional societies or associations (63%, n=164), with the minority developed by international bodies (3%, n=7). National bodies (e.g. National Institute for Health and Care Excellence (NICE)) produced higher quality guidelines when compared to international guidelines, professional societies and clinician/academic-led guidelines. Guideline quality varied across topics, subpopulations and producers. Resource-constrained guideline developers than cannot afford de novo guideline development have access to an expanding pool of high-quality prehospital guidelines to translate to their local setting. Conclusion: Although some high-quality CPGs exist relevant to emergency care, none directly addresses the needs of prehospital care in LMICs, especially in Africa. Strengthening guideline development capacity including adaptive guideline development methods that use existing high-quality CPGs is a priority.

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Raising ethical issues in the dead: An exploration of ethical challenges in Forensic Medicine

Celeste de Vaal (self)

This presentation is a summary of my master's thesis in philosophy in applied ethics. I will present ethical challenges in the field of forensic medicine which is largely unexplored, yet important, terrain. Pivotal to forensic pathology are the deceased and the medico-legal investigation. The unique relationship between the forensic doctor and the deceased is distinctly different to the doctor-patient relationship of most other medical disciplines. Focused ethical deliberation is required. I will briefly explore the deceased as an entity with moral status worthy of moral deliberation by means of five concepts, namely, human properties, relational considerations, moral agency, symmetry, and cultural and religious considerations. This in turn gives rise to certain obligations. South Africa's recent history demonstrates the existence of ethical concerns in forensic medicine. I will identify and explore some of the ethical issues pertinent to forensic pathology in the South African context. The major ethical issues revolve around current dual loyalty concerns that involve the deceased and the intricately linked judicial system, under which the forensic doctor works. The second major area of ethical concerns relates to retained post mortem interests of the deceased. I will briefly highlight how the principlism approach can be used as an ethical framework in forensic medicine. The four principles of justice, beneficence, non-maleficence and autonomy will each be applied to the deceased in the context of forensic pathology. Raising ethical issues in the dead is not merely a clever play on words, but indeed warrants further exploration.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 21

Being Paracelsus - the toxicology educational card game

Carine Marks (Stellenbosch University), Catharina Du Plessis (Stellenbosch University), Cherylynn Wium (Stellenbosch University), Helmuth Reuter (Stellenbosch University)

Objective Undergraduate toxicology students are frequently overwhelmed by the volume and complexity of information they are expected to learn. Health care-based educational games will enhance the communication, social interaction and critical thinking skills of the students. The objective of this study was to introduce a fun, alternative learning technique to (i) assess student learning and (ii) to assess student satisfaction with the learning experience. Methods The card game centred on poisoning scenarios and the treatment thereof. Two decks of cards were developed; one set with the poisoning exposure and the other with treatment. Students needed to pair the poisoning exposure with the correct treatment. Twenty-one 5th year medical students voluntarily agreed to participate in the game. The students were given relevant toxicology literature to aid them in the game. Three staff members from the Tygerberg Poisons Information Centre supervised the students. After the game, they were asked to anonymously complete a questionnaire. Results Students indicated that the card game was a competitive and engaging non-lecture approach to teaching toxicology. All students indicated that Paracelsus immersed them in course material and they would recommend this type of learning above didactic teaching. However, students need basic toxicology lectures before playing. Groups should be limited to 10 participants, for larger groups could have an influence on the level of participation. Supervision by toxicologists are initially necessary but once students have mastered the game they can self-facilitate and thereby increase peer-to-peer learning. Conclusion The game was an effective adjunct to toxicology lectures. This can lead to significant increases in toxicology assessment marks. A process of computerising this game should be undertaken and further research should focus on the incorporation of this type of game in the different fields of medical studies.

ABSTRACT NUMBER / ABSTRAKNOMMER: 22

Evaluating patient satisfaction with primary care consultations in the Helderberg sub-district of South Africa.

Lawson Eksteen (Stellenbosch University; Family Physician Stellenbosch Hospital), Robert Mash (Division of Family Medicine and Primary Care Faculty of Medicine and Health Sciences Stellenbosch University)

Background Effective primary care is vital for improving health outcomes. Patient-centred consultations are important and one way of assessing this is to evaluate patient satisfaction. The Medical Interview Satisfaction Scale (MISS) has not been used in South Africa. Aim To test validity and reliability of the MISS and evaluate patient satisfaction with consultations. Setting Primary care facilities in the Helderberg sub-district, South Africa. Methods The MISS tool was adapted and validated by a panel of experts. The internal consistency was evaluated on 150 consultations. The level of patient satisfaction on 23 items, in consultations by nurses and doctors, was measured. Respondents indicated agreement with each item on a scale (1=very strongly disagree, 7=very strongly agree). Results The wording of the items were adapted and translated into Afrikaans and Xhosa. There was good overall internal consistency (Cronbach alpha 0.889), but not in all subscales. Patients were most satisfied with rapport (Median score 6.2 (IQR 5.3-5.9)) and understanding of their concerns, fears and beliefs (5.7 (IQR 5.1-6.3)). They were less satisfied with the ability to foster an acceptable management plan (5.5 (IQR 4.5-6.5)) and with accuracy of information (5.0 (IQR 4.2-5.8)). Scores for nurses and doctors were not significantly different. Conclusion Further work is needed to improve the reliability of MISS subscales in the South African context and the best internal consistency was found with 21 items. Patients showed high levels of satisfaction with primary care consultations, although other studies suggest this may reflect low expectations rather than high quality consultations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 23

Evaluating the impact of adherence clubs on the clinical outcomes amongst ART patients in the Cape Winelands district of Western Cape Province of South Africa

Colette Gunst (Western Cape Department of Health), Dillon Wademan (Stellenbosch University), Graeme Hoddinot (Stellenbosch University), James Kruger (Western Cape Department of Health), Leonard Maschilla (Western Cape Department of Health), Nelis Grobbelaar (ANOVA), Peter Bock (Stellenbosch University), Rory Holtman (Western Cape Department of Health), Sue-Ann Meehan (Stellenbosch University)

Background: Implementing WHO recommendation for lifelong ART regardless of CD4 count for all HIV positive individuals, has resulted in increasing numbers of individuals on ART and increased client burden at health facilities. One consequence has been worse clinical outcomes. Referring stable HIV positive individuals to adherence clubs is one strategy to manage increased numbers of HIV-positive individuals. This study aimed to evaluate the impact of adherence clubs on the clinical outcomes amongst ART patients. Methods: This retrospective cohort study was conducted in the Cape Winelands district and included individuals aged ≥ 18 years, who started ART January 2014-December 2015. Routine data from electronic datasets was analyzed. Participants were followed up until December 2016. Descriptive statistics and multivariate analysis was used to determine factors associated with referral to a club and loss to follow up (LTFU). Results: 465 individuals were included in the study. At baseline, the majority (64.3%) were women, median age was 32 years and median baseline CD4 count was 375 cells/ μL . Overall, 184 (39.6%) of participants had a viral load reported, of which 162 (88%) were virally suppressed. Median time to referral to the adherence club was 14.1 months (IQR 9.9-19.1). Individuals with baseline CD4 > 500 (aHR = 1.86, 95% CI 1.13-3.08) and women pregnant at initiation of ART (aHR = 1.70, 95% CI 1.07-2.68) were more likely to be referred to an AD club. LTFU over time was lower in individuals referred to adherence clubs ($P=0.002$) compared to those who remained in the health facility. Conclusions: Participants were more likely to be retained in care if referred to an adherence club. The large proportion of missing data regarding viral load reporting needs further investigation. Viral load suppression remained high for those reported. Adherence clubs are one strategy to manage increasing numbers of HIV-positive individuals outside of healthcare facilities.

ABSTRACT NUMBER / ABSTRAKNOMMER: 24

Implementing community-based adherence clubs for stable HIV-infected patients in South Africa. Lessons learned from patient and health worker experiences.

Blia Yang (Stellenbosch University), Colette Gunst (Western Cape Department of Health), Dillon Wademan (Stellenbosch University), Graeme Hoddinott (Stellenbosch University), James Kruger (Western Cape Department of Health), Leonard Maschilla (Western Cape Department of Health), Nelis Grobbelaar (ANOVA), Peter Bock (Stellenbosch University), Rory Holtman (Western Cape Department of Health), Sue-Ann Meehan (Stellenbosch University), Vikesh Naidoo (Stellenbosch University)

Background: South Africa has the largest burden of HIV globally. Implementation of the WHO guidelines; offering ART to everyone living with HIV, has resulted in increased burden on health facilities with longer patient waiting times. Referring stable HIV positive individuals to community-based adherence clubs is one strategy to manage increased numbers of HIV-positive individuals. This study aimed to generate lessons learned on the implementation of community-based adherence clubs from patient and health worker perspectives. Description: The Cape-Winelands Health district have implemented community-based adherence clubs since 2012 according to department of health guidelines. "Clubs" are supported by non-governmental organizations. Stable HIV-positive patients are referred to clubs to collect pre-packed medication. This study enrolled 59 patients and 20 health workers from two "clubs". An electronic self-administered questionnaire comprising closed- and open-ended questions was used to collect data. Descriptive statistics and thematic analysis was used to analyse data. Lessons learned: The majority of participants reported that "clubs" are best led by counselors, should have ≥ 20 patients and take place in a community hall or church. From the patient perspective, "clubs": provide group identity (not alone in living with HIV) are empowering (motivated to stay adherent) are less time

consuming (short queues) From the health worker perspective, "clubs" are effective at decongesting health facilities, reduce the burden of work for facility staff, empower health workers to tailor their support to individual needs, are labour intensive and teamwork between stakeholders is critical. Conclusions: Community-based adherence clubs are a good way to deliver high quality health services for people living with HIV. Implementation of "clubs" is not simple. Optimal functioning is reliant on strong co-ordination of a multidisciplinary team with clear roles and responsibilities with standardized strategies that are specific to the needs and resources of the community.

ABSTRACT NUMBER / ABSTRAKNOMMER: 25

Internal research funding in a health science faculty, an 8-year review: Did we invest wisely?

Dr Tania Brodovcky (Research Development and Support, Faculty of Medicine and Health Sciences, Stellenbosch University), Ms Tonya Esterhuizen (Division of Epidemiology and Biostatistics, Department of Global Health, Faculty of Medicine and Health Sciences)

Our researchers are encouraged to apply for internal research funding that is made available within the Faculty of Medicine and Health Sciences (FMHS), Stellenbosch University, South Africa, particularly to assist in the development of postgraduate students, postdoctoral fellows and early-career clinical and non-clinical researchers. This study undertook to describe the research funding distribution within the FMHS, to establish participation and success rates and to evaluate whether it contributed to research outputs. A retrospective record review of internal funding application and award data, as maintained by the Research Capacity Development and Funding Office at the FMHS, as well as publication output data, was undertaken for seven different internal funding mechanisms covering the period 2009 to 2016. Captured data were verified and analysed using statistical software. The distribution of internal research funding according to applicant demographics, research theme, discipline and funding mechanism was described. In addition, the relative participation and success rates and contribution towards research outputs were analysed. This was the first review of internal research funding undertaken at the FMHS and these results will facilitate the strategic evaluation of current funding call mechanisms and approaches to ensure optimal future utilisation of this limited resource.

ABSTRACT NUMBER / ABSTRAKNOMMER: 26

Negotiating conflicting discourses around citation and plagiarism in health information systems

Arlene Archer (University of Cape Town), Karis Moxley (Stellenbosch University)

The successful communication of data and knowledge is a core component of health information systems, and citation in these communications is fundamental, especially when constructing academic discourse. There has been much discussion in the literature concerning the considerable difficulties tertiary students experience when writing using sources. One challenge frequently encountered is the predominantly negative discourse that surrounds the value and purpose of referencing. The contesting discourses around plagiarism involve notions of honesty and dishonesty, integrity and punishment, trust and deceit. The focus on citation in higher education and health training spaces is too often on the consequences of academic integrity breaches, which usually involve "severe punishment", including disciplinary action and possibly expulsion. This is compounded by the rise of text-matching software, such as Turnitin. The effect of this discourse of punishment is that students conceive of referencing as strategy to avoid plagiarism, not as a valuable rhetorical practice in the sharing of knowledge. This can cripple the confidence of young writers. Health educators can strive to work against this culture of deterrence, detection, and punishment of students, but there is a need to promote suitable strategies that enable positive discourses around writing and citation. We highlight the features of an alternate (positive) discourse and propose teaching strategies for addressing plagiarism in health training centres in ways that serve to empower students.

ABSTRACT NUMBER / ABSTRAKNOMMER: 27

Perceived enablers and constraints of undergraduate research in a Faculty of Medicine and Health Sciences: What role does choice play?

Bart Willems (Western Cape Dept of Health), Debbie Marais (Research Development & Support Division, Faculty of Medicine & Health Sciences, Stellenbosch University), Jessica Kotlowitz (The Green Dietician), Nicola Barsdorf (Health Research Ethics Office, Faculty of Medicine & Health Sciences, Stellenbosch University), Susan van Schalkwyk (Centre for Health Professions Education, Faculty of Medicine & Health Sciences, Stellenbosch University)

Background: Enhancing evidence-based practice and improving locally driven research begins with fostering the research skills of undergraduate students in the medical and health sciences. Research as a core component of undergraduate curricula can be facilitated or constrained by various programmatic and institutional factors, including that of choice. Self-Determination Theory (SDT) provides a framework for understanding the influence of choice on student motivation to engage in research. Aim: This study aimed to document the enablers and constraints of undergraduate research at Stellenbosch University's Faculty of Medicine and Health Sciences (FMHS) and to explore how the presence or absence of choice influenced students' engagement with research. Methods: This exploratory descriptive study involved 11 students and 10 staff at the FMHS who were recruited using purposive sampling. Semi-structured interviews were transcribed and thematically analysed. Findings were interpreted using Self-Determination Theory, focusing on how choice at various levels affects motivation and influences research experiences. Results: Many of the programmatic and institutional enablers and constraints – such as time and supervisory availability – were consistent with those previously identified in the literature, regardless of whether research was compulsory or elective. Choice itself seemed to operate as both an enabler and a constraint, highlighting the complexity of choice as an influence on student motivation. SDT provided insight into how programmatic and institutional factors – and in particular choice – supported or suppressed students' needs for autonomy, competence, and relatedness, thereby influencing their motivation to engage in research. Conclusion: While programmatic and institutional factors may enable or constrain undergraduate research, individual-level factors such as the influence of choice on students' motivation play a critical role. The implication for curriculum development is that research engagement might be enhanced if levels of choice are structured into the curriculum such that students' needs for autonomy, competence, and relatedness are met.

ABSTRACT NUMBER / ABSTRAKNOMMER: 28

Poisons Information Service of South Africa

Carine Marks (Division Clinical Pharmacology), Catharina du Plessis (Division Clinical Pharmacology), Cherylynn Wium (Division Clinical Pharmacology), Cindy Stephen (Red Cross Hospital Poison Information Centre), Farahnaz Mohammed (Red Cross Hospital Poison Information Centre), Kate Balm (Red Cross Hospital Poison Information Centre), Linda Curling (Red Cross Hospital Poison Information Centre)

South Africa initiated a Poisons Information service over 45 years ago, which was strengthened by the establishment of the Tygerberg Poison Information Centre (TPIC) and Red Cross Children's Hospital Poisons Information Centre (RXHPIC). In 2015, the two centres combined their telephone service to form the Poisons Information Helpline of the Western Cape (PIHWC). The PIHWC provides a 24/7 consultant based telephone service to medical professionals and the public. Consultants, known as specialists in poisons information (SPIs), assist with the prevention, diagnosis and management of poisoning. Seven of the fifteen SPIs are medical doctors, one of whom is always available to provide clinical support to non-medical SPIs. Data from poisoning calls are entered, real-time, onto a server-hosted database, the AfriTox TeleLog. The locally compiled AfriTox poisons information database underpins call data entry, providing for both substance definitions and treatment advice given. The PIHWC provides a system of toxicovigilance, which contributes epidemiological data on poisoning, describes new hazards, provides information on national trends, and identifies potentially vulnerable

populations. Where necessary, the WHO is informed about any potentially serious or unusual public health impacts. The PIHWC is actively involved in education and research. It offers regular toxicology workshops and formal lectures to under- and post-graduate students. Public education and information programmes on prevention and immediate management of acute poisoning are essential activities. Research findings are regularly published in peer-reviewed journals and staff members actively participate in national and international conferences, as well as international WHO workshops.

ABSTRACT NUMBER / ABSTRAKNOMMER: 29

PREHOSPITAL PROVIDERS PERSPECTIVES FOR CLINICAL PRACTICE GUIDELINE IMPLEMENTATION AND DISSEMINATION: STRENGTHENING GUIDELINE UPTAKE IN SOUTH AFRICA

Lynn Hendricks (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Michael McCaul (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Raveen Naidoo (National Department of Health, Director Emergency Medical Services & Disaster Medicine)

Background & IntroductionIn 2016 the first African emergency care clinical practice guideline (CPG) was developed for national uptake in the prehospital sector in South Africa. Comprehensive uptake of CPGs post development is not a given, as this requires effective and efficient dissemination and implementation strategies that take into account the perceptions, barriers and facilitators of the local end-users, namely private and public prehospital providers.
Objectives / GoalWe aimed to identify prehospital providers perceptions of the emergency care guidelines, including barriers and facilitators of guideline implementation and dissemination, for national decision makers, to strengthen CPG uptake in South Africa.
MethodsWe conducted a qualitative study using an interpretivist phenomenology approach. We convened nine focus groups with 56 prehospital providers, across four major provinces in South Africa. Data was analysed using thematic content analysis in Atlas.ti.
Results & DiscussionProviders perceived the guidelines both positively and negatively which was influenced by previous CPG experience and exposure, unofficial communication and difference between expectations and perceived reality. Challenges to guideline implementation included autocratic communication, lack of career direction and changes in scope of practice. Providers recommended using local champions, electronic end-user documents, clear communication and enabling a clear prehospital career pathway from stakeholders to strengthen guideline implementation. Implications for guideline developers / users
Decision makers must consider providers perceptions and needs from the start to strengthen guideline dissemination and implementation.
ConclusionIn order to disseminate and implement an emergency care CPG, decision makers must take into account the perceptions, barriers and facilitators of local end-users. This study provides clear recommendations to support this.

ABSTRACT NUMBER / ABSTRAKNOMMER: 30

Roles of nurses in ensuring quality and effectiveness of blood sample collection during household visits

Gerald Maarman (Stellenbosch University), Noluvo Rhode (Stellenbosch University), Nomsa Apleni (Stellenbosch University), Nomtha Mandla (Stellenbosch University), Nulda Beyers (Stellenbosch University), Peter Bock (Stellenbosch University)

BACKGROUND: Blood specimen collection is central part to clinical research, as it forms the basis for diagnosis and linkage to healthcare. Nurses often do phlebotomy in a research study, and their effectiveness is key. **OBJECTIVES AND METHODS:** After completing several research phases of the PopART study, nurses have documented important lessons learned about phlebotomy best practice at household visits. **FINDINGS:** (1) we frequently encountered participants with difficult to locate/rolling veins and having team of two nurses (one being more experienced) helps. (2) There are many study protocols that nurses have to know and implement, and having refresher phlebotomy training is helpful. (3) Proficiency testing by a phlebotomy-training provider is also helpful, as it helps nurses to (4) learn from mistakes and receive advice on how to improve their skill. (5) In a long-term study as PopART, it

is good that management provide such testing and training on a regular basis throughout study implementation (perhaps quarterly). Lastly, (6) nurses' effectiveness in phlebotomy can be aided if daily sample receive monitoring reports are created by the lab team and discussed with nurses. If generated on a daily basis and discussed with nurses, these reports can highlight when we should improve blood specimen quality or quantity. CONCLUSIONS: These lessons learned, may strengthen nurses' phlebotomy effectiveness and have positive impact on study outcomes and delivery of health services/linkage to care.

ABSTRACT NUMBER / ABSTRAKNOMMER: 31

Use of Cochrane nutrition reviews in guidelines: appraising the 'payback' on investing in nutrition evidence synthesis

Anne Eisinga (Cochrane UK), Celeste Naude (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Emma Carter (Cochrane UK), Kim Anh Nguyen (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Marianne Visser (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Selena Ryan-Vig (Cochrane UK), Solange Durao (Cochrane South Africa, South African Medical Research Council)

Background: Systematic reviews (SRs) are important tools for evidence-informed guideline development. The extent to which Cochrane nutrition SRs have informed guidelines is unknown. Objectives: To describe the number and proportion of Cochrane nutrition SRs which were cited in published health guidelines, per Cochrane Review Group (CRG), guideline developer, guideline type, and guideline publication year. Methods: This was a retrospective analysis of citations of nutrition SRs in published health guidelines. We built a nutrition database by screening all active records in the Cochrane SR Database (31 Dec 2017) to identify nutrition reviews using pre-specified eligibility criteria. We checked which of these were in Cochrane UK's dataset used to inform evidence-based guidance worldwide. This resource is populated by checking online, open access sources of accredited guidelines (those freely available at point of use) for the word 'Cochrane'. Results: We included 569 (78.6%) completed reviews in 47 CRGs. Nutrition SRs were cited 919 times in 450 guidelines, including 379 (84%) clinical and 71 (16%) public health guidelines. National professional associations cited reviews most frequently (n=327 in 155 guidelines), followed by national government agencies (n=306 in 161), intergovernmental agencies (n=84 in 37) and international professional associations (n=72 in 37). Pregnancy and Childbirth (18.5%) reviews were cited most. The earliest citations identified in the dataset were in 2010 (n=1) and 2012 (n=47), and then as the sources searched expanded with open access becoming available, increased sharply in 2013 (n=144), 2014 (n=208), 2015 (n=195), and 2016 (n=254). Conclusions: The number of citations of Cochrane nutrition SRs identified in guidelines has increased from 2012, revealing a wide pattern of use of nutrition evidence, mostly by national professional associations, national government agencies, and in clinical guidelines. These findings serve as proxy of the 'payback' on investment in nutrition evidence synthesis for informing guidelines to bridge the knowledge-to-action gap.

Theme 2 / Tema 2
Infectious Diseases /
Infeksiesiektes

ABSTRACTS/ABSTRAKTE

Oral Presentations / Referate

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

A STUDY OF CHRISAL PROBIOTICS FOR MORE EFFICIENT CLEANING IN TYGERBERG BURNS UNIT AND AS A METHOD OF DECREASING NOSOCOMIAL INFECTIONS

Andrew Whitelaw (Stellenbosch University), Edwin Kotzee (Stellenbosch University), Mishal Ebrahim (SU), Rishika Prag (SU), Wayne Kleintjes (Stellenbosch University)

Introduction: Biofilm in hospital environments provides the ideal environment for pathogenic bacteria to thrive. Cleaning and disinfection does not affect bacteria 'hiding' in the biofilm. By using environmentally friendly probiotic bacteria to eliminate biofilm there may be reduced the risk of hospital acquired infection. A prospective controlled study was designed to investigate this. Aim(s): The primary objective of the study was to determine whether probiotics can reduce hospital acquired infections (HAI's) in the Burns unit. The secondary objective was to establish a reduction and/or elimination of biofilm. The third objective was to determine the cost effectiveness and cost reductions. Methods: The Burn Unit was divided into different areas and assigned a number to each test and comparative normal cleaning treatment zone in different rooms. We informed the cleaning staff to use only the Probiotic products in each of the designated test areas. A baseline surface swab for culture was done in each area. Swabs were taken again for culture weekly. Ethical considerations: Stellenbosch University Health Research Ethics approval N17/04/045 Results: The results indicate that probiotic cleansing in the hospital environment may be a cost-effective way of decreasing environmental biofilms and HAI's. Conclusion/Recommendations: Based on the results further recommendations as to the application of probiotics are indicated, and a prospective study looking at the effects on wound cleaning is planned.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Acute Myocarditis - Clinical Presentation, Aetiology and Short-to-Medium Term Outcomes in a Single Centre in Sub-Saharan Africa

Anton Doubell (Stellenbosch University), Charles Kyriakakis (Stellenbosch University), Dan Zaharie (Stellenbosch University), Gert Van Zyl (Stellenbosch University), Karim Hassan (Stellenbosch University), Philip Herbst (Stellenbosch University)

Introduction: The aetiology and estimated incidence of acute myocarditis (AM) remains undefined in South Africa. Whilst cardiac magnetic resonance (CMR) provides for a provisional non-invasive diagnosis, endomyocardial biopsy (EMB), which is infrequently performed, remains the gold standard. The developed world has experienced a shift in the viral epidemiology of AM and the European Society of Cardiology's most recent position statement on myocarditis recommends both CMR and EMB as the standard of care in suspected cases. We report on the interim results of our study. Methods: All patients presenting or referred to Tygerberg Hospital with suspected AM are investigated according to the ESC guidelines on myocarditis, which includes blood tests (inflammatory markers, cardiac enzymes, HIV and Hepatitis C serology), standard electrocardiogram, transthoracic echocardiogram, coronary angiogram, CMR and EMB. All patients also undergo follow up CMR after 3 months of appropriate therapy. A cohort of patients from Tygerberg Hospital fulfilling either the Lake Louise criteria on CMR or WHO Marburg Classification on histology for AM between January 2017 and December 2022 will be recruited. Results: 15 patients have thus far been recruited. 9 presented with symptoms of acute coronary syndrome, 4 with arrhythmia (3 with ventricular tachycardia and 1 with heart block) and 2 with heart failure. At presentation 9 had an elevated hs-Trop T. CRP was elevated in 6 of these, and in isolation in another 2. AM was confirmed on histology with immunohistochemistry in 9 patients. 12

were polymerase chain reaction (PCR) positive for cardiotropic viruses: 6 for Parvovirus B19, 3 for Epstein-Barr (EBV), 2 for human herpes virus-6 and 1 for Parvovirus B19 and EBV. Conclusion: Preliminary results of this study demonstrates the heterogeneity in presentations and provides insight into the possible viral pathogens within our local setting, which appears to be similar to those in the developed world.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

A cluster for an iron-sulphur cluster synthesis regulator

Annalisa Pastore (King's College London), Brandon Weber (University of Cape Town), Danicke Willemsse (Stellenbosch University), Monique Williams (Stellenbosch University), Robin Warren (Stellenbosch University), Salvatore Adinolfi (University of Turin)

Iron-sulphur clusters (Fe-S) are cofactors utilised by proteins involved in several important cellular processes. Mycobacterium tuberculosis (Mtb) has one Fe-S cluster synthesis system. Fe-S cluster synthesis must be tightly regulated due to the toxicity of Fe-S clusters. In cyanobacteria, SufR is a transcriptional repressor of the Fe-S cluster synthesis system. SufR coordinates an Fe-S cluster via three conserved cysteine residues, and binding of an Fe-S cluster to SufR changes its affinity for DNA, thereby allowing adaptation of gene expression based on Fe-S cluster availability. In this study, we investigated the ability of Rv1460, a SufR homologue, to coordinate an Fe-S cluster and study the importance of three conserved cysteine residues for Rv1460's function. Recombinant Rv1460 protein was produced and purified, and reconstitution of the Fe-S cluster performed by enzymatic and chemical methods. The reconstitution reactions were monitored by circular dichroism (CD). Three cysteine conserved residues were mutated, individually and in combination, to serine residues and the ability of these variants to complement a Rv1460 M. tuberculosis mutant was tested. A promoter reporter assay was used to determine the ability of the Rv1460 serine variants to repress transcription relative to the wild-type repressor. The CD spectrum of Rv1460 reconstitution reactions showed peaks at 330 and 420 nm, characteristic of the formation of a 2Fe-2S cluster on Rv1460. Serine variants were less efficient at complementing the Rv1460 mutant, indicating that these residues are required for Rv1460's function, presumably through affecting Fe-S cluster coordination. Mutation of the conserved serine residues did not reduce the ability of Rv1460 to repress transcription from the Rv1460 promoter. The role of the Fe-S cluster in the binding of Rv1460 to DNA therefore needs further investigation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Antiretroviral therapeutic drug monitoring in children at Tygerberg Hospital_ 2012-2017

Anton Engelbrecht (MBChB VI, Faculty of Medicine and Health Sciences, Stellenbosch University), Eric Decloedt (Division of Clinical Pharmacology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch Unive), Helena Rabie (Department of Paediatric and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University), Jennifer Norman (Division of Clinical Pharmacology, Department of Medicine, Health Sciences Faculty, University of Cape Town), Lubbe Wiesner (Division of Clinical Pharmacology, Department of Medicine, Health Sciences Faculty, University of Cape Town)

Background In South Africa therapeutic drug monitoring (TDM) is not routinely used in the management of HIV, but may be useful in evaluating causes of treatment failure, guiding dosing and predicting efficacy of antiretrovirals. There are differences in pharmacokinetics between children and adults which may be further complicated by concomitant disease. Children at Tygerberg Hospital (TBH) can access TDM through the Clinical Pharmacology service at Groote Schuur Hospital. We reviewed the indications for TDM at TBH from 1 January 2012 to 30 June 2017. Methods Children < 18 years of age that had a therapeutic level were identified from the results database. Clinical data was collected to identify the TDM indications. Data was captured in Access and results analysed with Stata. Results Eighty six levels were done in 79 patients. In 80% (63/79) of patients lopinavir levels were requested, 18% (14/79)

efavirenz and 2% (2/79) nevirapine, The median age of children on efavirenz was 84 months and those on lopinavir 12 months. In our preliminary results lopinavir was mostly requested in patients with virological failure, when adherence measures did not correlate with the clinical picture and for therapeutic dose monitoring in neonates. Efavirenz levels were requested when toxicity was suspected and nevirapine in patients receiving concomitant rifampicin. Lopinavir TDM confirmed non-adherence in 50% (8/16) of patients with virological failure or when adherence measures did not correlate with the clinical picture. Efavirenz TDM confirmed toxicity in 88% (7/8) of patients. Conclusion Based on our preliminary results, we found that TDM is mostly requested in children with virological failure and when adherence measures did not correlate with the clinical picture or when toxicity was suspected. Lopinavir TDM confirmed non-adherence in only 50% of patients while efavirenz TDM confirmed toxicity in 88% of patients.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Early continuous ART and successful viraemic control in first 2 years of therapy predicts HIV-1 persistence after 8 years on treatment

Anita Janse van Rensburg (Department Paediatrics and Child Health, Stellenbosch University and Tygerberg Children's Hospital, South Africa), Barbara Laughton (Department Paediatrics and Child Health, Stellenbosch University and Tygerberg Children's Hospital, South Africa), Charise Cilliers (Department Paediatrics and Child Health, Stellenbosch University and Tygerberg Children's Hospital, South Africa), Gert van Zyl (Division of Medical Virology, Stellenbosch University and National Health Laboratory Service, Tygerberg), Kirsten Veldsman (Division of Medical Virology, Stellenbosch University), Mark Cotton (Department Paediatrics and Child Health, Stellenbosch University and Tygerberg Children's Hospital, South Africa), Shahieda Isaacs (Division of Medical Virology, Stellenbosch University)

Background: The impact of early initiation of antiretroviral therapy (ART) on HIV-1 persistence has been characterised in adult cohorts and in well-suppressed children on continuous therapy. Studies investigating the additional effects of therapy interruption or on-going viraemia are rare in paediatric cohorts. We aimed to investigate total HIV-1 DNA kinetics in early treated children on continuous versus interrupted therapy and varying degrees of viraemic control. Methods: HIV-1 DNA was quantified with a sensitive in-house real-time PCR assay in forty participants, selected from a study that randomised participants into either elective early time-limited treatment or delayed continuous treatment. Viraemia was defined as an HIV-1 RNA load > 200 copies/mL \geq 3 months on treatment. Generalised linear and mixed effect regression models were implemented using R software version 3.4.3 Results: In interrupted participants (n=27) there was no difference in pre- and post-interruption total HIV-1 DNA levels. Continued therapy, defined since therapy start, in uninterrupted patients, or after interruption (median duration 7 (IQR: 5-9) months), exhibited two HIV-1 DNA decay slopes: 1) a faster phase in the first 2 years on therapy and 2) a slower phase thereafter. In phase 1, HIV-1 DNA decay was significantly faster in suppressed patients: $t_{1/2}$ of 4.8 (95% CI 3.9-6.2) versus 19.1 months (95% CI includes positive slope) in viraemic patients. However, in phase 2, decay was similar in well-suppressed and viraemic individuals: HIV-1 DNA $t_{1/2}$: 3.4 (95% CI: 2.7 -4.5) years. Significant independent predictors of endpoint HIV-1 DNA after 8 (IQR: 7.7-9.5) years on treatment were baseline HIV-1 DNA and viraemia during the first 2 years on treatment. Conclusion: Early therapy initiation and treatment adherence in the first 2 years of therapy are pivotal in reducing the overall levels of HIV infected cells and may have important implications for HIV-1 remission and cure.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

Oral, sputum and gut microbiota are disrupted in treatment-naïve patients with active tuberculosis

Benjamin Wu (New York University), Charissa Naidoo (Stellenbosch University), Georgina Nyawo (Stellenbosch University), Gerhard Walzl (Stellenbosch University), Grant Theron (Stellenbosch

University), Leopoldo Segal (New York University), Robin Warren (Stellenbosch University), Yonghua Li (New York University), Zaida Palmer (Stellenbosch University)

Background: Tuberculosis (TB) is the leading infectious cause of death globally and, in South Africa, kills more people than any other condition however, its association with the microbiome is poorly understood. Methods: To characterize the microbiome, oral washes, induced sputum and stool were collected from 105 pre-treatment patients with presumptive TB. Cases were classified based on a positive Mycobacterium tuberculosis culture, Xpert or Ultra result (n=58) and symptomatic controls classified based on negative culture or Ultra result (n=47). Up to two healthy household contacts (culture- or Ultra-negative; n=155) per patient had the same specimens collected. Microbial DNA was extracted and sequencing of the V4 16S rRNA gene region done using the Illumina MiSeq. Data was analysed using QIIME and phyloseq in R. Linear discriminant analysis effect size (LEfSe) was used for biomarker discovery. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) was used to infer microbial functional content in specimens. Results: Although alpha- and beta diversity was similar between cases and controls, cases were enriched with anaerobes, Paludibacter and Prevotella, in oral washes and induced sputum, respectively. In stool, cases had higher microbial diversity than healthy controls (Shannon's diversity; p=0.025) and clustered separately from both symptomatic and healthy controls during Principal Coordinates Analysis (p<0.01). Healthy gut commensal, Bifidobacterium, was significantly depleted in cases, who were instead enriched with Erysipelotrichaceae members of which are highly immunogenic and positively correlate with tumor necrosis factor alpha levels. Top-ranking functions predicted by PICRUSt in cases included pyruvate, butanoate and propanoate metabolism. Conclusions: Distinct microbiota and functional pathways were associated with active TB, most notably in stool. The gut microbiome may regulate lung immunity via the gut-lung axis and should be investigated as a potential marker for TB. Future analyses will explore the association of microbial metabolites and immune markers with TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

The Potential of Rifabutin for the Treatment of Rifampicin Resistant Tuberculosis

Annelies Van Rie (Global Health Institute, Epidemiology and Social Medicine), Elise De Vos (Global Health Institute, Epidemiology and Social Medicine), Elizma Streicher (Stellenbosch University), Guido Groenen (Belgian Lung and Tuberculosis Association), Lesley Scott (National Health Laboratory Services), Michael Whitfield (Stellenbosch University), Rob Warren (Stellenbosch University), Vanessa Mathys (Scientific Institute of Public Health), Wendy Stevens (National Health Laboratory Services)

Background: Use of the Xpert MTB/RIF assay (Xpert) has increased the number of people diagnosed with rifampicin resistant tuberculosis (RR-TB), especially in South Africa where the assay is used as the initial diagnostic for all individuals presenting with symptoms of TB. We hypothesized that a proportion of patients diagnosed with RR-TB by Xpert can be treated with a rifabutin-containing regimen. Methods: Rifabutin susceptibility by rpoB mutation was assessed in two population-based cohorts of individuals diagnosed with RR-TB, 349 individuals from South Africa and 172 from Belgium. rpoB polymorphisms were identified by Sanger sequencing. Rifampicin and rifabutin resistance was assessed by phenotypically by drug susceptibility testing (DST) in Belgium or minimum inhibitory concentration (MIC) in South Africa. In addition, a systematic review was performed to comprehensively collate information on rifabutin susceptibility by rpoB polymorphism. Rifabutin susceptibility (susceptible, resistant or indeterminate) was assigned to rpoB polymorphism with 10 or more rifabutin MIC or DST results available. Results: In total, 112 different rpoB polymorphisms were identified in the isolates of 2045 RR-TB patients, of which 17 polymorphisms occurred in 10 or more patients. Five of these 17 polymorphisms were associated with rifabutin susceptibility. The rpoB 516 GTC mutation was the most common, representing 72% and 83% of all rifabutin susceptible rpoB polymorphisms in South Africa and Belgium, respectively. At a population level the rpoB 516 GTC mutation occurred in 23% of South African and 13% of Belgian RR-TB patients. Conclusion: Identification of the exact rpoB polymorphisms leading to the diagnosis of RR-TB has the potential to include rifabutin, a potent rifamycin, into the treatment regimen of a substantial proportion of RR-TB patients. A randomized

controlled trial evaluating the efficacy of a rifabutin-containing TB treatment regimen in these selected patients is needed to provide the evidence required for a change in policy.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

Baseline CD4 count as a predictor of clinical outcomes when providing antiretroviral treatment regardless of CD4 count at government clinics within the HPTN 071 (PopART) trial.

Peter Bock on behalf of HPTN 071 (PopART) team (DTTC, Department of Paediatrics and Child Health, Stellenbosch University)

Background In 2015 WHO recommended antiretroviral treatment (ART) for all HIV-positive individuals regardless of CD4 count and set a target for Universal Access to ART, that >80% of HIV-positive individuals should be on ART. This study, nested within the HPTN 071 (PopART) trial aimed to evaluate the association between baseline CD4 count and attrition, TB incidence and renal dysfunction on ART when providing ART to all HIV-positive individuals. **Methods** The study analysed routine data on a cohort of adults (≥18 years of age) initiating ART regardless CD4 count at three department of health (DOH) clinics in the Western Cape, South Africa; between January 2014 and November 2015. Cohort follow-up was completed at the end of May 2016. **Results** Overall 2423 adults with a median baseline CD4 of 328 cells/μL (IQR 195-468) were included. A total of 636 (26.2%) adults in the cohort experienced attrition during the follow-up period. Attrition was higher amongst individuals with baseline CD4 >500 cells/μL compared to individuals with baseline CD4 0-500 cells/μL (aHR 1.28, 95%CI 1.07-1.55). Overall TB incidence was 4.4 cases/100PY. TB incidence was lower amongst individuals with baseline CD4 counts > 500 cells/μL compared to those with baseline CD4 0-500 cells/μL (aHR=0.27; 95% CI 0.12-0.62). The prevalence of renal dysfunction in the cohort was low (1.9%), as was the rate of incident renal dysfunction on ART (1.9 cases/100PY). There was no significant association between baseline CD4 and incident renal dysfunction occurring on ART. **Conclusions** Overall this study demonstrated both benefits and challenges when routinely initiating ART at baseline CD4 counts >500 cells/μL and supports the drive to start ART as early as possible in HIV positive adults. Strategies to improve HIV retention in ART care and ART adherence, in these contexts, should be a priority for programme implementers in high-burden settings.

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

Variable Clinical and Molecular Phenotypes of IFNGR1 Mutations in Mendelian Susceptibility to Mycobacterial Disease in South Africa

Ansia van Coller (Stellenbosch University), Brigitte Glanzmann (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Caitlin Uren (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Craig Kinnear (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Mardelle Schoeman (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Marlo Møller (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Michael Urban (Stellenbosch University, South African Medical Research Council Centre for Tuberculosis Research), Monika Esser (Stellenbosch University, National Health Laboratory Service), Richard Glashoff (Stellenbosch University, National Health Laboratory Service)

Background: Mendelian Susceptibility to Mycobacterial Disease (MSMD) is characterised by a predisposition to infection by weakly-pathogenic mycobacteria. In countries with high prevalence of tuberculosis, individuals with MSMD are prone to severe, persistent, unusual or recurrent infections by virulent Mycobacterium tuberculosis. Several MSMD-associated genes have been described, many resulting in a disruption of IL-12 and IFN- γ cytokine axis, which is essential for control of mycobacterial infections. This genetic heterogeneity results in at least 18 distinct disorders which vary in their mode of inheritance and clinical presentation. The aim of this study was to identify the disease-causing

mutations in three MSMD patients using whole exome sequencing, followed by in-house functional profiling to determine their physiological effects. Methods: Whole exome sequencing was performed and the data was processed using an in-house bioinformatics pipeline, TAPER. Candidate variants were validated using Sanger sequencing. In-house flow cytometric and ELISA assays were used for functional profiling. This involved assessment of IFN- γ expression and signalling, as well as in vitro IFN- γ -induced IL-12 production. Results: Variants in IFNGR1 were identified in all three patients. Two of these variants, namely IFNGR1 (c.864 C>G; p.I288M and c.698C>T p.G233A) are novel. The final variant identified was a 4-bp deletion (818del4) that had previously been associated with MSMD. Functional profiling is still ongoing; however, preliminary data has shown that IFN- γ expression varies among the three patients. Conclusions: IFN- γ mediated immunity is essential for the control of mycobacterial infections. Defects within the same gene, IFNGR1, can lead to variable phenotypes, as evidenced by functional profiling of different variants.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

Genome-wide associations between host genotypes and *M. tuberculosis*

Craig Kinnear (Stellenbosch University), Eileen Hoal (Stellenbosch University), Elizabeth Streicher (Stellenbosch University), Gerard Tromp (Stellenbosch University), Gian van der Spuy (Stellenbosch University), Haiko Schurz (Stellenbosch University), Marlo Muller (Stellenbosch University), Rob Warren (Stellenbosch University), Stephanie Pitts (Stellenbosch University)

TB is a complex disease caused by infection with Mycobacterium tuberculosis (M. tb). While the majority of infected, immune-competent individuals remain asymptomatic, approximately 10% will develop active disease. Numerous studies have investigated the association of candidate genes with TB, and with different M. tb clades, with one recent study investigating genome-wide associations in a Thai cohort. This study aimed to investigate genome-wide association(s) between the host genotype and the genome of the infecting M. tb pathogen. Sputum and blood samples were collected from TB patients residing in a suburb in Cape Town. Genotyping was performed using the Affymetrix 500k SNP array, and M. tb clades were identified using spoligotyping and IS6110 RFLP. Genotypes passing strict quality control (QC) filters were phased followed by imputation. Multinomial logistic regression (MLR) was performed using SNPTest and the standard genome-wide significance cut-off of $\alpha = 5 \times 10^{-8}$ was used. The cohort was dominated by LAM, followed by the Haarlem/LCC, Beijing/CAS1, Other, and Quebec superclades. MLR was performed using ~7 million SNPs for 445 samples, and the five M. tb superclades. The strongest association was with SNP rs9389610 (g.139039029G>A) on chromosome 6, at a p value of 1.6×10^{-7} . Individuals with the A allele of this SNP were twice as likely to be infected with a member of the Beijing/CAS1 superclade, as compared to the Haarlem/LCC (OR: 0.49) or LAM (OR: 0.46) superclades. Although the association did not reach genome-wide significance, the results suggest replication of this approach in a larger cohort of this population may provide significant associations with the infecting M. tb clade, thereby improving our understanding of TB pathobiology. This is the first study to analyse associations between gene variants and M. tb superclades at a genome level, and this working method will now be used to investigate a Ghanaian cohort.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

RANDOMIZED TRIAL OF SAFETY OF ISONIAZID PREVENTIVE THERAPY DURING OR AFTER PREGNANCY

Adriana Weinberg (University of Colorado, Aurora, CO), Amita Gupta (Johns Hopkins University, Baltimore), Gerhard Theron (Stellenbosch University, Obstetrics and Gynaecology, Cape Town), Grace Montepiedra (Harvard T. H. Chan School of Public Health, Center for Biostatistics in AIDS Research, Boston), Katie McCarthy (FHI 360, Durham), Lisa Aaron (Harvard T. H. Chan School of Public Health, Center for Biostatistics in AIDS Research, Boston), Timothy Sterling (Vanderbilt University Medical Center, Nashville TN), Tsungai Chipato (University Of Zimbabwe College of Health Sciences, Dept of Obstetrics and Gynaecology, Harare)

Background: The safety, efficacy, and optimal timing of isoniazid preventive therapy (IPT) for HIV-positive pregnant women on antiretroviral therapy (ART) is unknown. We hypothesized that IPT can be safely initiated during pregnancy. **Methods:** A Phase IV randomized, double-blind, placebo-controlled trial compared initiation of 28 weeks of IPT in antepartum (AP; immediate) (arm A) versus at 12 weeks postpartum (PP; deferred) (arm B) in HIV-positive women from TB-endemic areas in Africa, Asia, and Haiti. Randomization 1:1 was stratified by gestational age. Mother-infant pairs were followed to week 48 PP. The primary safety endpoint was treatment-related maternal adverse events (AE) > grade 3 or permanent drug discontinuation due to toxicity. The non-inferiority margin (NIM) was an incidence rate (IR) of 5/100 person-years (PY). **Results:** Among 956 enrolled, median age was 29 years, median CD4 was 493 cells/ μ L, 955 (>99%) were on ART (85% efavirenz-based), 63% had plasma HIV-1 RNA undetectable. Median follow-up was 58.6 weeks. 147 (15%) reached the primary outcome (74 in arm A, 73 in arm B), 171 women discontinued the study prematurely; 6 died (2 in arm A, 4 in arm B), with 3 deaths due to treatment-related hepatotoxicity (1 in arm A, 2 in arm B) and one non-treatment-related in arm A. There were no statistical differences in IRs of any maternal grade \geq 3 AE or all-cause hepatotoxicity between arms. There was no difference in maternal TB or infant TB by study arm. Adverse pregnancy outcomes however were significantly higher in arm A vs. B (23% vs 17%; $p=0.009$). **Conclusions:** IR for the primary safety outcome was higher than expected and similar for immediate vs. deferred IPT. TB incidence was low. Immediate IPT was associated with excess adverse pregnancy outcomes. The recommendation to initiate IPT during pregnancy in HIV-positive women on ART needs re-evaluation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

Analysis of Cytomegalovirus UL97 Drug resistance Mutations in Patients Receiving Ganciclovir

Dr. H. Smuts (Division of Medical Virology, NHLS Groote Schuur Hospital, UCT), Dr. N Nkosi (Division of Medical Virology, NHLS Tygerberg Hospital, US), Dr. N. Hsiao (Division of Medical Virology, NHLS Groote Schuur Hospital, UCT), Dr. S. Korsman (Division of Medical Virology, NHLS Groote Schuur Hospital, UCT)

Background Cytomegalovirus (CMV) drug resistance mutations, because of the widespread use of ganciclovir, are widely reported in international literature, particularly in the post-transplant setting. However, a genotypic assay to detect CMV drug resistance is not available in South Africa and the prevalence of these mutations is unknown. **Objectives** We aimed to document the prevalence and types of CMV UL97 mutations following exposure to ganciclovir in adult and paediatric oncology patients, transplant recipients and HIV-infected patients in Red Cross War Memorial Children's Hospital, Groote Schuur Hospital and Tygerberg Hospital. **Methods** The study had two components, the first being a retrospective cross-sectional study using stored extracted DNA from patients with serially elevated CMV viral load levels. Thirty-three samples were tested for this component. The second component was a prospective case series on patients referred by clinicians for genotypic testing in whom CMV drug resistance was suspected. Eight samples were tested. The CMV UL97 gene was amplified by conventional nested polymerase chain reaction (PCR) and Sanger sequencing performed. **Results** CMV UL97 mutations were identified in five of thirty-three (15%) retrospective samples and three of eight prospectively tested patients (38%). Overall 8/41 (20%) patients had CMV UL97 mutations. A trend of higher risk for development of drug resistance mutations among haematological oncology patients 7/23 (30%) compared to solid organ transplant recipients 1/10 (10%) was observed, however, this difference was not statistically significant ($P=0.306$). **Conclusion** This study identified the presence of CMV UL97 mutations conferring resistance to ganciclovir in the haematological oncology, primary immunodeficiency and solid organ transplant patients in the Western Cape. The assay successfully detected CMV UL97 drug resistance mutations in whole blood and cerebrospinal fluid clinical samples. Ongoing viral replication in the background of intensive immunosuppression and prolonged antiviral therapy selects for the emergence of CMV UL97 drug resistance mutations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

Carriage of resistant Enterobacteriaceae in Cape Town children

Dr Anne-Marie Demers (Desmond Tutu TB Centre, Dept of Paediatrics), Dr. Mae Newton-Foot (Division of Medical Microbiology; and NHLS Tygerberg Hospital), Prof. Andrew Whitelaw (Division of Medical Microbiology; and NHLS Tygerberg Hospital), Prof. Anneke. C Hesselning (Desmond Tutu TB Centre, Dept of Paediatrics), Remous Ocloo (Stellenbosch University)

Background: Antimicrobial resistance (AMR) is a global threat. Despite many studies documenting increasing resistance rates, relatively little has been done to quantify the AMR burden in developing countries. Similarly, data on paediatric AMR is lacking, and where available, focuses on hospitalized patients. Information about resistance rates in the community setting can improve overall understanding of the burden of resistance, risk factors, and may inform interventions. Aim: To describe the carriage rates of resistant *E. coli* and *Klebsiella* spp. in the stools of healthy children in Cape Town. Methods: This study is nested within TB-CHAMP, a randomised controlled TB prevention study. After informed consent, stool samples were collected from healthy children, prior to intervention (daily fluoroquinolone vs placebo). *E. coli* and *Klebsiella* spp. were isolated, and susceptibility testing performed for commonly used antibiotics. Isolates non-susceptible to cephalosporins or fluoroquinolones were subjected to PCR to identify resistance genes. Results: From 32 stool samples, 28 *E. coli* and 11 *Klebsiella* spp. were isolated. Of the *E. coli* isolates, 50% (14) were quinolone resistant and 32% (9) were extended spectrum beta lactamase (ESBL) producers; 25% (7) were both ESBL-producers and quinolone resistant. Of the *Klebsiella* isolates, 55% (6) were quinolone resistant, 36% (4) were ESBL-producers; and 27% (3) were both quinolone resistant and ESBL-producers. Quinolone resistance was due to *qnrS* in four *E. coli* isolates, and *qnrB* in all resistant *K. pneumoniae* isolates. CTX-M was the most prevalent ESBL type. Conclusion: Preliminary results suggest that resistant *E. coli* and *Klebsiella* spp. are frequently carried in the stools of children in Cape Town communities. This may pose a risk to empiric treatment practices. This resistance may reflect "spillover" from hospital settings. The presence of the potentially mobile elements *qnrS* and *qnrB* is concerning, and may result in increased quinolone resistance through horizontal gene transfer.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

Deciphering the transcriptomic stress response of *Mycobacterium smegmatis*

Monique Williams (Stellenbosch University), Nastassja Steyn (Stellenbosch University), Nico Gey van Pittius (Stellenbosch University), Rob Warren (Stellenbosch University), Samantha Sampson (Stellenbosch University), Tiaan Heunis (Stellenbosch University)

The ability of *Mycobacterium tuberculosis* to adapt to adverse environmental conditions such as hypoxia, nutrient starvation and acid stress is well known. Investigation into the transcriptional responses of the organism to these stresses has improved our understanding of how *M. tuberculosis* can persist within the host environment. Methodologies used to investigate these transcriptional responses are often limited to investigating known transcriptional regulators, one at a time. This is problematic as the adaptation of the pathogen to these adverse conditions is likely the response of several transcriptional regulators. Furthermore, little is known about RNA-associated proteins and how they influence protein expression. Nucleoprotein-Mass Spectrometry (NP-MS) facilitates the identification of nucleic acid associated proteins through affinity purification of formaldehyde cross-linked RNA polymerase transcriptional complexes and tandem mass spectrometry. This approach was used to investigate the stresses encountered by the study organism *Mycobacterium smegmatis* during early stationary growth. NP-MS successfully identified several transcriptional regulators known to be required by mycobacteria for the adaptation to environmental stress. These included the dormancy response regulator DevR, the heat shock protein HspX, and the ribosome hibernation promoting factor Hpf. To date, a large number of predicted genes in the *M. tuberculosis* genome encode for proteins of

unknown function. We speculate that several of these proteins may be transcriptional regulators which may be involved in adaptation to stress. In this study we demonstrated the ability of the developed approach, NP-MS, to identify proteins associated with DNA and RNA during adaptation to environmental stress. We propose that NP-MS can be used to investigate the proteins associated with the RNA polymerase complex under adverse growth conditions in not only mycobacterial organisms, but in other bacterial species as well.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

High frequency of phenotypic bedaquiline-resistance in programmatically-treated patients with unfavourable clinical outcomes

Brigitta Derendinger (Division of Molecular Biology and Human Genetics Faculty of Medicine and Health Sciences Stellenbosch University), Frik Sirgel (Division of Molecular Biology and Human Genetics Faculty of Medicine and Health Sciences Stellenbosch University), Grant Theron (Division of Molecular Biology and Human Genetics Faculty of Medicine and Health Sciences Stellenbosch University), Leen Rigouts (Institute of Tropical Medicine, Antwerp), Margaretha de Vos (Division of Molecular Biology and Human Genetics Faculty of Medicine and Health Sciences Stellenbosch University), Robin Warren (Division of Molecular Biology and Human Genetics Faculty of Medicine and Health Sciences Stellenbosch University), Siemon Gabriels (Institute of Tropical Medicine, Antwerp), Tania Dolby (National Health Laboratory Services, Green Point, Cape Town)

Background and objectives: Drug resistant tuberculosis (DR-TB) is a crisis in South Africa, where <50% of DR-TB patients are treated successfully. New drugs such as bedaquiline (BDQ) may improve outcomes and shorten treatment. However, we lack data on how susceptibility changes during treatment, whether this causes unfavourable clinical outcomes, and what the underlying mycobacterial genetic resistance-associated variants are. We aimed to describe the prevalence of BDQ-resistance in patients with unfavourable outcomes (culture-positive after 2 months) and resistance^{â€™}s associated with prior clofazamine (CLF)-usage. We also explored the relationship between minimum inhibitory concentration (MIC) and variants in resistant-causing genes. Method: Treatment monitoring isolates were collected from 34 patients with unfavourable clinical outcomes receiving BDQ at Brooklyn Chest Hospital (BCH), Cape Town. Drug susceptible testing (DST) was done in MGIT (1 μ g/ml) and MICs on Middlebrook 7H11 (0.008-2.0 μ g/ml). DST was done on 12 baseline isolates. PCR and Sanger sequencing of Rv0678 and atpE was done. Clinical and outcome data were collected. Results: 18/34 (53%) of isolates were BDQ-resistant and 26/32 (81%) patients received previous CLF. 17/18 (94%) resistant isolates and 9/16 (56%) susceptible isolates had prior CLF-usage. From the 18 BDQ-resistant isolates, 8/18 (44%) had variants in Rv0678. From the 16/34 (47%) BDQ-susceptible isolates, 5 showed a variant in the promoter region of Rv0678 which was associated with increased susceptibility and lowered MIC (4/5; 80%). 8/8 (100%) baseline isolates were BDQ-susceptible. Conclusion: This preliminary study in programmatically-treated patients with unfavourable clinical outcomes shows high numbers being phenotypically- and genotypically-resistant to BDQ. Although numbers are small, all isolates were susceptible at baseline, suggesting that resistance was acquired. Isolates with variants found in the promoter region of Rv0678 may indicate a hyper-susceptibility to BDQ. Due to the small numbers, future studies that include more patients are needed. This study highlights the knowledge-gap for BDQ-resistance mechanisms.

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

Spinal tuberculosis in children: treatment duration and orthopaedic follow-up at a major tertiary hospital in the Western Cape

HS Schaaf (Stellenbosch University), Johan Davis (Stellenbosch University), Robin Dyers (Western Cape Government: Health), Theresa Mann (Stellenbosch University)

Objectives Children with spinal tuberculosis (TB) are at risk of debilitating kyphotic deformity both during and after the active phase of the disease. Management guidelines include 9 months of TB treatment and orthopaedic follow-up until skeletal maturity. However, little is known about adherence to these recommendations. This study investigated the duration of TB treatment and orthopaedic follow-up among children with spinal TB at a tertiary hospital in the Western Cape. **Methodology** This retrospective review included all children diagnosed with spinal TB at Tygerberg Hospital between January 2012 and December 2015. Clinical, demographic and TB treatment duration data was extracted from medical records and from a dataset obtained from the Western Cape Department of Health. Orthopaedic follow-up duration was calculated from the start of TB treatment to the last spine clinic appointment up until May 2018. **Results** Thirty four children (median age 7 years, range 2-15 years; 12 (35%) boys) were diagnosed with spinal TB during the study period; 28 (82%) had kyphotic deformity and 21 (62%) received corrective surgery. Mean TB treatment duration was 11 ± 6 months with 12 (35%) children completing <9 months of treatment. Four (12%) children had no orthopaedic follow-up with 12 (35%) lost to follow-up within <9 months, 13 (38%) lost to follow-up within 9-53 months and 5 (15%) remaining in follow-up. **Conclusions** Adequate treatment and ongoing monitoring are essential to help reduce the risk of progressive deformity in children with spinal TB. However many children received a shorter than recommended course of TB treatment and the large majority did not receive appropriate orthopaedic follow-up.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

A putative new HIV-1 A, C, D complex circulating recombinant form (CRF) is emerging in South Africa

Graeme Brendon Jacobs (Stellenbosch University), Olivette Varathan (Stellenbosch University), Susan Engelbrecht (Stellenbosch University)

Background: South Africa has the highest number of HIV-1 infected individuals, estimated at 7.1 million people, predominantly infected with HIV-1 subtype C. Our laboratory is one of the few in the country that routinely screen patients for HIV-1 drug resistance. From this we have maintained a large sequence database. We did phylogenetic analysis on the sequences from this database to identify possible emerging HIV-1 recombinant forms. **Methods:** After routine PCR amplification and sequencing of the HIV-1 pol gene, sequences are deposited in the Virology database. Subtypes are identified using the REGA and jumping profile Hidden Markov Model online programs. To confirm these preliminary subtyping results, we infer maximum likelihood (ML) phylogenetic trees. Selected samples are further analysed using HIV-1 near-full length genome (NFLG) amplification and sequencing. Viral RNA and DNA were extracted from selected patient samples and amplified targeting the NFLG in two fragments. After Sanger sequencing, sequences were further analysed using the Quality Control tool at LANL. Subtypes were inferred on the NFLGs using ML phylogenetic analysis with bootstrapping. **Results:** Two samples, a 31 year old female from the Eastern Cape and a 34 year old female from the Western Cape were used to obtain NFLGs of 7928 bp (HXB2 position 0776 to 8704 bp). Breakpoints for these two sequences were similar and both samples were identified as complex A, C, D recombinant forms. **Conclusions:** The results indicate that a putative new HIV-1 complex Circulating Recombinant Form (CRF) consisting of subtype A, C and D, is emerging in South Africa. The identification of a new CRF indicates that the epidemic is complex and constantly changing. Information gained from NFLG characterisation of HIV-1 can be used in vaccine development and studies on the future dynamics and spread of the HIV-1 epidemic in South Africa

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

Clostridium difficile associated diarrhoea in a South African tertiary hospital population: A retrospective, descriptive study.

Andrew Whitelaw (US), Jantjie Taljaard (US), Lederi Kearney (US)

Background: The prevention and control of *Clostridium difficile* infection (CDI) in health care facilities has become a global public health concern. *Clostridium difficile* associated diarrhoea (CDAD) is now the leading cause of gastroenteritis-associated deaths and is the most common cause of health care associated infections in the USA. There is limited data available with regards to CDI epidemiology in South Africa. A multitude of risk factors for the development of CDI have been identified in several studies, of which antibiotic use has been proven to be the most important. **Method:** A retrospective descriptive study from Tygerberg Academic Hospital between 1 October 2010 and 30 September 2016. Patients over the age of 18 years with a positive stool sample result for *Clostridium difficile* during this period were included. Clinical records were evaluated using an electronic health record system. **Results:** 253 patients were identified. The majority of cases were hospital acquired (n=206; 81.42%) with 18.58% (n=47) classified as community acquired. Degree of severity was equally distributed with mild disease in 32% (n=81), moderate disease in 34.8% (n=88) and severe disease in 33.2% (n=84) of cases. Overall, 74.5% of patients receive antibiotics prior to the onset of CDAD – 65.9% of patients in the CA group received no antibiotics versus only 17.5% of patients in the HA group. In-hospital mortality for all patients was 28.9% (n=73). HIV infection was the only risk factor significantly associated with higher in-hospital mortality. Disturbingly, only 44.3% of patients had evidence of specific treatment prescribed for CDI. **Conclusion:** Antibiotic use is an important risk factor for the development of hospital acquired CDAD in our setting. Additionally, HIV is significantly associated with increased in-hospital mortality. The lack of CDAD treatment is alarming. The general awareness of CDAD and correct management of the condition need to be addressed urgently.

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Combining datasets from different biotechnological platforms for integrative bioinformatic analysis in the context of TB biomarker discovery

Elizna Maasdorp (Division of Molecular Biology and Human Genetics), Gerard Tromp (Division of Molecular Biology and Human Genetics)

Rationale: Predictive biomarkers are needed for diagnosis, predicting disease progression, treatment or vaccine response and treatment outcomes, across the tuberculosis (TB) spectrum, from latent infection to post-TB lung disease or even death. They can be pathogen or host-based, originate from a variety of tissues, and be measured across different medium to high throughput biotechnological platforms. Data from two or more platforms have not yet been analysed together to discover predictive TB biomarkers. The proposed analysis will investigate combining data derived from different platforms, but the same cohort of people, in a combined analysis in the context of biomarker discovery. **Methods:** RNA sequencing, metabolomics and Luminex cytokine data from a longitudinal study of household contacts of TB patients, with 18 months follow-up and progression to active TB disease as outcome of interest, will be combined for predictive biomarker discovery. A test set of 40% of each dataset will be set aside to test the final models on. The unprocessed datasets will likely have different distributions, scales and unique features like negative value component, missingness and technology-specific artefacts. These challenges to combined analysis will be addressed during pre-processing, by data transformation, scaling, imputation, dimension reduction and feature engineering. To establish a baseline accuracy to compare subsequent combined analyses to, primary separate predictive modelling of each training dataset will first be done. Then modelling of the same dataset with an alternative, candidate method for the ultimate combined analysis, will be done. Finally combined analysis of the three training datasets will be done, iterating over pre-processing and modelling until an acceptable area under the curve is achieved. A final pre-processing approach and model will be selected to apply to the combined test sets. The areas under the curve of receiver operator characteristic curves will be compared to the baseline accuracies of the datasets.

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Correlation of the mycobacterial killing capacity of natural killer cells with the number of activating killer immunoglobulin-like receptors expressed on their surfaces.

Dr Craig Kinnear (Stellenbosch University), Dr Marlo MÅ¶ller (Stellenbosch University), Prof Eileen Hoal (Stellenbosch University), Talani van Schalkwyk (Stellenbosch University)

TB is a curable disease, but continues to kill and remains a major health problem. While infection with the causative agent, *Mycobacterium tuberculosis* (M.tb) is necessary for the development of TB, it is not sufficient to cause disease in most infected individuals. The precise factors associated with progression to clinical disease are still largely uncharacterized. However the involvement of host genetics in TB has been proven unequivocally. Natural killer (NK) cells are important in the immune system and are regulated by two receptor superfamilies with one of those being the immunoglobulin-like superfamily (Killer immunoglobulin-like receptors). An investigation of the role of KIRs in TB susceptibility found that an overexpression (â‰¥ 5) of the activating killer immunoglobulin-like receptors (aKIRs) offers protection against developing active TB disease. In the present study the aim was to compare the efficiency of mycobacterial killing of NK cells of individuals with five or more aKIRs versus individuals with less than five aKIRs. The KIR genotypes of 30 individuals were determined. Five individuals with less than five aKIRs (group 1) and five individuals with five or more aKIRs (group 2) were identified. Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood. NK cells were then isolated from the PBMCs through negative selection. The cells were stimulated with M.tb H37Rv and CFU counts were used to determine the mycobacterium's viability. No statistical significant difference was observed between the two groups ($p = 0.60$). The levels of cytokine production following the stimulations were determined by Luminex immunoassays. A higher expression of IFN-Î³, perforin, IL-17A and RANTES was observed for group 2. RANTES expression was statistically significant ($p = 0.04$). This pilot study was the first to contribute towards a protocol to determine the killing efficiency of NK cells against fighting TB infection while incorporating the KIR genotype.

ABSTRACT NUMBER / ABSTRAKNOMMER: 21

De novo assembly of an admixed human genome

Anel Sparks (Stellenbosch University), Brigitte Glanzmann (Stellenbosch University), Craig J. Kinnear (Stellenbosch University), Eileen G. Hoal (Stellenbosch University), Gerard Tromp (Stellenbosch University), Gian D. van der Spuy (Stellenbosch University), Marlo MÅ¶ller (Stellenbosch University), Paul D. van Helden (Stellenbosch University)

South Africa has a unique cultural and genetic history and is home to some of the most diverse populations in the world. These ethnic groups include KhoeSan, Bantu-speaking populations, European-descent groups and groups of complex inter-continental admixture. The genetic ancestry present in a South African admixed population was previously harnessed to identify novel tuberculosis (TB) susceptibility genes. These analyses were facilitated by the publicly available human reference genome, which was derived from the DNA of multiple white individuals and first became available in 2001. Even though this reference genome has been updated, the latest build still has hundreds of gaps and unplaced scaffolds, due to the presence of different haplotypes from the original donors. Additionally, despite the universal application of this genome, approximately 2 to 5% of total high quality next generation sequencing reads fail to map to it. These sequences may contain the genomic regions and variants necessary to elucidate disease susceptibility, evolution and population diversity. De novo assembly of population-specific reference genomes are needed to advance research in these fields and have been done in multiple populations with success. We used DNA from two unrelated individuals to perform Next Generation Sequencing (NGS) with multiple insert sizes. The produced reads were used to generate a de novo assembly using the De Bruijn graph approach best suited for short, high quality reads. We are currently assessing and annotating the assembled genome. This genome will facilitate genetic research in this population, including studies on infectious diseases, such as TB, but especially

those on ancestry-dependent non-communicable diseases, such as diabetes mellitus and ischemic heart disease. Most importantly, this resource can aid ancestry-informed precision medicine in South Africa.

ABSTRACT NUMBER / ABSTRAKNOMMER: 22

Deciphering the Mechanisms of Isoniazid Resistance in Mycobacterium tuberculosis with Whole Genome Sequencing.

Anzaan Dippenaar (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), Cindy-Lou Hayes (National Health Laboratory Services, Port Elizabeth, South Africa), Elizabeth M. Streicher (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), James E. Posey (Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for), Margaretha De Vos (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), Marisa Klopper (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), Paul D. van Helden (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), Robin M. Warren (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of), Scott Burns (Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers fo), Simon Nagel (SA MRC Centre for Tuberculosis Research, DST/NRF Centre of Excellence for Biomedical Tuberculosis research, Division of)

Isoniazid (INH) serves as the backbone of combined anti-tuberculosis therapy. However, the effectivity of this drug has been compromised due to increasing resistance in Mycobacterium tuberculosis, arising through spontaneous mutations in certain genomic regions. In South Africa, the current algorithm dictates that only rifampicin resistant cases are tested for INH resistance. This is done by the MTBDRplus line-probe assay (LPA), which reports INH resistance based on mutations in katG gene and inhA promoter, followed by a phenotypic drug susceptibility test (DST) to confirm INH susceptibility. However, discrepancies between the results of these tests are frequently reported. This may result in incorrect diagnoses and the prescription of improper drug treatment regimens. This study investigates 398 clinical isolates obtained from NHLS Port Elizabeth with discrepant LPA and DST results. Method: The isolates were investigated by means of a series of standardized methods such as minimum inhibitory concentration (MIC) determination, Sanger sequencing, whole genome sequencing (WGS) and spoligotyping. This was done to determine if the reasons for the discrepancies between the LPA and phenotypic DST were due to novel mechanisms of resistance to INH. Results: WGS revealed several genomic features that may explain INH resistance in the absence of the canonical mutations detected by LPA. These include large deletions spanning the katG gene, heteroresistance (where an underlying population possesses a known mutation), as well as several potential novel resistance-causing mutations. Conclusion: While genotypic testing is conveniently rapid and accurate in the majority of cases, phenotypic DST is necessary to detect resistance conferred by less common mechanisms. WGS can be applied to inform researchers and clinicians of such alternative resistance markers. The results obtained in this study will ultimately be used to improve current diagnostic methods for detection of INH resistance.

ABSTRACT NUMBER / ABSTRAKNOMMER: 23

Determining the host range of Neoromicia capensis coronavirus by using viral pseudoparticles

Andrea Kotz (Stellenbosch University), Tasnim Suliman (Stellenbosch University), Wolfgang Preiser (Stellenbosch University)

Background: NeoCoV coronavirus was discovered in the South African bat species *Neoromicia capensis*. It is 85.5% genetically identical to Middle East respiratory syndrome coronavirus (MERS-CoV) and believed to be a possible ancestor. The host-switching events that gave rise to present-day MERS-CoV are unclear. With the coronaviral spike protein being responsible for host cell attachment and entry, its characterisation is key to studying host range. This study aims to determine which species NeoCoV, MERS-CoV and severe acute respiratory syndrome coronavirus (SARS-CoV) can infect by using pseudoparticles that express these viruses' spike proteins. Methods: Pseudoparticles bearing different spike proteins were constructed using BHK-21 cells transfected with plasmids that contain NeoCoV, MERS-CoV and SARS-CoV spike protein inserts. Transfected cells were infected with a recombinant vesicular stomatitis virus pseudotyped system, resulting in pseudoparticles that express green fluorescent protein (GFP) upon infection. The pseudoparticles have been used to infect Vero E6 and *N. capensis* kidney cells. The amount of GFP-expressing cells were visualised through fluorescence microscopy and used to determine the infection rate. The pseudoparticles will be used to infect *Camelus dromedarius* kidney, *Pipistrellus pipistrellus* kidney and Vero EMK cells. GFP expression will be measured by flow cytometry and the infection rate will be determined by the percentage of GFP-expressing cells. Results: The NeoCoV-pseudotype had the highest infection rate in Vero E6 cells but was quantitatively less in comparison to SARS-CoV in *N. capensis* kidney cells - an unexpected result seeing as NeoCoV was first detected in *N. capensis*. Another surprising discovery was that MERS-CoV was the least successful in infecting *N. capensis* kidney cells, even though it is more closely related to NeoCoV than SARS-CoV is. Experiments using the other aforementioned cell lines are being performed and will be presented at the event. Discussion: Results indicate that NeoCoV replicates more efficiently in primate than bat cells.

ABSTRACT NUMBER / ABSTRAKNOMMER: 24

Developing best practices and implementing a pipeline for the analysis of multiplex immunoassays data for biomarker discovery

Gerard Tromp (Stellenbosch University), Ncita L. Da Camara (Stellenbosch University)

Background & Scope: Cytokines are fundamental to the immune response in health and disease, e.g. infection. Currently available analytical tools, e.g. multiplexed enzyme-linked immunosorbent assays (ELISA) such as the Luminex platform, enable the detection and quantification of multiple cytokines simultaneously from small amounts of sample. The utility of these assays for diagnostic and prognostic use demands that analyses be reproducible and robust. The aim of this study is to develop, evaluate, and implement a pipeline for the analysis of multiplex immunoassays data. Design & Approach: Programming and statistical analysis will be done to implement best practices for data generation, management and quality control to provide high quality data for analysis. A variety of analytical approaches will be investigated and a set of robust analysis options will be provided together with appropriate bioinformatics tools in the newly developed pipeline. The methods will be validated using existing de-identified data sets from the Stellenbosch University Immunology Research Group and their collaborators as well as data from public data repositories. Subsequently, we will apply the pipeline to newly generated data. Conclusions: The newly developed pipeline is expected to speed up identification of diagnostic markers, prognostic markers, as well as prognostic treatment response markers. We will implement this approach in our department, and promote its use more generally. This research is supported by the Strategic Health Innovation Partnership Grant from the South African Medical Research Council and Department of Science and Technology/SA Tuberculosis Bioinformatics Initiative (SATBBI).

ABSTRACT NUMBER / ABSTRAKNOMMER: 25

Development of direct detection tools for the diagnosis of tuberculosis in African elephants and rhinoceros.

Candice De Waal (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Eduard Roos (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Josephine Chileshe (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Michele A. Miller (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Paul van Helden (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Peter E. Buss (Veterinary Wildlife Services, South African National Parks, Kruger National Park), Sven D.C. Parsons (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Tanya Kerr (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University), Wynand J. Goosen (Divison of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University)

African elephants and rhinoceroses are susceptible to developing tuberculosis. The recent discovery of *Mycobacterium tuberculosis* disease (Mtb) in a bull elephant in the Kruger National Park and cow in a South African zoo emphasizes the impact this disease may have on wild and captive populations of African elephants in South Africa and the interface between people and wildlife. Recently, *Mycobacterium bovis* infection (bTB) in free-ranging African rhinoceros have also been discovered and has led to movement restrictions imposed by the Department of Agriculture, Forestry and Fisheries (DAFF) on rhinoceros in Kruger National Park. Currently, some of the largest populations of rhinoceros exist in areas where bTB is endemic in other wildlife species (Kruger National Park and Hluhluwe-iMfolozi Park). Unfortunately, large knowledge gaps exist regarding risk factors for tuberculosis transmission, infection and progression to disease; prevalence in these species and populations; and impact on ecology and conservation. Understanding these aspects requires reliable tools to diagnose individuals and to screen populations. However, there is a paucity of available techniques for the detection of mycobacterial infection and disease in elephants and rhinoceros. Further studies are critically needed to address these knowledge gaps to create an effective strategy to minimize disease spread while facilitating translocation and metapopulation management of these threatened and endangered species. Therefore, in this study we aim to improve and develop existing and novel direct detection techniques using ante-mortem and post-mortem samples for the detection of tuberculosis in African elephants and rhinoceros.

ABSTRACT NUMBER / ABSTRAKNOMMER: 26

Differential gene expression in antigen stimulated whole blood from patients with Tuberculosis and Tuberculosis-Diabetes comorbidity.

Gerhard Walzl (Stellenbosch University), Happy Tshivhula (Stellenbosch University), Katharina Ronacher (The University of Queensland), Leanie Kleynhans (Stellenbosch Univeristy)

Introduction: Patients with tuberculosis-diabetes comorbidity (TB-DM) are more likely to fail TB treatment compared to TB patients without co-morbidities despite having higher circulating concentrations of Th1 and Th17 cytokines. The aim of this study was to characterize antigen-specific immune responses in TB and TB-DM patients. Methods: Whole blood from patients with TB (n=10) and TB-DM (n=11) at baseline and end of treatment (month 6) were stimulated with *Mycobacterium tuberculosis* (Mtb) antigen cocktail (ESAT-6, CFP-10 and TB 7.7) and differential expression of 594 genes involved in immune regulation was determined using the Nanostring technology. RESULTS: We demonstrate that genes associated with innate and adaptive immune cell types are differentially represented in unstimulated and antigen stimulated whole blood from TB and TBDM patients at baseline and month 6. At baseline unbiased hierarchical clustering showed clear separation of TB-DM from TB patients based on whole blood mRNA expression profiles. Genes involved in Jak-Stat signalling pathways were significantly upregulated in TB-DM compared to TB patients, whereas genes involved in the iNOS and IL-12 signalling pathways were downregulated. CONCLUSION: Our results show differential gene expression and activation of immunological pathways in TB-DM compared to TB patients after stimulation with Mtb antigens. Alterations of these immunological pathways could be

contributing factor in delayed Mtb clearance and unfavourable TB treatment outcomes in TB-DM patients and offer targets for host-directed therapeutic approaches to treat TB-DM comorbidity.

ABSTRACT NUMBER / ABSTRAKNOMMER: 27

Dissecting QC variability in mid-scale “Shotgun” proteomic data

David Tabb (University of Stellenbosch, Molecular Biology and Human Genetics division), Marina Pauw (University of Stellenbosch, Molecular Biology and Human Genetics division)

“Shotgun” protein mass spectrometry is widely acknowledged as a platform with low sensitivity and lingering questions concerning reproducibility. The global tendency of moving towards a “equality by design” approach to research has fueled the creation of quality control software in this field. Free software packages such as the ID-free version of QuaMeter have allowed researchers to inspect the quality of their research independent of the instrument. This allows for the comparison of proteomic techniques across laboratories. Here, a large-scale analysis is conducted to assess different aspects of proteomic experiment design. When the cost of LC-MS instrument time is considered, the value of adding technical repeats to the study must be assessed. We therefore compare the amount of distinct peptides gained by adding technical replicates of a sample as opposed to analyzing different fractions of the same sample. We show here that in the datasets inspected, only 15% of the samples would have at least doubled the amount of distinct peptides by the addition of a second technical replicate and none of the peptides would have doubled the amount of distinct peptides gained by the addition of a third technical replicate. Different fractionation strategies, SDS-PAGE fractionation, MudPIT, OFFGEL and RPLC, are investigated in the realm of quality control metrics. Within datasets, we illustrate the clear progression of certain quality trends as a function of time. Our findings therefore emphasize the importance of randomization of datasets. We also demonstrate the use of quality metrics to determine quality outliers and infer the reason for the anomaly. The study shows that quality metrics are an appropriate tool to compare techniques, assess the quality of a dataset, determine outliers and infer the reason behind a change in quality.

ABSTRACT NUMBER / ABSTRAKNOMMER: 28

Diversity and Ecology of Astroviruses in South African Bats

Dr Ndapewa L. Ithete (Faculty of Medicine and Health Sciences, Department pathology, Division Medical Virology, Stellenbosch University), Dr Stacey Schultz-Cherry (St. Jude Children’s Research Hospital, Memphis, United States of America), Karlien Barnard (Faculty of Medicine and Health Sciences, Department pathology, Division Medical Virology, Stellenbosch University), Prof Wolfgang Preiser (Faculty of Medicine and Health Sciences, Department pathology, Division Medical Virology, Stellenbosch University)

BACKGROUND Emerging infectious diseases are a global health concern, and most of these diseases are zoonotic in origin. The search for wildlife hosts of potential zoonotic diseases has found that bats (Chiroptera) play an important role as reservoirs for numerous potential zoonotic diseases. Astroviruses (AstVs) are among a wide variety hosted by bats. Astroviridae comprise two genera, Mamastroviridae (infecting mammals) and Avastroviridae (infecting birds). AstVs are transmitted via faecal oral route and cause acute gastroenteritis and in rare cases encephalitis and hepatitis. Little is known about AstVs occurring in southern African (SAn) bats. OBJECTIVE Investigate the diversity and ecology of SAn bat AstVs using molecular- and phylogenetic techniques and statistical analyses. METHODS Six hundred bat faecal samples were screened for the presence of AstVs using screening assay that targets the RNA-dependent RNA polymerase (RdRp) gene. The amplification of astroviruses and coronaviruses (CoVs) were monitored over the span of a year in a specific bat colony using real-time assays. Phylogenetic analyses were carried out using various phylogenetic programmes (MEGA v7, Geneious R12). Statistical analyses and modelling was done in R (3.3.4).RESULTS AND DISCUSSIONAn overall

prevalence of 10% was noted for AstVs in SAn bats. Twenty five novel RdRp sequences were obtained. Phylogenetic analyses suggest that clustering is not according to species or geographical location, suggesting that they can easily cross species barriers. Strains isolated within a colony did not always cluster together, suggesting that multiple strains could be circulating within the colony. The colony study indicated that AstVs and CoVs amplification is most likely influenced by colony size and not seasonality. Statistical analyses indicated that species identity, sex and the biome, in which the bats were trapped could potentially influence AstV positivity.

ABSTRACT NUMBER / ABSTRAKNOMMER: 29

Diversity of paramyxovirus-related sequences identified in South African shrews

Bronwyn Kleinhans (Stellenbosch University), Dr Ndapewa Ithete (Stellenbosch University), Prof Corrie Schoeman (University of KwaZulu-Natal), Prof Sonja Matthee (Stellenbosch University), Prof Wolfgang Preiser (Stellenbosch University)

Introduction Over the past three decades, Hendra virus and Nipah virus (genus Henipavirus, family Paramyxoviridae) have demonstrated the ability to cross the species barrier with a severe impact on veterinary and human health. Species-rich small mammals, such as rodents and shrews, have been implicated as hosts for paramyxoviruses. A recent study revealed a high prevalence of henipa-related paramyxovirus sequences in wild shrew populations in Zambia. To date, the presence of paramyxoviruses has not been reported from South African shrew populations. As part of general surveillance of paramyxoviruses in South African small mammals, the presence and prevalence of paramyxovirus-related sequences in South African shrews were investigated. Methods Rodent and shrew specimens from various locations within South Africa were obtained from collaborators. Kidney specimens were homogenised, then total RNA extracted, followed by the synthesis of cDNA with random hexamer primers. A highly sensitive and broadly reactive PCR assay targeting a conserved region within the L-gene of paramyxoviruses was used for screening. Positive PCR products were sequenced for phylogenetic analysis. Results To date, a total of 190/634 (30%) individual small mammals screened positive for paramyxovirus sequences, including 14/31 (45.2%) shrews (*M. cafer* and *C. flavescens*), family Soricidae. Phylogenetic analysis of study sequences showed that they cluster with paramyxovirus sequences within the Henipavirus genus. Conclusion The prevalence and diversity of paramyxoviruses in shrews are severely understudied and poorly understood. In addressing these shortcomings, this study has revealed a high prevalence of henipavirus-related sequences in South African shrew populations. Viral sequences show to cluster according to species and not necessarily biome. Within South Africa, *C. flavescens* commonly occur along the coastline, while *M. cafer* is restricted to patches of Afromontane and forest areas (10-30 individuals per hectare). More comprehensive characterisation, attempts at virus culture and viral load testing in organs and between individuals are ongoing.

ABSTRACT NUMBER / ABSTRAKNOMMER: 30

Effect of pharmacologically-induced Myeloid Derived Suppressor Cell maturation on immune reactivity against Mycobacterium tuberculosis.

Anca Dorhoi (Friedrich-Loefer Institut), Gerhard Walzl (Stellenbosch University), Nelita du Plessis (Stellenbosch University), Vinzeigh Leukes (Stellenbosch University)

Development of active Tb disease is attributed to failure of an effective host Tcell helper1 (Th1) response during Mycobacterium tuberculosis (M.tb) infection. Immune mechanisms exist that suppress effector responses in the presence of persistent antigens to limit immune mediated tissue pathology. Myeloid derived suppressor cells (MDSC), an immature myeloid population, suppress T cell responses in various infectious diseases. All-trans retinoic acid (ATRA), induce maturation of MDSC resulting in decreased suppressive ability. We hypothesized that ATRA induced MDSC modulation improves immunity during M.tb infection. We aimed to measure the effect of ATRA on anti-Tb immune responses

and evaluate the effect of ATRA treatment on MDSC frequency. We also investigated the effect of ATRA supplementation on MDSC-mediated T cell suppression. Preliminary results show a significant decrease in Total MDSC (T-MDSC) frequencies following ATRA treatment ($p=0.0051$), driven by a significant decrease in the monocytic MDSC (M-MDSC) subset ($p=0.0028$). Co-culture experiments revealed that ATRA treatment does not affect T-cell activation, proliferation, memory formation or T-cell trafficking. ATRA treatment of MDSC does however reduce the number of regulatory T cells. The effect of ATRA treatment on soluble cytokine responses remains to be determined. This is the first investigation into ATRA treatment of MDSC from Tb patients. We propose to further evaluate drugs with direct effects on MDSC suppressive mechanisms, such as PDE-5 inhibitors (Sildenafil), as these will have a more pronounced effect on MDSC immunosuppression. To elucidate this, future work on Sildenafil as adjunctive therapy for Tb is necessary.

ABSTRACT NUMBER / ABSTRAKNOMMER: 31

Elucidating the position of ESX-3 components in the membrane of *Mycobacterium smegmatis*

Caitlyne Young (Stellenbosch University), Dr Nastassja Kriel (Stellenbosch University), Professor Samantha Leigh Sampson (Stellenbosch University)

Mycobacterium tuberculosis is a high prevalence pathogenic organism, which causes millions of deaths each year. *M. tuberculosis* encodes for a specialised Type VII secretion system known as ESX-3, which has been shown to be essential for the in vitro growth and survival of *M. tuberculosis* through its role in zinc and iron metabolism. Previously the cytoplasmic component of the ESX-3 secretion system, EccA3, was shown to be unipolarly localised at the growing pole in the closely related study organism *Mycobacterium smegmatis*. The results from this study suggested that ESX-3 was either unipolarly localised in *M. smegmatis* or recruited to a single polar region by EccA3. In this study, we aimed to identify the location of ESX-3 in the membrane of *M. smegmatis* through fluorescent tagging of the membrane component EccE3. The gene encoding for EccE3, was cloned into a conditional expression plasmid, pCG. Co-transformation with pTEK-4S-0X allowed for the regulated expression of EccE3 as a fusion protein with green fluorescent protein (GFP) in the presence of anhydrous tetracycline. Expression was confirmed by immunoblotting prior to determining the location of the fluorescently tagged protein in *M. smegmatis* using confocal microscopy. The regulated expression of EccE3-GFP was confirmed using immunoblotting and fluorescent intensity measurements. Confocal microscopy showed that EccE3-GFP was located throughout the membrane however, conditional expression showed the localisation of EccE3-GFP at both a single pole in the membrane of *M. smegmatis*, and throughout the membrane. Polar and membrane localisation of EccE3-GFP could suggest that the ESX-3 secretion system is inserted into the growing pole, followed by distribution throughout the membrane as the organism grows. Understanding how these secretion systems are assembled and incorporated into the nascent membrane could provide us with novel pathways to investigate with the ultimate aim of disrupting these processes.

ABSTRACT NUMBER / ABSTRAKNOMMER: 32

Evaluation of effects of read length and sequencing depth on experimental design of RNA-sequencing experiments

Darryn Zimire (University of Stellenbosch), Gerard Tromp (University of Stellenbosch)

RNA-sequencing, (RNA-seq), has become a standard method for quantifying gene expression due its ability to detect rare events, copious amounts of data output and dynamic range. Despite its strengths, this technology can be expensive and requires good experimental design for optimal downstream analysis and results. Read length and sequencing depth are two essential parameters to consider when designing RNA-seq experiments and should a priori be determined as they play a critical role in downstream analysis and can have a significant impact on cost of experiments as well as the biological

conclusions drawn from the generated data. Determining the optimal parameter values can help in designing adequately powered experiments and assist researchers in avoiding unnecessary experimental costs, wasted resources and choosing the most suitable high-throughput sequencing technology. The aims of the research project are to investigate the effects of read length and sequencing depth on downstream analysis and designing RNA-seq in their experiments, provide guidelines and standards for optimal read length, sequencing depth and base-call quality. The focus of the research will be human and bacterial Illumina single-end and paired-end RNA-seq data. We will model the effects of varying read lengths, sequencing depths and error profiles on differential expression and alternative splicing events. Successful models will inform researchers who are planning RNA-seq experiments on optimal parameter values that will allow the design of adequately powered experiments at the lowest cost that will produce data enabling sound biological conclusions. These will also lay the foundation for development of a bioinformatics tool for experimental design of RNA-seq experiments.

ABSTRACT NUMBER / ABSTRAKNOMMER: 33

Feasibility of ultra-deep high fidelity amplicon sequencing (SMOR) on genomic DNA from used Xpert MTB/RIF (G4 and Ultra) cartridges for full genotypic drug susceptibility testing

Ashley Ruiters (National Health Laboratory Services), Christopher Allender (Translational Genomics Research Institute), Dave Engelthaler (Translational Genomics Research Institute), Elizabeth Streicher (Stellenbosch University), Frik Sirgel (Stellenbosch University), Grant Theron (Stellenbosch University), John Metcalfe (Division of Pulmonary & Critical Care Medicine, San Francisco General Hospital, University of California, San Francisco), Margaretha de Vos (Stellenbosch University), Robin Warren (Stellenbosch University), Rouxjeane Venter (Stellenbosch University)

Drug-resistant tuberculosis (DR-TB) is a public health crisis. Key barriers to drug susceptibility testing (DST) are test rapidity, sensitivity, and completeness (i.e., full DST). We have shown that mycobacterial genomic DNA from used Xpert MTB/RIF G4 (Xpert) cartridges can be used for MTBDRsl DST and that single molecule overlapping reads (SMOR), a targeted next-generation sequencing approach, improves sequencing error and read depth in a highly multiplexed manner, thereby allowing the detection of cryptic micro-heteroresistance to first and second-line drugs. We evaluated whether SMOR could be done using the cartridge extract (CE) from Xpert and Xpert MTB/RIF Ultra (Ultra). Xpert-positive RIF-susceptible (n=24), Xpert-positive RIF-resistant (n=7), and Ultra-positive RIF-susceptible (n=20) cartridges were collected and CE used for SMOR. Paired cultures were done when possible for the latter two types [3/7(43%) and 16/20(80%), respectively]. Phenotypic DST (pDST) was done on isolates (rifampicin, isoniazid, ofloxacin, amikacin, kanamycin, pyrazinamide). Ultra CE displayed a trend towards less actionable reads (>10 total reads and, if resistant, >0.1% reads indicated resistance) when compared to Xpert CE [8/20(40%) vs 14/24(58%);p=0.22] and less mycobacterial load [median CTmin (IQR)] for non-actionable results (Xpert 27.3 [22.7-9.9] vs Ultra 18.3 [17.1-23.1];p=0.007); indicating that SMOR on Ultra CE is less likely to work on paucibacillary specimens without further optimisation. CTmin at which SMOR will yield actionable results were 23.15 and 16.75 for Xpert and Ultra, respectively. At this threshold, Ultra had a specificity of 90%. Xpert CTmin <23.15 had a sensitivity and specificity of 100% and 75%, respectively. pDST results showed concordance with SMOR on Ultra actionable results for all drugs but rifampicin. This proof-of-concept shows that SMOR is feasible on CE and could lead to fast and effective full drug-resistant diagnosis. Further optimisation will be done to improve SMOR on Ultra CE and confirm the sensitivity of SMOR on CE for resistance.

ABSTRACT NUMBER / ABSTRAKNOMMER: 34

Genotypic analyses of HIV-1 Integrase from South African patients failing first and second line antiretroviral treatment

Adetayo (Stellenbosch University), Graeme (Stellenbosch University), Kamalendra (Missouri University), Mathilda (Stellenbosch University), Ruben (University of the Western Cape), Ujjwal (Karolinska Institute)

Background: South Africa has the largest HIV combinational antiretroviral therapy (cART) roll-out program worldwide. HIV-Integrase (IN) has proven to be a viable target for highly specific HIV-1 therapy. Our aim was to analyze the HIV-1 IN gene in a South African context and identify RAMs against first and second generation Integrase inhibitors (INIs). Methods: We performed genetic analyses of 80 South African HIV-1 infected patients who failed both first and second line cART. Plasma samples were obtained from the National Health Laboratory Services (NHLS) diagnostic section of the Division of Medical Virology, Stellenbosch University. The NHLS routinely screens for HIV-1 drug RAMs through the characterization of viral strains through analysis of the viral Protease (PR) and Reverse-Transcriptase (RT) gene fragments. In this study, we targeted the IN gene to analyze the presences of RAMs. Drug resistance analyses were carried out using HIV Stanford Drug Resistance Database. Results: A total of 66 (82.5%) of the 80 samples could be successfully sequenced. Genotypic analyses revealed the absence of major and accessory RAMs in the cohort collected failing first and second line therapy in South Africa. However, E157Q, an accessory mutation emerged at the rate of 3.0% (2/66), which most likely confers low-level resistance to raltegravir (RAL) and elvitegravir (EVG), but do not confer resistance to second-generation dolutegravir (DTG). Most common subtype in our cohort was HIV-1 subtype C (98%, n=65/66). We also identified CRF02_AG (1.5%) n=1/66. Conclusion: Our data suggest the prevalence of INI RAMs, is low in South Africa, but natural polymorphisms and subtype-specific differences may influence the effect of individual treatment regimens. In the South African context, INIs are potentially a viable option for salvage therapy. However, there is still a need for surveillance of the RAMs to ensure patients receive the best possible treatment and care.

ABSTRACT NUMBER / ABSTRAKNOMMER: 35

Global transcriptomic investigation of human macrophage response to infection with pathogenic/non-pathogenic mycobacteria

Abhilasha Madhvi (Stellenbosch University)

Global transcriptomic investigation of human macrophage response to infection with pathogenic/non-pathogenic mycobacteria Background and objective: Tuberculosis caused by *Mycobacterium tuberculosis* (M.Tb) continues to be one of the biggest global health hazards, claiming millions of lives every year. Despite the emphatic nature of the disease, it develops in only 10% of infected individuals which explains the intricate mechanism of host immunity to contain bacteria. The answer to the enigma of TB infection and development to active diseases are hidden in host immune responses to M.tb. Disease causing M.tb survives while non-pathogenic does not survive inside human macrophages, where human monocyte derived macrophages (HMDMs) are considered to be the primary host cellular defence against M.Tb. We initiated to study the HMDMs response by infecting them with mycobacterial strains grown in tween-free media as tween decreases bacterial virulence by altering its cell wall. Approach: In this study, we propose to investigate the role of host immune response to pathogenic and non-pathogenic M.tb which may reveal the important determinants (molecules) that are involved in M.tb intracellular survival. We intend to access the early and late (12 and 96 hours post infection) transcription profiles between host and pathogenic/non-pathogenic mycobacterial strains (grown in tween-free medium) which will be assessed through RNAseq and validated through qPCR. Statistical analysis of relative gene expression difference will be assessed by Two-way ANOVA. The potential transcriptomes will be further knocked up/down in-vitro hence broadening the scope for drug targets that will afford the development of host-based therapeutics. Preliminary findings: Preliminary results of RNAseq with excellent RNA quality (RIN score 10) depict few differentially expressed transcriptomes with p-value ≤ 0.01 .

ABSTRACT NUMBER / ABSTRAKNOMMER: 36

HIV testing patterns in two community-based approaches to Universal Test and Treat in the HPTN 071 (PopART) intervention in South Africa

Abdul Sakoor (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Bliya Yang (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Bongwiwe Cimi (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Dolapo Awoniyi (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Helen Ayles (Zambia AIDS Related Tuberculosis Project, University of Zambia), Jacqueline Hlalukana (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Nulda Beyers (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Peter Bock (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Phumlani Ramncwana (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Phumza Siboto (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Richard Hayes (London School of Hygiene & Tropical Medicine, Dept of Infectious Disease Epidemiology), Rosa Sloot (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Sam Griffith (FHI360), Sarah Fidler (Imperial College, Department of Infectious Disease Epidemiology), Sheldon Hendricks (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health), Sian Floyd (London School of Hygiene & Tropical Medicine, Dept of Infectious Disease Epidemiology), Yvonne Saunders (Desmond Tutu TB Centre, Stellenbosch University, Dept of Paediatrics and Child Health)

Background: HPTN 071 (PopART) is a community-randomised trial conducted in 21 communities in Zambia and South Africa (SA) with a population of over 1 million, to measure the impact of a combination HIV prevention intervention on population-level HIV incidence; delivered by Community HIV-care Providers (CHiPs), who provide home-based HIV testing services (HTS). In response to a lower proportion of men being reached during home-based HTS (HBHTS), CHiPs offered HTS in tents. We analysed HTS data to determine whether more men were tested through tent-HTS as compared to HBHTS, and compared other demographic characteristics to understand HIV testing patterns. Methods: During annual round three from April 2017-December 2017, when both HBHTS and tent-HTS were offered by CHiPs in six SA communities, tent-HTS was conducted at public transport hubs(4days), shopping centres(13 days), schools/libraries(6 days), and a community event(1 day). HTS was offered through a finger-prick rapid test. CHiPs collected data on an electronic register. Multivariable logistic regression analysis was used to compare the population reached through HBHTS versus tent-HTS on gender, age, history of prior HIV testing, status as a presumptive TB case, and community. Results: 32,032 HIV tests were done through HBHTS and 402 during tent-HTS. Those testing through tent-HTS were more likely than those testing through HBHTS to be men (aOR 1.9, 95%CI 1.5-2.3), more likely to be from the older age-groups of 25-29/30-39/40-49/50+ (p-values of all aOR's < 0.01), and more likely to be residents of communities SA5/SA6 (agricultural communities further from Cape Town). Conclusions: Tent-HTS in high traffic areas proved successful in reaching a higher proportion of men, although the absolute number of additional tests was relatively small. Tent-HTS was relatively more successful in agricultural areas. Studies with larger sample size are required to understand differences in HIV testing patterns between HBHTS and tent-HTS.

ABSTRACT NUMBER / ABSTRAKNOMMER: 37

Important viruses with zoonotic potential in South African bats and their associated ectoparasites: influenza A viruses, hantaviruses and insect-specific viruses.

Karmistha Poovan (Stellenbosch University), Ndapewa L. Ithete (Stellenbosch University), Wolfgang Preiser (Stellenbosch University; National Health Laboratory Service (NHLS), Tygerberg)

Emerging infectious diseases pose a global threat to human health, economic stability and biodiversity. Recent research has focused on identification of reservoirs, disease vectors and virus-host evolution, leading to the discovery of influenza A-like viruses in South and Central American bats and new viral host species of hantaviruses, which now include bats and shrews. Research centring on insect-specific

viruses (ISVs) has improved insights into the evolutionary history of the Bunyavirus genus. More recently, a novel orthoreovirus was identified from bat flies, a bat ectoparasite, in South Africa. Consequently, the aim of the current study is to determine if influenza A-, hanta- and insect-specific-viruses (ISVs) are circulating in South African bat species and their associated ectoparasites, respectively. Various sample types and ectoparasites from numerous South African bat species were collected between 2014 and 2016. To date, 283 faecal samples have been screened for influenza A- and 264 faecal, 100 tissue and 144 saliva and urine swab samples for hantaviruses using PCR assays. All samples screened have yielded a negative result. However, screening is ongoing. Ectoparasites, namely bat flies (72), were used to seed C6/36 insect cells to test for the presence of ISVs. No cytopathic effect was observed in inoculated cell cultures, but cell culture supernatants and additional ectoparasite samples (366) are available for screening using PCRs assays. The detection of these viruses may allow for the assessment of the potential viral threat and increased knowledge to the evolutionary history of the diseases these viruses may illicit. Moreover, studies such as the current one can shed light on the evolutionary relationships between virus and host.

ABSTRACT NUMBER / ABSTRAKNOMMER: 38

Investigation of the effect of Curdlan-functionalized PLGA nanoparticles on Mycobacterium tuberculosis infected RAW264.7 macrophages

A. Dube (University of Western Cape), S. Du Plessis (Stellenbosch University), S.L. Sampson (Stellenbosch University)

Introduction Host directed therapy (HDT) is an alternative therapeutic approach against Tuberculosis (TB) that modulates and targets the host immune system instead of the pathogen itself. The attachment of curdlan onto the surface of Poly-lactic-co-glycoside (C-PLGA) nanoparticles (NPs) transforms them into target specific molecules that stimulate the Dectin-1 receptor present on macrophages (MPs) and consequently activate downstream bactericidal pathways. In addition, encapsulation of a conventional antibiotic in the core of these functionalised C-PLGA NPs will enable the sustained release of the drug within the specific Mycobacterium tuberculosis infected cell compartment. This multimodal approach makes it possible to simultaneously maximize pathogen killing and control inflammatory responses. Aim Determine the growth inhibitory effect of C-PLGA NPs on M. tuberculosis infected macrophages. Methods RAW264.7 MPs will be infected at a MOI of 10:1 with M. tuberculosis H37Rv::pMV306hsplux. Different NP formulations will be applied to the infected MPs and luminescence readings will be obtained over a period of 72h to track bacterial numbers. Results Based on preliminary data, we expect a decrease in relative light units that directly correlates with a decrease in bacterial cell counts, indicative of the inhibitory effect of C-PLGA NPs. Conclusion We intend to demonstrate the eradication of intracellular M. tuberculosis through macrophage-specific immune responses stimulated by C-PLGA NPs. Demonstrating the inhibitory effect of C-PLGA NPs may contribute towards the application of these particles as a novel approach against the control of TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 39

Investigation of X-chromosome variants in susceptibility to pulmonary tuberculosis: an XWAS approach

Brenna Henn (University of California), Chris R Gignoux (University of Colorado), Craig Kinnear (Stellenbosch University), Eileen Hoal (Stellenbosch University), Genevieve L Wojcik (Stanford University School of Medicine), Gerard Tromp (Stellenbosch University), Haiko Schurz (Stellenbosch University), Marlo MÃ¶ller (Stellenbosch University), Paul D van Helden (Stellenbosch University), Stephanie Pitts (Stellenbosch University)

Tuberculosis (TB), caused by Mycobacterium tuberculosis is a complex disease. Not only is disease progression influenced by environmental and socioeconomic factors, but both the host and pathogen genomes as well as age and sex contribute. A clear sex bias exists, with TB notification rates nearly

twice as high in males compared to females. Although socioeconomic, behavioral and sex hormones influence this male sex bias these factors do not fully explain it. We hypothesise that X-linked genetics further contribute towards the male sex bias since males only have one X chromosome. We genotyped 800 admixed South African individuals using the Illumina Multi ethnic genotyping array and conducted a sex-stratified analysis to determine if X-linked variants contribute to the male sex-bias. No significant associations were identified in the X-linked or autosomal association analysis with TB susceptibility, but interaction analysis revealed 11 interactions that passed Bonferroni correction for the genome-wide interaction analysis. These significant interactions further confirm the complexity of TB and highlight the need for in-depth analysis in large data sets.

ABSTRACT NUMBER / ABSTRAKNOMMER: 40

Mortality amongst HIV-positive female tuberculosis patients in South Africa

C van Schalkwyk (SACEMA, Stellenbosch University, Stellenbosch), M Borgdorff (Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands.), MM Claassens (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa.), P Naidoo (Bill and Melinda Gates Foundation, Seattle, Washington.), R Dunbar (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa.)

Background: Studies show that antiretroviral therapy (ART) may reduce mortality among HIV-positive tuberculosis (TB) patients on treatment. In 2011, the South African National TB Programme changed its policy regarding ART for TB patients to initiate all HIV-positive TB patients on ART, irrespective of CD4 count. We investigated the impact of this policy on mortality, using data from the South African National electronic TB register (ETR.net). Methodology: ETR.net data from 2009-2013 were used in conjunction with the Thembisa model for population denominators. Newly registered adults who were not transferred or moved were included and individuals with missing data excluded. An adjusted Cox regression model was developed, as well as the standardised mortality ratio (SMR) determined. Results: 1,155,924 individuals were included. ART coverage increased from 36% to 87%, similar in both sexes; the Cox model showed a 23% reduction in mortality risk amongst TB patients between 2009-2013 (aHR 0.77 95%CI 0.75-0.78). In both sexes, the highest mortality risk reduction was seen in age groups 15-24 and 25-34 years. Mortality risk reduced by 22% in HIV-positive women and 25% in HIV-positive men; it was stable in both HIV-negative groups. However, in HIV-positive women, the SMR increased significantly each year from 9.62 (95%CI 9.38-9.88) in 2009 to 16.46 (95%CI 16.05-16.89) in 2013. In HIV-positive men, the SMR showed no significant difference. Conclusion: A substantial decline of mortality was observed in HIV-positive TB patients, while among HIV-negative TB patients mortality was stable. The SMR showed mortality amongst HIV-positive women decreased at a slower rate in TB patients than in the general population. This might be explained by women not accessing HIV care as early or frequently as men because of family commitments but the data are limited by not including time of ART initiation, CD4 count or ART adherence and should be further investigated.

ABSTRACT NUMBER / ABSTRAKNOMMER: 41

Motivating people living with HIV to initiate antiretroviral treatment at high CD4 counts in three HPTN 071 (PopART) health facilities in the Western Cape, South Africa

Colette Gunst, (Western Cape Winelands DoH), Constance Mubekapi- Musadaidzwa (Stellenbosch University), Dillon Wademan (Stellenbosch University), Françoise Louis, (Kheth' Impilo), Gabriela Carolus, (Stellenbosch University), Graeme Hoddinott (Stellenbosch University), James Kruger, (Western Cape DoH), Karen Jennings, (City of Cape Town Health), Nelis Grobbelaar, (ANOVA Health Institute), Neshaan Petton (Western Cape DoH), Peter (Stellenbosch University), Portia Hendricks (Western Cape DoH), Rheiner Mbaezue, (City of Cape Town Health)

Background – In 2016 South Africa adopted WHO ART regardless of CD4 count recommendations. That same year ART coverage was estimated at 56% and increased uptake of ART at higher CD4 counts

is still needed. Historically, health-messaging about ART initiation highlighted side effects, resistance-risks, and triage of available treatment. CD4-count eligibility criteria and pre-ART counselling reinforced a perception that PLHIV must be "sick enough" to initiate ART. A messaging shift is critical to increase uptake and ensure adherence. The study provides insight on ART messaging pre-national ART policy shift. How can we explain this shift to PLHIV and motivate initiation? Methods Patients at three health facilities in the Western Cape, were eligible for ART regardless of CD4 count outside of guidelines between June 2014 and September 2016. We conducted 134 randomly reviewed clinical patient folders to characterise the socio-demographic profile of ART initiators. We interviewed 12 key informants about their experiences explaining initiating ART at high CD4 counts. The evaluation design was exploratory through case descriptions. Findings The mean age of patients initiating ART at CD4 count >500 was 34.6 (range: 17-65; SD = 9.13), most were women (74.7%), married (65.3%), and employed (42%). These characteristics were similar to patients initiating ART at CD4 counts ≤ 500. Key informants indicated no radical shift was necessary to explain ART regardless of CD4 count. They (i) used metaphors to emphasize the importance of building a strong foundation and not waiting until HIV weakened the body, (ii) reiterated that ART prevents opportunistic infections, and (iii) emphasized that management of HIV through ART is comparable to other chronic diseases. Conclusion Motivating patients to initiate ART at high CD4 counts is possible even in high burden settings. Messaging about reduced risk of onward transmission was not a core component of health workers' narratives.

ABSTRACT NUMBER / ABSTRAKNOMMER: 42

Mouse macrophages display differential expression of certain cell-surface receptor and signalling genes when comparing infection between pathogenic and non-pathogenic mycobacteria

Bienyameen Baker (Stellenbosch University), Carel van Heerden (Stellenbosch University), Gina Leisching (Stellenbosch University), Jeanie Sieberhagen (Stellenbosch University), Ray-Dean Pietersen (Stellenbosch University)

The disease causing agent, *Mycobacterium tuberculosis*, survives inside human macrophages but not non-pathogenic mycobacteria. Comparing the host response between infection with pathogenic and non-pathogenic mycobacteria might reveal important determinants (molecules) that are involved in *Mycobacterium*'s intracellular survival strategy. Previously, we observed through RNA-Seq data that mouse macrophages express RNA molecules at different levels, when comparing infection between pathogenic (*Mycobacterium tuberculosis* H37Rv and clinical isolate R179) and non-pathogenic mycobacteria (*Mycobacterium smegmatis* and *bovis* BCG). Here we report on the validation of this RNA-Seq data using qPCR for certain RNA molecules coding for macrophage surface receptors and signalling molecules involved in immune functions. Mouse macrophages were infected with the same strains as used for the RNA-Seq analysis, followed by extraction of macrophage RNA, conversion to cDNA and determining the relative expression levels through qPCR. Expression levels compare very closely between the data from the RNA-Seq and qPCR experiments. CLEC4a1 and CLEC4n code for Dectins which are involved in binding and uptake of pathogens and also stimulate immune cells. Except for *M. smegmatis*, infection with the other three strains resulted in an upregulation of these Dectins. Interestingly, only *M. smegmatis* normally gets killed inside these macrophages as compared to the other three strains. Likewise, *Pilrb2*, coding for an activating receptor involved in cell signalling, was unchanged for *M. smegmatis*, and BCG, but up regulated for H37Rv and R179. Interferon-stimulated gene 15 (*Isg15*), which has been linked to providing immunity during infections, is highly upregulated upon infection with all the strains, but with a more than double fold change for the pathogenic over the non-pathogenic strains. Selected genes may now be studied in further detail. The next question to answer is whether the knocking down of upregulated genes will affect the intracellular survival of the pathogenic strains.

ABSTRACT NUMBER / ABSTRAKNOMMER: 43

Mycobacterial genomic DNA from used Xpert MTB/RIF Ultra cartridges can be utilised for accurate second-line genotypic drug susceptibility testing

Brigitta Derendinger (Stellenbosch University), Charissa Naidoo (Stellenbosch University), Grant Theron (Stellenbosch University), Margaretha de Vos (Stellenbosch University), Rob Warren (Stellenbosch University), Rouxjeane Venter (Stellenbosch University), Stephanie Minnies (Stellenbosch University)

Background and objectives: Drug resistant tuberculosis has intensified the global TB crisis. First- and second-line drug susceptibility testing (DST) is recommended if Xpert MTB/RIF (Xpert) detects rifampicin resistance. This requires an additional sputum that can cause treatment initiation delays. We showed Xpert cartridge extract (CE) can be used for downstream genotypic DST but Xpert Ultra (Ultra) has superseded Xpert. We aim to determine the feasibility and concordance (vs. sputum) of MTBDRsl on Ultra CEs and evaluate whether usable Mycobacterium tuberculosis (Mtb) genomic DNA can be recovered from other cartridge chambers. An isoniazid line probe assay (Genoscholar INH-TB II; Genoscholar) was tested on Xpert CE to see if could identify isoniazid susceptibility in Xpert rifampicin-resistant CEs. Method: Clinical sputa (n=40) from patients with RIF-resistant TB were tested with Ultra. MTBDRplus and MTBDRsl were done on Ultra CE and paired sputa. To collect CE, the diamond-shaped amplification chamber at the back of the cartridge was pierced under sterile conditions and the contents extracted. Liquid was also extracted from other chambers for a 16S Mtb qPCR assay. CEs from 11 Xpert-positive rifampicin-resistant in vitro specimens were tested on Genoscholar. Results: MTBDRplus on CE showed [2/12(17%)] Xpert and [0/12(0%)] Ultra TUB-band positive results. MTBDRsl CE with a semi-quantitation category \leq (CT<26.25) was accurate. 13/19(68%) of the CEs with MTBDRsl-detected resistance were also resistant on sputum, whereas 18/20(90%) CEs with MTBDRsl-detected susceptibility were susceptible on sputum. Four CE-susceptible, sputum-resistant and two CE-resistant, sputum-susceptible MTBDRsl results were obtained. Of the four chambers tested, two chambers contained Mtb genomic DNA, one of which was comparable Mtb genomic levels to the diamond ($p < 0.001$). Genoscholar was unfeasible. Conclusion: MTBDRsl on Ultra CE gives valid results at CT <26.25. The other chambers hold promise for recovering genomic DNA. These data can reduce additional specimen collection and demand for culture.

ABSTRACT NUMBER / ABSTRAKNOMMER: 44

Nanotechnology in Analytical and Drug Development Research

Gasen Naidoo (Stellenbosch University), Sarfaraaz Vallie (Stellenbosch University)

The research focus will primarily focus on the nano drug delivery systems (NDDS) within the PK context. The aim is to improve efficacy by using a sustained and targeted drug release mechanism. The main aim would be to use nanomedicine to improve TB (Tuberculosis) drug efficacy by adapting the cancer drug developments and strides made in improving cancer drug efficacy using the NDDS. The research will include the lipid-based prodrug nano-carrier formulation, free drug versus Prodrug and carrier variants, and related safety issues. Rapid TB and HIV-TB Patient Drug Level Determination to Support Patient Treatment using Therapeutic Drug Monitoring (TDM) to determine the systemic concentrations of the prodrug vs free drug. A biological compatible power source to support a Nano robotic drug delivery mechanism is also of interest and will be further studied. Platinum (Pt) nano particles have a dual function: (1) Pt nano particle carrier for prodrugs and (2) Pt nano particles as the core component of the membrane electrode assembly (MEA) catalyst in the carriers power source. NP phenomenon was encountered during HPLC (High Performance Liquid Chromatography) and LCMS (Liquid Chromatography Mass Spectrometry) drug assaying and analytical method development may result from once solubilized drugs recrystallizing into nano-sized seed particles facilitating recrystallization and growth of particles large enough to block stationary phases. The scanning electron microscopy (SEM) observed particles sizes were in the nano-size range of 2 to 50 nm. Larger crystalline particles in the 200 - 500 nm range were also observed. The chromatography systems (CS) including the HPLC and LCMS are generally fitted with narrow internal diameters (\sim) range of columns are 2.1 - 4.6mm,

particle size 2 - 5 Åµm and the pressures exceeding 350bar. Ambient and sub-ambient temperature drug in plasma precipitation was evident although more volatile buffers were used.

ABSTRACT NUMBER / ABSTRAKNOMMER: 45

No evidence of a modulating effect in M. bovis infected African lions by FIV: A pilot study

Andre G. Loxton (Stellenbosch University), Michele A. Miller (Stellenbosch University), Paul van Helden (Stellenbosch University), Sven D.C. Parsons (Stellenbosch University), Tashnica Taimé Sylvester (Stellenbosch University)

Background: In lions, feline immunodeficiency virus infection has not been associated with the development of severe AIDS-like disease, as in domestic cats. Nonetheless, immune suppression may still occur in this species. Methods and Materials: The present study aimed to determine if FIV infection status was associated with altered immune responses to M. bovis. We investigated M. bovis specific responses in FIV-infected and uninfected lions by comparing antigen-induced expression of genes involved in cell-mediated immunity, i.e. IL8, IL10, CD4, CCL2, TNFA, GATA3, TBX21 and CXCL11as well as FCGR1A. Results: No significant changes in specific antigen stimulated expression of immune genes were detected in FIV-infected and uninfected M. bovis-infected lions. However, the expression ratio of IL10/TBX21 was significantly lower in the FIV-infected group. Additionally, IL10/TNFA and FCGR1A/TBX21 ratios were observed to be lower for FIV-infected lions in the unstimulated sample, although not statistically significant. Conclusions: These results suggest FIV does not modulate antigen-specific immune responses in M. bovis-infected lions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 46

Parallel testing using the single comparative intradermal tuberculin test (SCITT) and an interferon gamma release assay (IGRA) increases detection of Mycobacterium bovis-infected African buffaloes (Syncerus caffer)

Charlene Clarke (Tygerberg campus Stellenbosch University), Dave Cooper (KZN Wildlife), Eduard Roos (Tygerberg campus Stellenbosch University), Michele Miller (Tygerberg campus Stellenbosch University), Netanya Bernitz (Tygerberg campus Stellenbosch University), Paul van Helden (Tygerberg campus Stellenbosch University), Robin Warren (Tygerberg campus Stellenbosch University), Roxanne Higgitt (Tygerberg campus Stellenbosch University), Sven Parsons (Tygerberg campus Stellenbosch University), Tanya Kerr (Tygerberg campus Stellenbosch University), Wynand Goosen (Tygerberg campus Stellenbosch University)

The diagnosis of Mycobacterium bovis infection in African buffaloes (Syncerus caffer) relies on the detection of the cell-mediated immune response to M. bovis antigens using the single comparative intradermal tuberculin test (SCITT) and interferon gamma release assays (IGRAs), however these assays are imperfectly sensitive. To determine whether parallel testing using the SCITT and IGRAs increases the number of M. bovis-infected buffaloes identified by these tests, buffaloes in the M. bovis endemic regions were tested. Seventy-one culture-confirmed buffaloes were included in this study. Buffaloes in cohort A were tested using the SCITT, Bovigam® PPD, Bovigam® PC-EC and Bovigam® PC-HP IGRA. Buffaloes in cohort B were tested using the SCITT, Bovigam® PPD IGRA and the Qiagen Cattletype IGRA. No test, whether SCITT or IGRA, identified all buffaloes in either cohort. In both cohorts, the SCITT used in parallel with selected IGRAs, identified all buffaloes and this was a significantly greater number than identified by these tests individually. In cohort A (n=35), the SCITT used in parallel with either the Bovigam® peptide IGRA identified all buffaloes, and in cohort B (n=36), the SCITT used in parallel with the Bovigam® PPD IGRA identified all buffaloes. Overall (n=71), the SCITT identified 63/71 buffaloes, the Bovigam® PPD IGRA identified 64/71 buffaloes and used in parallel, these assays identified all but one buffalo. These findings are in agreement with cattle studies supporting the use of the SCITT and IGRAs in parallel to identify the greatest number of M. bovis-infected animals. The authors suggest that this parallel testing algorithm be strategically applied

to maximize the detection of *M. bovis* infection in known bovine tuberculosis-positive buffalo herds but when testing buffalo herds with no-known history of *M. bovis* or extremely valuable individuals, that a different strategy may need to be used to minimize the risk of false-positive test results.

ABSTRACT NUMBER / ABSTRAKNOMMER: 47

Patterns of facility-based HIV Testing Services (HTS) at two public health facilities participating in the HPTN 071 (PopART) universal test-and-treat intervention, in Cape Town, South Africa

Karen Jennings (City of Cape Town Health Services), Kerry Nel (DTTC, Department of Paediatrics and Child Health, Stellenbosch University), Muhammad Osman (DTTC, Department of Paediatrics and Child Health, Stellenbosch University), Nulda Beyers (DTTC, Department of Paediatrics and Child Health, Stellenbosch University), Peter Bock (DTTC, Department of Paediatrics and Child Health, Stellenbosch University), Rosa Sloot (DTTC, Department of Paediatrics and Child Health, Stellenbosch University)

Background Efforts toward ensuring that 90% of people living with HIV know their HIV status are ongoing. Men and adolescents are recognized as groups difficult to reach with HIV testing services. Various strategies at increasing testing in these groups are under investigation. Universal antiretroviral therapy eligibility at participating health facilities was commenced in January 2014 as part of the PopART intervention. The aim of this study is to investigate patterns of HIV testing among individuals, including men and adolescents, attending these health care facilities over time. Methods A retrospective analysis was conducted on routine HIV Testing Services data (2013-2016) of two Public Health facilities (PHF) participating in the PopART intervention. All individuals that received clinical services (headcount of PHF) during this study period were included in the analysis. Chi-squared tests for trend investigated changes in the proportion of individual tested for HIV and HIV positivity over time. Analyses were done separately for each PHF and stratified by gender and age. Results The proportion of individuals who had an HIV test done at both PHF during 2013-2016 increased significantly over time, and the increase was higher among males compared to females. At one PHF, the proportion of individuals who had an HIV test done increased for all age groups, but was most pronounced in young adults aged 15-24 years. HIV positivity among males and females tested for HIV was highest in 2014 and decreased during the years 2015 and 2016 at both PHF (p-values of all Chi-squared tests for trend <0.01). Conclusions Our findings show that during the implementation of a household delivered community wide HIV test and treat policy, an increase in HIV testing is observed at health facilities located within these communities. The decrease in HIV positivity over time may reflect overall increased HIV testing coverage.

ABSTRACT NUMBER / ABSTRAKNOMMER: 48

Peripheral blood Myeloid-Derived Suppressor Cells express the surface proteins Toll-like Receptor 4 and Caveolin-1 during active TB disease.

Andrea Gutschmidt (Stellenbosch University), Gerhard Walzl (Stellenbosch University), Leigh Ann Kotz (Stellenbosch University), Martin Kidd (Stellenbosch University), Nelita du Plessis (Stellenbosch University)

Myeloid-derived suppressor cells (MDSC), a heterogeneous population of innate immune cells, have recently gained attention in the TB field for their apparent involvement in bacterial infections. It is well known that inadequate T cell responses contribute to poor *Mycobacterium tuberculosis* (*M.tb*) infection control, as is seen during HIV co-infection, but the factors responsible for this are inconclusive. We have previously shown MDSC to be expanded in peripheral blood of TB patients and have shown the T-cell suppressive effect of TB patient-derived MDSC. MDSC are, therefore, of particular interest, as the mechanism of MDSC-mediated T-cell suppression during TB is unknown. Previous work in a murine *M.tb* infection model highlighted the presence of live *M.tb* within MDSC, suggesting MDSC-mediated internalization of the bacteria, but no proof exists in human studies; unpublished data has also shown

the existence of caveosome-like structures on human MDSC. Caveosomes are cholesterol-rich, endocytic vesicles made up primarily of caveolin-1 (Cav-1) proteins which aggregate on the surface of phagocytic cells, including poorly phagocytic MDSC. These proteins, possibly activated through pathogen binding of adjacent surface receptors like Toll-like Receptor 4 (TLR4), have the potential to create a niche for bacterial host immune evasion. In this study, we postulate that MDSC play a key role in the suppression of host immune responses to M.tb infection through the combined activities of Cav-1 and TLR4, which may facilitate pathogen uptake into MDSC while bypassing conventional uptake methods, and allow M.tb bacilli to escape host protective immune responses. We, therefore, investigated the frequency of M.tb-specific MDSC from the peripheral blood of active TB and latent infection cases, their cytokine profile, as well as the expression of Cav-1 and TLR4.

ABSTRACT NUMBER / ABSTRAKNOMMER: 49

Pharmacokinetic study of anti-TB drug PAS and metabolites and its possible relationship with the development of toxicity

Helmuth Reuter (Stellenbosch University), Kim Adams (Stellenbosch University), Marietjie Stander (Central Analytical Facilities)

Background: Since the introduction of PAS, gastrointestinal (GI) intolerance was noted, including reports of nausea, bloating, and diarrhoea, Therefore, PAS was replaced with better tolerated agents. However, the extent of drug resistant tuberculosis has prompted its reintroduction and generation of a granular slow-release formulation that delays the premature release in the stomach thus avoiding high PAS concentrations. In previous studies tolerability of PAS under two dosing regimens (8g once-daily vs 4g twice-daily) was investigated and showed no distinctive difference in the extent of the GI events, indicating that these adverse effects were not necessarily attributed to higher PAS concentrations. It was found that once-daily dosing was associated with equivalent or less intolerance. These findings have led to the speculation that the rate of absorption and metabolism of PAS to APAS through acetylation and GPAS through glycine-conjugation, may be the causative of GI adverse effects as opposed to the notion of high PAS concentrations. Purpose: Firstly, is to develop a method using Ultra-performance Liquid Chromatography (UPLC) in tandem with Mass spectrometry (MS) to simultaneously assay PAS, APAS and GPAS, in human plasma. Secondly, is to perform non-compartmental analysis (NCA) for establishing pharmacokinetic (PK) parameters of each compound. Lastly, to correlated PK parameters with adverse effects, determined by Visual Analogue Scale (VAS). Methods: PAS, APAS and GPAS were assayed using Waters triple quadrupole MS connected to a UPLC system, and NCA was performed using Winnonlin version 5.0. Thereafter, PK parameters were correlated with VAS scores using Spearman's rank coefficient to determine the relationship. Results: Statistical significances were observed for APAS, with bloating ($p= 0.025$) and diarrhoea ($p=0.044$). Similarly, GPAS showed a significance with diarrhoea ($p= 0.041$). Although significant, the strength of the correlation as described by Spearman's rho were all below 0.05 and thus represents a low correlation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 50

The clinical presentation and treatment outcomes of infants with tuberculosis in Cape Town, South Africa

(), Ruth Aryao (Paediatric Department, Tygerberg Hospital)

Clinical presentation and treatment outcomes of infants with tuberculosis in Cape Town, South Africa Aryao R , Dramowski A , van der Laan L Hesselning AC , Schaaf HS Bekker A Department of Paediatrics and Child Health, Stellenbosch University Introduction: We describe the clinical presentation, course and outcome of infants initiated on first line antituberculosis drugs. Methods: Infants with tuberculosis admitted to Tygerberg, Khayelitsha District and Brooklyn Chest Hospitals (March 2014 - March 2015) were enrolled. Antituberculosis treatment was administered .Study evaluations took place at entry, 3 and 6 months post initiation of antituberculosis treatment. Results: Of 39 infants treated for tuberculosis,

33 (85%) had pulmonary, 1 (2%) had extrapulmonary and 5 (13%) had both pulmonary and extrapulmonary tuberculosis. The median age was 6 months (IQR: 3-7) and median weight 6.1 kg (IQR: 5-7.3) at tuberculosis diagnosis. Of the 22/39 (56%) of HIV-exposed infants, 5 (13%) were HIV-infected. Tuberculosis was culture-confirmed in 14/39 (36%), 22 (56%) infants had probable tuberculosis and 3 (8%) had possible tuberculosis using international consensus criteria. Common presenting symptoms were failure to thrive (24; 62%), weight loss (14; 36%), lethargy (14; 36%) and persistent cough (13; 33%). Nine infants (23%) had bronchoscopy for lymph nodes causing severe airway obstruction; 3 required surgical lymph node decompression. A tuberculosis source case was identified in 21/39 (54%) infants; the mother was the source case in 11/21 (52%). Only 4/21 (19%) infants were started on isoniazid preventive therapy prior to tuberculosis diagnosis. Tuberculosis treatment outcomes were favourable in 33 (85%) infants (4 cured; 29 completed treatment), 6 (15%) had unfavourable outcomes (4 interrupted treatment for >2 months but were re-initiated and completed treatment, 2 were lost to follow-up). Conclusions: Failure to thrive was common in infants with tuberculosis. Good treatment outcomes were observed in this cohort with additional study follow-up.

ABSTRACT NUMBER / ABSTRAKNOMMER: 51

The effects of HIV-proteins and antiretroviral therapy on aortic endothelial cells (AECs)

Amanda Genis (Stellenbosch University Division of Medical Physiology), Clara Marincowitz (Stellenbosch University Division of Medical Physiology), Hans Strijdom (Stellenbosch University Division of Medical Physiology), Sana Charania (Stellenbosch University Division of Medical Physiology)

Introduction: Endothelial dysfunction (ED) is an early precursor of cardiovascular disease characterized by decreased nitric oxide (NO) and increased oxidative stress creating a pro-inflammatory environment. Increased ED and cardiovascular risk have been observed in HIV-1 infected patients as well as in those receiving antiretroviral therapy (ART). The aim of this study was to investigate ED as a pathophysiological consequence of HIV-infection and ART. Aims: Establishing an in vitro HIV-1 model and determining the effects of non/nucleoside reverse transcriptase inhibitors (NRTI/NNRTIs) and protease inhibitors (PIs) on endothelial function. Both these aims were subject to dose- and time-response investigations. Methods: The in vitro HIV model was created by adding three recombinant HIV-1 proteins (Tat, Gp160 and Nef) to growth medium. ARTs used were efavirenz/emtricitabine/tenofovir (ART1) and lopinavir/ritonavir (ART2). Cell viability, NO-production and oxidative stress were measured. Results: HIV-1 (100ng/ml, 24 hours) caused a decrease in NO (100 \pm 1.25% vs. 76.00 \pm 3.67%; $p < 0.05$), with no effect on cell viability and oxidative stress. Oxidative stress increased in ART1+HIV-1 (control: 100 \pm 1.42% vs. low: 85.66 \pm 2.37%; medium: 78.86 \pm 1.70%; high: 81.87 \pm 4.36%; $p < 0.05$) and ART2+HIV-1 (control: 100 \pm 0.91 vs. low: 91.22 \pm 2.46; medium: 91.51 \pm 4.08; high: 78.66 \pm 1.98%; $p < 0.05$). ART2+HIV-1 caused a decrease in NO (control: 100 \pm 0.72% vs. medium: 94.47 \pm 1.91%; high: 84.67 \pm 1.41%; $p < 0.05$). Discussion and Conclusion: HIV-proteins (100ng/ml, 24 hours) decreased NO production in AECs. This lowering effect was not observed upon treatment with NRTI/NNRTIs, but with PIs. A decrease in baseline oxidative stress was associated with both NRTI/NNRTIs and PIs. In our model, NRTI/NNRTIs seemed to ameliorate the NO-lowering effect of treatment with HIV-1 proteins.

ABSTRACT NUMBER / ABSTRAKNOMMER: 52

The humoral immune response in tuberculous meningitis: an immunohistochemical analysis

A.M. van Furth (VU University), D.J. Franken (VU University), M. van der Kuip (VU University), S.D. Zaharie (Stellenbosch University), S.L. van Elsland (Stellenbosch University)

Tuberculosis (TB) is a devastating infectious disease, contributing to the global burden of disease. The most severe clinical manifestation of extra-pulmonary TB is tuberculosis of the central nervous system

(CNS), which occurs in approximately 1% of all patients with active TB. CNS TB manifest either localised (tuberculoma) or diffuse (meningitis). TB meningitis (TBM), the more common, and more severe form of CNS TB, is associated with significant morbidity and a mortality rate of up to 23%. The pathogenesis of CNS tuberculosis, and in particular of TBM is poorly understood. This study aims to explore the humoral immunity response in granulomas in patients with tuberculous meningitis. In this post-mortem study, conducted in Tygerberg hospital, Cape Town, South Africa, specimens from 46 patients, diagnosed between 1976 and 2010 with TBM were examined. Formalin-fixed, paraffin-embedded brain tissue were cut and stained with hematoxylin-eosin (HE) to identify TB granulomas, as well as immunohistochemical stains for clusters of differentiation (CD20, CD23, CD27, CD38, and CD138) and immunoglobulins (IgD, IgG and IgM). The specimens were systematically examined for the presence and distribution of the humoral immune cells (B-lymphocytes) and immunoglobulins. Diffuse intercellular presence of IgD and IgG in the granulomas were observed. The presence of CD20+ B-cells were restricted to the outer layers of the granulomas, surrounded by CD38+ late plasmablasts. CD20+ B-cells, present as lymphoid aggregates in the lower part of subarachnoid space near the pia mater, also stained IGD+. No stains were positive for CD23 (maturing B-cells), CD27 (maturing B-cells), CD138 (plasma cells), and IgM. This study demonstrates the presence of a humoral immune response in TBM in addition to the cellular immune response. Challenging the historical view of TBM as a disease with only a cellular immune response – our findings suggest the potential for new immunomodulating therapy in TBM.

ABSTRACT NUMBER / ABSTRAKNOMMER: 53

Tuberculous lymphadenitis is associated with changes in the microbiome at the site of disease

Benjamin Wu (New York University School of Medicine, New York), Charissa Naidoo (Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University), Georgina Nyawo (Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University), Grant Theron (Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University), Leopoldo Segal (New York University School of Medicine, New York), Pawel Schubert (Division Anatomical Pathology, Faculty of Medicine and Health Sciences, Stellenbosch University), Robin Warren (Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University)

Tuberculous lymphadenitis (TBL) is the most common presentation of extrapulmonary tuberculosis (EPTB). The microbiome in EPTB is largely undefined and may reveal new targets for understanding host-pathogen interactions and diagnostic or therapeutic targets. The study aimed to characterize the site-of-disease microbiome and inferred metagenome in patients with lymphadenopathy undergoing investigation for active TB in Cape Town, South Africa. Fine needle aspirates (FNAs) were collected from the necks of 23 pre-treatment TB cases (Xpert- or culture-positive) and 19 controls (Xpert- and culture-negative) with suspected TB lymphadenitis. Background specimen sampling controls (skin swab, saline needle flush) were collected. 16S rRNA gene sequencing was done using Illumina MiSeq. Taxonomy was assigned to 16S sequences using Greengenes. Overall, skin had the highest microbial diversity (alpha diversity), and FNA microbial composition was more similar to skin than saline (PERMANOVA, $p=0.001$), indicating that contamination from saline was not in FNAs. Cases had a different microbial composition compared to symptomatic controls (PERMANOVA, $p=0.009$). Furthermore, cases with HIV co-infection had a distinct microbial composition compared to HIV-negative cases (PERMANOVA, $p=0.006$). In addition to *Mycobacterium* spp, several other members of the Actinobacteria phylum (e.g., *Dermacoccus*, *Atopobium*) were enriched in cases, while gram-negative Bacteroidetes phylum were abundant in symptomatic controls. While HIV-positive cases only had the Enterobacteriaceae family enriched, HIV-negative cases enriched several taxa, including gut (*Bifidobacterium*, *Veionella*) and oral (*Streptococcus*) commensals. Functional analysis using PICRUSt revealed metabolic functions involving fatty acid metabolism and amino-acid metabolism enriched in cases compared to symptomatic controls, whilst transporters, ribosome and ABC transporters functions were enriched in symptomatic controls. These findings show for the first time that patients with TBL

have a distinct site-of-disease microbiome, comprised of Mycobacteria (most abundant), as well as many non-Mycobacteria taxa, compared to symptomatic controls, and demonstrate a shifted functionality compared to controls known to be associated with inflammation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 54

Undetected isoniazid mono resistance in the rural Eastern Cape Province

Charnay van der Merwe (Stellenbosch University), Marisa Klopper, Elizma Streicher, Margaretha De Vos, Rob Warren

Tuberculosis (TB) is ranked second to HIV/AIDS co-infection as posing a major global health challenge. In addition, the emergence of drug-resistant TB (DR-TB) has exacerbated the problem raising concerns to potential significant threats relevant to TB treatment and control programs. The largely rural Eastern Cape Province (EC) is an area of significant interest, with an alarmingly high TB case load while the percentage of multidrug-resistant (MDR) TB cases is among the highest in South Africa. Current diagnostic algorithms ignore the possibility of new and retreatment TB cases presenting with isoniazid (INH) mono resistance (IMR), which may subsequently lead to potential undetected cases that may contribute to amplification of resistance and, eventually MDR-TB if not properly managed. The study aims to use molecular epidemiological tools to describe the epidemiology of IMR at a community level in South Africa. Methods incorporated include drug susceptibility testing by agar proportion method; spoligotyping; LATE-PCR and Sanger sequencing. Whole genome sequencing will also be used to detect the presence of alternative resistance-causing mutations. Preliminary results showed a high diversity of strains with the predominant strain, namely Beijing. Majority of samples were shown to be wild-type for *katG* and *inhA* promoter. We were able to identify 16 confirmed mutations to date, the most prevalent being *katG* (315ACC). The DR-TB epidemic in the EC is a major concern, with increased risks of additional resistance leading to MDR-TB development and poor treatment outcomes. Hence, informing public health policy to improve the diagnostic strategy currently available upon implementing effective tools aimed to rapidly identify IMR cases might potentially halt the progression to MDR and control future spread of TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 55

Using aerial photography in longitudinal community studies.

Mark Theart (Desmond Tutu TB Centre)

INTRO: Retention of participants in community-based longitudinal studies is crucial. Communities are dynamic and contextual changes can contribute to increased loss to follow up from research cohorts. Monitoring and understanding contextual changes in communities using aerial photography can help researchers to adapt retention strategies during the life of the study. **AIM:** The aim of this study was to demonstrate the use of aerial photography to monitor changes in the built environment of study areas during completion of a community cohort study. **METHODS:** The HPTN 071 (PopART) trial, a community randomized trial in 21 communities in South Africa and Zambia that aims to determine the impact of two community-level combination prevention packages on population-level HIV incidence. The PopART population cohort followed up more than 16 000 participants in nine study communities in the Western Cape over 4 years. Google Earth provided time series aerial photography, which were customised for study purposes. Maps were updated regularly and the information derived fed back to study teams for management purposes. For this study, we have reviewed changes in the built environment of study communities over time to illustrate how these data can be used to improve fieldwork efficiency. **RESULTS:** (Sequential maps will be displayed for presentation) Sequential maps completed over time showed significant changes in study communities including: 1. Formal housing replacing informal housing 2. Vacant land being replaced by informal housing and new residents in-migrate. Furthermore, the maps provided the study team with critical information that they used to re-organised fieldwork activities more efficiently. **CONCLUSION:** Communities are dynamic with in- and out

migration of people and changes to housing structures. Aerial photography can provide critical insight to guide study teams and understand retention patterns in community research.

ABSTRACT NUMBER / ABSTRAKNOMMER: 56

Validation of a fluorescent reporter for monitoring Rv1460 expression in vivo

Lucinda Baatjies (University of Stellenbosch)

The shortcoming of current Tuberculosis (TB) immunodiagnostics highlights the need for new TB biomarkers. One strategy to identify proteins with diagnostic potential is to investigate Mycobacterium tuberculosis (M.tb) proteins that are specifically induced during infection. Kumar et al (2011) detected Rv1460 in serum of TB patients, suggesting that this regulator may play a role during M.tb growth within the human host. Aim: To validate a fluorescent reporter for monitoring Rv1460 expression in vivo. Method: A fluorescence reporter was constructed by cloning two regions (123 bp and 211 bp) upstream of a promoterless mCherry gene. The reporter was transformed into the Mycobacterium tuberculosis strain H37Rv (wild type, wt) and the growth of the strains was monitored under standard growth conditions by optical density (600nm was measured over 22 days). Fluorescence intensity (FI) for each strain was measured using a 96-well plate reader at day 4, 10 and 14. The colony forming units (CFUs) per well was determined by plating serial dilutions of the culture on solid media at each time point. FI was expressed per CFU. A one millilitre aliquot of each culture was sonicated in a waterbath sonicator to disrupt clumps and fixed with 4% formaldehyde for analysis by flow cytometry. Results: No growth defect in reporter strains was observed when compared to wt. An increase in fluorescence intensity was observed overtime, with the biggest difference observed between day 4 and day 10. Flow cytometry was more sensitive technique, showing a difference in the fluorescence signal between the two reporter strains. The final step in validation will involve comparing the fluorescent intensity to mRNA levels at the three time points.

ABSTRACT NUMBER / ABSTRAKNOMMER: 57

Validation of a Novel Interferon Gamma Release Assay for Detection of Mycobacterium bovis Infection in Free-Ranging African Rhinoceros (Diceros bicornis, Ceratotherium simum)

Eduard Roos (Stellenbosch University), Josephine Chileshe (Stellenbosch University), Michele A. Miller (Stellenbosch University), Paul van Helden (Stellenbosch University), Peter E. Buss (Veterinary Wildlife Services, South African National Parks, Kruger National Park, Skukuza), Sven D.C. Parsons (Stellenbosch University), Wynand Goosen (Stellenbosch University)

Tuberculosis (TB) in captive African rhinoceros has been sporadically reported. However, mycobacterial infection has only recently been observed in rhinoceros in different countries. Between 2016 and 2018, Mycobacterium bovis infection was confirmed in one black and five white rhinoceros in Kruger National Park, South Africa. The South African Department of Agriculture, Forestry, and Fisheries issued a quarantine notice in December 2016, which has prevented further rhinoceros translocations until a management plan is created to test rhinoceros for TB. A novel interferon-gamma (IFN- γ) release assay (IGRA), based on the human QuantiFERON[®] TB Gold In-Tube (QFT) (Qiagen, Hilden, Germany) whole blood stimulation platform (Qiagen, Hilden, Germany) and a commercially available equine IFN- γ ELISA (Mabtech AB, Nacka Strand, Sweden) for cytokine detection, was developed and tested in known M. bovis-infected and uninfected rhinoceros. In this study we sought to optimize and validate the IGRA in free-ranging African rhinoceros. Optimization included determining monoclonal antibody specificity, sample matrix, sample dilution, incubation time, reproducibility, limit of quantification and parallelism. Following optimization, the IGRA was validated using rhinoceros in bovine TB endemic areas. Screening of free-ranging and boma confined rhinoceros has detected individuals that have had consistent positive IGRA results on serial samples, suggesting that these may be infected and require further confirmatory testing. These preliminary findings indicate that this IGRA, using commercially

available reagents, has promise as a diagnostic tool to screen African rhinoceros for mycobacterial infection and facilitate future translocations, especially from TB endemic populations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 58

“NGO-initiated research - translating community needs to academia”

Dr Ana Houston (Hope Cape Town), Prof Monika Esser (Stellenbosch University), Prof Wolfgang Preiser (Stellenbosch University)

Introduction:HOPE Cape Town was established in 2001 in response to the paediatric HIV/AIDS crisis. At the time antiretroviral treatment (ART) was unavailable in the public sector, and infected infants fell ill and died. In close partnership with Tygerberg Academic Hospital (TBH), HOPE Cape Town as non-governmental organisation (NGO) addresses gaps in the care of HIV-infected children; employing community healthcare workers, doctors, nurses, social workers and an occupational therapist. During the early years, a sponsorship programme provided ART for infected children. Later on, as the national HIV programme stepped up with free ART for all, other areas of need such as enrollment, resistance and retention in care were addressed.HOPE Cape Town directly addresses the HIV pandemic through education and treatment support in partnership with governmental health structures, other Community Based organisations (CBOs) and communities themselves.**Materials and Methods:**The structure of HOPE Cape Town makes it ideally suited for grassroots research to document the needs within the paediatric HIV community as well as suggested interventions for improvement. HOPE Cape Town has conducted this collaborative research with Stellenbosch University over the last 13 years. Research topics include: Engaging with traditional healers (2005); The real cost of ART - beyond pharmaceutical costs (2007); Using the paediatric ART visit to engage mothers in care through Point of Care CD4 testing (2013); Role of paediatric resistance testing (2014) Virological failure in a community paediatric ART clinic, with suggestions for improvement. (2014)**Results:**This poster gives several examples demonstrating the benefit of research partnerships and the role of NGO-led research. The topics also reflect the changing scope of practice and needs within the paediatric ART field over the last decade. **Conclusions:**Partnership between NGOs and academic institutions can produce excellent and clinically relevant results that may benefit the community and inform medical practice.

ABSTRACT NUMBER / ABSTRAKNOMMER: 59

AUTOPHAGIC CLEARANCE OF MYCOBACTERIUM TUBERCULOSIS; HOW INVOLVED IS PARKIN?

Ben Loos (Stellenbosch University), Craig Kinnear (Stellenbosch University), Glynis Johnson (Stellenbosch University), Naomi Okugbeni (Stellenbosch University)

AUTOPHAGIC CLEARANCE OF MYCOBACTERIUM TUBERCULOSIS; HOW INVOLVED IS PARKIN?**Background:**Following infection with Mycobacterium tuberculosis (M.tb), macrophages phagocytose the bacteria for intending degradation. However, M.tb has developed mechanisms to damage the phagosome and escape degradation. This damage triggers a selective degradation pathway namely Autophagy, which is initiated by the ubiquitination of damaged phagosomal membranes. This ubiquitination is, in part, mediated by the E3 ubiquitin ligase, PARKIN. In this study, we aim to elucidate the role of PARKIN in following M.tb infection and to track the progression of autophagy in M. tb-infected macrophages.**Methods:**To investigate the role of PARKIN in Tuberculosis immunity, wild-type, and PARKIN-deficient THP-1 macrophages were infected with M.tb H37rv for 4, 24, 48 and 72 hours. Subsequently, the cells were lysed and the culture lysate was plated onto 7H11 plates for mycobacterial colony forming units (CFU) counts. In order to track the progression of autophagy, RAW 264.7 macrophages were infected with m-cherry-transformed M.tb H37rv for 4 hours, labeled with a green fluorescent protein-tagged anti-LC3 antibody and visualized by super-resolution confocal microscopy.**Results:**Infected PARKIN deficient cells had consistently higher CFU counts compared to wild-type cells at all time-points except 4 hours post-infection. We also observed recruitment of PARKIN

to M.tb bacilli at 4 hours. Moreover, confocal microscopy revealed that, as expected, number of bacilli were encapsulated in LC3 positive compartments. What was unexpected was that some of these bacteria were encapsulated in the extracellular milieu. We also observed "empty" bacilli-shaped vacuoles as well as "free" bacilli without LC3 encapsulation. Conclusion: Our results confirm that PARKIN plays a crucial role in host response to M.tb infection and that the autophagic response to infection with M.tb can vary even within the same cell. Further studies to elucidate this complex pathway is currently underway.

ABSTRACT NUMBER / ABSTRAKNOMMER: 60

Evidence of persisting chronic inflammation in early treated HIV infected children at 8 years of age: Is gut permeability to blame?

Barbara Laughton (FAMRU), Mark Cotton (FAMRU), Richard Glashoff (Stellenbosch University), Shalena Naidoo (Stellenbosch University), Tongai Maponga (Stellenbosch University)

Background: Early combination antiretroviral therapy (cART) has reduced mortality and morbidities. However, even with virological suppression and reconstituted CD4 counts, the immune system remains in dysregulation. Microbial translocation, low-level viremia, co-infections and other adverse events play a significant role in the persistence of chronic inflammation. The effects of HIV-related chronic inflammation is poorly understood in infected children under long-term therapy and virally suppressed. Methods: Plasma and PBMC samples were evaluated. ART was initiated within 9 months with sustained viral suppression at 8 years of age. Plasma biomarkers including; IL-1 β , IL-1 α , IL-2, IL-6, IL-10, IP-10, IFN- γ , MIP-1 α , MIP-1 β , TNF- α , TNF- β , CD40L, INF- γ , FGF, RANTES, TGF β ^{1,2,3}, sCD14, sCD163, IL-18, hsCRP and LBP were measured using ELISA and Luminex[®] Multiplex assays. Age-matched controls were measured for the same biomarkers. Results: 161 samples were evaluated. Median pre-therapy viral load was 738,501 copies/ml. Median CD4-percentage at baseline was 36.9% (range: 23.1-57.1%). At 8 years of age, there were no significant differences between the CD4-percentage of the HIV-infected (38.3%) and control groups (40.0%) (p=0.261). All children, except five, showed undetectable viral loads at sampling. HIV-infected children showed highly significant increase (p<0.001) in levels of IL-1 α , IL-2, IL-13, IP-10, MIP-1 β , TNF- β , CD40L, INF- γ , TGF β ^{1,2}, sCD14, sCD163, IL-18, hsCRP and LBP. Significantly lower levels for the following biomarkers were noted for the HIV-infected group: IL-1 β , IL-6, IL-10, TGF β ^{2,3}, IL-15, IL-17A, INF- γ , TNF- α and RANTES. Conclusion: Despite early therapy, viral suppression and normalized CD4 counts, HIV-infected children display persistent inflammation as defined by signature biomarkers (sCD163, hsCRP, CD40L, IP-10, IL-18, IL-2). We showed dysregulation in the adaptive immune compartment characterized by lower levels of IL-4, IL-10, TGF β ^{2,3}, IL-17A, IFN- γ and RANTES suggestive of immune exhaustion. The increase in sCD14 and LBP levels are indicative of the monocyte-gut translocation axis, and highlight a potential mechanism driving this chronic inflammation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 61

Percutaneous pericardioscopy in a population with a high prevalence of tuberculous pericarditis "improving the diagnostic yield and advancing the time to diagnosis

Andrew Whitelaw (Division of Medical Microbiology, Department of Pathology, Stellenbosch University and Tygerberg Hospital), Anton Doubell (Division of Cardiology, Department of Medicine, Stellenbosch University and Tygerberg Hospital), Charles Kyriakakis (Division of Cardiology, Department of Medicine, Stellenbosch University and Tygerberg Hospital), Cornelia Rautenbach (NHLS Microbiology Laboratory, Tygerberg Hospital), Mae Newton-Foot (Division of Medical Microbiology, Department of Pathology, Stellenbosch University and Tygerberg Hospital), William Bates (Division of Anatomical Pathology, Department of Pathology, Stellenbosch University and Tygerberg Hospital)

Background: Establishing a definite diagnosis of tuberculous (TB) pericarditis via direct detection of Mycobacterium tuberculosis (MTB) is challenging and not always possible using conventional

investigations. Previous studies have demonstrated a low yield using either direct microscopy or mycobacterial culture on pericardial fluid alone. We evaluated the potential advantage of minimally invasive percutaneous pericardioscopic biopsy of the pericardium in the diagnosis of TB pericarditis. Methods: Patients presenting with a moderate-to-large pericardial effusion were offered pericardiocentesis via a standard procedure, followed by percutaneous pericardioscopy and pericardial biopsy. Pericardial fluid evaluation included biochemistry, cell count, smear microscopy and TB culture. Pericardial biopsy specimens underwent direct smear microscopy for acid fast bacilli (AFBTMs), TB culture and histological examination. Definite TB pericarditis was defined as at least one specimen positive for AFBTMs, MTB culture, or presence of granulomas on histology. Results: 100 patients participated. 59 were males, mean age 37.9 ± 13.5 years, and 60 were HIV infected (mean CD4 = 192.7 cells/μL). Pericardial biopsy could be obtained in 82 participants, and 54 (65,8%) of these had definite pericardial TB. The yield by examining pericardial tissue was significantly higher than by examining pericardial fluid (96,3% (52/54) vs 72,2% (39/54); p<0.05). 34 tissue samples were positive by smear and/or histology (11 AFB positive, 12 had granulomas, and 11 had both), whilst 15 tissue samples were only culture positive. Of the 39 culture positive fluid samples, 10 were smear positive. Conclusions: Histological and microbiological examination of pericardial tissue resulted in a significantly higher yield than examination of pericardial fluid, with 15 of the 54 confirmed cases (27,7%) identified only on examination of pericardial tissue. In contrast to the assessment of pericardial fluid where a definite diagnosis of TB was mainly dependent on culture, pericardial biopsy enables a more rapid diagnosis by microscopy or histology.

ABSTRACT NUMBER / ABSTRAKNOMMER: 62

Evidence of persisting chronic inflammation in early treated HIV infected children at 8 years of age: Is gut permeability to blame?

Barbara Laughton (FAMRU), Mark Cotton (FAMRU), Richard Glashoff (Stellenbosch University), Shalena Naidoo (Stellenbosch University), Tongai Maponga (Stellenbosch University)

Background: Early combination antiretroviral therapy (cART) has reduced mortality and morbidities. However, even with virological suppression and reconstituted CD4 counts, the immune system remains in dysregulation. Microbial translocation, low-level viremia, co-infections and other adverse events play a significant role in the persistence of chronic inflammation. The effects of HIV-related chronic inflammation is poorly understood in infected children under long-term therapy and virally suppressed. Methods: Plasma and PBMC samples were evaluated. ART was initiated within 9 months with sustained viral suppression at 8 years of age. Plasma biomarkers including; IL-1[±], IL-1[±], IL-2, , IL-6, IL-10, IP-10, IFN-[±], MIP-1[±], MIP-1[±], TNF-[±], TNF-[±], CD40L, INF-[±], FGF, RANTES, TGF[±]1,2,3, sCD14, sCD163, IL-18, hsCRP and LBP were measured using ELISA and Luminex[®] Multiplex assays. Age-matched controls were measured for the same biomarkers. Results: 161 samples were evaluated. Median pre-therapy viral load was 738,501 copies/ml. Median CD4-percentage at baseline was 36.9% (range: 23.1-57.1%). At 8 years of age, there were no significant differences between the CD4-percentage of the HIV-infected (38.3%) and control groups (40.0%) (p=0.261). All children, except five, showed undetectable viral loads at sampling. HIV-infected children showed highly significant increase (p<0.001) in levels of IL-1[±], IL-2, IL-13, IP-10, MIP-1[±], TNF-[±], CD40L, INF-[±], TGF[±]1,2, sCD14, sCD163, IL-18, hsCRP and LBP. Significantly lower levels for the following biomarkers were noted for the HIV-infected group: IL-1[±], IL-6, IL-10, TGF[±]3, IL-15, IL-17A, INF-[±], TNF-[±] and RANTES. Conclusion: Despite early therapy, viral suppression and normalized CD4 counts, HIV-infected children display persistent inflammation as defined by signature biomarkers (sCD163, hsCRP, CD40L, IP-10, IL-18, IL-2). We showed dysregulation in the adaptive immune compartment characterized by lower levels of IL-4, IL-10, TGF[±]3, IL-17A, IFN-[±] and RANTES suggestive of immune exhaustion. The increase in sCD14 and LBP levels are indicative of the monocyte-gut translocation axis, and highlight a potential mechanism driving this chronic inflammation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 63

Comparison of Xpert MTB/RIF (G4) and Xpert MTB/RIF Ultra diagnostic accuracies in patients with a recent history of tuberculosis

Byron Reeve (Stellenbosch University), Grant Theron (Stellenbosch University), Hridayesh Mishra (Stellenbosch University), Jhon Simpson (National Health Laboratory Services, Green Point, Cape Town), Judy Cladwell (City of Cape Town Metropolitan Municipality), Robin Warren (Stellenbosch University), Tania Dolby (National Health Laboratory Services, Green Point, Cape Town)

Background and Objectives: After completion of tuberculosis (TB) treatment, Mycobacterium tuberculosis (Mtb) genomic DNA can persist in patients and cause positive PCR results in the absence of culturable bacilli or active disease. There is limited data on diagnostic accuracy of Xpert MTB/RIF G4 (Xpert) and its successor Xpert MTB/RIF Ultra (Ultra) in such patients, who form a significant part of the TB burden in many settings. **Method:** Sputum sediments (n=352) from patients not on treatment who had finished their prior treatment within two years (101 culture-positive, 251 culture-negative; culture served as reference standard) were included. Sediments were randomly allocated to Xpert or Ultra done per the manufacturer's protocols. **Results:** The sensitivity and specificity of Xpert was 92% (47/51) and 84% (107/127), respectively, and 86% (38/44; p=0.359) and 69% (86/124; p=0.005) respectively for Ultra. After reclassifying the lowest Ultra semi-quantitative category ('trace') to negative, specificity of Ultra changed to 85% (105/124) from 69% (86/124; p=0.004), indicating an increase of 16% (6-19%) (similar overall specificity to Xpert). The sensitivity of Ultra after reclassification changed by -5% (-13-4%). In a situation representative of Cape (culture-positivity rate of ~20% in presumptive patients previously treated within two years), the PPV of Ultra, Ultra (trace reclassified), and Xpert will be approximately 40%, 55%, and 62%, respectively in this subpopulation. **Conclusion:** Ultra has lower specificity than Xpert in patients with recent previous TB. With Ultra, ~3/10 culture-negative patients will be false-positive, compared to ~1/7 with Xpert. Furthermore, with Ultra, only 4/10 positive results in recently treated patients will be true-positive, compared to 6/10 with Xpert. These data have implications for diagnostic algorithms, the implementation of new TB diagnostic tests with high analytical sensitivity, and underscore the need for culture, adjunct diagnostic tests, and clinical decision making in previously-treated patients.

ABSTRACT NUMBER / ABSTRAKNOMMER: 64

Clonal expansion of colistin resistant Acinetobacter baumannii isolates in Tygerberg Hospital, South Africa

Andrew Christopher Whitelaw (Stellenbosch University), Mae Newton-Foot (Stellenbosch University), Motlatji Reratlwe Bonnie Maloba (University of the Free State), Yolandi Snyman (Stellenbosch University)

Background: Acinetobacter baumannii is an opportunistic Gram-negative nosocomial pathogen recognized worldwide as a significant concern. Treatment of A. baumannii infections is hampered by increasing multidrug resistance, including resistance to carbapenems and the last resort antibiotic, colistin. This study describes colistin resistance mechanisms and strain diversity of Acinetobacter spp. isolates in Cape Town, South Africa. **Methods:** Colistin-resistant Acinetobacter spp. isolates, identified using the Vitek® 2 AES, were collected from the Tygerberg Hospital referral microbiology laboratory from May 2016 to August 2017. Colistin resistance was confirmed using broth microdilution and the SensiTest Colistin assay. The plasmid-mediated colistin resistance genes, mcr-1-5, were detected by PCR and confirmed by Sanger sequencing. Strain typing was performed by rep-PCR. **Results:** Of the thirty colistin-resistant isolates collected, twenty-four were confirmed colistin-resistant by broth microdilution or SensiTest. Five were isolated in 2016, and 19 in 2017, from tertiary (18) and district/regional level (5) hospitals and a primary healthcare clinic (1). mcr-4.2 was identified in a single A. nosocomialis isolate obtained from a district hospital. Sixteen A. baumannii isolates were identical by rep-PCR; all from patients admitted to Tygerberg Hospital during 2017 and carbapenem resistant. The remaining colistin-resistant isolates were unrelated. **Conclusion:** An increase in colistin-

resistant *A. baumannii* isolates from Tygerberg Hospital in 2017 appears to be clonal expansion of an emerging colistin-resistant strain within the hospital. This strain was not detected in 2016 or in isolates from other hospitals. The lack of plasmid-mediated *mcr* genes suggests that colistin-resistance may be due to chromosomal mutations selected by the use of colistin; further investigation of the resistance mechanisms is planned. To our knowledge, we also describe the first detection of *mcr*-4.2 in a clinical isolate in South Africa, and the first detection of an *mcr* gene in a *Acinetobacter* isolate.

ABSTRACT NUMBER / ABSTRAKNOMMER: 65

Rapid, Culture-free Method for Mycobacterial Viability Discrimination and Cell Enumeration

Jomien Mouton (Stellenbosch University), Samantha Sampson (Stellenbosch University), Trisha Parbhoo (Stellenbosch University)

In majority of *Mycobacterium tuberculosis* infected individuals, infection persists in a clinically asymptomatic state with the ability to resuscitate and cause active tuberculosis. Risk factors such as HIV infection, malnutrition and diabetes are known to increase progression into the active state. Current methods for detection of *M. tuberculosis* take weeks, as a result of its slow growth, emphasizing the need for rapid, culture-free methods for viability discrimination and cell enumeration. In addition, colony forming unit (CFU) plating relies on viable cells to grow on solid media, however cell damage, environmental or antibiotic stressors contribute to limited culturability, resulting in the underrepresentation of the actual bacterial load in a sample. To address this, we optimised and developed a rapid, growth-independent flow cytometry based method for identification and enumeration of the various physiological states of mycobacteria within a heterogeneous population. We optimized the LIVE/DEAD BacLight Bacterial Viability kit using the model organism *Mycobacterium smegmatis*, with the fluorescent dyes SYTO9 and propidium iodide detecting live and dead cells, respectively. Bacterial enumeration was achieved using a bead-based approach, exploiting flow cytometry and compared with plating for CFU determination. A clear distinction between viable and non-viable *M. smegmatis* was detected. Additionally, bacterial numbers determined by our flow cytometry-based method showed good correlation with CFU plating. In addition, the effect of isoniazid and rifampicin treatment on *M. smegmatis* could be determined using this flow-cytometry-based method. For application on clinical samples, *M. tuberculosis* will be recovered and enumerated from spiked sputum. An Alexa Fluor 405 labelled anti-*M. tuberculosis* antibody will be used in sputum samples that contain mixed bacterial populations, providing an accurate culture-free estimation of the mycobacterial load. Enumerating live and dead bacteria using our optimized method will allow rapid and accurate assessment of the bacterial load in samples, supporting both basic research and clinical applications.

ABSTRACT NUMBER / ABSTRAKNOMMER: 66

Evolution of Low-level Kanamycin Resistance in Extensively Drug-resistant *Mycobacterium tuberculosis* in the Western Cape Province of South Africa

Lizma M Streicher (Stellenbosch University), Margaretha de Vos (Stellenbosch University), Rob M Warren (Stellenbosch University), Samantha Pillay (National Health Laboratory Services), Serej D. Ley (Stellenbosch University), Yuri F. van der Heijden (Vanderbilt University Medical Center)

Background: South Africa has one of the highest tuberculosis (TB) burdens globally and a high rate of extensively drug-resistant TB (XDR-TB, resistance to isoniazid, rifampicin, any fluoroquinolone, and any second-line injectable drug) that requires an estimated 45% of the country's TB control budget. Low-level resistance to kanamycin (second-line injectable drug) can be due to *eis*-promoter mutations, but the prevalence of these mutations in TB high burden regions is unknown, as is the frequency of mutations that are not included in current diagnostic tools. Method: We performed Illumina whole genome sequencing (WGS) on 216 *Mycobacterium tuberculosis* (*Mtb*) isolates collected from 40 patients

in the Western Cape Province between 2007 and 2017. These Mtb isolates show evolution from multidrug-resistance to XDR-TB while on treatment. We assessed these strains for eis-promoter mutations and confirmed them using targeted Sanger sequencing and GenoType MTBDRsl. We then screened WGS data from an additional 2368 Mtb isolates (stored convenience sample) for eis-promoter mutations. Results: Nine of 40 patients were infected with an Mtb strain carrying at least 1 eis-promoter mutations. Screening of 2150 additional biobanked whole genome sequences revealed 38 with eis-promoter mutations, two of which carried mutations that are not included in the MTBDRsl assay (eis-promoter -8 and eis-promoter -15). Conclusion: Until 2017, eis-promoter mutations and phenotypic kanamycin resistance were not routinely tested for in South Africa. This could have led to undetected resistance, leading to partially empiric treatment regimens with decreased effectiveness. Additional analyses are required to determine the prevalence of eis-promoter mutations, including those not detectable by MTBDRsl in the Western Cape Province of South Africa. In the future, (targeted) WGS might be considered for diagnostic purposes to determine the complete drug-resistance profile of each patient to avoid the emergence of incurable TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 67

How does Xpert Ultra compare to Xpert MTB/RIF in patients with TB symptoms in a mixed ancestry and African population in Cape Town, South Africa?

Byron Reeve (Stellenbosch University), Grant Theron (Stellenbosch University), Hridayesh Mishra (Stellenbosch University), Zaida Palmer (Stellenbosch University)

Tuberculosis (TB) is a widespread disease that is responsible for the most South African deaths annually and is the single biggest killer of people with HIV/AIDS. Rapid point of care TB tests like Xpert MTB/RIF (Xpert) have been successfully implemented in clinics for this research study, however, the benefit or next generation Xpert Ultra (Ultra) compared to Xpert in such a setting has not been determined. The aim of the study is a head-to-head evaluation of the diagnostic accuracy of Xpert vs Ultra. Mixed ancestry and African study participants with TB symptoms were screened using Xpert and liquid culture tested on induced sputa as part of the participant's routine care (n=302). An additional induced sputum was collected and biobanked for later Ultra testing. Head-to-head comparison data analysis was only performed on patients with matching specimens and actionable results (n=239). The HIV prevalence was 20%, and 39% of patients had a history of previous TB. Overall, the sensitivity of Xpert is 81% (confidence interval (CI) 70-89) compared to Ultra's 87% (CI 76-94; p=0.371) and Xpert has a significantly increased specificity of 99% (CI 95-100) vs 90% (CI 84-94; p<0.001) for Ultra. If "MTB trace detected" Ultra results (n=13) are reclassified as "MTB not detected", then the sensitivity of Ultra is 81% (CI 70-89; p>0.999) with a decreased specificity of 95% (CI 91-98; p=0.040). If trace results are excluded from the analysis, the sensitivity of Xpert is 81% (CI 70-90) and similar compared to Ultra's 86% (CI 75-93; p=0.493), but the specificity of Xpert is 99% (CI 96-100) compared to a significantly decreased Ultra specificity of 95 (90-98; p=0.032). Decreased specificity was observed for HIV and previous TB patients as well. Ultra has similar sensitivity compared to Xpert, but Ultra is offset by significantly decreased specificity even if trace results are excluded.

ABSTRACT NUMBER / ABSTRAKNOMMER: 68

Investigating the role of a novel protein in iron-sulphur cluster biogenesis in mycobacteria

Dr BW Weber (University of Cape Town), Dr MJ Williams (Stellenbosch University), Nandi Niemand (Stellenbosch University)

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb) infection, is the leading cause of death attributable to a bacterial pathogen. The current rise in drug-resistance and co-infection cases puts a strain on TB control programs, highlighting the need for development of new, more effective anti-TB drugs. Numerous uncharacterized genes have been identified in Mtb, and the essentiality of these genes for survival of the organism is currently being investigated. Rv2204c in Mtb and its homologue,

MSMEG_4272 in *Mycobacterium smegmatis*, are uncharacterized genes that produce hypothetical proteins that share homology with A-type carrier proteins. These proteins are thought to be involved in Fe-S cluster biogenesis. Iron-sulphur (Fe-S) clusters are ubiquitous co-factors that contribute to a diversity of biological processes within prokaryotic and eukaryotic organisms. Clusters do not assemble spontaneously, but require multiprotein complex for their formation and transfer to target proteins. Iron, for cluster formation, is obtained from an unknown source and A-type carrier proteins are proposed to be involved in iron scavenging. In this study, we aim to investigate the role of these proteins in Fe-S cluster biogenesis and mycobacterial metabolism. The Rv2204c-encoded protein was produced, within *E. coli* Rosetta II expression strain, and purified using Nickel-NTA gradient elution and gel filtration chromatography. The ability of Rv2204c protein to bind iron was investigated using Isothermal Titration Calorimetry (ITC). Rv2204c was observed to have a high binding affinity for iron in its reduced form (Fe(II)), but had no interaction with oxidized iron (Fe(III)). This provides the first insight into the role of Rv2204c and MSMEG_4272 in mycobacterial physiology.

ABSTRACT NUMBER / ABSTRAKNOMMER: 69

Dried Plasma Spot Testing: a Possible Solution to Enhance Blood Transfusion Safety in Africa

Arthur Richard Bird (WPBTS), Charlotte Pistorius (WPBTS), Wolfgang Preiser (Stellenbosch University)

Sub-Saharan Africa has a unique set of challenges pertaining to blood transfusion. Two contributing factors are the very common occurrence of diseases that require blood as a lifesaving intervention (e.g. malaria) and the high burden of infectious diseases transmissible through transfusion. While testing for viral genomes (nucleic acid testing, NAT) combined with serological testing is the gold standard for ensuring infection safety of donated blood, the vast distances and high temperatures experienced over much of Africa make transport of plasma samples a logistical nightmare. Our hypothesis is that NAT of dried blood (DBS) or dried plasma spots (DPS) may offer a viable alternative, allowing transport to remote testing centres and thus making NAT more widely available in Africa. The project evaluated the diagnostic sensitivity and specificity of testing DPS and DBS samples in comparison to testing plasma samples and determined the stability of DPS and DBS and sample integrity after storage. Samples from 900 negative new donors and 100 confirmed positive donors, as determined by routine screening at WPBTS, were used. After completion of routine testing, one DBS and one DPS sample per donor was prepared and analysed with the Ultrio Elite Assay on the Panther analyser. Preliminary results look very promising. Specificity was superb as was sensitivity for HIV and HCV. Sensitivity for HBV was not as high which could be due to very low and erratic viral loads. We conclude that especially DPS are a highly suitable sample type for screening blood donors as. Logistically they are easy to obtain (fingertip samples could be used), transport is simple (samples will not leak or haemolyse) and storage at room temperature is sufficient.

ABSTRACT NUMBER / ABSTRAKNOMMER: 70

Impact of iron on biofilm formation in *Mycobacterium smegmatis*

Danicke Willemse (Stellenbosch University), Monique Joy Williams (Stellenbosch University), Tsaone Tamuhla (Stellenbosch University)

Background and objectives Biofilms have become synonymous with drug resistance in bacteria as they have been shown to harbour drug tolerant bacteria. *Mycobacterium tuberculosis* has a propensity to form biofilms, but the significance of these biofilms during infection is currently unclear. Iron has been linked to biofilm formation in mycobacteria, however the mechanism is not understood. The aim of the study was to investigate the impact of media components and iron concentrations on pellicle biofilm formation in mycobacteria. Methods *Mycobacterium smegmatis* is a non-pathogenic, fast-growing mycobacteria that is closely related to *Mycobacterium tuberculosis* and it was used as a model organism in this study. Pellicle biofilms were cultured in 24 well plates over 5 days using different media. Biomass

formation was assessed visually for Sautonâ€™s media, chelex treated metal defined media (MM) and MM media supplemented with a range of iron concentrations (0 to 2 μM). Results Both the Sautonâ€™s media and MM media with 2 μM supplemental iron were able to support the growth of biofilms with a fully developed extracellular matrix after five days, with Sautonâ€™s media resulting in the greatest biomass. Mature biofilms were not formed in MM supplemented with less than 2 μM iron, and progress through the steps of biofilm formation, i.e. cell aggregation, matrix formation and matrix maturation, was halted earlier by decreasing iron supplementation. Planktonic growth under iron limitation ruled out the maturation defect was due to growth inhibition. Conclusion Formation of an extracellular matrix is the final stage in biofilm formation. Our results suggest that iron is needed for formation of an extracellular matrix in pellicle biofilms in *M. smegmatis*. Further work to elucidate the mechanism through which iron influences maturation of the pellicle biofilms is still needed.

ABSTRACT NUMBER / ABSTRAKNOMMER: 71

Longitudinal change in host transcriptome during tuberculosis disease progression

Gerard Tromp (Stellenbosch University), Stuart Meier (Stellenbosch University)

Mycobacterium tuberculosis (*M.tb*), which causes tuberculosis (TB), is responsible for more human deaths globally than any other single pathogen. While one third of the worldâ€™s population is infected with *M.tb* most remain healthy and fewer than 10% progress to active TB disease. A number of studies have shown that the TB infection and disease state is reflected in the blood transcriptome of patients. The Grand Challenges 6 (GC6) longitudinal study followed household members of index cases who were newly diagnosed with TB. Whole blood was collected from exposed individuals and RNA was extracted for sequencing at specified time points up to 18 months post enrollment. Here we analysed the RNA-seq data generated in the GC6 study, which included ~390 samples collected from ~320 individuals, to identify genes that are differentially expressed (DE) at different stages of progression prior to TB diagnosis compared to individuals who remained healthy. The DE analysis identified over 6,000 genes whose expression was significantly ($\text{FDR} < 0.05$) altered at different stages of disease progression with a clear progressive increase in the number of up-regulated genes at times that approached TB diagnosis with approximately 3,000 DE genes (~20% of expressed genes) identified four months prior to disease diagnosis. A gene ontology and KEGG pathway analysis of the identified DE genes showed a strong enrichment in genes annotated to function in host immune and defence responses including those annotated to function in the KEGG TB pathway (hsa05152). The results of this study provide a longitudinal snapshot of host transcriptome responses prior to TB diagnosis and will contribute to our understanding of the biology of host defence responses during progression of TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 72

Longitudinal transcriptomic profiling of whole blood during tuberculosis treatment

Gerard Tromp (Stellenbosch University), Stuart Meier (Stellenbosch University), Trust Odia (Stellenbosch University)

Previous studies showed that it is difficult to predict which patients will respond well to tuberculosis (TB) treatment, and relapse or be reinfected (recurrent TB). Individual clinical variability and adherence to treatment are therefore factors to be considered in TB treatment outcome. The goal of this study is to identify underlying biological processes associated with treatment outcomes, among patients diagnosed with Pulmonary TB. Whole-blood samples of 99 individuals (as well as 29 healthy controls) were collected at defined time points for transcriptomic analysis using RNA-seq, as part of a longitudinal study to investigate patient responses to TB treatment. PET-CT scans were used to monitor patients at intervals during treatment. The expression data will be analysed for correlation with disease severity as previously determined by lung PET-CT scans. First, we will determine the proportion of cell types by deconvolution of RNAseq data; next, we will perform statistical analyses using mixed and multilevel

models, conditioned on covariables, such as disease severity and other clinical and demographic observations, to determine differential or correlated expression between outcomes such as successful treatment as well as degree of resolution of lung disease. Gene set enrichment and metabolic pathway analyses will be performed to identify processes involved in these outcomes. The genes and pathways identified in this study will provide novel insights into successful treatment of TB.

ABSTRACT NUMBER / ABSTRAKNOMMER: 73

Neurodevelopmental outcome at 11 months in HIV-infected infants initiating very early Antiretroviral therapy

(), Anita Janse van Rensburg (Stellenbosch University), Barbara Laughton (Stellenbosch University), Els Dobbels (Stellenbosch University), Gert van Zyl (Stellenbosch University), Kirsten Veldsman (Stellenbosch University), Mariana Kruger (Stellenbosch University), Mark Cotton (Stellenbosch University), Mary-Grace Katusiime (Stellenbosch University), Michael Boivin (Michigan State university), Richard Glashoff (Stellenbosch University), Shalena Naidoo (Stellenbosch University)

Background: Early antiretroviral therapy (ART) in perinatally infected children, especially before 2 months of age improves outcomes and limits HIV reservoir size. The long term outcomes of early exposure to ART are unknown. We report neurodevelopment at 11.5 months, of perinatally HIV-infected children who started ART within the first weeks of life. Materials and Methods: Participants were enrolled from the public sector birth HIV-diagnosis program both in community and hospital. Inclusion criteria were: gestation >36 weeks or birth weight >2000g, commencing ART < 6 weeks and no Cytomegalovirus disease. ART included Zidovudine/Lamivudine/Nevirapine for the first 2 weeks, the latter replaced by Lopinavir/Ritonavir. Once body weight >3kg and post conception age >44 weeks, Abacavir replaced Zidovudine. Neurodevelopment was assessed at 10-12 months using the Griffiths Mental Development Scales (GMDS). Results: Of 30 children assessed, 23 (77%) were girls. Mean birth weight was 2961g \pm 541g. Seven (23%) had no PMTCT, 20(60%) received PMTCT (3 unknown). Median [IQR] baseline viral load (VL) was 6915[392; 23405] copies/ml, age starting ART was 5.0 [0; 13] days and time to VL suppression was 25.5 [15; 44] weeks. Seven participants had detectable VL at the GMDS assessment, three had suppressed earlier but experienced virological rebound. Mean CD4% closest to the GMDS was 33.3 \pm 8.6 (range 18-53) and mean CD4 count 2074 \pm 732 (range 863-3790). GMDS was performed at a mean age of 11.5 \pm 0.8 months. Mean quotients were within the average range: Global Griffiths Score 103.3 \pm 11.1 and mean quotients on the subscales ranged from lowest 95 \pm 13.8 for Locomotor to highest 112.6 \pm 11.1 for Speech and Hearing. These scores are similar to CHER participants on ART from a median of 7 weeks and for uninfected controls. Conclusion: Neurodevelopmental outcome at 11.5 months of perinatally HIV-infected infants starting ART at median age of 5 days is within the normal range.

ABSTRACT NUMBER / ABSTRAKNOMMER: 74

The epidemiology and virulence characteristics of Staphylococcus aureus isolates from bacteraemic patients at Tygerberg Hospital, South Africa.

Amike van Rijswijk (Stellenbosch University), Andrew Whitelaw (Stellenbosch University/National Health Laboratory Services), Mae Newton-Foot (Stellenbosch University/National Health Laboratory Services), Shima Abdulgader (Stellenbosch University)

Staphylococcus aureus is a highly virulent pathogen causing life-threatening infections. Data on the molecular epidemiology of S. aureus and its association with clinical outcome in South Africa is limited. This study aimed to determine the molecular epidemiology and the agr associated virulence characteristics of S. aureus isolates from bacteraemic patients at Tygerberg Hospital; and to investigate the impact of strain characteristics on clinical outcomes. Two hundred isolates were collected from blood cultures from February 2015 to March 2017. Genotyping was performed using spa and agr typing.

Related spa types were clustered into spa-CCs. Agr functionality was assessed using the phenotypic \hat{I} -haemolysin assay. Clinical data was collected prospectively and logistic regression models were performed to describe associations between strain characteristics and clinical outcome. Fifty-five (27.5%) of the isolates were MRSA, and 106 (53%) were HA infections. Of the CA isolates, 5% were MRSA. The overall mortality was 29%, with no difference in mortality between MRSA and MSSA bacteraemia (35% vs. 27%; $p=0.41$). Sixty-five different spa types were identified which clustered into 12 spa-CCs. spa-t045 ($n=21$; 11%) was the most prevalent type and found mainly in paediatric wards ($n=19$); all except one spa-t045 isolate were MRSA. Agr type I was the dominant type ($n=98$; 49%), and 30 (15%) isolates were agr dysfunctional. There was no significant association between genotype or agr functionality and methicillin resistance, hospital acquisition or mortality. Hospital acquisition was associated with bacteraemia without focus ($p<0.001$). In this study, heterogeneous strains were identified from bacteraemic patients, with single genotype predominating in paediatric wards, suggesting on-going transmission. The lack of association between strain type and outcome may be a reflection of the small sample size. Additional experiments are planned to further investigate the mechanisms and role of the agr locus in *S. aureus* physiology, virulence and clinical disease.

ABSTRACT NUMBER / ABSTRAKNOMMER: 75

Impact of an online interactive educational tool as an adjunct to community engagement and informed consent practices in HIV Clinics in the Western Cape.

Farah Cassim (CMEL, SU), Keymanthri Moodley (CMEL, SU), Melany L. Hendricks (CMEL, SU), Zulpha Geyer (CMEL, SU)

The uptake of ARV[™]s remains low in developing countries. There are encouraging developments in the field of HIV cure research. However, the complex nature of cure research renders the informed consent process challenging. Educational material evaluated is expensive and not easily reproducible or translatable. The CMEL developed an animated video using POWTOON animated software which is culture neutral, transcends age barriers and stimulates learning in visual and audio modalities. It is easy to use thus can be used to educate patients in hospital waiting rooms. This study evaluates the impact of an interactive online HIV educational tool. A questionnaire assessing the content of the intervention was administered to adults recruited from the waiting room at the FAMCRU Clinic, Tygerberg hospital in South Africa. 50% of participants watched an educational video on HIV prior to the study. All participants had access to educational HIV pamphlets. Adults who gave voluntary informed consent completed the questionnaire in English before and immediately after completing the intervention. Scoring was carried out according to a predetermined scoring grid, with a maximum score of 10.51 participants (median age 25.0 years; 91% female) completed the pre- and post-online tool questionnaires. Most participants (63%) were unemployed; 49% (25) had a grade 11 and 12 level of education and 2% (1) had a tertiary level of education at the time of testing. 47% (31) had a grade 7 to 10 level of education. There was a significant increase in knowledge scores from an average of 57% to 68% ($p=00006$) immediately after the intervention was completed. The POWTOON animation improved participants' [™] knowledge related to HIV treatment, prevention and cure research. It compares well to other educational interventions and is easily reproduced making it a useful adjunct to community engagement and the informed consent process in the research setting.

ABSTRACT NUMBER / ABSTRAKNOMMER: 76

The effect of environmental conditions on growth and phenotype switching in *Mycobacterium smegmatis*

Davina-Nelson Apiyo (Stellenbosch University), Jacoba Mouton (Stellenbosch University), Samantha Sampson (Stellenbosch University), Tobias Louw (Stellenbosch University)

The ability of bacteria to survive antibiotic treatment, despite being genetically susceptible, is the underlying cause of latent tuberculosis (TB) infections. These drug-tolerant bacteria, that are either

non-growing or slowly growing, are known as “persisters”TM, and they exist as a small, viable but non-replicating (VBNR) population. Very little is known about them, since these cells are very difficult to study, owing to their small numbers within a bacterial population and their dormant state. Nevertheless, recent work has developed and exploited a dual fluorescent reporter for use in *Mycobacterium tuberculosis* to identify, isolate and characterise VBNR persister populations. A biofilm system has been proposed to investigate the formation, fate and physiology of persisters, since biofilms generate a spatially heterogeneous microenvironment that could lead to phenotype switching of individual cells and subsequent population heterogeneity. The growth, metabolism and persister formation of *Mycobacterium smegmatis* – a non-pathogenic model of *M. tuberculosis* – will be assessed under different environmental stresses involving nutrient starvation and the addition of antibiotics. Growth conditions will be assessed in vitro using techniques such as respirometry, CFU plating, flow cytometry and dry cell biomass. Data from these experiments will then be used to estimate the growth parameters of *M. smegmatis* using a computational modelling approach. This model will be used to predict the effect of varying experimental conditions on growth and persister formation in a biofilm. Such a study will be particularly useful in developing novel treatment strategies that target drug-tolerant *M. tuberculosis* cells.

ABSTRACT NUMBER / ABSTRAKNOMMER: 77

Human Adenovirus and Human Papillomavirus in the Pathogenesis of Pterygium

Derrick Smit (Tygerberg Ophthalmology), Ernst Van der merwe (Tygerberg Ophthalmology), Jean Maritz (Pathcare), Kayla Delaney (Medical Virology)

Introduction: Our understanding of the pathogenesis of pterygium is incomplete at this stage. One theory proposes a multi-step model (also called a two-hit model) for the pathogenesis of pterygium, with the suggestion that ocular surface viral infections might play an important role. Human Papillomavirus (HPV) has been identified as a co-factor in susceptible hosts and Human Adenovirus (HAdV) has also been implicated as a causative organism. This paper describes the frequency with which these 2 viruses were isolated from excised pterygia in a Namibian population. **Methods:** In this prospective descriptive study the primary objective was to determine the prevalence of HPV and HAdV isolated from pterygium samples of patients operated in a Namibian population. Viral nucleic acid extraction and PCR was done on 66 tissue samples. **Results:** Of the 66 samples, 21 (31.8%) had a positive PCR. Of these, 15 (22.7%) were HPV+ and 6 (9.1%) were HAdV+. The mean age for the HPV+ patients were >8 years younger than the HPV- patients and the mean age for the HAdV+ patients were >7 years older than the HAdV- patients. Of the 9 Human Immunodeficiency Virus positive patients, only 1 (11.1%) tested positive for HPV and none tested positive for HAdV. **Conclusion:** The HPV prevalence of this study is in accordance with other similar studies and the HAdV prevalence is significantly lower than the one other similar study. The significance of the average age differences and the link with HIV needs further investigation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 78

In-hospital mortality of acute kidney injury in those with and without HIV at a tertiary hospital in South Africa: a 2-year retrospective cohort study

Mogamat-Yazied Chothia (Medicine, Tygerberg hospital; Nephrology, Stellenbosch university), Nikash Ramsunder (Internal Medicine Tygerberg hospital)

Background: Acute kidney injury (AKI) in HIV patients is a common cause for hospitalisation and is associated with high morbidity and mortality. There is a paucity of data regarding the outcome of AKI in those with and without HIV. The primary outcome was to determine the overall in-hospital mortality. **Methods:** This was a single centre study of patients with AKI referred to the renal unit at Tygerberg Hospital from 1 January 2015 to 31 December 2016. AKI was defined as a normal serum creatinine (< 3 months) and normal kidney sizes on ultrasound. Those with proteinuria > 3.0 g/day were excluded.

Kaplan Meier curves and logistic regression were used to assess survival and identify factors predicting mortality. Results: We identified 291 patients with AKI of which 116 (39.9%) were HIV positive. Overall, 91 (31%) patients died of which 40 (34.5%) were HIV positive and 51 (29.1%) were HIV negative ($P = 0.34$). At hospital admission, more HIV positive patients had tuberculosis (81.5% vs. 18.5%, $P < 0.01$) and had higher admission serum creatinine ($551.1 \pm 190 \mu\text{mol/L}$ vs. $190 \pm 190 \mu\text{mol/L}$, $P < 0.01$). Of those that died, the HIV positive patients were younger (41 years vs. 52 years, $P < 0.01$), were predominantly Black (87.5% vs. 23.5%, $P < 0.01$) and were predominantly admitted to medical wards (92.5% vs. 41.2%, $P < 0.01$). There was no difference in mortality regardless of renal replacement therapy ($P = 0.50$). Logistic regression identified Mixed race (OR 2.47, $P = 0.02$), HIV (OR 2.69, $P < 0.01$) and surgical ward admission (OR 2.05, $P = 0.03$) as strong predictors for death. Conclusion: Overall in-hospital mortality of AKI was high. HIV was associated with a greater risk of death that may be the result of late presentation of both the AKI as well as the HIV

Theme 3 / Tema 3
Mental Health and Neurosciences /
Geestesgesondheid en
Neurowetenskappe

ABSTRACTS/ABSTRAKTE

ORAL PRESENTATIONS / REFERATE

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

AN ATTEMPT TO STEM THE TIDE : EXPLORING THE EFFECT OF A 90-DAY TRANSITIONAL CARE INTERVENTION ON READMISSIONS TO AN ACUTE MALE PSYCHIATRIC UNIT IN SOUTH AFRICA

Dana Niehaus (Dept Psychiatry, US), Liezl Koen (Dept Psychiatry, US), Marise Coetzee (Stikland Hospital), Ulla Botha (Dept Psychiatry, US)

Introduction: Pressure on inpatient beds often results in premature discharges, which may precipitate early readmission. This has prompted an increased interest in transitional care interventions to bridge the gap between in- and outpatient care to reduce such readmissions. Our study aimed to assess the effect of a Transitional Care Service (TCS) on readmission rates in a high pressure inpatient service which utilizes a premature discharge policy to address bed pressures.
Methods: Sixty male patients identified for crisis discharge were offered a TCS for the first ninety days after discharge. Patients received a structured intervention consisting of four phone calls and one home visit, focusing on maintaining adherence, appointment reminders and psychoeducation. The TCS patients were retrospectively compared to a matched control group in terms of readmission after 90 days. Data was collected on adherence to medication, attendance of appointments and incidence of substance use.
Results: There was no significant difference in readmission rates. Prevalence of substance use was very high (90%), especially methamphetamine use (48%). Adherence dropped from 45% (n=27) at one week post-discharge to 25% (n=15) at 90 days.
Conclusion: Structured telephone-based transitional interventions have no effect on readmission rates in this setting. Prematurely discharged patients require more comprehensive support with focus on comorbid substance use.
Keywords: Transitional care, premature discharges, adherence, telephone-based interventions, early readmissions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Burnout among rural hospital doctors in the Western Cape: Comparison with previous South African studies

Andrew Liebenberg (Stellenbosch University), Francois Coetzee (Stellenbosch University), HOFFIE CONRADIE (Stellenbosch University), Johan Coetzee (Stellenbosch University)

Background: Burnout among doctors negatively affects health systems and, ultimately, patient care.
Aim: To determine the prevalence of burnout among doctors working in the district health system in the Overberg and Cape Winelands districts of the Western Cape Province and to compare the findings with those of previous South African studies.
Setting: Rural district hospitals.
Methods: During 2013, a validated questionnaire (Maslach Burnout Inventory) was sent to 42 doctors working in the district health system within the referral area of the Worcester Hospital, consisting of the Overberg health district and the eastern half of the Cape Winelands.
Results: Response rate was 85.7%. Clinically significant burnout was found among 81% of respondents. High levels of burnout on all three subscales were present in 31% of participants. Burnout rates were similar to those of a previous study conducted among doctors working in the Cape Town Metropolitan Municipality primary health care facilities. Scores for emotional exhaustion (EE) and depersonalisation (DP) were greater than those of a national survey; however, the score for personal accomplishment (PA) was greater. EE and PA scores were similar to that of a study of junior doctors working in the Red Cross Children's Hospital; however, EE was smaller.
Conclusion: This study demonstrates high burnout rates among doctors working at district level hospitals, similar to the prevalence thereof in the Cape Town Metropolitan primary health care facilities.

Health services planning should include strategies to address and prevent burnout of which adequate staffing and improved work environment are of prime importance.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

Medical students' experiences of mistreatment by clinicians and academics at Stellenbosch University and Tygerberg Hospital, South Africa

Dr Kenneth David Crombie (UCT), Dr Maria Christodoulou (SUN), Kathleen Eva Crombie (SUN), Prof Soraya Seedat (SUN)

Although a number of international studies on mistreatment of medical students have been published, to date no South African studies have been done on the topic. OBJECTIVES: To identify experiences of mistreatment of medical students by their superiors (clinicians and academics) at Stellenbosch University and Tygerberg Hospital and to describe the demographic characteristics, mistreatment, mental health correlates and knowledge of current reporting systems. METHODS: This cross-sectional descriptive study was conducted through a questionnaire survey of second to sixth year medical students at Stellenbosch University. All enrolled medical students in second to sixth year were included in this study. Participation was voluntary and anonymous and the survey was completed online (using SurveyMonkey). Three email invitations were sent out, each one week apart with participants required to provide online consent. RESULTS: 78.2% of students reported having been mistreated which occurred mostly in the departments of Internal Medicine and Surgery. Being ignored/excluded (61.8%) was the most prevalent form of mistreatment, followed by gestures e.g., eye rolling, scoffing, glaring (52.4%), verbal abuse (43.1 %), racial discrimination (24.5%) and gender discrimination (21.3%). Students felt that registrars were the main perpetrators (57.5%). 25.5% of students met criteria for a mood/anxiety disorder and 66.9% of these students felt that mistreatment by senior doctors contributed to their psychological distress to some degree. 80.9% of students were not aware of a system in place to report mistreatment.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Profiles of Traditional Healers and their healing practices in Eastern Cape Province of South Africa

Berta Van der Wat (MA Psychology by Thesis, Department of Psychiatry Stellenbosch University), Karis Moxley (PhD Department of Psychiatry Stellenbosch University), Ntombinele Menze (Psychiatry Registra), Prof Soraya Seedat (MD, PhD Department of psychiatry Stellenbosch University)

Background: Despite the widespread use of traditional healers in the management of mental health problems among South Africans, there is a knowledge gap of their practices that needs to be narrowed in order to develop a more collaborative and integrated mental health system. There is a need to better understand traditional practices from the perspective of the healers themselves, and how these align with Western approaches. Aim: We specifically explored the journey towards becoming a traditional healer, the types of interventions and key practices in the management of mental disorders, and the extent to which traditional healers collaborate with conventional medical practitioners. Methods :This mixed methods study involved 77 traditional healers who practice in the Eastern Cape Province of South Africa. We administered semi-structured interviews to gather data on healer training, experiences and practices. The Patient Health Questionnaire (PHQ-9) to screen for depression. All interviews were conducted in isiXhosa at participants' homes. Results: Most healers were female (80.5%), and only half 49% had a traditional healing certificate. Healer training typically consisted of six key steps and was mostly facilitated by a non-family member/trainer, as directed by the ancestors. Most healers treated physical illnesses (86%), and called on their ancestors to assist with diagnosis (90%). Only 40% treated mental illness. While some healers revealed tensions in working with Western practitioners, the majority were open to collaboration (71%). Conclusions: Traditional healers may have an important role to play in the development of culturally-relevant mental health care in South Africa. This study

contributes to a greater understanding of what it means to be a traditional healer, and the types of treatment provided. Findings emphasise that conventional mental health practitioners need to make equal efforts to collaborate, especially if we are to provide culturally-relevant mental health care in traditional South Africa settings.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Enabling health and wellbeing in later life: A Cross-sectional Survey of the Role of Occupational Therapy in Care Homes in South Africa

Nicola Ann Plastow (Occupational Therapy)

This oral presentation was first delivered at the World Federation of Occupational Therapists 2018 Congress in Cape Town, South Africa. Introduction: Although more than half of older people in South Africa live in extended family households (Census 2011), the need for residential care is likely to increase as the ageing population grows. Despite the value of occupational therapy, very few care homes employ an occupational therapist. Additionally, those who do work in this setting report low levels of support and a poorly defined role. Objectives: The purpose of this study was to describe the current role of occupational therapy in care homes in South Africa. Methods: We used a cross-sectional online survey to gather data across South Africa. Occupational therapists were recruited using convenience sampling from care homes (n = 333), our networks (n = 35), and snowballing (n = 4). Data analysis included descriptive statistics and principal components analysis with IBM SPSS 22.0.0.0 software. Results: Of the 77 occupational therapists we identified, 30 completed the survey. Almost all used at least one formal assessment, most often worked with residents in groups, and focussed on meaningful activity. Those working more hours also worked with staff and families. The occupational therapy role included three components: 1) Promoting meaningful activity and independence among residents with specific health conditions; 2) Providing indirect services to reduce risk, modify the environment, and manage; and 3) Education and advocacy for residents, their families, and staff. Conclusion: Occupational therapists in South Africa are providing innovative services within the interdisciplinary care home team. This research will enable occupational therapists to more clearly delineate their role within those teams.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

Reliability and validity of the Stuttering Severity Instrument (SSI): A scoping review.

Chanelle Stewart (Stellenbosch University), Jillian Petersen (Stellenbosch University), Prelene Kannemeyer (Stellenbosch University), Stacey Brummer (Stellenbosch University)

ABSTRACT Background: The Stuttering Severity Instrument-3 was designed to be utilised in clinical settings and research where either a single, numerical score or a descriptive label is desired. Limitations and inconsistencies have been identified which impact the credibility of the studies, all of which involve qualified speech therapists conducting the Stuttering Severity Instrument-3. These inconsistencies reflect on the use of the instrument in the clinical setting and the positive and negative factors influencing the reliability and validity of the Stuttering Severity Instrument-3. Aim: Focus was on identifying factors that influence the reliability and validity thereof. Method: For this investigation, the inclusion criteria includes literature published in English, dates ranging from 1971 to 2018, all age groups of individuals who stutter and research reviews that occur in developed and developing countries. Arksey and O'Malley methodology for conducting a scoping review was utilised by searching several databases. Results: The subjectivity of the instrument presents a significant influence of the clinician's judgement and perception of various aspects of stuttering behaviours. It introduces a variability among clinicians in the interpretation of results thus reducing its accuracy and making it unreliable. It is incapable of measuring stuttering behaviours that are specific in differentiating between the stuttering severity, the presence of normal dysfluency and interiorized stuttering in preliterate children which reduces the validity of the tool. Conclusion: The validity of the Stuttering Severity

Instrument-3 as a diagnostic assessment tool has been influenced by the reliability. The Stuttering Severity Instrument-3 is unreliable and has reduced validity as an assessment tool due to variability. Keywords: Stuttering Severity Instrument-3, reliability and validity, variability, unreliable, reduced validity.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

Cannabis use and hippocampal subfield volume in First Episode Schizophrenia

Bonga Chiliza (Stellenbosch University), Frederika Scheffler (Stellenbosch University), Hilmar Luckhoff (Stellenbosch University), Laila Asmal (Stellenbosch University), Lebogang Phahladira (Stellenbosch University), Robin Emsley (Stellenbosch University), Sanja Kilian (Stellenbosch University), Stefan du Plessis (Stellenbosch University)

Schizophrenia and exposure to antipsychotic medication are known to impact brain volume. Furthermore, the cannabis use literature also suggests an impact on brain volume in otherwise healthy populations as well as in First-Episode Schizophrenia (FES) samples. In particular, hippocampal volume is implicated in cannabis use. However, very little is known regarding specific hippocampal subfield volumetric differences in the context of schizophrenia and cannabis use. In this study, we investigated hippocampal subfield volume differences between cannabis using and non-using patients and controls at baseline assessment. We assessed whole hippocampal and subfield volumes bilaterally in patients with a first episode of a schizophrenia spectrum disorder and healthy controls matched for age, gender, and education both with and without cannabis use. Patients and controls were scanned on a 3T MRI scanner at baseline and the images were processed using the latest Freesurfer v6.0 with improved hippocampal subfield segmentation compared to previous versions. Psychopathology, functionality and cognitive performance were also assessed at baseline entry into the study. Differences in hippocampal subfield volumes were assessed between patients and controls who are cannabis users and non-users to determine if there is an interaction effect between illness-status and cannabis use. We found differences in the parasubiculum, CA3 and fimbria. The relationship between schizophrenia spectrum disorder, cannabis use and the impact on hippocampal subfields was further explored with sub-group comparisons between cannabis using and non-using patients as well as between cannabis using and non-using otherwise healthy controls. This study demonstrates the impact of cannabis use on hippocampal subfield volumes already present at the first episode of a schizophrenia spectrum disorder.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

Childhood trauma and hippocampal subfields in first-episode schizophrenia

Freda Scheffler (Department Psychiatry, Stellenbosch University), Laila Asmal (Department Psychiatry, Stellenbosch University), Lebogang Phahladira (Department Psychiatry, Stellenbosch University), Robin Emsley (Department Psychiatry, Stellenbosch University), Sanja Kilian (Department Psychiatry, Stellenbosch University), Stefan du Plessis (Department Psychiatry, Stellenbosch University)

There is a growing body of evidence that suggests childhood trauma (CT) plays an important role in the development of schizophrenia. Increased levels of childhood adversity has been linked with increased risk for psychosis, trauma related co-morbidities, cognitive impairment as well as poorer premorbid functioning. Increased levels of stress mediated hormones/transmitters involved in synaptogenesis could potentially impact vulnerable brain regions known to be involved in schizophrenia. Regions such as the hippocampus and related structures have been identified as being particularly vulnerable. The CA1/CA3 hippocampal subfields are of particular importance, as they are known to undergo complex changes during neurodevelopment. Although it is known that CT impacts the hippocampus in otherwise healthy adults, relatively little work has been done to explore the potential relationship between hippocampal subfield morphometry and childhood trauma in schizophrenia. Here we aim to investigate potential differences in childhood trauma and schizophrenia. As there are potential gender differences in vulnerability to childhood trauma, we will also explore gender

effects. Since differences in the various hippocampal subfields are potentially complex, we will take into account correlations between the various subfields, by entering them as dependent variables into a Multivariate Analysis of Co-Variance (MANCOVA), modeling for interactions between diagnosis, childhood trauma total score and gender while controlling for substance abuse, scanner sequence and age. We found a significant interaction effect between gender, childhood trauma total score severity and hippocampal subfield morphometry. There was a significant positive relationship between childhood trauma total score and the CA3 hippocampal subfield in male schizophrenia patients, which was not present in other groups. Our results support structural changes in the hippocampus in schizophrenia, with early life trauma being associated with changes in hippocampal subfields known to be affected in schizophrenia. Gender differences contributed significantly to this vulnerability.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

Perceptions and Experiences of the Opioid Substitution Clinic at Stikland Psychiatric Hospital

Abdul Kader Domingo (Stellenbosch University)

Background: Opioid use disorder is a chronic, relapsing disease that can be fatal if untreated. Opioid substitution therapy (OST) has not been widely used in South Africa, which means that little is known about the clinical utility of this treatment in our local setting. Furthermore there is a paucity of research that explores the subjective experiences of patients undergoing OST treatment. There is a need for qualitative data to provide a more accurate interpretation of the effectiveness and quality of OST, and to identify areas in which service delivery could be improved. Aim: To explore patients' perceptions and experiences of attending the OST outpatient clinic (OST-OC) at Stikland Hospital. Methods: This qualitative study, conducted between January to June 2017, involved 8 patients who had been attending OST-OC for at least 6 months. Semi-structured interviews were conducted based on five established indicators and assessment areas for evaluating OST clinics. Interviews were audio-recorded and transcribed verbatim, and data were analysed in Atlas.ti using a phenomenological approach to identify emerging themes. Results: Patients felt OST was helpful and contributed to maintaining a sober lifestyle. Family support and interaction emerged as a vital theme contributing to successful patient outcomes. The preference for methadone and buprenorphine treatment depended on individual experiences. Patients reported that improved interactions with non-clinical staff could better facilitate treatment. Conclusions: Patients' subjective experiences of the OST-OC at Stikland Hospital highlight that OST has assisted clients in maintaining sobriety, but that the choice of medication should be individualised. Patients have further to this highlighted the significant role that clinical-staff have, but also that of non-clinical and institutional considerations. These findings may contribute to optimised service delivery and improved quality of care in this OST-OC, and may help to develop future policy concerning the treatment of opioid use disorders, both locally and abroad.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

STRUCTURAL AND FUNCTIONAL BRAIN NETWORK CONNECTIVITY IN PRENATAL ALCOHOL EXPOSED NEONATES AS ASSESSED BY MULTIMODAL BRAIN IMAGING

Annerine Roos (Stellenbosch University), Dan Stein (Stellenbosch University / University of Cape Town), Heather Zar (University of Cape Town), Jean-Paul Fouche (University of Cape Town), Jonathan Ipser (University of Cape Town), Katherine Narr (University of California, Los Angeles), Kirsten Donald (University of Cape Town), Roger Woods (University of California, Los Angeles)

Introduction: Prenatal exposure to alcohol (PEA) compromises the development of brain networks underlying core behavioral functions in neonates, but studies have not attempted to integrate structural and functional data after PEA. The aim of this study was to apply graph theoretical analysis (GAT) to multimodal MRI data, allowing the simultaneous characterization of disruptions in structural

and functional brain network organization after PEA. Methods: A sample of 11 neonates prenatally exposed to alcohol (ALC) and 14 healthy controls (CON) from the Drakenstein Child Health Study, aged 2-4 weeks, were included in this analysis. Resting state functional and diffusion weighted structural MRI data were acquired during natural sleep. GAT was applied to create covariance networks for each of the two data sets, controlling for variance in age and sex. Hubs in regional brain networks were operationalized as clusters with connectivity two standard deviations above that of the mean for that network. Nonparametric permutation tests were employed to identify group differences in the connectivity of global network hubs. Results: Functional network hubs in ALC were the amygdala, pallidum and superior temporal lobe; while functional hubs in CON included the posterior cingulate and precuneus. ALC and CON had similar hubs in their structural networks including middle cingulate, parahippocampal and fusiform gyri. Conclusion: In the functional network analysis, we observed early signs of functional disruption that suggest suboptimal integration of functional networks even at this early age. Larger apparent group differences in functional compared to structural brain organization suggests that structural differences may only become evident with further maturation of neural development and as functional demand increases.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

The neurological phenotype of patients with HIV associated neurocognitive disorder (HAND) on antiretroviral therapy

Eric H. Decloedt (Division of Clinical Pharmacology, Department of Medicine, Faculty of Medicine and Health Sciences, University of Stellenbosch), John A. Joska (Division of Neuropsychiatry, Department of Psychiatry and Mental Health, Faculty of Health Sciences, University of Cape Town), Michael Mccauley (Biostatistics Unit, Centre for Evidence-based Health Care Department of Global Health, Faculty of Medicine and Health Sciences), Ned C. Sacktor (Johns Hopkins University, Johns Hopkins Bayview Medical Center, Baltimore, Maryland, USA), Sean Glen Anderson (Faculty of Medicine and Health Sciences, University of Stellenbosch, Cape Town, South Africa)

Background: All forms of HIV associated neurocognitive disorder (HAND) remain highly prevalent despite effective antiretroviral therapy (ART). Neurological findings have been well described in regions where clade B HIV subtype dominates but not in South Africa where clade C predominates. The primary endpoint was to describe neurological manifestations in patients with HAND in the era of ART and to explore associations with Global Deficit Score (GDS). The secondary endpoint was to determine associations between efavirenz (EFV) and its metabolite (8-hydroxy efavirenz [OH-8-EFV]) with neurological manifestations. Methods: We conducted cross sectional analyses of the neurological examination findings of patients screened and/or enrolled in a HAND randomised controlled trial. Neurological examination data was grouped into clusters made up of clinically related neurological signs. Multiple linear regression models were used to explore associations between neurological parameters and GDS, as well as plasma and cerebrospinal EFV and OH-8-EFV concentrations. Results: We included 80 participants. 90% were female with a median age of 35 and a median GDS of 0.94 (interquartile-range (IQR) 0.63-1.36). The patients were established on ART for a median of 40 months and at entry had a median CD4+ T-cell count of 498 cell/mm³. We found statistically significant associations between HAND severity and neurological clusters: gait [slow walking speed ($p=.03$; $R^2=.06$), gait ataxia ($p<.01$; $R^2=.21$), abnormal gait appearance ($p<.01$; $R^2=.18$)]; coordination [upper limb bradykinesia ($p<.01$; $R^2=.10$) and lower limb bradykinesia ($p=.01$; $R^2=.10$)]; primitive reflexes [jaw jerk ($p=.04$; $R^2=.05$) and palmo-mental response ($p=.03$; $R^2=.06$)]; smooth pursuit ($p=.01$; $R^2=.09$) and saccades ($p<.01$; $R^2=.15$). No significant associations were found between plasma and cerebrospinal EFV or OH-8-EFV concentrations and any neurological sign. Conclusion: We found the neurological sign clusters of gait, coordination, primitive reflexes, smooth pursuits and saccades were associated with GDS and could be used in clinical practice to assess for HAND severity.

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

Investigation of familial Parkinson's disease in a South African family of Indian ancestry using whole exome sequencing

Dr Karisha Roopnarain (Stellenbosch University-Division of Neurology, Tygerberg Hospital), Dr William Haylett (Stellenbosch University-Division of molecular biology and human genetics), Prof Jonathan Carr (Stellenbosch University-Division of Neurology, Tygerberg Hospital), Prof Soraya Bardien (Stellenbosch University-Division of molecular biology and human genetic)

Introduction: Whole exome sequencing (WES) has been successfully used in the discovery of new genes involved in Parkinson's disease (PD). Not much is known about the genetic architecture of PD in the Indian population in South Africa. The aim of this project was to identify the possible genetic factors contributing to PD in a South African family of Indian ancestry using WES. Methods: We identified a family with multiple PD-affected members and performed a neurological evaluation. We collected DNA from three affected and seven unaffected family members. We did WES on three affected siblings using the Ion Proton System. A bioinformatics pipeline was used to identify rare coding variants shared between the three affected siblings. We further prioritised the variants using various bioinformatics and computer based prediction tools. We performed Sanger sequencing confirmation of the prioritised variants. We then did High Resolution Melt (HRM) screening of > 120 control DNA samples to determine the population frequencies of prioritised variants. Results: WES found 166 rare coding variants in total shared by all three affected family members. We did not find any variants in known PD-causing genes. A list of 11 variants was prioritised for Sanger sequencing validation, which validated all 11 variants. HRM screening of 3 variants demonstrated that these variants are very rare in SA populations. Conclusion: We have confirmed 11 possible candidate genes for PD in the family studied, using WES. Of interest is that one of those confirmed was a variant in the gene LRRK1. A few other studies in PD families in other countries also found variants in the LRRK1 gene. LRRK1 is a homolog of the gene LRRK2 which has already been strongly linked with PD, they may share similar functions and pathways. We would like to further study these genes by doing functional studies.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

MitoSPARK- Mitochondrial DNA Sequencing of South African Parkinson's disease patients

Amica C. MÅller-Nedebock (Stellenbosch University), Francois H. van der Westhuizen (North-West University), Joanna L. Elson (Newcastle University), Jonathan A. Carr (Stellenbosch University), Marianne Pretorius (North-West University), Soraya Bardien (Stellenbosch University)

Background: The burden of age-related disorders is expected to increase in Sub-Saharan Africa, with Parkinson's disease (PD) predicted to affect approximately 3 million Sub-Saharan Africans older than 60 by 2050. PD is an incurable neurodegenerative condition with both environmental and genetic contributors, severely compromising the quality of life of those affected by it. Despite this knowledge, PD remains understudied in Africans. Inherited mitochondrial DNA (mtDNA) variation differs between ethnicities and is suggested to underlie mitochondrial dysfunction implicated in PD pathogenesis, yet the association between mtDNA and PD remains controversial. Previous association studies between mtDNA and PD using the haplogroup association method, have produced largely inconsistent results. Methods: Here, as part of a pilot study we sequenced whole mitochondrial genomes of 40 South African PD patients from different ethnic groups (Black, Afrikaner Caucasian, English-speaking Caucasian, Mixed Ancestry) using Next Generation Sequencing (NGS). Subsequently, employing the MutPred variant load hypothesis, we calculated individual variant loads (<http://mutpred.mutdb.org>). Results: As expected, Black participants had the most mtDNA variation (average of 57.3 variants per person) and English-speaking Caucasians had the least (average of 21.5 variants per person). Black and Mixed Ancestry ethnic groups had similar counts of homoplasmic, non-synonymous variants per person (average of 10.3 variants). Afrikaner and English-speaking Caucasians also had comparable counts of these variants per person (average of 5.7 and 5.8 variants, respectively). 73% of cases (n=29), on average 7 from each ethnicity, had mildly deleterious MutPred variant loads >0.5. Future

Work: On the premise that there are no published studies on mtDNA variation in Black African PD cases, future work will include sequencing whole mtDNA of 100 PD cases and 200 controls of Black, South African ethnicity and applying the MutPred variant load hypothesis to determine whether inherited mtDNA variation contributes to PD development in this ethnic group.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

The gut microbiome in mental health: an investigation in South African PTSD patients

Dr Leigh van den Heuvel (Stellenbosch University), Dr Stefanie Malan-Muller (Stellenbosch University), Prof Sian MJ Hemmings (Stellenbosch University), Prof Soraya Seedat (Stellenbosch University)

Background Violence and trauma are highly prevalent in South Africa and subsequently, our population is at an increased risk of developing trauma-related disorders. Inadequate immunoregulation and elevated inflammation may be risk factors for posttraumatic stress disorder (PTSD), and microbial inputs are important determinants of immunoregulation. A recent pilot study by our group found that a particular trio of bacteria is present at very low levels in PTSD patients compared to trauma-exposed controls (TEC). These altered bacteria may negatively affect immune regulation in patients, with subsequent negative sequela on the central nervous system and its functioning. The aim of this study was to expand on the pilot study by investigating the gut microbiome composition in a larger sample size of 80 PTSD patients, 59 TEC and 45 healthy controls, to identify microbial signatures associated with trauma, PTSD and lifestyle variables. Methods PTSD was diagnosed using the Clinician-Administered Posttraumatic Stress Disorder Scale for DSM-5 (CAPS-5). Microbial DNA was extracted from stool samples of 80 PTSD patient and 59 TEC and 45 healthy controls. Bacterial 16S ribosomal RNA (rRNA) V4 amplicons were generated and sequenced. Microbial community structure, alpha-diversity, and beta-diversity will be analyzed. Random forest analysis will be used to identify associations between bacterial taxa and PTSD. Results Results are currently being generated and will be presented at the meeting. Conclusion This study will be the second gut microbiome investigation in PTSD patients and the largest one to date. The gut microbiome is an easy target for interventions, therefore, studies that can identify bacterial signatures associated with disease can pave the way for future psychobiotic (pre/probiotics that improve psychiatric symptoms) applications to alleviate symptoms of mental health disorders.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

The significance of general intelligence in social cognition assessment.

Alex Doruyter (Division of Nuclear Medicine, Stellenbosch University), Christine Lochner (SU/UCT MRC Unit on Risk & Resilience in Mental Disorders, Stellenbosch University), Dan J Stein (SU/UCT MRC Unit on Risk & Resilience in Mental Disorders, University of Cape Town), Lian Taljaard (SU/UCT MRC Unit on Risk & Resilience in Mental Disorders, Stellenbosch University)

Introduction: Social anxiety disorder (SAD) has been associated with abnormalities in social cognition, i.e. problematic thought processes concerning knowledge of self and others¹. There is no data however on the role of general intellectual ability in social cognition. The current study aims to address this caveat in the SAD literature. Methods: A case-controlled study compared outcomes on social cognition assessments between SAD patients and matched healthy controls. The Liebowitz Social Anxiety Scale (LSAS) was used to assess illness severity, and the Wechsler Abbreviated Scale of Intelligence (WASI) to estimate intelligence quotient (IQ). Social cognition, entailing emotion recognition (ER) and social knowledge (SK) was assessed using the Reading the Mind in the Eyes Test (EYES) and The Awareness of Social Inference Test (TASIT), respectively. Results: 19 SAD (57.9% female) patients and 17 controls (52.9% female) took part. In the SAD group, the mean age of onset was 8.47 years (SD $\hat{A}\pm 9.59$), and

LSAS total 92.89 (SD $\hat{A}\pm 23.9$). Results from multivariate linear modeling indicated that there was a significant main effect for IQ and ER, $F(1,35)=20.61$, $p<.001$, and SK, $F(1,35)=31.152$, $p=.001$. When controlling for IQ, group (patients vs. controls) did not significantly predict performance on ER ($p=.484$), or SK ($p=.325$). However, SAD patients performed significantly worse than controls on ER $F(1,35)=4.587$, $p=.039$ and a strong tendency to perform worse on SK ($p=.059$), when not controlling for IQ. Conclusion: Our findings suggest that IQ is significant in social cognition in SAD. The current study highlights the importance of assessing general intelligence when investigating social cognition. Increased IQ may serve as a protective factor for impaired social cognition. In addition, addressing faulty social cognition in CBT may assist in reducing social anxiety severity. However, IQ may potentially influence treatment outcome and prognosis.

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

Cluster analysis of disorders characterized by impulsivity in patients with methamphetamine use disorder

Christine Lochner (SU/UCT MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, SU), Dan Stein (SU/UCT MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry and Mental Health, UCT), Edrich Rall (SU/UCT MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, SU), Martin Kidd (Center of Statistical Consultation, Department of Statistics and Actuarial Science, SU)

Background: There is an association between substance use disorder (SUD) and impulsivity. Patients with methamphetamine use disorder (MUD), for example, often present with comorbidities with impulsive features. These comorbidities include impulse-control disorders, substance use disorders (SUDs), neurodevelopmental disorders, and some personality disorders. There has been little systematic investigation of comorbidity with impulsive features in MUD however. Methods: A cluster analysis of lifetime comorbid disorders with impulsive features was performed on 65 MUD patients (female: 66%), ages ranging between 18 - 49 years. Illness severity was assessed with the YBOCS-du and impulsivity using the UPPS-P. Results: Five "impulsive" conditions were detected in this cohort (i.e. borderline personality disorder [BPD], antisocial PD [ASPD], SUDs [methamphetamine and cannabis] and alcohol use disorder (AUD)) and included in the analysis. CA divided cases into 4 clusters. Cases in Cluster 1 had comorbid AUD only ($n=12$). Cluster 2 cases had no comorbidity ($n=19$). Cluster 3 cases had other SUDs and increased rates of ASPD ($n=15$) and Cluster 4 had other SUDs and increased rates of BPD ($n=19$). In Cluster 3, 80% of cases had ASPD, 26% had cannabis use disorder (CUD), 80% methamphetamine use disorder (MxUD), and 46% of the cases met diagnosis of AUD. In Cluster 4, 42% had BPD, 89% met a diagnosis of CUD, 63% MxUD, and 63% AUD. Illness severity differed between clusters ($p=0.04$), with Cluster 2 being least severe. Impulsivity rates also differed significantly between clusters ($p=0.02$), with cases in Clusters 3 and 4 being most impulsive. Conclusion: Comorbidity with impulsive features increases illness severity in MUD. Personality pathology (i.e. ASPD and BPD) is associated with increased impulsivity in MUD. These findings contribute to data on impulsivity in MUD, and showed impulsivity is a heterogeneous concept, manifesting differently in different cases with MUD.

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

Patient Experience of Living with Trichotillomania (Hair-pulling Disorder)

Derine Sandenbergh (Stellenbosch University)

Trichotillomania or Hair-pulling Disorder (HPD) is a disorder that hasn't received much research consideration in the South African context, compared to other mental health disorders, like Schizophrenia, Substance Use Disorder, and Post-Traumatic Stress Disorder. Patients with HPD were recruited for a cognitive training intervention study. To add to a richer understanding of HPD, including perceptions of treatment, each contact session (pre- and post-intervention, and 3 months post-

intervention) included a qualitative interview. The aim was to explore the participant's experience of living with HPD, as well as their experience of being part of the research study. The qualitative data of 95 interviews, with 37 participants, were transcribed and then analyzed using an interpretative phenomenological approach, utilizing the qualitative data analysis and research software, ATLAS.ti. The major themes and subthemes highlighted during the process will be presented to reflect the daily challenges patients with HPD face, and how they understand, make sense of and manage the disorder. Preliminary themes include the experience of hair-pulling, emotions linked to the behaviour, the role of relationships, interventions trialed, self-reflection, as well as reflection on being part of the research and engaging in online training.

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Association of childhood maltreatment with internalizing and externalizing disorders in trauma exposed adolescents

Jani Nothling (Stellenbosch University), Leigh van den Heuvel (Stellenbosch University), Milo Koning (Stellenbosch University), Soraya Seedat (Stellenbosch University)

Introduction: South African adolescents experience high levels of trauma, including various types of childhood maltreatment. Different types of maltreatment often co-occur. Previous research suggests that childhood maltreatment provokes a latent liability to internalizing and externalizing dimensions of psychopathology. Our objective was to examine the effects of childhood maltreatment on internalizing and externalizing disorders in trauma-exposed adolescents, and to assess the mediating effect of posttraumatic stress disorder (PTSD) on these associations. Methods: A cross-sectional study was conducted with 262 trauma exposed adolescents (aged 12-18 years) in South Africa. Childhood maltreatment and PTSD severity were assessed using the Childhood Trauma Questionnaire and the Child PTSD Checklist respectively. Psychiatric disorders were diagnosed utilizing the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version and were grouped into internalizing and externalizing disorders. Hierarchical logistic regression was used to assess the association of childhood maltreatment types with internalizing and externalizing disorders, controlling for statistically significant sociodemographic characteristics, with PTSD severity added to the final model as a potential mediator. Results: Sexual abuse was significantly associated with internalizing disorders ($B = .07, p = .011$), although this effect was mediated by PTSD severity ($B = .05, p < .001$; not included as an internalizing disorder). In contrast, physical abuse ($B = .09, p = .004$) and gender ($B = .70, p = .035$) were associated with externalizing disorders, but the addition of PTSD severity did not significantly alter these associations. Conclusion: The association between sexual abuse and internalizing disorders was fully mediated by PTSD symptom severity. Gender and physical abuse severity, but not PTSD severity, was associated with the presence of externalizing disorders. Adolescents displaying internalizing or externalizing psychopathology need to be assessed for exposure to childhood physical and sexual abuse and PTSD comorbidity.

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Change in telomere length and cognitive function over 12 months in the context of HIV, major depressive disorder and childhood trauma

Georgina Spies (Stellenbosch University), Jacqueline Womersley (Stellenbosch University), Sian Hemmings (Stellenbosch University), Soraya Seedat (Stellenbosch University)

Background: HIV-associated neurocognitive disorders continue to prevail in countries affected by HIV/AIDS despite improved access to antiretroviral therapies. Previous research from our group suggested that the interaction of childhood trauma (CT) and depression may increase the risk of neurocognitive decline, and that telomere length (TL) attrition, a marker of biological aging, may mediate this relationship. We expanded our investigation of whether change in TL is predictive of declining neurocognitive function as this has implications for timely intervention. Methods: HIV-positive

(n=61) and negative (n=49) women underwent a battery of neuropsychological tests to measure seven domains of cognitive function: motor skill, verbal fluency, attention and working memory, processing speed, learning, recall, and executive function, from which a global cognitive score was calculated. Participants completed the Childhood Trauma Questionnaire and the Centre for Epidemiological Studies Depression Scale. Quantitative polymerase chain reaction using primers specific to telomeric repeats and the reference gene human β -globin was performed on DNA extracted from peripheral blood mononuclear cells. Neurocognitive tests and TL measurements were performed at baseline and at 12 months and change scores were calculated. Multiple linear regression models using the R statistical language were used to assess the relationships between HIV, CT, depression, change in TL and change in cognitive scores. Results: Depressive symptoms alone, and in interaction with CT, were associated with increased TL shortening across participants ($p = 0.037$ and $p=0.017$ respectively). HIV seropositivity was strongly associated with worsening global cognitive scores over one year ($p=2 \times 10^{-4}$). Finally, the interaction of CT experience, HIV status and change in TL was associated with a decline in cognitive performance ($p=0.025$). Conclusions: Our longitudinal data support the deleterious impact of HIV on cognitive function and suggest that TL attrition is predictive of worse cognitive performance in the context of CT and HIV.

ABSTRACT NUMBER / ABSTRAKNOMMER: 21

Structural brain differences in adolescents with anxiety proneness and childhood trauma.

Fatima Ahmed (Stellenbosch University), Lindi Martin (Stellenbosch University), Soraya Seedat (Stellenbosch University)

Introduction: Studies have shown that anxiety disorders are among the most prevalent category of psychiatric disorders among adolescents and they are more prone to suffer brain volumetric reductions compared to controls. Individuals with childhood trauma are at greater risk of developing anxiety disorders. The aim of this study was to compare brain structure among adolescents with childhood trauma and anxiety proneness. Our hypothesis was that adolescents with high levels of childhood trauma and high level of anxiety will demonstrate significantly more pronounced volumetric reductions compared to adolescents with comparable levels of childhood trauma but who also have low levels of anxiety. Method: Participants (N=94) were selected from schools in the Cape Town area, and underwent structural magnetic resonance imaging at CUBIC. The sample consisted of 23 participants with high anxiety/high trauma, 24 with high anxiety/low trauma, 19 low anxiety/high trauma and 28 healthy controls, with low anxiety and low trauma. We used Freesurfer to assess brain volumes and SPSS v.25 to conduct analysis to calculate the possible significant volumetric differences in brain regions. Results: Results revealed a trend for significance in the right Anterior Cingulate Cortex between high anxiety/low trauma and high anxiety/high trauma ($p = 0.069$) participants, and between low anxiety/high trauma and high anxiety/high trauma ($p = 0.084$) for the left PFC and low anxiety/high trauma and low anxiety/low trauma for the right PFC ($p = 0.089$) participants respectively. Conclusion: We unfortunately did not find any significant values, but our results that led towards significance for both the trauma exposed and anxiety groups speaks volumes about the role of both on brain structure. The effects of childhood trauma on brain structure are known, but as we are dealing with adolescents whose brains are still developing, the role of anxiety proneness needs further analysis.

ABSTRACT NUMBER / ABSTRAKNOMMER: 22

A profile of adult acute admissions to Lentegour Psychiatric Hospital, South Africa

Herman Franken (Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University), John Parker (Lentegour Psychiatric Hospital, Department of Psychiatry and Mental Health, University of Cape Town), Robert Wicomb (Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Capital and Coast DHB), Robin Allen (Lentegour Psychiatric Hospital, Departments of Psychiatry, University of Cape Town and Stellenbosch University)

Introduction: The Western Cape Province has the highest documented lifetime prevalence of common mental disorders in South Africa. To ensure the efficient, equitable and effective distribution of current resources, there is a need to determine the profile of patients seeking psychiatric treatment. The aim of this study was to describe patients admitted to the Acute Adult Admissions Unit at Lentegeur Hospital (LGH) which is situated in Mitchells Plain, Cape Town. Methods: This retrospective study involved an audit of all patients (18-60 years of age) admitted between 1 January 2016 and 30 June 2016. Results: A total of 573 adult psychiatric patients were profiled. The median age of the cohort was 29 years. The majority of patients (63%) were educated to the secondary level. Only 12% of patients were employed and 37% received disability grants. More than 90% of cases presented with psychotic symptoms. Of these, 28% presented with first episode psychosis. Of all patients, 20% were referred with manic symptoms and 7% with depressive symptoms. Many patients (62%) used substances in the period leading up to admission. Significantly more males (73%) used substances compared to females. Cannabis was the most widely used substance (51%), followed by methamphetamine (36%). Violence was a contributing factor to 37% of admissions. A total of 70 patients (13%) tested positive for HIV, while 49 (9%) tested positive for syphilis. Conclusion: We found the average patient requiring admission to be an urban young male who would likely have a secondary level (grade 8-12) education, but be unemployed. This patient would also likely be a user of illicit substances, would present psychotic, and would likely display violent behaviour prior to referral. Substance use and a propensity for violence were identified as significant factors that influence the likelihood of admission.

ABSTRACT NUMBER / ABSTRAKNOMMER: 23

Burnout and job satisfaction of nursing staff in a South African acute mental health setting

Anthea Payne (Stellenbosch University), Inge Smit (Stikland Hospital), Liezl Koen (Stikland Hospital)

Psychiatric nurses are a fundamental component of the mental health care system in South Africa. However, high levels of burnout and job dissatisfaction amongst nursing staff has been associated with reduced empathy and quality of care, and poor service delivery. This cross-sectional study used the Copenhagen Burnout Inventory and an established job satisfaction questionnaire to assess burnout and job satisfaction amongst 129 nursing staff at Stikland Psychiatric Hospital. Although scores for personal, work-related and client-related burnout were relatively high, job satisfaction was also high. Higher levels of burnout were significantly associated ($p=0.01$) with lower levels of job satisfaction in this population of mostly female nurses. There were no significant associations between burnout/job satisfaction and gender or rank. These findings emphasise that supportive or preventative structures should be implemented to reduce the prevalence of burnout.

ABSTRACT NUMBER / ABSTRAKNOMMER: 24

The subjective experiences of extrapyramidal side effects (EPSEs) in first episode psychosis patients treated with flupenthixol decanoate

Francois-Pierre Joubert (Stellenbosch University)

Abstract Background: Schizophrenia remains one of the most devastating of mental illnesses. Cost-effective treatments of First Episode Schizophrenia (FES) are important for improving long-term outcomes in resource-constrained settings, such as South Africa. The long-acting injectable antipsychotic, flupenthixol decanoate, has been suggested as a viable treatment option in FES. However, the development of extrapyramidal side effects (EPSEs) represents a major barrier to the routine use of this drug in FES. Aim: Therefore, the aim of this study was to describe the nature, occurrence and severity of EPSEs, and their impact on patients with First Episode Schizophrenia over 12 months of treatment with flupenthixol decanoate. We explored both the objective (clinician rated) and subjective (patient reported) experience of EPSEs, and the relationship between these ratings and clinical symptoms of schizophrenia. Methods: This was a sub-study of a larger study which examined

several outcomes in patients with FES treated with the lowest effective dose of flupenthixol decanoate. The Extrapyramidal Symptom Rating Scale (ESRS) was used to assess both subjective experience and objective measures of EPSEs in a cohort of FES patients (N=130). The relationship between demographic and clinical risk factors for individual subsets of EPSEs was also determined. Results: There was good tolerability of the medication over a twelve-month follow-up period. Subjective ESRS scores rose before objective measures and both decreased to baseline levels by the end of the follow-up period. Clinical and demographic variables were identified as risk factors for Parkinsonism, dystonia and akathisia with ethnicity being particularly important. Conclusions Flupenthixol decanoate is a well-tolerated in FES. Several risk factors predicting the development of individual side effects were identified in this cohort, suggesting a complex interplay between clinical and demographic features and the development of EPSEs. This warrants further investigation in the future.

ABSTRACT NUMBER / ABSTRAKNOMMER: 25

The impact of a psychiatry clinical rotation on the attitude of South African final year medical students towards mental illness

Caro De Witt (Dept of Psychiatry, Stellenbosch University), Dana Niehaus (Dept of Psychiatry, Stellenbosch University), Esme Jordaan (Biostatistics Unit, Medical Research Council, South Africa and Statistics and Population Studies Department), Inge Smit (Dept of Psychiatry, Stellenbosch University), Liezl Koen (Dept of Psychiatry, Stellenbosch University), Ulla Botha (Dept of Psychiatry, Stellenbosch University)

Background: Stigmatising attitudes of health care professionals towards mental illness can impede treatment provided for psychiatric patients. Many studies have reported undergraduate training to be a critical period for changing the attitudes of medical students, and one particularly valuable intervention strategy involves time spent in a clinical psychiatric rotation. In South Africa, medical students are exposed to a clinical rotation in psychiatry but there is no evidence to show whether this has an effect on attitudes toward mental illness. Aim: This study assessed whether medical students' attitudes toward mental illness changed after a clinical rotation in psychiatry. Methods: This prospective cohort study involved a convenience sample of 112 South African medical students in their 5th or 6th year of undergraduate training. This sample attended a 7-week psychiatry rotation. The Attitudes to Mental Illness Questionnaire (AMIQ) was used to assess students' attitudes toward mental illness before and after the clinical rotation which includes exposure to a number of psychiatric sub-divisions and limited didactic inputs. Results: There was a significant improvement ($p < 0.01$, t-test) in the students' attitude toward mental illness following the psychiatric rotation. Females displayed a more positive attitude towards mental illness at the end of the rotation compared to males. The participants' attitude significantly deteriorated for the non-psychiatric vignette describing diabetes (< 0.01 , t-test). Conclusions: Our findings suggest that clinical training and exposure to a psychiatric setting impacts positively on medical students' attitude towards mental illness, even when this training does not include any focused, didactic anti-stigma input

ABSTRACT NUMBER / ABSTRAKNOMMER: 26

Genome-wide differentially methylated genes associated with PTSD in female rape survivors

Jani Ntshing (Stellenbosch University), Naeemah Abrahams (South African Medical Research Council), Sian Hemmings (Stellenbosch University), Soraya Seedat (Stellenbosch University)

BACKGROUND: Alterations to the epigenome in response to psychological trauma have been reported as a mechanism mediating gene and environmental interaction. Differentially methylated genes involved in the biological pathways associated with the adverse phenotypic behavioural presentations in posttraumatic stress disorder (PTSD) has previously been identified. However, the majority of studies

have focussed on differential methylation of single candidate genes in participants exposed to heterogeneous index traumas. The objective of this study was to identify genome-wide differences in methylation profiles of a group of women exposed to rape, with and without PTSD. METHODS: Female isiZulu participants (n=48) between 18 and 40 years of age, who reported an incident of rape within the previous twenty days, were recruited from two Thuthuzele Rape clinics in KwaZulu Natal. Rape-exposed participants with and without PTSD were matched on HIV status, age, childhood maltreatment and other lifetime trauma exposure, body mass index and smoking status. DNA was extracted from peripheral blood and analysed using the Illumina Epic BeadChip microarray. Logistic regression models, adjusting for multiple comparisons, were used to identify differentially methylated genes in participants with and without PTSD at three months post-rape. RESULTS: Four hundred twenty-three differentially methylated genomic regions were associated with PTSD status. Paired box 8 (PAX8) $p=9.14E-20$ and Zinc Finger Protein 57 (ZFP57) $p=4.84E-18$ were among the top twenty genomic regions significantly associated with PTSD in this dataset and previously found to be associated with PTSD in other traumatised cohorts. CONCLUSION: PAX8 may be involved in PTSD symptoms related to sleeping difficulties and ZFP57 is believed to be involved in susceptibility to stress governed by differential methylation in hippocampal cells. This is the first study, to our knowledge, to investigate genome-wide profiles of women exposed to rape in Africa. Confirmation of these findings will require replication in larger cohorts.

ABSTRACT NUMBER / ABSTRAKNOMMER: 27

The profile of seekers of mental health information in South Africa

Mandi Broodryk (University Stellenbosch)

AbstractIntroduction: Knowing the profile and needs of mental health information seekers can serve a number of purposes, including assistance with website foci, streamlining awareness campaigns, and development of printed media, amongst others. Here we describe the demographic characteristics and needs of individuals that contacted the Mental Health Information Centre (MHIC) of Southern Africa (www.mentalhealthsa.org.za) during 2017. **Method:** Profile information of first contact emails, phone calls and website messages were recorded between January and December 2017. Descriptive analyses were employed to produce percentages and frequencies of each demographic variable. **Results:** A total of 460 individuals contacted the MHIC during 2017. After excluding missing data, 76% of callers (n = 206) were female, 53.4% (n = 101) were between the ages of 21 and 39 and callers' first languages were English (62.7%, n = 173), Afrikaans (28.3%, n = 78) and Xhosa (8.7%, n = 24), respectively. The callers predominantly included Caucasian individuals (63.9%, n = 154), followed by individuals of Black (14.9%, n = 36), Mixed race/Coloured (14.9%, n = 36) and Indian descent (5.8%, n = 14), respectively. February and October were when the most contacts were made. Eighty six percent (n = 240) of contacts found out about the MHIC via Internet searches. Lastly, 63.9% (n = 177) of contacts were made via email/the website, followed by 34.3% (n = 95) by telephone. A large variety of disorders and topics were queried, with the most questions relating to diagnostics (e.g. depression, schizophrenia, anxiety disorders and obsessive-compulsive disorder), treatment avenues, cost, and referrals to suitable centres / clinicians. **Conclusion:** Help seekers from South Africa seem to be quite diverse. Information regarding reason for contacts suggest that MHIC serves an important role and that there is a need for information on mental health matters despite loads of information on

ABSTRACT NUMBER / ABSTRAKNOMMER: 28

Insights into Foetal Alcohol Spectrum Disorder: The Role of the Microbiome

A. S. Marais (Stellenbosch University), J. S. Womersley (Stellenbosch University), M. M. de Vries (Stellenbosch University), M. Parker (Stellenbosch University), N. Kitchin (Stellenbosch University), P. A. May (University of North Carolina and University of New Mexico), S. M. J. Hemmings (Stellenbosch University), S. Malan-Muller (Stellenbosch University), S. Seedat (Stellenbosch University)

Prenatal alcohol exposure can alter the development, function and regulation of neural and physiological systems, manifesting its effects through cognitive and behavioural deficits, changes in stress and immune function, and increased vulnerability to mental health disorders. Foetal Alcohol Spectrum Disorder (FASD) is an overarching term describing four diagnoses along a severity spectrum. Despite the fact that prenatal exposure to alcohol is one of the most preventable causes of birth defects, developmental disorders and mental retardation, the prevalence of FASD in South Africa is 13.5 to 20.8%, significantly higher than the global prevalence of 0.77%. The gut microbiome, the catalogue of the microbes and their genes in the human gut, plays a role in regulating neuroimmunity and metabolic and immunological development. Excessive alcohol intake results in alterations in the gut microbiome composition. Changes in the maternal gut microbiome may influence foetal development via transfer of bacteria through the placenta. The aim of this study is to assess gut microbial composition in women with and without alcohol use during pregnancy. A total of 78 pregnant women were recruited from Robertson and Wellington - 48 who consumed alcohol during pregnancy and 30 who did not. Microbial DNA extraction was performed on stool samples, followed by 16S rDNA sequencing of the V4 region. The Dada2 pipeline will be used to pre-process the fastq sequencing files and to create an operational taxonomic unit table. PhyloSeq will be used to assign taxonomy, create phylogenetic trees, and perform analyses to determine whether there are compositional differences between the two groups. R will be used to compute the statistical analyses of microbial composition and calculate \hat{H}^{\pm} -diversity and \hat{H}^2 -diversity. If differences in gut microbial composition between the two groups are identified, it is possible that the gut microbiome may serve as a mechanism whereby alcohol exposure affects foetal health.

ABSTRACT NUMBER / ABSTRAKNOMMER: 29

PTSD SYMPTOM SEVERITY, TRAUMA LOAD AND SLEEPING DIFFICULTIES IN TRAUMA EXPOSED, TREATMENT SEEKING ADOLESCENTS

Carissa van Aarde (Stellenbosch University), Jani Ntshing (Stellenbosch University), Soraya Seedat (Stellenbosch University)

BACKGROUND: Sleep disturbances are associated with various anxiety and trauma related disorders and specifically with post-traumatic stress disorder (PTSD). Two of the core symptoms of PTSD are recurrent distressing dreams about the traumatic event and difficulty falling or staying asleep (insomnia). Sleep is essential for functioning with poor sleep compromising cognitive, emotional and behaviour regulation. Sleep is also of particular importance for brain development and information processing in children and adolescents. The aim of this study was to determine if PTSD symptom severity and trauma load is associated with nightmares and insomnia in a sample of trauma exposed, treatment seeking adolescents. **METHODS:** Three hundred thirty-eight South African adolescents, between 12 and 18 years of age, exposed to at least one DSM-5 qualifying traumatic event, were assessed for PTSD related sleep difficulties using the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS). Childhood exposure to ten common trauma types was also recorded using the KSADS trauma checklist. PTSD symptom severity was measured using the Child PTSD Checklist (CPC). **RESULTS:** Gender ($B=.040, p=.465$), age ($B=.15, p=.072$) and grade ($B=-.11, p=.182$) were not significant demographic predictors in a regression model predicting PTSD symptom severity. Nightmares ($B=.14, p=.026$) and insomnia ($B=.25, p<.000$) were significant predictors of PTSD symptom severity. Trauma load ($B=.14, p=.14$) and perceived stress ($B=.51, p<.000$) were significant moderators of PTSD. The regression model explained 63.1% of the variance predicting PTSD symptom severity. **CONCLUSION:** Assessing and treating sleep difficulties related to PTSD in trauma exposed adolescents, in an effort to reduce the developmental impact of trauma on brain development and general functioning, should not be overlooked. Longitudinal studies may contribute to a better understanding of the long-term effects of trauma related insomnia and nightmares on mental and physical health outcomes.

ABSTRACT NUMBER / ABSTRAKNOMMER: 30

Caregiver and youth self-reported emotional and behavioural problems in Ugandan HIV infected children and adolescents

Eugene Kinyanda (MRC/UVRI Uganda Research Unit on AIDS), Jean B Nachega (University of Pittsburgh Graduate School of Public Health), Jonathan Levin (University of the Witwatersrand), Kenneth D. Gadow (Stony Brook University), Leigh van den Heuvel (Stellenbosch University), Richard S. Mpango (MRC/UVRI Uganda Research Unit on AIDS), Soraya Seedat (Stellenbosch University), Vikram Patel (Harvard Medical School)

IntroductionWe determined the prevalence of, and factors associated with, self-rated emotional and behavioural problems (EBPs) and assessed agreement between self-rated and caregiver rated EBPs in the Mental health among HIV infected Children and Adolescents (CA-HIV) in Kampala and Masaka, Uganda (CHAKA) study. Existing literature demonstrates that CA-HIV face increased mental health challenges related to a broad range of biological and psychosocial factors. There is scarce data on self-reported EBPs in CA-HIV.
MethodsIn a cross-sectional sample, caregiver reported EBPs were assessed with the Child and Adolescent Symptom Inventory-5 (CASI-5) and self-reported problems were evaluated with the Youth Inventory-4 (YI-4) in 469 adolescents aged 12-17 years and the Child Inventory-4 (CI-4) in 493 children aged 8-11 years. Logistic regression models were utilised to determine factors related to self-reported EBPs.
ResultsSelf-reported emotional problems (EPs) were present in 28.8% of the adolescents and were associated with caregivers being separated and having a lower level of education. Among adolescents, 14.5% had self-reported behavioural problems (BPs) and these were associated with caregiver unemployment and food insecurity. Self-reported EPs were reported by 36.9% of children and were associated with rural study sites, having missed school and caregivers having a lower level of education. There was only modest agreement (maximum $r = 0.29$) between caregiver and CA-HIV reported EBPs, with caregivers reporting more EPs whereas adolescents reported more BPs.
ConclusionsSelf-reported EBPs are frequently endorsed by CA-HIV and these problems are related to unique psychosocial factors. Including CA-HIV self-report measures can assist in identifying problems that caregivers may not be aware of, particularly BPs.

ABSTRACT NUMBER / ABSTRAKNOMMER: 31

The Effects of Metabolic Syndrome and Sleep on Neurocognitive Functioning

Leigh van den Heuvel (Stellenbosch University), Sanja Kilian (Stellenbosch University), Sharain Suliman (Stellenbosch University), Soraya Seedat (Stellenbosch University)

Background: The incidence of metabolic syndrome (MetS), a cluster of metabolic risk factors in a single individual, is increasing worldwide. Accumulating evidence has suggested sleep deprivation/fragmentation is one of the key factors involved in the onset and treatment resistance of MetS components. Moreover, bidirectional associations between sleep complaints and MetS have been described. Additionally, there is mounting evidence of the effect of MetS on cognitive functioning. **Aims:** In the present study we aim to assess whether MetS and sleep complaints are associated with clinically determined neurocognitive disturbances in a sample of participants with MetS symptoms, ranging from none to all criteria met.
Methods: Participants comprise 153, mixed race, individuals from the Western Cape province of South Africa. Sleep (Pittsburg Sleep Quality Index), neurocognition (Repeatable Battery for the Assessment of Neuropsychological Status) and anthropometric (MetS components) assessments were performed on all participants. A hierarchical regression model, including potentially confounding variables (IQ, demographic variables (e.g., age, gender), clinical variables (e.g., bmi, cholesterol) was then constructed. **Results:** The model was significant: Adjusted R square = 0.486; $F(13,110) = 9.952$, $p < 0.0001$. The demographic variables accounted for 32.3% of variability. This increased to 48.5% when the clinical variables were added. Sleep and metabolic criteria only added 0.1%.
Discussion: Although we did not find sleep and metabolic factors to significantly influence cognition when other factors were accounted for, further investigation into risk and outcome factors, such as these, may assist in the identification of mechanistic links, which may also improve management of patients who are at risk, thereby improving health outcomes.

ABSTRACT NUMBER / ABSTRAKNOMMER: 32

The clinical and social profile of patients with serious mental illness institutionalised at Lentegeur Hospital

Bonga Chiliza (University of Kwa-Zulu Natal), John Parker (Lentegeur Hospital), Lebo Phahladira (University of Stellenbosch), Schalk Wiehan Van Der Merwe (University of Stellenbosch)

Background. South Africa has a large number of psychiatric patients requiring long term care in state-run psychiatric hospitals. These patients are considered institutionalized. The WHO, in line with current global trends for mental health care, has been advocating deinstitutionalization and community based care. In South Africa, reasons why some patients will require long term inpatient care are unclear and poorly described. Objective. To assess the demographic, social and clinical profile of patients currently institutionalized at Lentegeur Hospital, a tertiary psychiatric hospital, in the Western Cape. Method. Clinical folders of patients in adult psychiatric units meeting inclusion criteria were reviewed in terms of demographics (age, sex, race), social factors (marital status, family support, residence), comorbidity (psychiatric and medical), current diagnosis and current pharmacological treatment. Results. We identified 35 patients fulfilling inclusion criteria. Of these institutionalised patients, 65.71% remained institutionalised due to being considered a high risk. The other 34.28% were not considered a high risk, but remained institutionalized for other reasons, including their families being unable to take care of them. Most institutionalised patients were male (78.1%), single (77.14%), of African descent (51.43%) and had a diagnosis of schizophrenia (57.14%). The most frequently prescribed medications were sodium valproate (65.71%), amisulpride (54.29%) and clozapine (48.57%). Conclusion. The high percentage of subjects that remain institutionalized for reasons other than being a high risk (34.29%) was our most troubling finding. Further research is necessary in order to ascertain predictors of long term institutionalization in the South African context. Key words: institutionalization; deinstitutionalization; mental health care; state-run psychiatric hospitals; long-term in-patient care

ABSTRACT NUMBER / ABSTRAKNOMMER: 33

Weight gain and metabolic change as predictors of symptom improvement in first-episode schizophrenia spectrum disorder patients treated over 12 months

Bonginkosi Chiliza (Department of Psychiatry, Nelson R Mandela School of Medicine, University of Kwazulu-Natal, South Africa), Freda Scheffler (Department of Psychiatry, Stellenbosch University, South Africa), Hilmar Luckhoff (Department of Psychiatry, Stellenbosch University, South Africa), Laila Asmal (Department of Psychiatry, Stellenbosch University, South Africa), Lebogang Phahladira (Department of Psychiatry, Stellenbosch University, South Africa), Robin Emsley (Department of Psychiatry, Stellenbosch University, South Africa), Sanja Kilian (Department of Psychiatry, Stellenbosch University, South Africa), Stefan du Plessis (Department of Psychiatry, Stellenbosch University, South Africa)

Background: Multiple studies have reported that treatment-emergent weight gain is associated with antipsychotic efficacy in schizophrenia patients treated with clozapine and olanzapine. However, few studies have investigated this relationship in first-episode patients treated with other antipsychotics. The aim of the present study was to investigate the relationships between weight gain and associated metabolic changes with psychopathology improvement in relation to age, sex, ethnicity, substance use, treatment duration and antipsychotic dose in first-episode schizophrenia spectrum disorder patients. Methods: This single site cohort study included 106 minimally treated or antipsychotic-naive patients treated with flupenthixol decanoate over 12 months. Psychopathology was evaluated using the Positive and Negative Syndrome Scale (PANSS) and BMI, fasting blood lipids and glucose were assessed at regular intervals. Hierarchical linear regression models were constructed to determine the effects of socio-demographic, clinical and metabolic factors as predictors of change in total PANSS score and factor-derived domains. Results: BMI change scores were inversely correlated with change in PANSS total ($R = -0.25$; $p = 0.011$), positive ($R = -0.23$; $p = 0.019$), depressive-anxiety ($R = -0.21$; $p = 0.031$) and

disorganized symptoms ($R = -0.32$; $p < 0.001$). Clinically significant weight gain was associated with a greater decrease in disorganized symptoms ($p = 0.034$). Hierarchical regression showed that increased BMI predicted improvement in global psychopathology and disorganized symptoms independent of age, sex, ethnicity, substance use, modal antipsychotic dose and treatment duration. **Conclusions:** Our findings suggest that the relationship between treatment-emergent weight gain and psychopathology improvement is not limited to patients treated with antipsychotics most associated with weight gain, and is not confounded by treatment duration and dose.

ABSTRACT NUMBER / ABSTRAKNOMMER: 34

The integration of neuroimaging and genetics to investigate antipsychotic treatment response

Emma Frickel (Stellenbosch University), Kevin O'Connell (Stellenbosch University), Louise Warnich (Stellenbosch University), Nathaniel McGregor (Stellenbosch University)

Antipsychotics remain the only available option for the treatment of schizophrenia, however only about 50% of patients respond to treatment. In order to address the need for new therapeutic strategies, a thorough understanding of the underlying mechanisms involved in antipsychotic response is required. Antipsychotic response can be largely attributed to genetic differences. Additionally, variations in brain structure have been implicated in differential treatment outcomes. However, pharmacogenetic, pharmacoepigenetic, and neuroimaging research has not progressed enough for the clinical utility of findings. As treatment outcome is complex and multifactorial, it would be prudent to start embracing more holistic study approaches. This would contribute to the potential for multi-faceted profiles of patients, and more effective therapeutic interventions. The integration of neuroimaging and genetics has gained traction as a relevant approach to investigate the aetiology of neuropsychiatric disorders such as schizophrenia. Imaging genetics may thus be an applicable strategy to investigate the complex underlying mechanisms of antipsychotic response. The aim of this study is therefore to explore the potential interplay between genetics and brain structural variation in terms of antipsychotic treatment outcome. The patient cohort comprises 103 South African first episode schizophrenia individuals, treated with a long-acting injectable antipsychotic. Fourteen genes that overlap between brain structure and antipsychotic response were identified and selected as candidate genes for the study. Genome-wide genotype data is available for the cohort, from which data for all genetic variation within the candidate genes has been extracted. Variants will be prioritised for investigation based on potential functional and regulatory mechanisms, using bioinformatics in silico prediction tools. Seven brain regions of interest (based on previous implication in antipsychotic response) have been identified in literature for inclusion in the analyses. Several measures of antipsychotic treatment response will also be considered, and linear mixed-effects regression models will be employed for all association analyses.

ABSTRACT NUMBER / ABSTRAKNOMMER: 35

Telomere-related gene expression in childhood trauma, depression and HAND

Georgina Spies (Stellenbosch University), Jacqueline Womersley (Stellenbosch University), Morne Du Plessis (Stellenbosch University), Patricia Swart (Stellenbosch University), Sian Hemmings (Stellenbosch University), Soraya Seedat (Stellenbosch University)

HIV infection can exert pathological effects on the central nervous system. Collectively referred to as HIV-associated neurocognitive disorders (HAND), these effects include symptoms such as neurocognitive impairment, emotional disturbance and motor abnormalities that exist along a spectrum of severity. The risk of developing HAND has been linked to the experience of depression and childhood trauma. Accelerated telomere shortening, an indicator of biological aging, has been independently associated with HIV, depression and childhood trauma, and previous studies in our laboratory have suggested that telomere shortening may act as a biomarker for HAND. The aim of this study is to investigate how the expression of two genes related to telomere length maintenance, telomere reverse

transcriptase (TERT) and poly(ADP-ribose) polymerase 1 (PARP1), is associated with HIV status, childhood trauma, depression and cognitive function. RNA will be extracted from blood samples collected from a cohort of HIV-negative (n = 95) and -positive women (n = 105) who experienced moderate to severe childhood trauma. Gene expression will then be assessed by polymerase chain reaction using primers specific for TERT and PARP1. Regression models will be used to investigate the relationships between cognitive function, HIV, childhood trauma, depression and TERT and PARP1 expression. The data generated will supplement our current research on the psychological and genetic determinants of HAND in South African women.

ABSTRACT NUMBER / ABSTRAKNOMMER: 36

Functional MRI analysis of the auditory cortex in HIV infected children

Barbara Laughton (Stellenbosch University), Ernesta Meintjes (University of Cape Town), Haley Elliott (Stellenbosch University), Keri Woods (University of Cape Town), Marcin Jankiewicz (University of Cape Town), Peter Torre III (San Diego State University), Tzy-Jyun Yao (Harvard T.H. Chan School of Public Health)

Introduction: Perinatally HIV infected children have a higher prevalence of hearing loss than HIV uninfected children [1]. The underlying mechanisms for the high prevalence of hearing loss in HIV infected children are not well understood, nor have there been studies using neuroimaging of the central auditory system in HIV infected children. **Methods:** We acquired data from 77 African and Coloured children (mean age $\hat{\pm}$ sd: 11.47 $\hat{\pm}$ 0.37 years): 42 vertically infected with HIV (35 African, 19 males) and 35 uninfected controls (25 African, 22 males). All scans were performed on a 3T Skyra (Siemens, Erlangen, Germany). Children were scanned while hearing pure tones of 500, 1500 or 4000 Hz, monaurally, or silence. 2s tones (or silence) were interleaved with 2s rest intervals during which scanner noise occurred due to data acquisition. The child heard each tone 8 times in each ear, and 15 silent stimuli, in randomized order. **Functional MRI analyses** were performed using SPM12 [2]. Preprocessing included correction for different slice acquisition times, spatial smoothing, and motion correction. Analyses were performed inside a mask of the auditory cortex (including Brodmann areas 22, 41 and 42), using the general linear model with predictors based on known experimental blocks convolved by the canonical hemodynamic response function. Activation between controls and HIV infected children were compared using second level analyses. Cluster-level thresholding was used to determine minimum cluster-size of significant regions with $p=0.005$ and $\hat{I}\pm=0.05$. **Results:** After controlling for sex and race, HIV infected children show less activation of the left primary auditory cortex (Brodmann area 41) when hearing tones (of all frequencies) than control children (mean percent signal change $\hat{\pm}$ sd: controls = 0.25 $\hat{\pm}$ 0.74; HIV = -0.33 $\hat{\pm}$ 0.68, $t(75)=3.59$, $p<0.001$). **Conclusion:** HIV affects activation in the auditory cortex when listening to pure tones.

ABSTRACT NUMBER / ABSTRAKNOMMER: 37

Childhood trauma associated white matter abnormalities in first-episode schizophrenia

Bonginkosi Chiliza (University of KwaZulu Natal), Frederika Scheffler (Stellenbosch University), Jean-Paul Fouche (University of Cape Town), Laila Asmal (Stellenbosch University), Paola Dazzan (King's College London), Robin Emsley (Stellenbosch University), Sanja Kilian (Stellenbosch University), Soraya Seedat (Stellenbosch University), Stefan du Plessis (Stellenbosch University)

Schizophrenia is associated with brain connection irregularities within and between brain regions. Childhood trauma increases the risk of schizophrenia suggesting that the relationships between childhood trauma and brain connectivity requires further investigation. Here, we examine the relationship between childhood trauma (as measured by the Childhood Trauma Questionnaire) and fractional anisotropy (FA) in 54 minimally treated first-episode schizophrenia patients and 51 community matched controls. Patients who experienced high levels of trauma had significantly lower FA in the inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), and inferior fronto-occipital

fasciculus (IFOF) compared to controls who experienced high levels of childhood trauma. A history of childhood sexual abuse in patients was associated with lower FA in the IFOF, ILF, SLF and forceps major compared to patients without a history of sexual abuse. However, patients who had experienced childhood emotional neglect had higher FA in the right SLF compared to patients with low levels of emotional neglect. Our findings highlight altered cortico-limbic circuitry in first-episode schizophrenia patients compared to controls and differential effects of childhood emotional neglect and sexual abuse on white matter in patients. Although stress-related WM pathways appear to be involved in both schizophrenia and otherwise healthy controls previously exposed to childhood trauma, the pattern of disruption of WM integrity in FES patients appears to be distinct.

ABSTRACT NUMBER / ABSTRAKNOMMER: 38

Accelerated theta-burst rTMS for depression in South Africa: A series of nine cases

Dr. Leigh van den Heuvel (Stellenbosch University - Medical Campus), Erine BrÄcker (Stellenbosch University - Medical Campus), Prof Soraya Seedat (Stellenbosch University - Medical Campus)

This case series documents local experience using accelerated theta-burst repetitive transcranial magnetic stimulation (rTMS) as a supplementary treatment for depression in both Major Depressive Disorder (MDD) and Bipolar Disorder (BD). Nine consenting patients (MDD=7; BD (major depressive episode)=2) each received the accelerated theta-burst protocol consisting of three magnetic pulses delivered 20ms apart and repeatedly delivered every 200ms resulting in a 5Hz theta rhythm over the left dorsolateral prefrontal cortex (DLPFC). Treatment was comprised 20 sessions delivered over 8 days. Accelerated theta burst rTMS treatment provides more stimuli over a shorter duration of time, thus potentially increasing feasibility and cost-effectiveness. Improvement was monitored using the Centre for Epidemiological Studies Depression Scale (CES-D) and the Clinical Global Impression scale (CGI) at baseline, day 5 and at day 8 of rTMS treatment. All patients remained on their prescribed medication for the duration of rTMS treatment. We performed a Wilcoxon matched pairs signed rank test to determine whether there was a difference in scores from baseline to post treatment. The CES-D scores decreased significantly from baseline (Mdn 38.0; IQR 31.0; 51.0) to post-treatment (Mdn 17.0; IQR 11.0; 28.5; $Z = -2.55$, $p = 0.011$). The CGI severity scores also decreased significantly between baseline (Mdn 4.0; IQR 4.0; 5.0) and post-treatment (Mdn 3.0; IQR 3.0; 4.0; $Z = -2.43$, $p = 0.015$). Five patients demonstrated at least a 50% symptom reduction on the CES-D. The most commonly reported adverse effect was mild headache which lasted a few hours during and post rTMS treatment. The caveat to these findings is that this was a small case series without a control arm, however, the findings suggest that the accelerated theta burst rTMS protocol for depression was well tolerated with most patients also experiencing symptomatic improvement by day 8.

ABSTRACT NUMBER / ABSTRAKNOMMER: 39

Exploring Parameters of Unplanned Pregnancy in South African Women with Mental Illness

Dana Niehaus (University Stellenbosch), Elsa du Toit (University Stellenbosch), Esme Jordaan (Medical Research Council), Jukka Leppanen (University of Tampere), Liezl Koen (University of Stellenbosch)

Much has been written about the possible causes and adverse consequences of unplanned pregnancy, yet it remains a common phenomenon, especially among women from lower socio-economic backgrounds. During our research with a group of pregnant South African women with diagnoses of psychiatric illness, we became increasingly aware of the complexities and subtleties surrounding pregnancy planning and the dynamic nature of a woman's relationship towards her pregnancy. We realised that simply categorising pregnancies as either planned or unplanned is insufficient and possibly even detrimental, as reducing a multi-dimensional concept to a dichotomous variable over-simplifies a very complex matter. Therefore, we went in search of a more nuanced tool to measure aspects of pregnancy planning and found it in the London Measure of Unplanned Pregnancy (LMUP). In this quantitative descriptive study, we compared existing literature regarding the parameters included in

the LMUP questionnaire with the results from our study cohort (170 women who completed the LMUP), in order to establish to what extent general findings about the various aspects of pregnancy planning also apply to women with mental illness living in a developing country. Results revealed similar findings as various other studies in terms of contraception use, pregnancy timing, pregnancy intent, desire to have a baby, partner involvement and health-promoting behaviours during pregnancy and highlight the importance of gaining a more nuanced insight into women's fertility circumstances in order to stage meaningful interventions, especially among vulnerable women, such as those living with mental illness and socio-economic difficulties.

ABSTRACT NUMBER / ABSTRAKNOMMER: 40

Neurocognitive norms for people living with HIV/AIDS in low-resource countries: A scoping review

Dr. Georgina Spies (Stellenbosch University), Dr. Sharain Suliman (Stellenbosch University), Mr. Edward Ackling (Cardiff University), Mrs. Melanie Cilliers (Stellenbosch University), Prof. Soraya Seedat (Stellenbosch University)

HIV is capable of inducing neurological injury, which is characterised by a progressive decline in neurocognitive functioning. Early identification of HIV-related cognitive decline is crucial and can be achieved through a reliable and valid neurocognitive assessment of HIV-associated neurocognitive disorders (HAND) incorporating the multiple domains of cognitive functioning that are impacted by HIV infection. However, most research on neurocognitive battery development and validation has been carried out in developed countries. Since cultural and educational differences contribute to cognitive performance, norms identified in developed countries cannot be generalised to resource limited settings. The lack of appropriate normative data in resources limited countries potentially undermines the accuracy of interpretation of neurocognitive performance and can contribute to the inaccurate diagnostic classification of HAND. The present study aims to review normative data generated in resource-limited countries for test batteries to measure cognitive decline in HIV-positive patients. This was done by conducting a scoping review on the current available literature. An electronic search was conducted in five bibliographic databases to identify potentially relevant studies. Gray literature and reference bibliographies of identified full text articles were also used to identify possible studies. Two reviewers independently screened the titles and abstracts of all articles obtained from the database searches to assess their potential relevance for inclusion. The study aims to summarize the research literature, identify research gaps, and to make recommendations for future research relating to this topic.

ABSTRACT NUMBER / ABSTRAKNOMMER: 41

An integrative, multi-omics approach to identify genetic risk and expression quantitative trait loci associated with PTSD in a South African Mixed Ancestry population.

Cathryn Lewis (Department of Medical and Molecular Genetics, King's College London), Leigh van den Heuvel (Department of Psychiatry, Stellenbosch University), Patricia C. Swart (Department of Psychiatry, Stellenbosch University), Sian M.J. Hemmings (Department of Psychiatry, Stellenbosch University), Soraya Seedat (Department of Psychiatry, Stellenbosch University)

South Africa has a high rate of traumatic events, which leaves susceptible individuals vulnerable to developing posttraumatic stress disorder (PTSD). Symptoms depend on the severity of exposure and the type of traumatic event as well as intrinsic factors such as genetic heritability and polygenicity. The genetic factors underlying the susceptibility (or resilience) towards developing PTSD are unknown and are further complicated by gene-environment interactions. Genome-wide association studies (GWAS) have been used to investigate the multiple genetic variants, each with modest effect sizes, that contribute to psychiatric disorders such as PTSD. The sum of the identified single nucleotide

polymorphisms (SNPs) and environmental interactions can be then used for polygenic risk score (PRS) analyses to provide a measure of genetic liability towards developing a complex trait. In addition, GWAS data can be used to identify associated functional genetic variants (expression quantitative trait loci (eQTLs)) when integrated with gene expression data (RNAseq). This project aims to establish an integrative, multi-omics approach to identify genetic risk and functional genetic variants associated with PTSD in a South African Mixed Ancestry population of PTSD patients and trauma-exposed controls. PRS analyses will be conducted using PLINK software and the GWAS (n = 300) and RNAseq (n = 120) data will be integrated using a publicly available algorithm such as matrixQTL in R, a statistical programming language, to identify eQTLs. We will present the results from these analyses, which will provide insight into the genetic underpinnings of PTSD. Further, this project is expected to build and validate a bioinformatics and statistical pipeline that can then be employed to determine genetic risk and functional genetic variants associated with other complex psychiatric disorders in the South African population.

ABSTRACT NUMBER / ABSTRAKNOMMER: 42

A prospective longitudinal study of the impact of pre- and postnatal maternal mental health disorders on the neurodevelopmental trajectories of children during the first 18 months. A Study Protocol

Dr M Unger (Stellenbosch University), Marlette Burger (Stellenbosch University), Prof C Einspieler (Medical University of Graz), Prof DJH Niehaus (Stellenbosch University)

BACKGROUND: Mental health disorders are one of the non-communicable diseases that contribute the most to the overall worldwide burden of disease. Worldwide about 10% of pregnant women and 13% of women who have given birth experience some type of mental health disorder and in low- and middle-income countries, ante- and postnatal mental disorders are even higher. A growing body of evidence from high-income countries links ante- and postnatal maternal mental health disorders with adverse effects on different aspects of infant neurodevelopment in the cognitive, behavioural and psychomotor domains.**METHODS/DESIGN:** The present study is a prospective longitudinal cohort design with repeated measures in which pregnant women are followed from the 1st trimester of pregnancy until their child is 18 months old. We plan to investigate the effect of antenatal and postnatal exposure to maternal mental health disorders on the early neurodevelopmental outcome of infants at 12-15 weeks postterm as well as at 6 and 18 months of age.**STUDY POPULATION AND SITE:**The study sample will be recruited from the catchment area of the northern suburbs of Cape Town. Pregnant mothers and their babies (n=250) attending Stikland Hospital's Maternal Mental Health Clinic will be eligible for inclusion in the study. **DISCUSSION:**The World Health Organization found that there is an extensive lack of awareness about maternal mental health and its impact on child development in resource-constrained, low- and middle income countries. Mothers and children from lower socio-economic areas in the Western Cape are disproportionately exposed to multiple and cumulative socioeconomic and environmental risk factors which may compromise the child's development. This will be the first study to evaluate the effect of ante- and postnatal maternal mental health disorders on different aspects of neurodevelopmental trajectories (namely cognitive, fine and gross motor and language) in young children in the Western Cape, South Africa.

ABSTRACT NUMBER / ABSTRAKNOMMER: 43

White matter changes in the corpus callosum in adults with HIV as seen by diffusion tensor imaging: a systematic review

Fatima Ahmed (Stellenbosch University), Georgina Spies (Stellenbosch University), Soraya Seedat (Stellenbosch University), Stefan du Plessis (Stellenbosch University)

Introduction: There has been no recent reviews of DTI studies in adults with HIV. Given all the advancements in DTI that have been made since 2008 and the well-known clinical changes in white

matter this is surprising. We undertook a review of DTI studies that utilized this imaging modality to investigate HIV disease progression in adults and to address the question of whether white matter is affected early on the disease or only evident at a later stage of disease progression. We felt it prudent to carry out a review determining the white matter changes associated with HIV disease. The reason for looking at DTI is because it is a more advanced tool, as it looks at diffusion parameters that are closely related to white matter integrity. Method: We used search engines Science Direct, Web of Science and PubMed. The search terms used were "HIV" coupled with "adults", "corpus callosum" and "DTI" or "Diffusion Tensor Imaging". We focused on DTI studies, focusing on the corpus callosum that included participants who had been diagnosed with HIV. We included studies that had both a patient and a non-HIV healthy control group, to allow us to clearly view any potential differences in white matter integrity between the HIV and healthy control groups, thereby excluding patient only studies. Results. We found 454 articles that met our search criteria, the total of included studies was 37 studies. Conclusion: As most studies in this review used FA as the measure of diffusion, it may be beneficial to examine MD also, as studies examining the diffusivity of white matter integrity in HIV (e.g., Pfefferbaum et al, 2009), have shown that despite no decrease in FA, there was an increase in diffusivity, suggesting that diffusivity may be a more sensitive marker of HIV-related neuropathology.

ABSTRACT NUMBER / ABSTRAKNOMMER: 44

Review on Trace Element Changes in Brain Tumors

Ben J Page (Stellenbosch University), Karen Cilliers (Stellenbosch University)

Trace elements have been implicated in the progression of cancer, since concentrations differ between cancerous and non-cancerous tissue, as well as between cancer types. A large number of studies focused on different cancer types; however, few studies have been conducted on brain tumors. Thus, this study aims to review the available literature on brain tumor elements, and to identify gaps in the literature. Tumor tissue has been compared to tissue from control brains, and to adjacent healthy tissue. Compared to control brains, tumors had significantly higher concentrations of arsenic, cerium, gadolinium, lanthanum, lutetium and thorium. Compared to adjacent tissue, tumors indicated increased magnesium, decreased copper, and contradicting results for zinc. Furthermore, different malignancy grades have been compared; the higher the malignancy grade, the lower the calcium, cadmium, iron, phosphorus and sulfur concentration, and the higher the lead, manganese, mercury, and zinc concentration. Carcinogenesis alters the elemental composition of cancerous and adjacent tissue. Therefore, by identifying the element changes, cancerous tissue can be identified, distinguished from adjacent non-cancerous tissue, classified into different cancer types, and categorized into different malignancy grades. Furthermore, information on the concentration and distribution of trace elements could assist with understanding the mechanisms associated with cancer and carcinogenesis. Trace elements have been considered as therapeutic agents; however, more studies need to be conducted to ascertain the effectiveness of these agents. In conclusion, different aspects of element concentration changes have been assessed. Trace element concentrations differ between cancerous and non-cancerous tissue, different cancer types, and different malignancy grades. Since studies research different aspects, it is impossible to compare data from these studies, and available data is still considerably inconclusive. Ideally, future studies should include a sufficient samples size, compare different tumor types, and compare tumors with healthy adjacent tissue as well as with samples from unaffected matched brains.

ABSTRACT NUMBER / ABSTRAKNOMMER: 45

Prognostic Value of Motor Timing in Treatment Outcomes and Relapse in Patients with Alcohol- and/or Cocaine Use Dependence in a Rehabilitation Program

Martin Kidd (Stellenbosch University), prof Soraya Seedat (Stellenbosch University), Susanne Young (Stellenbosch University)

Introduction: Individuals with SUD often have cognitive deficits in multiple domains, with recovery times of up to one year. These deficits influence treatment outcomes and abstinence. In addition, motor timing deficits have been found in SUD, but to our knowledge, timing deficits have not been investigated with regard to treatment outcome and relapse. Methods: This prospective study tested the theoretical basis for prognostic indicators in SUD with regards to motor timing. The study sample consisted of 74 abstinent in-patients at a private treatment programme for drug/alcohol dependence at the Momentum Mental Healthcare South Africa clinic in Somerset West, South Africa, diagnosed with alcohol and/or cocaine dependence. Participants were tested at three points (i) Within 72 hours of the start of the treatment programme (ii) after completion of the treatment programme at eight weeks (measure of treatment response) through filling out self-report questionnaires and experimental motor task testing, and (iii) a third visit followed through a telephonic interview at 12-months. Results: Motor timing alone predicted 27 percent of the variance in total score change on the Alcohol Self-Efficacy Scale. Specifically, spatial errors, synchronisation errors and IRI errors at baseline predicted self-efficacy at treatment completion. With regard to motor timing, change in cocaine self-efficacy scores at treatment completion explained 25 percent variance. Specifically, spatial errors and contact times were predictive at very high tempi (300m/sec). The sample size at 12 months did not allow for further analyses of prognostic values. Conclusions: This research provides novel insights on the prognostic value of treatment outcomes and relapse in SUD. To our knowledge, it is the first study of its kind. The results of this investigation show us that motor timing holds prognostic value with regard to treatment outcomes. Motor timing predictors for relapse remain unclear. This requires investigation going forward.

ABSTRACT NUMBER / ABSTRAKNOMMER: 46

Mental health information in the palm of your hand

Christine Lochner (MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, University of Stellenbosch, South Africa), Dan J. Stein (Department of Psychiatry and Mental Health, University of Cape Town, South Africa), Janine Roos (Mental Health Information Centre of Southern Africa), Mandi Broodryk (MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, University of Stellenbosch, South Africa)

Mental illness occurs in 30% of South Africans during their lifetime. Despite being highly treatable disorders far too few people receive optimal care. Challenges include stigmatization of mental illness and a lack of easy access to mental health information and professionals. The Mental Health Information Centre (MHIC) of Southern Africa aims to address these challenges through a website (www.mentalhealthsa.org.za) and online database of local mental health service providers. Through their website the MHIC also aims to build sustainable partnerships with mental health experts (service providers, volunteers, community organizations and institutional and corporate partners). By logging all calls and contacts to the MHIC (a combination of emails, phone calls and website messages) daily, we are able to know where we need to concentrate our efforts of delivering a service to the community, such as updating the website with the most recent mental health information and by motivating professionals to register on the database. Worldwide, over the last couple of years, there has been a sharp increase in the use of smartphones to access information fast. In 2014, it was estimated that 9.7 million South Africans were using smartphones with a projected increase to 25.47 million users in 2022. So the question can be raised whether this phenomenon has changed the way in which mental health information is sought. Previously, enquiries to the MHIC call centre were mainly made telephonically. The current status of contacts shows that 63.9% of enquiries to the MHIC are being made via email or the website, with more than half of the website contacts originating from smartphones, specifically Android, Blackberry and iOS devices. Smartphones and other mobile devices have the potential to contribute positively to accurate information and early referrals.

ABSTRACT NUMBER / ABSTRAKNOMMER: 47

The usefulness of 18 F-DOPA PET scan in challenging conditions at our movement disorder clinic

Mohamed Khider (Stellenbosch University)

BACKGROUND: Differentiating conditions characterized by degeneration of nigrostriatal pathways from conditions with features of Parkinsonism due to other causes or other tremor conditions may sometimes be difficult on clinical grounds, especially in the early stages of the disease, or atypical presentations. 18 F-DOPA PET scan is an investigation that can determine the degree of affectedness of presynaptic dopaminergic activity. The aim of this study was to determine the usefulness of 18 F-DOPA PET scan in challenging conditions at our movement disorder clinic. **METHODS:** A retrospective analysis was carried out for patients that underwent 18 F-DOPA PET brain scans between 2016-2017. The patients' medical records were assessed for the course of illness and length of follow-up. 18 F-DOPA PET scans were requested when there was uncertainty about the clinical diagnosis. Qualitative interpretation of the scan was performed based on the visual assessment of the uptake in the basal ganglia. A scan was considered abnormal when the visual assessment revealed a relative decrease in 18F-DOPA uptake in the striatum. The final clinical outcome was based on progression at follow-up and response to levodopa or other medications such as primidone. A correlation of the scan findings with the final clinical outcome was performed using statistical agreement test. **RESULTS:** Twenty-four patients were included (mean age, 57.7 years; 13 men, 11 women, mean follow up 13 months). Of the 24 scans, eight scans were reported as normal, while 16 scans were reported as abnormal. There was a good agreement between the scan results and the final clinical outcome ($\kappa = 0.80$). The scans were normal in essential tremor cases, dystonic tremor and drug induced Parkinsonism. **CONCLUSION:** When there is uncertainty about the diagnosis, 18 F-DOPA PET scan is a useful investigation to differentiate conditions due to nigrostriatal degeneration from those with overlapping clinical presentations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 48

Exploring parental reflective function and the quality of mother-infant interaction in a sample of women with peri-partum psychosis

Astrid Berg (UCT / Stellenbosch University), Dana Niehaus (Stellenbosch University / Stikland Hospital), JuanÃ© Voges (Stellenbosch University / Stikland Hospital)

The purpose of this exploratory study is to examine the impact of peri-partum psychosis on parental reflective function and quality of mother-infant interaction in a South African sample at high risk of developing attachment difficulties. Besides the effects of physical separation, attachment difficulties may arise from other maternal factors, such as a lack of reflective capacity or negative symptoms affecting the warmth with which she interacts with her child. This study will examine the quality of mother infant interaction to determine how the presence of psychotic symptoms during pregnancy or shortly after delivery affects aspects like maternal sensitivity, child social involvement and dyadic engagement. Ultimately, the study aims to investigate the association between psychosis, parental reflective functioning and quality of parent-infant interaction. The study follows a descriptive, observational design. Mothers were recruited if they experienced psychotic symptoms during pregnancy or within six months postpartum. Demographic information and psychiatric history was collected. Parental reflective function was assessed by the Parent Development Interview and quality of mother-infant interaction in an unstructured play interaction was coded with the Coding Interactive Behaviour. Eight participants, aged between 22 and 44, with diagnoses of Bipolar disorder, schizophrenia and MDD with psychosis were recruited. Parental reflective functioning showed marked variation with scores approaching and exceeding ordinary reflective functioning, typically found in non-clinical populations. Play interactions were mostly parent-led, with some surprising findings, such as a lower than anticipated frequency of parental negative affect, moderate maternal sensitivity and wide variation in scores for infant withdrawal noted. The results found in this small sample of mothers with peri-partum psychosis have presented unexpected results, both in terms of higher than anticipated

capacity for parental reflective functioning and interaction quality with their infants. Possible implications for future interventions will be discussed.

Theme 4 / Tema 4
Non Communicable Diseases /
Nie-oordraagbare Siektes

ORAL PRESENTATIONS / REFERATE

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

Clinical features and disease severity of ALS in the different ethnic population groups in the Western Cape province.

Franco Henning (Stellenbosch University), Kireshe Naidu (Stellenbosch University)

Introduction: Amyotrophic lateral sclerosis is a progressive neurodegenerative disorder, which can be subdivided into spinal, bulbar or respiratory onset. There is currently a paucity of data regarding ALS in Africa, and in general within black populations. We studied the demographic and clinical characteristics of ALS within the Western Cape province, which provided an ideal ethnically diverse study population. **Methods:** Data was collected prospectively as part of an ongoing epidemiological study of ALS in the Western Cape. Patients fulfilling the revised El Escorial criteria for ALS were included between 1 July 2014 and 31 January 2018. Demographic data (gender, ethnicity and age at onset) as well as clinical information regarding mode of presentation and disease progression were collected. **Results:** A total of 140 patients were included, with white South Africans constituting the largest ethnic group (51%), followed by mixed ancestry (37%), black (11%) and Asian (1%). There was a male predominance (60%), and the median age of onset was 57. Age of onset was youngest in the black population (median 47 years), followed by the mixed ancestry population (median 52 years), and oldest in the white population (median 65 years). The majority had spinal onset disease (81%), followed by bulbar onset (17%), and respiratory onset (2%). The median ALSFRS-R delta score, a measure of disease progression, was 0.74 for the entire cohort, but slightly higher in the black group (0.87). **Conclusion:** Our findings demonstrate that the dominant onset type (spinal) is similar amongst the ethnic subgroups. The age of onset appears to be youngest within the black population, oldest within the white population and in between these two groups in the mixed ancestry population. The rate of progression may be slightly higher in black patients; however, longitudinal data on the clinical course would be a more accurate measure to verify this.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Racial variation of QRS-duration for CRT qualification amongst systolic heart failure patients: why is the door still closed for Black patients?

Dale Peterson (Department of Medicine, Stellenbosch University & Tygerberg Academic Hospital), Marshall Heradien (Department of Medicine, Stellenbosch University & Tygerberg Academic Hospital), Paul Brink (Department of Medicine, Stellenbosch University & Tygerberg Academic Hospital)

BACKGROUND In sub-Saharan Africa decompensated heart failure is the commonest primary diagnosis for patients admitted to hospital with heart disease. Recent ESC guidelines propose that patients on optimal medical therapy, in sinus rhythm with a left bundle branch block (LBBB) and QRS-duration ≥ 150 ms are ideal candidates for cardiac resynchronization therapy (CRT). It is unknown whether race is associated with QRS-duration and LBBB prevalence. **METHODS** Consecutive patients with a new diagnosis of Heart Failure with a reduced Ejection Fraction (HFrEF) and dilated cardiomyopathy (DCMO) were enrolled. Race was self-reported. The cohort was sub-stratified into black and non-black racial groups and the predictors of response to biventricular therapy namely QRS duration, left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF). Means (SD) were compared with Student's t-test and relative proportions with Fisher's exact test. A p-value of <0.05 was considered significant. **RESULTS** Amongst 44 patients with a DCMO and HFrEF, medical treatment did not differ significantly, but ischaemic heart disease was more prevalent amongst white (n=15) than black (n=14) patients (77% vs. 57%; p=0.035). QRS duration was significantly shorter in blacks compared to whites (100.71ms vs. 127.15ms; p=0.0001). LBBB was less prevalent amongst black than white patients (7% vs. 53%; p=0.01). **CONCLUSION** Based on the QRS duration and LBBB prevalence,

black South African DCMO and HFrEF patients will seldom qualify for potentially life-saving CRT. Larger studies are urgently needed to investigate this relevant treatment issue.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

The state of our health: Are health workers at risk of Diabetes Mellitus?

Amanda Beukes (Tygerberg), Ankia Coetzee (Tygerberg Hospital), Jocely Hellig (Tygerberg), Mari van de vyfer (Tygerberg), Reinhardt Dreyer (Tygerberg), Roshni Mistry (Tygerberg), Salaamah Solomons (Tygerberg)

Background: The increasing prevalence of type 2 diabetes mellitus (DM) is predicted to overburden healthcare systems. Health workers (HW) are not only critical for the optimal functioning of health systems but also often serve as role models for their communities. HWs can, by raising awareness of DM, inspire wide reaching lifestyle changes. Since personal health has been shown to influence the way in which HWs advocate, it is essential that the risk factors associated with DM are identified and addressed in this population. Objectives: The objectives of this study were to a) determine the 10-year risk of HW to develop DM and b) to identify modifiable risk factors as targets for preventative strategies. Methods: Retrospective data analysis. A total of n=323 HWs at Tygerberg hospital, Western Cape, South Africa were screened for DM risk factors as part of an awareness campaign that was held on 14 November 2017. The 10-year DM risk was calculated using the validated "Test2prevent" calculator. Results: Eighty nine percent (n=288; 89%) of participants were female; under the age of 45 (n=184; 57%) and employed in the field of nursing (n=145; 49%). The majority (n=283; 88%) had elevated BMI (≥25 kg/m²) and almost two thirds (n=199; 59%) were obese (BMI ≥30 kg/m²). Low levels of physical activity coincided with daily consumption of (n=249; 77%) sugar sweetened beverages. More than half (n=168; 52%) of the workers had an elevated risk, with the prevalence of DM predicted to be 15% in 10 years' time. Conclusion: In HWs, a high prevalence of modifiable risk factors for DM was observed, with a concerning number of individuals at risk for future DM. Public health facilities should address the risk factors identified to prevent DM in the health workforce. Keywords: Diabetes mellitus; Health workers; obesity; risk factors; screening; HbA1c

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

An investigation of the potential neuroprotective role of curcumin in cellular models of Parkinson's disease

Annika Neethling (Stellenbosch University), Celia van der Merwe (University of Cape Town), Jonathan Carr (Stellenbosch University), Shameemah Abrahams (Stellenbosch University), Soraya Barden (Stellenbosch University)

Background: Parkinson's disease (PD) occurs in 1-2% of individuals older than 60 years and is recognized by resting tremors and bradykinesia. Potential mechanisms of PD include mitochondrial dysfunction and abnormal protein processing. Currently, no cure exists for PD while drug treatments only treat the symptoms and not the underlying cause of the neurodegeneration. Therefore, there is a need for a therapy directed at the underlying PD mechanisms. Curcumin is a polyphenol, attributed with antioxidant and anti-inflammatory properties. We recently showed that curcumin protected against mitochondrial dysfunction and cell death in a PINK1 knockdown SH-SY5Y cell model [1]. The aim of this study was, therefore, to follow-up on the PINK1 cell model and investigate the protective effect of curcumin in various cell lines including HEK293 cells and PD patient-derived fibroblasts. Methods: Neuroblastoma SH-SY5Y and human kidney HEK293 cells were commercially available. Dermal fibroblasts were obtained from mutation-positive PD patients. A MTT assay was used to determine the effect of paraquat and curcumin treatment on cell activity. Concentration and treatment duration curves for paraquat and curcumin treatments were performed. Results: We previously showed that paraquat decreased cell viability and curcumin (2 µM) rescued viability in the PINK1 SH-SY5Y cell model [1]. In the current study, curcumin post-treatment group (5 µM) showed increased viability in paraquat-

exposed HEK cells ($p=0.0003$). For the fibroblasts, we found that a high paraquat concentration (>10 mM) was needed to decrease cell viability. Studies are in progress to determine whether we see the same protective effect of curcumin in the fibroblasts. Conclusion: We previously showed that curcumin was protective in SH-SY5Y cells and now is also protective in HEK cells. Therefore, it would be interesting to observe the effect in patient fibroblasts. Successful results for curcumin in fibroblasts would further confirm its protective effect against PD pathology.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Transforming the workplace environment to prevent non-communicable chronic diseases: Participatory action research in a South African power plant

Darcelle Schouw (Division of Family Medicine and Primary Care, Stellenbosch University), Robert Mash (Division of Family Medicine and Primary Care, Stellenbosch University), Tracy Kolbe-Alexander (School of Health and Wellbeing, University of Southern Queensland, Ipswich, Australia)

ABSTRACT Background The workplace is highlighted as an important setting for the prevention of non-communicable diseases (NCDs). The policies for transformation of the workplace environment have focused more on “what to” do and less on “how to” do it. The aim of this study was to learn how to transform the workplace environment in order to prevent and control the risk factors for NCDs amongst the workforce at a commercial power plant situated along the coast in Cape Town, Western Cape. Methods The study design utilised participatory action research (PAR) in the format of a cooperative inquiry group (CIG), in which the researcher and participants used a cyclical process of planning, action, observation and reflection over a 2-year period. The group used outcome mapping to define the vision, mission, boundary partners and strategies required; to achieve the desired changes in transforming the workplace environment to prevent NCDs. At the end of the inquiry, the group reached a consensus on their key learning. Results Substantial change was observed in the four boundary partners: catering services (78% of progress markers achieved), sport and physical activities (75%), health and wellness services (66%), and managerial support (65%). Amongst a 10-point consensus on key learning, the major insights included: leadership; diverse composition and functioning of the CIG; value of outcome mapping in terms of a clear design and monitoring process; importance of managerial engagement in personal and organisational change; and making healthy lifestyle an easy choice. Conclusion This study demonstrates the potential value of improving health and wellness in the workplace and gives guidance on how to do this. Future studies will evaluate changes in the risk profile of the workforce as well as the costs and consequences for the organisation. Key words Non-communicable diseases, workplace environment, transformation, participatory action research, diversity, leadership

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

Assessment of comorbid conditions in hormone-positive postmenopausal breast cancer patients using the updated Charlson Comorbidity Index

Karin Baatjes (University of Stellenbosch), Maritha Kotze (University of Stellenbosch), Zelmarië Beselaar (University of Stellenbosch)

Introduction: The prevalence of cancer and comorbidities increase with advancing age. Scoring indices, such as the Charlson Comorbid Index (CCI), can aid clinician decision-making and prognostication in the elderly. The present study investigated the prevalence of comorbid conditions of the updated CCI in postmenopausal breast cancer patients, as well potential associations with biochemical markers and genotyping data. **Methods:** Clinical, biochemical and genetic data of postmenopausal breast cancer patients, aged 50-80 years old, recruited from Tygerberg Academic Hospital Breast clinic into study S13/05/103, were analysed. Further information was obtained from hospital records and lifestyle information were self-reported by patients in a questionnaire. Basic body measurements were taken to determine their body mass index (BMI). **Results:** Of the 122 participants, 14 had a CCI score greater

than 0, indicating comorbid diseases. Renal and chronic pulmonary disease were the most prevalent, identified in 35% each, followed by congestive heart failure (29%). Up to 66% of participants with the aforementioned diseases had a BMI above normal limits. No participant with rheumatic conditions had an increased BMI. Increased homocysteine (Hcy) levels were associated with a lower BMI in the comorbid population, with hetero- and homozygosity for MTHFR 677C>T detected in 2 and 1 patients, respectively. Discussion: Our analysis reveals that among breast cancer patients, the most prevalent comorbid conditions were renal disorders, chronic pulmonary disease and congestive cardiac failure, which differed from other studies. Many participants had an increased BMI, however there was no clear association between the CCI score and an increase in either BMI or Hcy, indicating that obesity might not be the driving force behind these conditions. MTHFR 677C>T, known to contribute to Hcy, was detected in patients with elevated levels. A small study sample and patient factors, including age, race and smoking, need to be considered when evaluating the results.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

Public condition/private affliction: Negotiating co-morbidity, confidentiality, and care in South Africa, a case-study from HPTN 071 (PopART) study

Graeme Hoddinott (Desmond Tutu TB Centre), Hanlie Myburgh (Desmond Tutu TB Centre), Lario Viljoen (Desmond Tutu TB Centre; Department of Sociology and Social Anthropology), Lindsey Jane Reynolds (Department of Sociology and Social Anthropology), Virginia Bond (Zambart, School of Medicine; Department of Global Health and Development, London School of Hygiene and Tropical Medicine)

For many individuals living in contexts precarity, negotiating care for chronic illness is a complex social process. This is further complicated when individuals are affected by multiple health conditions with different causes, prognoses and social meanings. We explore how people living with HIV (PLHIV) in a resource-constrained community in South Africa manage dual diagnoses and seek communal support and medical care through the negotiation of differing social interpretations of illness. The data are drawn from a qualitative cohort study nested within the HPTN 071 (PopART) HIV-prevention trial conducted in the Western Cape. We used a team-based approach informed by ethnographic research principles to conduct module-based interviews from 2015 to 2017. Of the 60 PLHIV in the cohort, 16 were living with other chronic conditions. A narrative analyses of data illustrates the complexity of navigating care across co-morbidities. We present the narrative of a young woman who manages dual diagnoses of HIV and epilepsy with family support. Her epilepsy diagnosis is publicly shared with the community, and she takes treatment accessed from the nearby clinic. Her HIV status, however, remains private, shared only with her parents and partner. She does not take antiretroviral treatment, despite increasing emphasis on "universal" HIV treatment in the public health system. The narrative highlights how choices about disclosure are informed by moral interpretations of illness acquisition, prognosis, and transmission. In this case, epilepsy is seen as "familial", non-communicable and visible; HIV is seen as sexualised, transmissible, and physically invisible. Negotiating care for chronic conditions is subject to more than treatment availability or distances to clinics, as individuals negotiate the daily realities of living with chronic illness. The complex layering of secrecy and disclosure complicates the management of illness in contexts where social constraints make it difficult to maintain boundaries between what is public and private.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

Stem cell therapy for diabetic wounds: Ex vivo anti-oxidant treatment, enhance the anti-inflammatory paracrine responsiveness of bone marrow mesenchymal stem cells to promote healing.

Mehrbani Azar, Yashar (SU/ Department of Medicine), Van De Vyver, Mari (SU/ Department of Medicine)

Obesity-associated type 2 diabetes cause severe co-morbidities such as non-healing wounds. Mesenchymal stem cell therapy is a promising therapeutic option, since MSCs can "sense" the clinical status of the wound microenvironment and respond accordingly to promote healing through paracrine signalling. Autologous MSCs from patients with diabetes are however less efficacious than their allogeneic counterparts, due to impaired paracrine responsiveness. This study, investigated the effectiveness of ex vivo antioxidant (Ascorbic acid 2-phosphate (AAP) and N-acetylcysteine (NAC)) conditioning to restore the paracrine response of impaired diabetic MSCs. Bone marrow- MSCs were isolated from healthy control (C57BL/6J) and obese prediabetic (B6.Cg-Lepob/J) mice and cultured in the presence or absence of AAP (0.62 mmol) and NAC (7.5 mmol). The "conditioned" and "unconditioned" MSCs were then exposed to chronic wound fluid for a period of 4h and their cytokine response assessed at mRNA (RT qPCR micro array; 84 genes) and protein (23 Plex bead-array) level. Impaired diabetic MSCs had a pro-inflammatory phenotype (IL1, Eotaxin, GCSF, IL3, KC, IL12, TNFa, RANTES and GMCSF over expressed) and impaired viability prior to antioxidant conditioning. AAP and NAC were however able to improve cellular viability and proliferation in culture. An upregulation in the anti-inflammatory response (IL6, IL10) was furthermore evident in the "conditioned" diabetic MSCs in response to stimulation with chronic wound fluid. Suggesting that prolonged exposure of MSCs to a pathological microenvironment in vivo skewed the phenotype of these cells to favour a destructive pro-inflammatory environment. Antioxidant treatment can however restore the anti-inflammatory paracrine response of diabetic MSCs.

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

Atrio-autonomic interaction amongst beta-blocker naïve males: predictor or modifier of atrial fibrillation risk?

Bonke Khwinani (SA Endovascular), Chris Greyling (Department of Medicine), Marshall Heradien (Department of Medicine), Paul Brink (Department of Medicine), Warren Stilwaney (Department of Medicine)

BACKGROUNDThe sinus node, AV node and atrio-pulmonary venous junctions are richly innervated by autonomic nerves, but it is unknown if cardio-autonomic tonal (CAT) changes are associated with left atrium hypertrophy (LAH), an atrial fibrillation risk factor. **METHODS**Hypertension-treated, beta-blocker naïve males (BBNM) underwent a transthoracic echocardiogram and Bruce protocol exercise stress test until tired. Patients with untreated thyroid disease, significant valvular heart disease, chronic kidney disease were excluded. Left atrial (LA) dimension was measured with M-mode echocardiography in the parasternal long/short axis. LAH was diagnosed if LA ≥ 45 mm (cases). Controls did not have LAH. Resting heart rate (RHR), PR-interval length and exercise-related heart rate profiles (HRP) were used to assess CAT. **RESULTS**LAH was diagnosed in 54 (28.7%) of 188 BBNM. Diabetes mellitus prevalence, office blood pressure and total anti-hypertensive drug use did not differ between groups. Cases were older (56.02 \pm 12.68 years vs. 50.05 \pm 11.95 years; $p=0.003$), had higher BMI (34.65 \pm 5.82 kg/m² vs. 31.33 \pm 5.32 kg/m²; $p=0.0002$) and more prevalent left ventricular hypertrophy (LVMI >115 g/m²: 65% vs. 40%; $p=0.002$) than controls. RHR was slower (67.26 \pm 11.52 bpm vs. 72.9 \pm 12.58 bpm; $p=0.005$) and PR intervals longer in cases than controls (182.20 \pm 37.20ms vs. 167.22 \pm 24.26ms; $p=0.001$). Total exercise time did not differ significantly, but peak exercise (PHR) and one-minute recovery heart rates (OMRHR) were slower in cases than controls (PHR: 142.19 \pm 17.82 bpm vs. 151.97 \pm 19.15 bpm; $p=0.001$; OMRHR: 111.41 \pm 18.25 bpm vs. 119.92 \pm 19.53 bpm; $p=0.007$). **CONCLUSION**Amongst BBNM, LAH is significantly associated with older age, obesity, LVH, slower HRP and slower AV-conduction, respectively. These effects may be due to increased vagal tone and/or reduced sympathetic tone which may be aggravated by anti-sympathetic or vagal tone increasing drugs/interventions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

In vitro assessment of an aspalathin-enriched green Rooibos (*Aspalathus linearis*) extract treatment in statin-induced hepatotoxicity

Christo Muller (SAMRC), Danielle Millar (Stellenbosch University), Sandra Bowles (SAMRC), Shantal Windvogel (Stellenbosch University)

Rooibos (*Aspalathus linearis*) is a shrub indigenous to South Africa. The leaves and stems are typically brewed into an infusion and enjoyed as a beverage. Rooibos is rich in numerous polyphenols, and of interest is aspalathin, found uniquely and abundantly in Rooibos. Rooibos is increasingly recognised for its health benefits; particularly its beneficial effects on metabolic disease which include antidiabetic and lipid-lowering properties, as well as hepatoprotective properties. In two cases, however, it has been reported that chronic consumption of Rooibos has been associated with hepatotoxicity. Statins, administered to lower increased cholesterol levels, act by competitively inhibiting hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. A side-effect of statin usage is the potential development of hepatotoxicity due to an increase in reactive oxygen species (ROS) production. The aim of this study was to investigate the interaction between Rooibos and statins in terms of whether Rooibos may infer hepatoprotective effects and ameliorate the statin-induced hepatotoxicity, or alternatively contribute to hepatotoxicity. To mimic the hyperlipidaemic state in vitro, C3A liver cells were pre-treated with palmitate. Cells were then exposed to ATV and Afriplex GRT (green Rooibos extract) and cell viability, function, and oxidative stress were measured by cellular ROS production, apoptosis/necrosis, and mitochondrial integrity were assessed. Higher concentrations of ATV induced hepatotoxicity, while high concentrations of GRT exerted hepatoprotective effects. In combination, GRT had modulating effects on ATV-induced hepatotoxicity in terms of cell death, mitochondrial integrity, and ROS production. This warrants further investigation into the herb-drug interactions in a chronic model.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

Regulations relating to the reduction of sodium in certain foodstuffs and related matters: Perspectives from adult consumers in the Tygerberg Health District, City of Cape Town, Western Cape, South Africa

Dominique Greeff (Stellenbosch University), Hanneke Schreuder (Stellenbosch University), Iman Gierdien (Stellenbosch University), Lebogang Mohlala (Stellenbosch University), Liezel Engelbrecht (Stellenbosch University), Lindsay Reid (Stellenbosch University), Maritha Marais (Stellenbosch University), Marizaan du Toit (Stellenbosch University), Megan Yates (Stellenbosch University), Nelene Koen (Stellenbosch University), Tessa Leng (Stellenbosch University), Yolande Smit (Stellenbosch University)

In South Africa, the prevalence of adult hypertension (HT), a condition linked to stroke and cardiovascular disease, has increased at an alarming rate in recent years. Salt reduction legislation is a cost effective way to reduce this burden, as salt is a driver of HT. This study aimed to determine City of Cape Town (CoCT) consumers' awareness, attitudes and practices relating to the current salt legislation and whether the legislation has influenced their consumption patterns. In this cross-sectional, descriptive study with an analytical component, an interviewer-administered survey was conducted on literate adult consumers (N=583) at four randomly selected shopping malls in the Tygerberg health district, CoCT. More than half (n=332; 56.9%) of all participants indicated they try to consume less salt and of those, 67.2% (n=223) said they do so because they think it is healthier. Processed foods were identified by 50.4% (n=294) of participants as a major source of salt in their diet. Twenty two percent (n=128) of participants indicated that they suffer, or have suffered from (HT), while significantly more HT sufferers chose lower salt containing products compared to those with no HT (p=0.008). Only 16.5% (n=96) of participants were aware of the current salt legislation. Though 47.9% of participants think that the legislation will affect the taste of food negatively, 80.9% reported they have not noticed a change after the first phase of the legislation had been implemented. The majority of participants were positive about the role of manufacturers to lower the amount of salt in

foods. Though many consumers try to consume less salt because they think it is healthier, they still consume processed foods regularly. In general, consumers do not have a negative attitude towards the salt legislation, suggesting it is a low-barrier intervention to decrease the populations' salt consumption.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

The Nutritional Status Assessment of Dialysis patients in Tygerberg and Groote Schuur hospital

Gareth Coetzee (University of Stellenbosch), Liezel Blaauw (University of Stellenbosch), Magda de Mooij (University of Stellenbosch), Megan Donald (University of Stellenbosch), Nazeema Esau (Tygerberg Hospital), Zarina Ebrahim (University of Stellenbosch)

Introduction: Chronic Kidney Disease (CKD) has many nutritional complications in dialysis patients. Research has shown malnutrition to be as high as 20-75%. However, recent studies show increasing trends in obesity. Therefore, this study aimed to assess the current nutritional status of dialysis patients using methods sensitive to under and over nutrition. Methods: A cross-sectional descriptive study was performed at Tygerberg and Groote Schuur Hospital dialysis units. Anthropometrical measurements include weight, height, BMI, waist circumference, triceps, mid-arm circumference and arm muscle area (AMA). RAPA 1 and RAPA 2 scores assessed physical activity levels. Biochemical measures included haematology, renal function and nutrition outcomes. Dietary intake assessment included 24-hour recalls. Statistica 13.3 was used to perform statistical analysis. Results: There were 102 patients who participated, 71% (n=72) hemodialysis patients and 29% (n=30) peritoneal dialysis patients. The age of the patients were 40.6 ± 10.61 , 42% were males (n=43) and 58% females (n=59). Patients were mostly unemployed with a household income less than R3000 per month. The BMI showed patients were mainly overweight 34% (n=35) and obese 19% (n=20). The AMA was low in the normal weight group. Biochemical results show mostly normal values, except for a high phosphate level. The RAPA scores showed that 77% (n=79) of patients did none to light aerobic activity and 80% (n=82) did no strength training exercises. Dietary intake showed suboptimal intake. High food costs as barriers to following dietary advice were identified in 76% (n=68) of patients. Conclusion: Overweight, obesity and low muscle mass area were common in this group of dialysis patients. Physical activity and dietary intake was suboptimal which could be due to a variety of factors. Interventions should aim to increase muscle mass in susceptible patients, increase physical activity, optimize dietary intake and reduce obesity. Financial assistance for food purchasing should be explored.

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

In vitro single muscle fibre contractility measurement to investigate mechanisms of weakness in idiopathic inflammatory myopathies.

Franco Henning (Stellenbosch University), Jonathan Carr (Stellenbosch University), Tertius Kohn (University of Cape Town)

Introduction: Polymyositis (PM), dermatomyositis (DM) and necrotizing autoimmune myopathy (NAM) form part of the spectrum of idiopathic inflammatory myopathies (IIMs). Although the pathomechanisms are different, the unifying feature is that of weakness caused, in some way or another, by an inflammatory attack on muscle. The mechanism by which weakness develops is still unclear, but experimental animal data suggest that dysfunction of the contractile apparatus might contribute to muscle weakness in these conditions. This study investigated the contractile function of single muscle fibres from patients with IIMs in vitro. Methods: Muscle biopsies obtained from patients with IIMs and healthy controls were dissected and chemically skinned. Single muscle fibres were dissected out and subjected to contractility measurement based on a standard protocol utilising a

permeabilised single fibre system. The myosin heavy chain (MyHC) composition of each fibre was determined by means of gel electrophoresis. Contractile force, shortening velocity and power output were calculated for each fibre and normalised to cross-sectional area (CSA), and compared between the two groups. Results: A total of 178 fibres from IIM cases and 174 fibres from controls were studied. Specific (normalised) force was 23%, 24% and 29% lower in the IIM group for all fibre types combined, type I fibres, and type IIa fibres, respectively. In individual IIM cases, the degree of clinical weakness correlated with specific force. Both shortening velocity and power output were increased in the IIM group, compared to controls. Discussion: The findings from this study suggest that weakness in IIMs may, at least in part, be caused by dysfunction of the contractile apparatus. Although the mechanism by which this develops has not been investigated, animal studies suggest a role for TNF- α . The findings of this study provide a basis for further investigation into the mechanisms underlying weakness in IIMs.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

Left ventricular hypertrophy in males is associated with increased vagal tone after adrenergic stress, regardless of beta-blocker usage.

Bonke Khwinani (SA Endovascular; Netcare Hospital), Chris Greyling (Department of medicine), Marshall Heradien (Department of Medicine), Paul Brink (Department of Medicine)

BACKGROUND: Ventricular ectopic beats disappear as heart rate increases, but typically re-appear during the recovery phase of an exercise stress test (EST). This phenomenon suggests that simultaneous sympatho-vagal discharge may have pro-arrhythmic effects on susceptible substrates e.g. left ventricular hypertrophy (LVH). Since the vagal system does not have beta-adrenergic receptors, we hypothesised that amongst males, LVH is associated with increased cardio-inhibitory vagal tone, regardless of beta-blocker (BB) treatment. **METHODS:** Males without pacemakers, untreated thyroid disease, chronic kidney disease or significant valvular heart disease underwent a transthoracic echocardiogram and routine Bruce-protocol treadmill EST until tired. Cases had LVH with a left ventricular mass index (LVMI) $>115\text{g/m}^2$. Controls did not have LVH. Peak minus one minute recovery heart rate (HRR) was used to assess vagal tone post-exercise. **RESULTS:** Amongst 286 males, 154 (56%) were identified as cases and 132 (44%) as controls. BB ^TM s were more frequently prescribed to cases than controls (43% vs. 24%, $p=0.001$). Age, resting systolic blood pressure, body mass index and total exercise time did not differ significantly between groups. Diastolic BP was lower ($p=0.009$) and QRS duration longer ($p=0.0001$) in cases than controls. Although not different between BB users and non-users, HRR was significantly quicker amongst cases than controls (32.29 ± 12.15 bpm vs. 28.9 ± 12.55 bpm; $p=0.02$). **CONCLUSION:** Male LVH is associated with pro-arrhythmic factors including lower diastolic pressure and broader QRS complexes which reduces coronary perfusion pressure and fractionates the depolarising electrical wave front, respectively. Furthermore, and regardless of BB-usage, males with LVH have increased post-exercise vagal function which may be pro-arrhythmic if it coincides with peak adrenergic outpour.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

MicroRNA signature of healthy vs impaired diabetic mesenchymal stem cells as biomarker for autologous stem cell therapy.

Ascentia Seboko (Division of Endocrinology, Department of Medicine, Stellenbosch University), Mari van de Vyver (Division of Endocrinology, Department of Medicine, Stellenbosch University)

Background Diabetes Mellitus has become a global burden affecting over 350 million people and approximately 15% of all diabetics are affected by chronic foot ulcers. The persistent hyperglycaemic microenvironment observed in diabetes results in vascular and neurological changes that compromise the healing of chronic foot ulcers that account for 20% of all hospitalisations associated with type 2 diabetes mellitus (T2DM) patients in Sub-saharan Africa. Therapeutic approaches to diabetic ulcers

include mesenchymal stem cell (MSC) therapy. MSCs are multipotent cells that have immunomodulatory and paracrine functions that promote healing of tissue, however, autologous stem cell therapies have shown very little improvement when utilizing MSCs from diabetic patients. We hypothesized that MSC impairment in T2DM is due to microRNA (miRNA) dysregulation of proteins associated with MSC maintenance. Due to their central role in developmental processes, perturbations in miRNA expression patterns can lead to pathologies. Thus, our aim was to gain mechanistic insight into the difference in miRNA expression between healthy control- and obese pre-diabetic mice MSCs. Methods Bone marrow MSCs were isolated from male and female healthy control (C57BL/6J) and ob/ob (B6.Cg-Lepob/J) mice. Total RNA was purified from MSC lysates and a broad miRNA profiling was performed using nanostring technology. Results Our data showed a higher proliferation rate in control mice MSCs compared to that of ob/ob mice. The following miRNAs (miR18b; miR21; miR139; miR155; miR191; miR376b; miR650 and let-7c) displayed differential expression between healthy and impaired MSCs. Conclusion The difference in the proliferation rate between MSCs from healthy and ob/ob mice, further demonstrated the impairment in these MSCs. The differential expression of miRNAs between the healthy and impaired MSCs demonstrated a role for miRNAs in MSC maintenance and pathology. Furthermore, we hope to establish a unique miRNA signature of healthy versus impaired MSCs, as a biomarker for autologous stem cell therapy.

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

Retrospective review of biological therapy in a resource limited setting within a community at high risk of tuberculosis

Jacques Wynand Rood (TBH), Riette du Toit (TBH)

Background: Biological disease modifying anti rheumatic drugs (DMARDs) have ultimately become the gold standard of treatment in well resourced countries for rheumatic conditions. There is a significant risk of infection and reactivation of latent infections in particular tuberculosis with the use of biological therapies. Their safety and role in a resource limited environment is still unclear. Method: We conducted a retrospective, descriptive folder review of all patients started on biological therapy for rheumatic conditions from November 2011 to December 2016. Primary objective was to describe the nature and frequency of adverse events as well as the main reason for discontinuation of treatment. Results: A total of 31 patients were included. The rheumatic diseases included in the study were ankylosing spondylitis (35%), rheumatoid arthritis (19%), systemic lupus erythematosus (16%), juvenile idiopathic arthritis (13%), vasculitides (10%) and psoriatic arthritis (7%). Adverse events occurred in 26 (84%) patients. Serious adverse events occurred in 14 (45%) patients with recurrent uveitis being the most common occurring in 5 (16%) patients. One patient developed pulmonary tuberculosis (PTB). Discontinuation or switching of biological therapy occurred in 13 (42%) patients. The main reason for discontinuation or switching of biological therapy was for serious adverse events and treatment failure occurring in 7 (23%) and 6 (19%) patients respectively. Median disease activity improvement in BASDAI; 5.8 [5-7] to 1.0 [0.75-2.0], and CDAI; 31.5 [24.5-42.8] to 7 [5-24] and occurred over median of 26 months [19-48] and 17 months [8-30] respectively. Conclusion: Recurrent uveitis occurred in almost half of the patients with ankylosing spondylitis and was also the main reason for discontinuation of biological therapy. We did not document an increased incidence of PTB. Disease activity scores showed significant improvement. The study is limited by the small number of patients on biological therapy - a reflection of the impact of severe resource constraints.

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

Evidence for the utility of antenatal HbA1c to predict diabetes after gestational diabetes.

Ankia Coetzee (Division of Endocrinology), David R Hall (Division of Obstetrics and Gynecology), Deidre Mason (Division of Obstetrics and gynecology), Magda Conradie (Division of Endocrinology), Mariza Hoffmann (NHLS, Chemical Pathology)

Aim To evaluate antenatal HbA1c at diagnosis and in the 4 weeks preceding delivery to predict early postpartum diabetes mellitus (DM) in women with Gestational Diabetes Mellitus (GDM). Methods Seventy-eight women with GDM were prospectively assessed. The ability of HbA1c at GDM diagnosis (t1) and in the 4 weeks preceding delivery (t2) to predict DM 6-12 weeks after delivery was investigated. Glucose assessment was performed between November 1, 2015, and November 1, 2016 at Tygerberg Hospital (TH), Cape Town, South Africa (SA). Individuals with known pre-existing diabetes were excluded. Results A HbA1c of 6.2% (44mmol/mol) and 6.5% (48mmol/mol) at t1 predicted DM with sensitivities of 95% and 90% and specificities of 62% and 70% respectively. At t2 the best cut-off for HbA1c, in accordance with t1, was also 6.2% (44mmol/mol; sensitivity 92%, specificity 56%). Of the 29 women with antenatal overt DM, 19 had HbA1C levels \geq 6.5% (48mmol/mol) at t1. The increased risk for postpartum DM with HbA1c \geq 6.2% (44mmol/mol) was four-fold (OR 3.97 CI 2.08-7.59 $p < 0.001$) at t1 and five-fold (OR 5.08 CI 1.60-16.25 $p = 0.006$) at t2. Conclusion HbA1c lower than 6.5% predicts early postpartum DM in women with GDM. HbA1c can serve as directive instrument to improve postpartum uptake.

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

Exome sequencing of the first reported South African X-linked primary immunodeficiency case identifies a hemizygous mutation in MSN

Brigitte Glanzmann (Stellenbosch University), Craig J. Kinnear (Stellenbosch University), Eileen G. Hoal (Stellenbosch University), Mardelle Schoeman (Stellenbosch University), Marlo MÅ¶ller (Stellenbosch University), Michael Urban (Stellenbosch University), Monika M. Esser (National Health Laboratory Service), Paul D. van Helden (Stellenbosch University)

Primary immunodeficiency diseases (PIDs) are a subgroup of immunological disorders that are inherited and which increase susceptibility to viral infections. Single-gene defects may lead to disease manifestations that range from extremely narrow infectious phenotypes to broad multisystem defects. Here, we present the findings of a patient who presented with non-resolving lymphopenia and neutropenia following a bout of pneumonia. Whole exome sequencing was performed and the data was processed using an in-house bioinformatics pipeline, TAPER. Candidate variants were subsequently validated using Sanger sequencing. A hemizygous missense mutation (c.511C>T; p. R171W) in exon 5 of MSN was identified. Sanger sequencing subsequently revealed that the variant was heterozygous in the mother and absent from the father of the index case. Moreover, the same mutation was identified in the maternal uncle of the index case who is also affected. The R171W mutation identified in MSN has previously been associated with PID, but this is the first known reported case in South Africa and only the eighth patient worldwide. Our findings not only emphasise the importance of an accurate molecular diagnosis, but also allow for improved patient management and treatment. Moreover, the use of WES is a cost-effective and accurate means of molecular diagnosis in resource constrained countries such as South Africa.

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Outcomes of 562 Echocardiographically Guided Pericardiocenteses over a 10-year period in a low-to-middle income country Tertiary Referral Centre

Anton Doubell (Stellenbosch University & Tygerberg Hospital), Charles Kyriakakis (Stellenbosch University & Tygerberg Hospital), Sumanth Karamchand (Stellenbosch University & Tygerberg Hospital)

Background: Echocardiographically-guided percutaneous pericardiocentesis (EGPP) is well-established as a safe procedure with a low rate of minor and major complications in high-income countries. Its feasibility and safety is poorly described in resource-limited regions. Objective: The primary objective of this study was to evaluate the major and minor complications associated with EGPP in a large South African tertiary referral centre and to compare the rate of complications with the internationally accepted standard. Secondary objectives included evaluating the optimal route of access

and identifying potential risk factors for procedure-related complications. Methods: All EGPP performed between 01/01/2008 and 31/12/2017 were included. Pericardiocentesis procedural reports and clinical notes were evaluated to determine the aetiology of the pericardial effusion, pericardial access site, procedural success, volume of fluid aspirated and procedure-related minor and major complications. Results: During the 10-year study period, 562 EGPP were performed on 502 patients (mean age: 40±14 years). The leading aetiology was tuberculous pericarditis (82.5%). Iatrogenic, cardiac catheterisation-related effusions comprised only 1.7%. Overall EGPP procedural success rate was 95%, with a total procedure-related complication prevalence of 6.99% (95% CI: 4.9–9.7%); (major: 1.98%; minor: 5.01%), compared to a complication rate of 4.7% (major: 1.2%; minor: 3.5%) in the largest series from the Mayo Clinic. The preferred site of access was the trans-apical route (66%). After adjusting for confounding variables in a multivariate analysis, pericardiocentesis in low-volume effusions (<300mL) was associated with procedure related complications, Odds Ratio 2.23 (95% CI: 1.01–4.98). There was no significant association between adverse outcomes and alternate (subxiphisternal/parasternal) routes of access. Conclusions: EGPP is associated with a low prevalence of complications in our centre (a resource-limited African country), with a major procedure-related complication prevalence comparable to that of a leading centre from a high-income country. Low-volume effusions were independently associated with an increased risk of procedure-related complications.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Evaluating the effect of the Practical Approach to Care Kit on teaching medical students primary care: Quasi-experimental study

Bob Mash (Stellenbosch University), Hilary Rhode (Stellenbosch University)

Background: South Africa is committed to health reforms that strengthen primary health care. Preparing future doctors to work in primary care teams with other professionals is a priority, and medical schools have shifted towards community-based and decentralised training of medical students. Aim: To evaluate the effect on student performance of the Practical Approach to Care Kit (PACK) (an integrated decision-making tool for adult primary care) during the final phase of medical student training at Stellenbosch University. Setting: Clinical rotations in family medicine at clinics in the Western Cape. Methods: Mixed methods involving a quasi-experimental study and focus group interviews. Student examination performance was compared between groups with and without exposure to the PACK during their clinical training. Student groups exposed to PACK were interviewed at the end of their rotations. Results: Student performance in examinations was significantly better in those exposed to the PACK. Students varied from using the PACK overtly or covertly during the consultation to checking up on decisions made after the consultation. Some felt that the PACK was more suitable for nurses or more junior students. Although tutors openly endorsed PACK, very few modelled the use of PACK in their clinical practice. Conclusion: The use of PACK in the final phase of undergraduate medical education improved their performance in primary care. Students might be more accepting and find the tool more useful in the earlier clinical rotations. Supervisors should be trained further in how to incorporate the use of the PACK in their practice and educational conversations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 21

Carotid intima media thickness (CIMT) in a cohort of HIV positive and negative individuals of South Africa

Festus Kamau (Stellenbosch University), Frans Everson (Stellenbosch University), Hans Strijdom (Stellenbosch University), Henry Cyster (Stellenbosch University), Ingrid Webster (Stellenbosch University), Mashudu Mthethwa (Stellenbosch University), Nandu Goswami (Medical University of Graz),

Nyiko Mashele (Stellenbosch University), Patrick De Boever (Flemish Institute for Technological Research (VITO)), Sana Charania (Stellenbosch University), Tim Nawrot (Hasselt University)

Background:In a resource limited country such as South Africa (SA), the rates of cardiovascular diseases are on a rise. Carotid artery intima-media thickness (CIMT) is a surrogate marker of subclinical atherosclerosis, which has been shown to predict future cardiovascular events in the general population. This study aims to investigate the relationship between CIMT and an array of cardiovascular risk factors and other control variables in study participants with and without HIV-infection.**Method:**The cross-sectional study was conducted in a population sampled from patients visiting health care clinics in Cape Town and Worcester. Anthropometric (BMI; waist-hip-ratio), cardiovascular (lipid profile; blood pressure [BP]; plasma glucose), and qualitative (medical history, life style), data were obtained from 261 participants (HIV+, n=136; HIV-, n=125). CIMT was measured according to international standardised guidelines via ultrasound using QIMTÂ® software.**Results:**The median CIMT in the cohort (mean age, 39 Â± 9.97) was 0.625mm. Age, waist circumference, systolic and diastolic BP, LDL-cholesterol as well as HBA1C% positively correlated with CIMT (p<0.05). Furthermore, both systolic and diastolic hypertension, as well as high LDL-cholesterol correlated with IMT (p<0.05). Upon regression analysis, age strongly associated with CIMT (p<0.01).**Conclusion:**In this cohort, CIMT values are associated with cardiovascular risk factors, independent of HIV related factors. The study confirms that age, waist circumference, systolic and diastolic BP, HBA1c% as well as serum LDL cholesterol levels are determinants for increased CIMT. This study further concludes that age is an independent predictor of sub clinical atherosclerosis.

ABSTRACT NUMBER / ABSTRAKNOMMER: 22

Glycated haemoglobin threshold for dysglycaemia screening, and application to metabolic syndrome diagnosis in HIV-infected Africans

Andre Pascal Kengne (Non-Communicable Diseases Research Unit, South African Medical Research Council, Cape Town), Anniza de Villiers (Non-Communicable Diseases Research Unit, South African Medical Research Council, Cape Town), Debora Jonathan (Non-Communicable Diseases Research Unit, South African Medical Research Council, Cape Town), Kim Anh Nguyen (Centre for Evidence Based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Nasheeta Peer (Non-Communicable Diseases Research Unit, South African Medical Research Council, Cape Town), Tandi. E. Matsha (Department of Biomedical Sciences, Faculty of Health and Wellness Science, Cape Peninsula University of Technology)

Background: Glycated haemoglobin (HbA1c) test has been increasingly promoted as an alternative to fasting plasma glucose (FPG) or oral glucose tolerance test (OGTT) to diagnose dysglycaemia, but the performance of HbA1c in HIV-infected Africans has yet to be established. This study aimed to assess the diagnostic accuracy of HbA1c for dysglycaemia including FPG-defined and OGTT-defined dysglycaemia in African population with HIV infection, and assess the effect of HbA1c-predicted dysglycaemia on Joint Interim Statement (JIS)-based prevalent metabolic syndrome (MS).**Methods:** A cross-sectional, multi-clinic-based study included 748 randomly selected participants (157 men). The recommended HbA1c cut-points were tested alongside optimal cut-points obtained from receiver operating characteristic curve analyses.**Results:** The optimal HbA1c cut-point of 5.75% showed 54% sensitivity, 84% specificity for FPG-defined dysglycaemia, and 52% sensitivity, 85% specificity for OGTT-defined dysglycaemia. The internationally advocated cut-point of 5.7% yielded similar performance with the study-specific cut-point for any dysglycaemia. MS prevalence by JIS criteria (28.2%) increased to 29.7% when using HbA1c \geq 5.75% and to 32.9% with HbA1c \geq 5.7%. The agreement between the original and modified criteria were very good (kappa=0.81) and good (kappa=0.76) respectively. **Conclusions:** This study agrees with the internationally recommended HbA1c cut-point for detecting dysglycaemia. Replacing FPG-based with HbA1c-predicted dysglycaemia in the JIS criteria to diagnose MS is feasible in HIV-infected Africans.

ABSTRACT NUMBER / ABSTRAKNOMMER: 23

Renal Cell carcinoma in South Africa: Review of the epidemiology and a first report on demographics, risk factors, staging and pathological profile

Andre van der Merwe (US), Danelo Estienne du Plessis (US)

Introduction: Little information currently exists in the literature regarding the epidemiology of Renal Cell Carcinoma (RCC) in South Africa, or indeed Africa. There are known racial and gender disparities with regards to incidence, stage at presentation and prognosis of renal cell carcinoma. Presentation in Africa is typically at a younger age and with more advanced stage. In this report we review the epidemiology, classification and risk factors of RCC and give a first report on the demographics, stage, pathological profile and risk factors for RCC in a South African Centre. **Methods:** We prospectively collected epidemiological, clinical and pathological data from 27 patients with RCC. **Results:** The presence of known risk factors for RCC such as obesity, smoking and hypertension was demonstrated in our population, in keeping with international trends. The most common mode of presentation was incidental finding on imaging (55%). Our median stage of presentation was pT2b, more advanced than international norms. Our study demonstrated that smoking, obesity and hypertension were risk factors for more advanced stage at presentation. The pathological profile and presenting symptoms in our population mimics that seen in Europe and United States, but differs from that seen in other African studies. However, patients in our study followed the trend of African patients to present at a younger age, although only 2 of our patients were black. This highlights complex interaction between genetic and environmental factors at play.

ABSTRACT NUMBER / ABSTRAKNOMMER: 24

Assessing risk factors for non-communicable diseases in the workforce at a commercial power plant, South Africa

Darcelle Schouw (Division of Family Medicine and Primary Care, Stellenbosch University), Robert Mash (Division of Family Medicine and Primary Care, Stellenbosch University), Tracy Kolbe-Alexander (School of Health and Wellbeing, University of Southern Queensland, Ipswich, Australia)

Abstract Background Non-communicable diseases (NCD) account for more than half of annual deaths globally and nearly 40% of deaths in South Africa. The workplace can be an important setting for prevention of NCDs. **Objective** The aim of this study was to assess risky behaviours and risk factors for NCDs amongst the workforce at a commercial power plant in the Western Cape. **Methods** 156 employees were randomly selected. Biometric testing included blood pressure, total cholesterol, random glucose, body mass index (BMI), waist circumference and waist to hip ratio (WHR). Questionnaires evaluated tobacco smoking, alcohol use, diet, physical activity, stress and prevalence of NCDs. The 10-year cardiovascular risk was calculated. **Results** Employees had a mean age of 42.8 years (SD 9.71) and 65% were male. Overall 26% smoked tobacco, 29% had harmful or dependent alcohol use, 73% had inadequate fruit and vegetable intake, up to 61% regularly consumed high fat foods and 64% were physically inactive. Systolic blood pressure was raised in 33% and diastolic in 35%, 62% had raised cholesterol, and 77% were overweight or obese. Overall 17% were diagnosed with hypercholesterolaemia, 17% with hypertension, 16% with depression and 34% had a moderate-high 10-year cardiovascular risk. **Conclusion** The workforce at a South African commercial power plant was at substantial risk of NCDs and this workplace could be an important setting for disease prevention. The findings will be used to monitor change as a result of a future action-research project to transform the organisational environment in order to prevent NCDs in the workplace. **Key words** Risk behaviour, risk factors, non-communicable diseases, workplace, cardiovascular diseases

ABSTRACT NUMBER / ABSTRAKNOMMER: 25

Skin cancer in a South African tertiary care dermatology clinic: A retrospective study.

Johann de Wet (Tygerberg Hospital), Minette Steyn (Stellenbosch University)

Background: Skin cancer is a growing health concern worldwide. It is the most common malignancy in South Africa and comprises mainly basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma (MM). Although it places a large stress on the overburdened public healthcare sector of South Africa there is very limited local scientific data available regarding skin cancer. Objectives: The aim of this study is to determine the (i) frequency; (ii) variations in body site; (iii) age, sex and ethnic distribution and (iv) histological type of skin cancers in a South African tertiary care dermatology clinic. Methodology: We will review the demographics of patients who underwent a biopsy for skin cancer as well as the clinical and histological features of skin cancers diagnosed between September 2015 and August 2016 at the Tygerberg Academic Hospital, Cape Town, Western Cape, South Africa. Results: A total of 696 biopsies were identified. The total number of participants were 443 with a mean age of 64 years at the time of biopsy. Clinical suspicion of skin cancer was histologically confirmed in 64.89% of cases. Most common sites of biopsies were as follows: head (25.47%), neck (15.97%), hand (15.25%), arm (11.65%), leg (8.06%) and chest (6.33%). The most common skin cancer identified was basal cell carcinoma (36.06%) followed by squamous cell carcinoma (12.50%), squamous cell carcinoma in-situ (5.32%), Kaposi sarcoma (4.45%) and cutaneous malignant melanoma (4.02%). Conclusion: Skin cancer remains a burden on South Africa's stressed health care system. There is a requirement for further local data regarding prevalence as well as reporting and prevention strategies.

ABSTRACT NUMBER / ABSTRAKNOMMER: 26

The validation of the visual screening tool for anxiety disorders and depression in people living with hypertension and/or diabetes

Dana JH Niehaus (Stellenbosch University; Stikland Hospital), Liezl Koen (Stellenbosch University; Stikland Hospital), Zimbini Ogle (Stellenbosch University)

Background: Depression and anxiety disorders remain poorly detected at primary health care, particularly in patients with hypertension and/or diabetes. A visual screening tool for anxiety disorders and depression (Vistad) has been developed for use in people living with hypertension and/or diabetes. Aim: We aimed to validate the Vistad in primary health care participants diagnosed with hypertension and/or diabetes. Setting: Participants were recruited from five primary health care centres in the Eastern Cape, South Africa (urban and peri-urban and rural). Methods: The study used a cross-sectional study design to validate the Vistad. The Vistad was validated against the MINI International Neuropsychiatric Interview (M.I.N.I). A demographic questionnaire was used to collect data on socio-economic variables. Results: Sixty-nine (87%) females, 10 (13%) males with a mean age of 49 (SD 8.6844) participated in the study. Fifty black (63%), 16 coloured (20%) and 13 white (16%) subjects participated in the study. The majority of the participants (77%) did not complete high school. The area under curve score (AUC) for the Vistad in screening for depression (Vistad) was 0.91, and for anxiety disorders, 0.87 post traumatic stress disorder, 0.87 panic disorder, 0.85 social phobia, 0.88 agoraphobia, and 0.83 generalized anxiety disorder revealing acceptable psychometric properties. Conclusion: The use of the Vistad as a screening tool at primary health care is hence recommended for depression and anxiety disorders, and could therefore play a key role in the prevention and early treatment of individuals diagnosed with hypertension and/or diabetes across cultures and levels of education.

ABSTRACT NUMBER / ABSTRAKNOMMER: 27

7-Year experience of Transcatheter Aortic Valve Implants (TAVI) in a Western Cape private healthcare setting

Andre Philips (Mediclinic Vergelegen, Somerset West), Anton Doubell (Division of Cardiology, Tygerberg Hospital & Stellenbosch University Department of Internal Medicine, Tygerberg Hospital), Barry Barnard (Mediclinic Vergelegen, Somerset West), Hellmuth Weich (Division of Cardiology, Tygerberg Hospital & Stellenbosch University Department of Internal Medicine, Tygerberg Hospital), Jacques van Wyk (Mediclinic Panorama, Panorama, Cape Town), Jurgens Jacobus Liebenberg (Division of Cardiology, Tygerberg Hospital & Stellenbosch University Department of Internal Medicine, Tygerberg Hospital), Mark Abelson (Mediclinic Vergelegen, Somerset West), Rocco Vivier (Mediclinic Panorama, Panorama, Cape Town), Tom Mabin (Mediclinic Vergelegen, Somerset West)

Background The rapid expansion of TAVI device technology and international implantation expertise is hampered in South Africa by resource constraints. We report our experience with 244 successive TAVI implants, the largest South African TAVI outcome report to date for a single heart valve team. Methods 244 patients underwent TAVI (October 2009 - September 2016) at 2 hospitals in the Western Cape. Outcome data was used to compile this report. Transcatheter devices used included the Edwards Sapien, Edwards Sapien XT and the Medtronic CoreValve. All endpoints are in accordance with the VARC 2 consensus report definitions. Results The average age of patients was 80 years, with a slight male preponderance (55% males). The majority of patients had significant comorbidities with a mean STS score and log EuroSCORE of 7.89% and 26.5% respectively. The femoral access route was preferred (75%) followed by the transapical and transaortic route (14% and 11%). Device implantation success was achieved in 89.3% of cases. One year survival rate was 81%. This was accompanied by a valve area increase from 0.7cm² to 1.6cm², a decrease in mean aortic valve gradients from 46mmHg to 10mmHg and a significant increase in effort tolerance (NYHA dyspnea grading: Pre-procedural 65% NYHA 3; Post-procedural 50% NYHA 1). Comparable to existing literature, we report a procedural mortality rate of 3.68%. Life threatening bleeding and major vascular complications were found in 4.5% and 5.73% respectively. Lower rates of vascular complications were seen with second generation devices and growing experience of the heart valve team. Conclusion Despite obvious constraints, we have shown outcome data in line with international reports. Furthermore, we have shown an improvement in patient outcomes with growing expertise and device development. This, along with other South African TAVI registry reporting ought to fuel local funding and interest in this rapidly evolving field.

ABSTRACT NUMBER / ABSTRAKNOMMER: 28

Pioneering informed consent towards ethical genetic research in Kenyan breast cancer patients

Kotze J Maritha (Stellenbosch University), Laing Nakita (Groote Schuur Hospital), Mining K. Simeon (Moi University), Sawe Rispah Torrorey (Stellenbosch University)

Title: Pioneering informed consent towards ethical genetic research in Kenyan breast cancer patients
Abstract Background: Obtaining informed consent from study participants is a key principle required for ethically conducted clinical research. Evaluation of genetic risk factors that may affect the burden of breast cancer in Africa has not previously been performed in Kenya. Objective: We report insights gained from the consent process and family history assessment using a breast cancer referral screening tool (B-RST[®],[†]) for genetic testing in Kenyan breast cancer patients. Methods: The informed consent form approved for genetic studies at the Moi Teaching and Referral Hospital, was adopted from a research study previously performed in South Africa. Initially, 16 females referred for breast surgery were guided through a process of pre-testing the informed consent form and the study questionnaire. Results: A total of 96 breast cancer patients were enrolled in the study from 2013-2016. These included 2 males and 94 females between the ages of 18 and 80 years (mean age 46.9 years). All participants signed the informed consent form. Use of the B-RST[®],[†] recorded a detailed self-reported family history in 13.5% of female patients (13, aged 35-70 years). Four patients were below the age of 40 years, and one diagnosed with bilateral breast cancer. Conclusion: The pre-test process pioneered in this investigation was critical to ensure that study participant have an adequate understanding of the project goals, given the challenges associated with the translation of sophisticated genetic terms into native

African languages. By adding the B-RSTâ„† our aim to identify predictors of genetic risk became clear to participants. Novel insights gained as a result of this study will be applied towards the development of a training and genetic counselling model for feedback on research results to patients.

ABSTRACT NUMBER / ABSTRAKNOMMER: 29

Prevalence of non-communicable diseases in adults living with Human Immunodeficiency Virus: An Overview of Systematic Reviews.

Prof. Taryn Young (Stellenbosch University), Shahista Mustafa Jaffer (Stellenbosch University)

Background: HIV infected people are now expected to live longer with good quality of lives. However, the number of Non-communicable diseases (NCDâ€™s) in this population is on the rise partly attributable to the use of anti-retro viral therapy (ART). Objectives: To determine the prevalence of one or more NCDâ€™s namely diabetes mellitus type 2, hypertension, dyslipidemia and depression in adults with HIV on ART. Methods: A comprehensive search strategy was undertaken on the 27th of February 2018 with no date limits in more than 3 databases to identify systematic reviews on the prevalence of NCDâ€™s in HIV patients. We included studies with population over 18 yrs of age, on ART and with the presence of one or more NCD. Findings: Our search yielded 1600 articles and after de-duplication and screening we remained with 11 studies for data extraction of which 3 are ongoing studies. Out of 11 studies identified, only 3 assessed the presence of multi-morbidity while the rest have all assessed the prevalence of co-morbidity of any 1 NCD in HIV patients. The years in which these systematic reviews were undertaken range from 2009 to 2017. We are currently extracting data from each study on a modified AMSTAR 2 tool in order to determine the prevalence of co-morbidity and multi-morbidity in this population. Conclusion: We aim to consolidate findings from several systematic reviews done on prevalence of NCDâ€™s in HIV in order to inform the existing body of research and provide information to healthcare for planning of healthcare services in this group of patients.

ABSTRACT NUMBER / ABSTRAKNOMMER: 30

An Index of Suspicion in a Case of Hyponatraemia

Annalise E Zemlin (NHLS, University of Stellenbosch), Ekkehard W Zollner (University of Stellenbosch), Mariza Hoffmann (NHLS, University of Stellenbosch), Marizna Barkhuizen (NHLS, University of Stellenbosch), Rajiv T Erasmus (NHLS, University of Stellenbosch)

Background: Serum indices can give valuable information and should be interpreted as a result in itself. Lipaemia can influence results through different mechanisms. An important interference affecting electrolyte determination, is the electrolyte exclusion effect. Lipaemia can also cause light scattering that interferes with spectrophotometric detection and partitioning that leads to nonpolar substances being partitioned in the lipid fraction of the sample. A case of pseudohyponatraemia due to the electrolyte exclusion effect is reported. Case description: A 15 year old female patient known with type 2 diabetes mellitus was seen at paediatric endocrinology with mild ketoacidosis. During recovery, her biochemistry (performed on Roche Cobas 6000) revealed severe hyponatraemia of 118mmol/L on serum analysis. At the time of blood collection, her capillary glucose was 13.7mmol/L with a corrected sodium of 122mmol/L. The result was identified as a critical value by the laboratory information system (sodium < 120mmol/L). During manual reviewing of the results, a lipaemia index of 3+ (absolute value 1320) was noted on the serum indices report, which was not flagged as it was below the critical lipaemia limit for sodium determination. On repeat analysis of the same sample on a blood gas analyzer (ABL80 FLEX, Radiometer Medical ApS) using a direct method, the serum sodium was 134mmol/L (sodium corrected for glucose = 138mmol/L). Due to the lipaemia, a triglyceride level was requested, which was severely raised (100mmol/L). Conclusion: The electrolyte exclusion effect is an analytical phenomenon that causes falsely low electrolyte concentrations in the presence of severe lipaemia or

hyperproteinaemia when using indirect analytical methods. This method is used on many modern-day automated chemistry analysers and should be considered in a patient with asymptomatic hyponatraemia.

ABSTRACT NUMBER / ABSTRAKNOMMER: 31

HIV/AIDS (ART-naive) and cardiovascular risk: Are retinal microvascular geometric features markers of effects?

Frans Everson (Stellenbosch University), Hans Strijdom (Stellenbosch University), Ingrid Webster (Stellenbosch University), M. Faadiel Essop (Stellenbosch University), Mashudu Mthethwa (Stellenbosch University), Nandu Goswami (Medical University of Graz), Nyiko Mashele (Stellenbosch University), Patrick De Boever (Vito), Sana Charania (Stellenbosch University), Tim S. Nawrot (University of Hasselt), Yolandi Espach (Stellenbosch University)

Background: HIV/AIDS per se is considered a cardiovascular risk factor while retinal blood vessel calibers and features describing the retinal vessel network complexity are considered surrogate markers of cardiovascular risk; however, the effects of HIV on these retinal metrics remain under-investigated. This study aimed to investigate the effects of HIV/AIDS on the retinal microvasculature in a HIV-infected study population in the Cape Town region. Methods: HIV-free and HIV-infected (without antiretroviral treatment; HIV+) participants were recruited from health clinics. Data were collected via health questionnaires, anthropometry, and biomarker analyses. Retinal images were captured, and retinal vessel metrics (vessel calibers and network patterns) quantified. Results: The study population (HIV-free: n=86; HIV+: n=32) had a mean age of 38.6±9.9 years. HIV+ vs. HIV-free significantly decreased BMI (20.8 (15.0-43.1) vs. 24.8 (14.7-46.6) kg/m³; p < 0.05), systolic (114±10.8 vs. 119 (78-179) mmHg; p < 0.05) and diastolic blood pressure (80±8.5 vs. 86±14.4 mmHg; p < 0.05), HDL-cholesterol (1.01 (0.69-2.38) vs. 1.30 (0.51-3.04) mmol/L; p < 0.05) and full blood count for haemoglobin (13.05±1.56 vs. 13.7±1.29 g/dL; p < 0.05). HIV+ significantly increased central retinal venular equivalent (CRVE) vs. HIV-free (243±27.3 vs. 235±18.8 µm; p < 0.05). HIV+ increased avg. arterial tree diameter vs. HIV-free (82±5.3 vs. 79±4.9 µm; p < 0.05). HIV+ was positively associated with CRVE (r = 0.224, p < 0.05) and avg. arterial tree diameter (r = 0.217, p < 0.05). Conclusion: HIV+ significantly altered various retinal microvascular features and exhibited a less favourable retinal microvascular status compared to HIV-free.

ABSTRACT NUMBER / ABSTRAKNOMMER: 32

High prevalence of vitamin D deficiency in postmenopausal breast cancer patients treated with aromatase inhibitors at Tygerberg Hospital

Baatjes K. B (Stellenbosch University), Erasmus R. T (Stellenbosch University), Kotze M. J (Stellenbosch University), Okunola Abisola Oyedele (Stellenbosch University), Sawe R. T (Stellenbosch University), Zemlin A. E (Stellenbosch University)

Introduction: The importance of vitamin D for prevention of osteoporosis and bone fractures is undisputed, while its role in cancer risk remains uncertain. Breast cancer patients treated with aromatase inhibitors represent an important target group for assessment of vitamin D status, since this drug is associated with increased risk of bone loss and fractures. The aim of this study was to determine vitamin D status in breast cancer patients with the luminal subtype, previously shown to correlate with clinical outcome. Methods: A total of 126 histologically confirmed postmenopausal breast cancer patients attending the Tygerberg Hospital Breast Cancer Clinic were included in the study. Baseline data entered between 2014 and 2017 was extracted from the research database. Estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2) status was determined by standard immunohistochemistry (IHC). Serum vitamin D levels were measured in the study participants by chemiluminescent immunoassay and their DNA stored for future genetic studies. The levels of vitamin D were classified as deficient (<20ng/ml), insufficient (20-29ng/ml) or sufficient

(30-150ng/ml).Results: Pathological tumor types included 14 (11.4%) invasive lobular carcinomas, 87 (71.3%) invasive ductal carcinomas, 5 (4.1%) ductal carcinoma in situ, and 5 (4.1%) were unknown. Vitamin D levels were deficient in 53.7% (Mixed ancestry 54, Caucasian 6, Black 2, Indian3) of the patients. Insufficient levels were detected in 37.1% (Caucasian 7; mixed ancestry 36), while sufficient levels were recorded in 11.2 % (Caucasian 2; mixed ancestry 11) of study participants.Conclusions: The finding that more than half of the patients have vitamin D deficiency highlighted the need for a comprehensive monitoring program aimed at improved clinical management at Tygerberg Hospital. The value of applied laboratory medicine in healthcare delivery lies in early detection of patients at increased risk of breast cancer recurrence and drug-induced side effects.

ABSTRACT NUMBER / ABSTRAKNOMMER: 33

Community engagement for H3Africa Biobanking Research

Anita Kleinsmidt (Centre for Medical Ethics & Law)

Biobanking research is increasingly important in the medical field but Africa lags behind even with the most varied genomes in the world. In order to address this shortcoming, H3Africa established a biobank in Africa, in which African samples are be stored. The development of research capacity in this field depends on the willingness of the community to participate and to this end, we developed material which facilitates community engagement within the Tygerberg context. The collection, storage and future re-use of biological samples raises cultural concerns for many communities, as well as fears of stigmatisation and discrimination. We developed activity books for Life Sciences matric students and have been invited to participate in curriculum development. We reviewed the literature and existing guidelines, and engaged with stakeholders in order to develop a community engagement model for Tygerberg hospital. Ubuntu was considered an essential component of the model, given the African context. 30 participants and 11 community advisory board (CAB) members were recruited from the adult lymphoma clinic at Tygerberg. In-depth interviews were conducted focussing on perceptions on community, biobanking and engagement methods using the educational material developed for this context and a genogram to initiate discussions about genetics. Participants's definitions of community varied. Definitions referenced familial connections, social connection and geographical proximity. Despite the different definitions of community, there was significant overlap in engagement methods. Community engagement based on Ubuntu requires that relationships are built on mutual respect with an openness to hear the other in the first phase. Ubuntu facilitates reciprocal learning and could possibly identify and address the needs of the researcher, the participant and the community. During phase 2, using identified phase 1 methods, consensus should be reached about the objectives through collective decision-making. The process is complete when the information collected is disseminated and community feedback is given.

ABSTRACT NUMBER / ABSTRAKNOMMER: 34

An audit of the number and indication of Prothrombin (Factor II) molecular tests requested at Tygerberg Hospital over a period of 12 years and the molecular screening of a newly identified Prothrombin (Factor II) mutation

Carmen Swanepoel (Division of Haematology, Department of Pathology, FMHS, Stellenbosch University; National Health Laboratory Service), Nomusa Mashigo (Division of Haematology, Department of Pathology, FMHS, Stellenbosch University; National Health Laboratory Service), Shafieka Isaacs (Division of Haematology, Department of Pathology, FMHS, Stellenbosch University), Shareefa Isaacs (Division of Haematology, Department of Pathology, FMHS, Stellenbosch University), Wardah Cerfontein (Division of Haematology, Department of Pathology, FMHS, Stellenbosch University; National Health Laboratory Service)

Heritable thrombophilia which predisposes individuals towards thrombosis is a multifactorial disorder with high mortality and morbidity. The more prevalent inherited risk factors are the gain-of-function

mutations in coagulation factors, Factor V-Leiden (FVL; F5G1691A) and Factor II or prothrombin (FII; F2G20210A). As the prevalence of FVL and FII mutations within our setting is unknown, we aim to conduct an audit on the number of molecular tests requested and investigate the prevalence of Factor II and screen for a novel mutation Arg596Leu; c.1787G>T in exon 14 of Factor II. Molecular reports reviewed over a period of 12 years to determine the number of FII requests and associated epidemiological data. One hundred patients with and without known positivity for the FII and FVL mutations will be screened for Arg596Leu; c.1787G>T mutation using RFLP and Sanger sequencing. For the audit, a total of 723 molecular thrombophilia request have been performed with an annual average of 60 tests requested and screened. Of this only 20% of the request were for FII highlighting that 80% was not screened for Factor II as it was not specifically requested. Of the total test requests, 3% was positive for the F5G1691A mutation while a higher incidence of 7% was positive for the F2G20210A mutation. The epidemiology of the FVL and FII mutations has not been well studied within the South African/African context. The fact that 80% of cases did not request FII while a higher incidence of the FII mutation was observed in our population highlights big gaps and shows that this requires further investigation as these results would aid in the improvement of thrombophilia screening at TBH. Likewise including the screening of a newly identified mutation as well as the Methylenetetrahydrofolate reductase (MTHFR C677T) mutation in our screening panel will aid in strengthening diagnosis.

ABSTRACT NUMBER / ABSTRAKNOMMER: 35

THE SURGICAL MANAGEMENT AND OUTCOME OF GASTROINTESTINAL STROMAL TUMOURS AT TYGERBERG ACADEMIC HOSPITAL AND ITS DRAINAGE AREA

Ailsa Leitch (University of Stellenbosch), Stefan Hofmeyr (University of Stellenbosch)

Introduction: Gastro-intestinal stromal tumours (GIST) are uncommon. Local data concerning their presentation, management and outcome are limited. Aims: To describe the mode of presentation, surgical management, anatomical location, histopathological characteristics and survival of GIST managed at Tygerberg Academic Hospital and its drainage area. Methodology: A retrospective cohort study of cases identified from the NHLS anatomical pathology database, between 01/2003 and 07/2016, was identified. University of Stellenbosch Health Research Ethics Committee approval was attained (HREC S16/07/137.) Inclusion criteria: Age > 13 years; patients treated at Tygerberg Academic Hospital and its referral hospitals. Exclusion criteria: Incomplete clinical records and patients without histopathological confirmation of GIST. Results: Of 85 patients identified, 71 met the inclusion criteria. The median age presentation was 63 (30-84). Female: male ratio was 1,5: 1. Gastro-Intestinal bleeding and abdominal pain were the most common presenting complaints. 28% of GIST were larger than 10 cm. 68% of specimens had a low mitotic count (< 5/50 HPU). The stomach was involved in 68%, small bowel 10%, large bowel 4%, duodenum 4% and other 14%. Metastases were present in 14 patients (20%). Imatinib use was infrequent (14%). 5 year overall survival was 67%. (International O.S. = 70.2%) Conclusions: GIST presented at a similar age to international data. The large size of GIST at presentation suggests that our cases present late. The distribution of GIST and presence of metastases and overall survival were similar to international findings. Recommendations: Collaboration between institutions will recruit larger numbers for the study of uncommon tumours and conditions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 36

ATM expression in Peripheral Blood Mononuclear cells as a Biomarker of Insulin Resistance.

Barbara Huisamen (Stellenbosch University, Division of Medical Physiology), Lois Williams (Stellenbosch University, Division of Medical Physiology)

Introduction: Ataxia Telangiectasia (AT) is an autosomal recessive disease caused by mutations in the ATM (AT mutated) gene causing protein deficiency/inactivation and presents with cerebellar neurodegeneration, immunodeficiency, increased predisposition for cancer, insulin resistance, a high risk of developing type II diabetes and ischaemic heart disease. Peripheral blood mononuclear cells (PBMC) can express part of the genome which is susceptible to environmental influences such as insulin resistance. ATM has previously been measured in PBMC thus a correlation will be investigated between the degree of insulin resistance and ATM expression. Methods: Male Wistar rats were fed a high fat diet (HFD) for 16 weeks to induce obesity and insulin resistance and compared to chow-fed age-matched controls (C). Body weight, intra-peritoneal (IP) fat and OGTTs were measured. After sacrifice PBMC were isolated from whole blood, lysates prepared and Western blotting done to determine ATM expression. Additional control animals were sacrificed at 12 weeks for an age comparison (YC). Results: Body weight differed between YC and C, $p=0.0001$, $n=7$; IP of HFD vs C differed significantly ($25.62\text{g} \pm 1.495\text{g}$ vs. $14.17\text{g} \pm 1.432\text{g}$; $p<0.0001$, $n=7-9$). Both fasting blood glucose levels ($p<0.05$) and OGTTs ($p<0.0001$), $n=12$, differed significantly, indicating insulin resistance in the HFD vs C animals. Total ATM levels did not differ between C and HFD animals but differed significantly between C and YC ($p=0.025$) and phosphorylated ATM levels differed significantly between YC and C ($p=0.018$). Conclusion: HFD is linked to the advancement of insulin resistance as HFD animals showed elevated levels of total IP fat, fasting blood glucose and AUC of the OGTTs when compared to controls. The correlation between ATM expression and insulin resistance should be further investigated while age showed a significant effect on active ATM.

ABSTRACT NUMBER / ABSTRAKNOMMER: 37

ATM regulates cardiac mitochondrial function

Amanda Lochner (University of Stellenbosch), Barbara Huisamen (SA-MRC Biomedical Research and Innovation Platform & University of Stellenbosch), Marguerite Blignaut (University of Stellenbosch)

Ataxia Telangiectasia (A-T) a rare, recessive genetic disease that arises due to a decrease or absence of Ataxia Telangiectasia mutated protein kinase (ATM). A-T is a neurodegenerative disease but patients also display insulin resistance, type 2 diabetes and ischaemic heart disease. The absence of ATM is furthermore associated with increased oxidative stress. In addition, ATM maintains myocardial glucose homeostasis. Using animal models, we demonstrated that myocardial ATM expression in the heart is (i) low in obesity-induced insulin resistance and (ii) located on the inner mitochondrial membrane. In light of the importance of mitochondrial dysfunction in cardiovascular disease, this study investigated the role of mitochondrial ATM in cardiac oxidative phosphorylation (oxphos) using male Wistar rats. Methods: TEM and SR-SIM microscopy and western blotting were employed to localize ATM. Ex vivo perfusion ($n=6-9/\text{group}$) of hearts \pm the specific ATM inhibitor, KU60019 (3 μM) or insulin (10 nM), was performed prior to mitochondrial isolation and oxphos measurements (Clarke-type electrode) using either a carbohydrate (glutamate) or fatty acid (palmitoyl-carnitine) substrate. Results: Sequential shearing off of mitochondrial membranes coupled to western blot analysis of marker proteins demonstrated the localization of ATM to the inner mitochondrial membrane. SR-SIM using fluorescently labelled antibodies confirmed this by showing co-localization with ANT (inner membrane) but not VDAC (outer membrane). Inhibition of ATM significantly decreased active and resting mitochondrial respiration which was associated with a decreased oxphos rate and respiratory control index (RCI) ($p<0.05$). In contrast, stimulation of hearts with insulin, increased mitochondrial respiration parameters that, in turn, were reversed by inhibition of ATM. Moreover, inhibition of ATM resulted in decreased total mitochondrial Drp1 levels indicating less fission. We therefore conclude that ATM may play an important role in mitochondrial oxidative phosphorylation potential as well as fusion and fission and may therefore be involved in mitochondrial dysfunction in insulin resistance.

ABSTRACT NUMBER / ABSTRAKNOMMER: 38

Revisiting chloroquine as a potential anti-diabetic drug and its effect on cardiac function

Barbara Huisamen (Stellenbosch University), Marguerite Blignaut (Stellenbosch University), Mignon van Vuuren (Stellenbosch University), Yolandi Espach (Stellenbosch University)

Purpose: Chloroquine-induced cardiotoxicity is a well-known side effect of the drug. Several studies have proposed chloroquine as a potential anti-diabetic but do not address cardiotoxicity. This study investigated the effect of acute chloroquine treatment in 1) glucose uptake and heart function 2) mitochondrial function in obesity and 3) chronic low-dosage treatment (5 mg/kg/day) on heart function. **Methods:** Glucose uptake (2-DG), cell viability (propidium iodide), heart rate and cardiac function (balloon model) was measured in lean, control male Wistar rat hearts in the presence of increasing chloroquine concentrations (10 μ M, 30 μ M, and 50 μ M). Mitochondrial function was assessed with a Clark-type oxygraph (Hansatech.) in obese male Wistar rat hearts that were perfused with either a vehicle control (n=8) or chloroquine (30 μ M, n=8). Cardiac function after chronic chloroquine treatment (5 mg/kg/day) was assessed in an insulin resistant, obese model (n= 4). **Results:** Acute chloroquine treatment becomes cardiotoxic to isolated cardiomyocytes at high concentrations (100 μ M), and had no effect on cardiomyocyte glucose uptake (2DG) at low (10 μ M), intermediate (50 μ M) or high (100 μ M) concentrations. This study shows that an acute chloroquine treatment at 10 μ M is sufficient to significantly decrease RPP and LVD ($p < 0.05$) in lean, control hearts, and significantly reduce heart at 30 μ M ($p < 0.05$). Acute treatment had no effect on mitochondrial function, but chronic low-dose chloroquine treatment significantly decreased aortic output and total work in hearts ($p < 0.005$) from insulin resistant, obese Wistar rats. **Conclusion:** Low and intermediate chloroquine doses administered either chronically or acutely is sufficient to result in myocardial dysfunction.

ABSTRACT NUMBER / ABSTRAKNOMMER: 39

Understanding the liver to protect the heart: investigating the link between insulin resistance and non-alcoholic fatty liver disease in obesity-induced myocardial dysfunction

Anel Boshoff (Stellenbosch University), Barbara Huisamen (Stellenbosch University), Rabia Johnson (South African Medical Research Council)

Introduction: The global rise in obesity has led to an increase in co-morbidities, such as insulin resistance and non-alcoholic fatty liver disease (NAFLD). Insulin resistance is thought to be a hallmark of NAFLD and is also a well-established risk factor for the development of type 2 diabetes mellitus (T2DM) and subsequent myocardial dysfunction. However, an alternative school of thought suggests that NAFLD can develop in the obese state, independent of insulin resistance, and that it can in fact lead to insulin resistance and myocardial dysfunction. **Aim:** To establish the age-dependent onset of insulin resistance, NAFLD and myocardial dysfunction. **Methods:** Obese male Lepr^{db/db} mice and lean controls were monitored weekly for body weight and fasting blood glucose. Serum lipogram assessed dyslipidaemia, and serum AST/ALT levels were measured as an indication of liver damage. Liver histology and gene expression analysis assessed lipid accumulation and inflammation. Heart function was monitored by echocardiography and expression analysis of genes involved in fibrosis, inflammation and insulin resistance. The onset of peripheral insulin resistance was established by gene expression analysis in fat and protein expression in skeletal muscle. **Results:** This study showed that Lepr^{db/db} mice were significantly overweight and dyslipidemic by the age of 6 weeks, and histological analysis revealed that hepatic steatosis was already present by this time. However, fasting blood glucose was normal at 6 weeks of age, indicating that insulin resistance was not yet present. Echocardiography and expression of fibrosis genes in the heart indicated the onset of myocardial dysfunction by 16 weeks of age. **Conclusion:** NAFLD can develop in the obese state, independent of insulin resistance. **Keywords:** Obesity, insulin resistance, non-alcoholic fatty liver disease, myocardial dysfunction

ABSTRACT NUMBER / ABSTRAKNOMMER: 40

The effect of green rooibos extracts in the histomorphology of the pancreas in rats fed a high fat diet

Dr. Nireshni Chellan (South African Medical Research Council), Jodie Layman (Stellenbosch University), Prof Barbra Huisamen (Stellenbosch University), Prof Sanet Kotze (Stellenbosch University)

The anti-diabetic effects of fermented rooibos, *Aspalathus linearis*, have been well described in vivo and in vitro. Afriplex GRT[®] is an unfermented green rooibos extract, which is postulated to be a nutraceutical with anti-diabetic properties. The study aimed to determine if the possible anti-diabetic effects of GRT shown in vitro is reflected in vivo on pancreatic histology in a diet-induced obese rat model. Male Wistar rats (N=28) were randomly sorted into four study groups (n=7) namely, control, GRT fed control (GRT), high-fat diet (HFD) and high fat diet, GRT supplemented (HFD-GRT). Pancreata were removed and processed to wax for histological sectioning. Each pancreas was sectioned at 4 µm in thickness at three levels 20 µm and 50 µm apart. Sections were labelled with anti-insulin and anti-glucagon antibodies and counterstained using haematoxylin. Islet area, alpha and beta cell areas as well as islet density were determined using morphometric techniques. Supplementation of GRT resulted in a significant increase in islet and beta cell areas in the GRT control group compared to the control. Alpha cell area was increased by GRT supplementation however, this was not significant. Islet density did not differ across the groups. Green rooibos and its extracts have improved glucose tolerance and metabolism as well as the expression of insulin signalling proteins in other rodent models. In the present study, GRT in isolation effectively increased glucose metabolism as indicated by the increase in islet and beta cell areas. However, histologically observable effects of GRT on the pancreas of the HFD-GRT group were negative as islet and beta cell area was significantly smaller compared to GRT and HFD groups. Thus, the anti-diabetic effects of GRT are not reflected on a histological level in terms of islet and beta cell areas in an obese rat model and its efficacy as a nutraceutical requires further investigation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 41

Beta secretase regulation and inflammation in pancreatic beta cells: the potential role of Rooibos

CJF. Muller (Stellenbosch University; South African Medical Research Council), J. Burger (Stellenbosch University; South African Medical Research Council), J. Lopes (Stellenbosch University), N. Chellan (Stellenbosch University; South African Medical Research Council)

Insights into the mechanisms involved in pancreatic β^2 -cell inflammation and the associated effect(s) of beta secretase (BACE), may reveal an opportunity for the development of novel therapeutics that directly protect and preserve β^2 -cells in type 2 diabetes (T2D). In β^2 -cells, BACE modulates the deposition of cytotoxic islet amyloid and subsequent induction of oxidative stress, making BACE inhibition a therapeutic target. Taking into consideration the antioxidant properties of aspalathin and phenylpyruvic acid glucoside (PPAG), both bioactive polyphenols of an aspalathin-enriched, unfermented Rooibos extract (GRT) as well as the possible BACE inhibitory properties of these phenolic compounds, we postulate that Rooibos may have anti-inflammatory effects in β^2 -cells and additionally may have the ability to modulate BACE, thus further enhancing the anti-diabetic effect. BACE inhibition profiling of GRT, aspalathin, and PPAG was assessed by using a fluorescence resonance energy transfer (FRET) purified enzyme assay, followed by kinetically assessing BACE activity in vitro. INS1 cell viability, function and oxidative stress were measured by cellular ATP production, apoptosis / necrosis, insulin secretion and content, and reactive oxygen species (ROS) production. Higher concentrations of aspalathin and moreso, GRT, showed a trend towards BACE inhibition, but reduced ATP content of INS1 cells. However, lower concentrations of aspalathin, GRT and PPAG may have a protective effect on inflamed pancreatic β^2 -cells as a slight increase in overall cell viability and function was observed, with a decrease in oxidative stress. From these data, GRT may potentially ameliorate inflammation-induced β^2 -cell stress, with some regulation of BACE activity; the effect on the interaction between BACE regulation and inflammation still needs to be investigated.

ABSTRACT NUMBER / ABSTRAKNOMMER: 42**A comparison of the effects of three indigenous South African herbal beverages on the vascular function of streptozotocin (STZ)-induced male diabetic Wistar rats**

Dawn Mahlangu (Stellenbosch University), Michelle Smit-van Schalkwyk (Stellenbosch University), Shantal Windvogel (Stellenbosch University)

Diabetes mellitus, a known risk factor for cardiovascular disease (CVD), is associated with oxidative stress, which leads to the production of reactive oxygen species (ROS). Endothelial dysfunction (ED) appears to be a response to cardiovascular risk factors, with nitric oxide (NO) playing a major role in the homeostasis of the vasculature. ED is an early, reversible precursor of atherosclerosis, which, in turn, is associated with CVD. ROS reduce the protective abilities of NO on the endothelium, which leads to ED. Rooibos (*Aspalathus linearis*), Honeybush (*Cyclopia intermedia*) and Sutherlandia (*Sutherlandia frutescens*) are indigenous South African herbal beverages which exert potent antioxidant and immune-modulating actions and are thus believed to be cardioprotective. This study aimed to compare the effects of treatment with Rooibos, Honeybush and Sutherlandia on the vascular function of STZ-induced male diabetic Wistar rats. Diabetes was induced by means of a single intraperitoneal injection of STZ (45 mg/kg bw). After confirmation of diabetes, Rooibos (fermented, 2%), Honeybush (unfermented, 4%) and Sutherlandia (4%, diluted in water to 0.01 ml/g rat weight) were administered in place of the drinking fluid for a treatment period of six weeks. Appropriate controls were included. Vascular function was determined by means of blood pressure measurements (in vivo) utilising the CODA non-invasive blood pressure system (tail-cuff method). Aortic ring isometric tension studies (contraction/relaxation studies) were carried out on fresh segments of aortic tissue (ex vivo) to determine endothelial and smooth muscle function.

ABSTRACT NUMBER / ABSTRAKNOMMER: 43**Evaluation and validation of the Cepheid GeneXpert BCR/ABL Monitor and Ultra test kits to identify and monitor the presence of the oncogenic BCR-ABL p210 variant transcript in CML patients**

Carmen Swanepoel (Stellenbosch University/NHLS), Chantal De Long (Stellenbosch University), Lynthia Paul (University of Cape Town/NHLS), Ravnit Grewal (Stellenbosch University/NHLS)

Chronic myeloid leukaemia is a disease of the white blood cells resulting from the reciprocal translocation between chromosome 9 and 22. The molecular consequence of this translocation is the generation of the BCR-ABL oncogene that encodes the chimeric BCR-ABL1 tyrosine kinase (TK) protein. Highly effective therapies have been developed for CML particularly the tyrosine kinase inhibitors (TKI) which targets the oncogenic activity of BCR-ABL, however it does not serve as a cure for the disease. Thus, molecular monitoring of the BCR-ABL transcript has become standard of care as it aids in prognosis, help with monitoring treatment response and help predict relapse. Quantitative reverse transcription PCR (qRT-PCR) is the method of choice used to monitor the treatment response by measuring the amount of BCR-ABL messenger RNA (mRNA) in blood cells. It is thus critical that the BCR-ABL test is accurate, adhere to an international scale (IS) and have improved sensitivity. The present study aims to evaluate and validate BCR/ABL Monitor and Ultra tests kits using the Cepheid GeneXpert instrument. No studies to date had been published in South Africa to compare the performance of the two kits and to verify the claim of greater sensitivity with the improved ULTRA kit. It also aims to do a cost and labour analysis of this automated qRT-PCR methodology compared to the manual methods used in other diagnostics settings. The anticipated result would be to find improved sensitivity in the Ultra kit, making it the preferred technique for diagnostic purposes and molecular monitoring of CML patients. Furthermore, it is anticipated that the automated qRT-PCR method would be less expensive and less labour intensive. The results of this comparison will be analysed in conjunction with the available clinical data.

Theme 5 / Tema 5
**Maternal and Child Health/
Moeder- en Kind Gezondheid**

ORAL PRESENTATIONS / REFERATE

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

Cochrane “Packaging and Push” in action: dishing up digestible nutrition evidence

Anel Schoonees (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Celeste Naude (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University), Jimmy Volmink (Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Stellenbosch University)

Background: Worldwide, 52 million children under the age of five years are wasted, of which 17 million have severe acute malnutrition (SAM). Fewer than 20% of children with SAM are able to access the treatment they need. Ready-to-use therapeutic food (RUTF) has been widely recommended for outpatient rehabilitation for children with uncomplicated SAM. In 2017/2018, we updated a Cochrane review on the effects of RUTF to treat children with SAM at home. Healthcare decision-makers need this new evidence to inform policies and practice. Objective: To develop and implement a knowledge translation plan for a priority nutrition review that enables user-friendly evidence to reach relevant users for uptake in decision-making. Methods: In line with theme 2 of the Cochrane Knowledge Translation (KT) Framework “Packaging, push and support to implementation”, we will: (1) define audiences and map specific stakeholders according to topic and context, using structured stakeholder mapping; (2) define suitable diffusion and dissemination strategies to address the objective; (3) develop fit-for-purpose products and activities linked to appropriate channels; and (4) implement the plan. Results: We will conceptualise the knowledge translation plan into a “Packaging and Push Action Table”, defining each product and activity, stakeholder, strategy, channel and implementation approach. Our main target audience includes policymakers, healthcare managers, researchers and research funders, with particular reference to key stakeholders such as UNICEF, WHO, and low- and middle-income country governments. Appropriate review-derived products will include a policy brief, blogshot, podcast and infographic and participation in targeted scientific meetings. Channels will include downloadable products on websites, newsletters, email, media, Cochrane member networks and the Cochrane KT department. Conclusion: This “Packaging and Push Action Table” will enable us to bridge the production, diffusion and dissemination of a priority nutrition Cochrane review, and can help ensure that users receive digestible evidence useful for making healthcare decisions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Dietary Diversity, Food Security and Coping Strategies of Households from Rural Communities in Limpopo Province

Gubela Mji (Stellenbosch University), Lindelani Mushphi (University of Venda), Nomusa Dlamini (CSIR), Sefora Makuse (University of Limpopo), Xikombiso G Mbhenyane (Stellenbosch University)

Introduction: The main aim of the study is to develop models for improving food security and nutritional status of households using indigenous foods among rural communities in the selected areas of Eastern Cape and Limpopo provinces. This paper reports on dietary diversity, household food security and coping strategies to food deprivation by households with a focus on children and women in Limpopo Province.

Methodology: The approach was a descriptive survey where purposive sampling was used to select study areas and the sample from two rural communities in Limpopo provinces. The project was submitted for ethical clearance at the Health and Research Ethics Committee of Stellenbosch University (Ref #: N16/06/083). Further permission was obtained from Traditional Leadership of the villages and participants signed consent for their participation and that of the children. Results: A total 280 households, 2520 participants of which 17% were children under 12 years

participated. 23.6% of households were food secure, 39.6% at risk of hunger while 36.8% were food insecure. The coping strategies occurring at least for 3 days (mode) in a week were: reliance on less preferred and less expensive foods (53.9%); reduce portion sizes until month end (36.4%); reduce number of meals eaten in a day (33.6%); and limit portion size at mealtimes (25%). Only 15% of the households with an occurrence of once week gathered wild food, hunt or harvest immature crops. Conclusion: High levels of food insecurity was reported in these two communities and household employ various approaches to cope with food deprivation to feed children with none utilisation of indigenous or wild foods.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

An investigation into the correlation between macroscopic signs and post-mortem biochemistry of dehydration at autopsy in a forensic pathology cohort of children under 1 year.

Björn Andrew Swigelaar (Stellenbosch University / Forensic Pathology Services)

Dehydration secondary to gastro-enteritis remains a significant cause of death in children. Forensic practitioners face challenges when making the diagnosis due to poor ante-mortem history, non-specificity of external features, difficulty in both obtaining post-mortem fluid samples and interpreting post-mortem results. Possible morphological artefacts arise in the setting of a delayed post-mortem interval (PMI). Could the morphological features of dehydration be a result of post-mortem drying out of the body due to a prolonged PMI, and do the biochemical analyses truly indicate ante-mortem dehydration? The aim is to investigate the correlation between post-mortem macroscopic and biochemical features of dehydration. A prospective analytical study was performed involving children under the age of 1 that underwent post-mortem examinations at the Tygerberg mortuary. Autopsies were performed due to the unexplained and sudden nature of the death. Cases underwent external, internal post-mortem examination and sampling of blood and/or ocular fluid. Chemical analyses were performed at the Tygerberg NHLS. Results were compared with the external findings seen at post-mortem examination and a correlation between macroscopic and biochemical features of dehydration was determined. Of the 95 cases, 20 were diagnosed with dehydration based on external examination. Sodium and chloride levels failed to show alterations consistent with dehydration in cases of dehydration based on external examination. Sodium and chloride results also failed to indicate statistically significant differences when comparing results of the dehydrated and non-dehydrated groups. Mean urea levels were statistically significantly higher in the dehydrated group vs the non-dehydrated group (p -value <0.001 for serum, 0.003 for ocular fluid). Mean ocular fluid creatinine levels showed statistically significant increases in the dehydrated group vs non-dehydrated group. Conclusions: Serum and ocular fluid urea, as well as ocular fluid creatinine, were associated with statistically significant increases in the dehydrated group.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Ten years of routine paediatric TB surveillance data in South Africa – high disease burden and poor treatment outcomes

Dr. Anneke C. Hesselning (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University), Dr. Karen du Preez (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University), Dr. Muhammad Osman (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University), Dr. Pren Naidoo (Bill and Melinda Gates Foundation, Seattle, Washington)

Background: Improving surveillance data for children with tuberculosis (TB) is a key priority. Evaluation of routine surveillance data is important for programmatic monitoring and evaluation and to understand local epidemiology and the impact of program changes. We evaluated 10 years' routine paediatric TB treatment surveillance data. Methods: Retrospective cohort analysis of all newly registered children

(<15 years of age) recorded in the routine South African National TB programme (SANTP) electronic TB register for drug-susceptible TB (ETR.Net) from 2004-2013. We report routinely collected demographic, clinical and treatment outcome data. Data was analysed in 4 age bands: 0-1, 2-4, 5-9, and 10-14 years. Results: A total of 456,441 paediatric TB cases (232,059; 50.8% males) were identified, contributing 11-14% of the total TB caseload amongst newly registered TB patients annually. Children <5 years comprised nearly two thirds (0-1 years: 140,758 [30.8%]; 2-4 years: 142,238 [31.2%]; 5-9: 113,520 [24.9%]; 10-14 years: 59,921 [13.3%]). The age distribution did not change over time. Documentation of HIV status improved over time (2004=0.3%, 2009=37.6%, 2013=82.6%). Annually since 2010, the proportion of children with HIV co-infection varied between 20 and 21%. Pre-treatment bacteriological test results were recorded in only 76,401(16.7%) children, with bacteriological confirmation in 41,501(9.1%). Diagnostic confirmation increased with age: 0-5 years=3.0%; 5-9 years=9.5%; 10-14 years=37.1%. Only 294,453(64.5%) had favourable outcomes (cured/treatment completed). Unfavourable outcomes included 7,660(1.7%) deaths, 114,388 (25.1%) moved/transferred out and 39,536 (8.7%) loss-to-follow-up/not evaluated. Conclusions: Many children have been treated for TB and reported in ETR.Net in South Africa. Although the proportion of children overall (11-13%), and proportion of these <5 years of age (62%) are consistent with that expected in high burden TB settings, the proportion of children with confirmed disease is low (9%). Further analysis should explore age, TB disease spectrum, HIV co-infection and treatment and reasons for poor treatment outcomes in children.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Paediatric antimicrobial use at a South African hospital

Andrew Whitelaw (Stellenbosch University), Angela Dramowski (Stellenbosch University), Eric de Cloedt (Stellenbosch University), Heather Finlayson (Stellenbosch University), Lotte Koopmans (Radboud University)

Background: Data on antimicrobial use among hospitalised children in Africa is very limited owing to the absence of electronic prescription tracking. Methods: We evaluated antimicrobial consumption rates, antimicrobial spectrum used and indications for therapy on a paediatric ward and the paediatric intensive care unit (PICU) at Tygerberg Hospital, Cape Town, South Africa. Antimicrobial prescription and patient demographic data was prospectively collected from 10 May 2015 to 11 November 2015. For the same period, data on antimicrobials dispensed and costs were extracted from the pharmacy's electronic medicine management system. The volume of dispensed antimicrobials (dispensing data) was compared with observed antimicrobial use (prescription data). Results: Of the 703 patients admitted, 415/451 (92%) paediatric ward admissions and 233/252 (92%) PICU admissions, received 1/more antimicrobials. In the ward, 89% of prescriptions were for community-acquired infections; 29% of PICU antimicrobials were prescribed for healthcare-associated infections. Ampicillin and 3rd generation cephalosporins were the most commonly prescribed agents. Antimicrobial costs were 67 541 South African Rands (ZAR) [5 680 United States Dollars (USD)] on the ward and 210 484 ZAR (17 702 USD) in PICU. Ertapenem and meropenem were the single largest contributors to antimicrobial costs on the ward (43%) and PICU (30%) respectively. The volume of antimicrobials dispensed by pharmacy (dispensing data), differed considerably from observed antimicrobial use (prescription data). Conclusion: High rates of antimicrobial consumption were documented. Community-acquired infections were the main indication for prescription. Although pharmacy dispensing data did not closely approximate observed use, it is a promising method for antimicrobial usage tracking in future.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

A scoping review on the perceptions of mothers with preterm infants regarding early communication development.

Elani Matthee (Stellenbosch University), Elanie van Schalkwyk (Stellenbosch University), Julia Miller (Stellenbosch University), Samantha Gay (Stellenbosch University)

Preterm infants are at risk for communication disorders/delays. In order to prevent or effectively address these possible communication disorders/delays, health professionals need to understand the perceptions and needs of mothers regarding the early communication development of their preterm infant. Although previous studies have focused on parents' and patients' perceptions of medical information received from health professionals, there is limited research regarding maternal perceptions of early communication development, specifically in the South African context, focusing on preterm infants. The aim of this study was to scope and summarize the range and nature of available research in the fields of early communication development and intervention in preterm infants, and specifically maternal perceptions thereof. This study followed the methodology of a scoping review. The scoping review followed five phases, namely: articulating the research question, identifying relevant studies, selecting appropriate studies, charting the data and collating, summarizing and reporting the results. Research articles were included only if they addressed the key concepts of our research question. Based on the results of this study, a need exists for further research within the field of early communication development and intervention in the preterm population. It is recommended that an empirical study aiming to establish the most effective strategies for communication-interaction training with mothers of preterm infants is conducted. A further recommendation would be to increase the awareness of early communication development and intervention in the preterm population amongst both health professionals and parents.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

THE EFFECT OF MATERNAL HIV STATUS AND DURATION OF TREATMENT ON BODY COMPOSITION OF HIV-EXPOSED AND HIV-UNEXPOSED PRETERM, VERY AND EXTREMELY LOW BIRTHWEIGHT INFANTS

Daniel Gerhardus Nel (Stellenbosch University), Evette Van Niekerk (Stellenbosch University), Klara Strydom (Stellenbosch University), Muhammad Ali Dhansay (Medical Research Council)

Background: There is an evidence gap regarding the relationship between HIV exposure, body composition (and the quality thereof) and preterm infants. Aim: The purpose of this study was to determine the body composition of HIV-exposed, preterm very low-birthweight (VLBW) and extremely low-birthweight (ELBW) infants and to assess the effect of maternal HAART duration on the body composition of this vulnerable population. Methods: A descriptive cross-sectional study was conducted between May and October 2016. HIV-exposed and -unexposed preterm infants (gestational age <37 weeks) with a birthweight of ≤ 1200 g were included. Each infant's maternal medical background was recorded. Infant anthropometric measurements including skinfolds were recorded weekly during the 28-day follow-up period. Results: Thirty of the preterm infants (27%) were HIV-exposed. HIV-exposed infants had significantly ($p=0.01$) lower gestational ages than HIV-unexposed infants (25-28 weeks) within the group. HIV-exposed infants had significantly lower measurements on day 21 and day 28 for triceps skinfold (TSF) (2.5 mm vs 2.7 mm, $p=0.02$ and 2.6 mm vs 2.9 mm, $p<0.01$), subscapular skinfold (SSSF) (2.3 mm vs 2.6 mm, $p=0.02$ and 2.4 mm vs 2.7 mm, $p<0.01$) and fat mass percentage (FM%) (0.9% vs 1.4%, $p=0.02$ and 1.0% vs 1.5%, $p=0.03$). HIV-exposed infants whose mothers received HAART for ≥ 20 weeks were heavier and had a higher FM% and lower fat-free mass percentage (FFM%) at birth than HIV-exposed preterm infants whose mothers received highly active antiretroviral therapy for <20 weeks. Conclusion: Mothers receiving HAART could have an increased risk of preterm delivery, and the duration of maternal HAART affects postnatal body composition of their infants. Body composition differs between HIV-exposed and HIV-unexposed preterm infants.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

Mother-to-child transmission of hepatitis B virus in Windhoek, Namibia: transmission dynamics and prevention

Charles Wiysonge (South African Cochrane Centre), Cynthia Tamandjou (Division of Medical Virology, Stellenbosch University), Dorothea Diergaardt (Division of Family Health, Directorate of Primary Health Care Services, Ministry of Health and Social Services), Etienne Nel (Department of Paediatrics and Child health), Josef Mufenda (Department of obstetrics and Gynaecology, Windhoek Hospital Complex), Monique Andersson (Division of Medical Virology, Stellenbosch University), Wilson Landuleni (Department of Paediatrics, Intermediate Katutura Hospital), Wolfgang Preiser (Division of Medical Virology, Stellenbosch University)

Mother-to-child transmission (MTCT) has emerged as a major driver of the hepatitis B virus (HBV) epidemic in sub-Saharan Africa (SSA). The tools to eliminate this route of transmission are available. This study aimed to assess the feasibility of preventing MTCT of HBV through a screen-treat-vaccinate intervention. Consented pregnant women, attending an antenatal clinic in Windhoek, were screened for HBsAg by means of the Alere Determine™ HBsAg rapid test. Venous blood was collected from HBsAg positive patients for further HBV serological markers (HBeAg, anti-HBe, anti-HBc IgM) testing. Viral load was determined using the AmpliPrep/COBAS TaqMan HBV test V2.0. Genotyping and mutation analysis were performed through online HBV genotyping tools. Positive mothers at high risk of MTCT were reviewed for antiviral prophylaxis. HBV-exposed babies were immunized as per national guidelines, and followed-up to determine the rate of MTCT. A total of 515 pregnant women participated to the study; 28 (5.4%) tested HBsAg-positive. Viral strains belonged to genotype E (8/11; 72.7%) and sub-genotype D1 (3/11; 27.3%). No drug resistance mutations were identified. Two (2/28; 7.14%) HBsAg/HBeAg-positive patients presented with viral load >106 IU/ml; one received antiviral prophylaxis with tenofovir, the other was offered prophylaxis but did not receive it. So far, 21 HBV-exposed babies have been followed-up at six weeks of age. All babies received birth dose vaccine and all tested negative for HBsAg, including both babies born to patients at high risk of MTCT. A 5.4% HBsAg seroprevalence was observed amongst pregnant women in Windhoek. Two women (7.14%) were at high risk of infecting their infants. All infants received HBV birth dose vaccination. Through MTCT, HBV infection is perpetuated within communities. Elimination is achievable. To that aim, scale-up of HBV antenatal screening, HBV birth vaccination and antiviral prophylaxis for mothers at high risk of MTCT is essential.

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

Neonatal listeriosis during a countrywide epidemic: a tertiary hospital's experience

Adrie Bekker (Stellenbosch University), Angela Dramowski (Stellenbosch University), Heather Finlayson (Stellenbosch University), Kessendri Reddy (National Health Laboratory Service), Lizel Lloyd (Stellenbosch University), Marina Aucamp (Tygerberg Hospital), Sandi Holgate (Stellenbosch University)

Background: A countrywide epidemic of *Listeria monocytogenes* (LM) began in the first quarter of 2017, rapidly becoming the world's largest LM outbreak to date. **Methods:** We describe the clinical course of neonates with culture-confirmed LM infection admitted to a tertiary neonatal unit at Tygerberg Hospital, Cape Town, South Africa (1 January 2017-31 January 2018). Current epidemic LM cases were compared with a historical cohort of sporadic neonatal LM cases at our institution (2006-2016). The global literature on epidemic neonatal LM outbreaks (1 January 1978 - 31 December 2017) was reviewed. **Results:** Twelve neonates (median gestational age 35 weeks; median birth weight 2020 grams) were treated for confirmed LM bacteraemia in 2017/18, presenting at a median age of 0.5 days. In 5 cases, neuro-listeriosis was suspected. Three neonates died (25%) versus 8/13 (62%) neonatal deaths in the sporadic listeriosis cohort (2006-2016) ($p=0.075$). The institution's neonatal LM infection incidence increased significantly in 2017 from a historic rate of 0.17 to 1.4/1000 live births ($p<0.001$). During the current LM epidemic, the crude neonatal fatality rate exceeded the average calculated global epidemic neonatal LM mortality (3/12 [25%] vs 50/290 [17%]; $p=0.448$). Possible contributing factors to the high mortality rate in this epidemic LM neonatal cohort may include more virulent disease associated with sequence-type 6 and the predominance of early-onset disease in this

cohort. Conclusions: Epidemic neonatal listeriosis at Tygerberg Hospital was associated with predominance of bacteraemic, early-onset disease. Listeriosis-associated mortality rates were higher than previously published, but lower than that of an historic institutional cohort.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

EXTREMELY LOW BIRTHWEIGHT INFANTS AND DISEASE-SPECIFIC WEIGHT CATEGORISATION AT TYGERBERG HOSPITAL, SOUTH AFRICA: MORTALITY OF INBORN BABIES AT THE LIMITS OF VIABILITY. A CROSS-SECTIONAL STUDY.

GB Theron (Stellenbosch University), GS Gebhardt (Stellenbosch University)

Introduction Extremely low weight at birth (ELBW) is defined as all babies weighing <1000g at delivery. Approximately 4% of babies born at Tygerberg Hospital falls into this weight category. For deliveries of birth weight 500-999g, where the baby was alive at the time of hospital admission, the main primary causes of death is hypertensive conditions of pregnancies and spontaneous preterm labour. **Aim**The aim of this study was to assess the disease-specific clinical outcomes for ELBW infants in 100g increments; starting at 500g and linking this to the corrected gestational age. **Methods**This was an observational cross-sectional study using data from the routinely collected PPIP database, electronic labour ward register and clinical data from patient folders. All inborn infants of 500-999g birthweight who delivered at Tygerberg Hospital between 1 January 2014 and 30 June 2016 were included in the study. **Results**Detailed folder review identified 93 additional deaths (up to 28 days after delivery) not included in the PPIP database. Complete maternal and neonatal data was available on 1028 patients. Live babies were tracked for a median of 296 days after birth. Eighty-two percent of all babies born to mothers with SEOPE and accurate gestation (early ultrasound) had a birthweight below the 10th centile for their gestational age. Overall survival was 50.8%, with 17% showing some form of disability at follow up, mostly related to severely stunted growth. With SPTL, survival into childhood was slightly lower- only n=45 (47%) of infants survived after discharge. The majority died within a few hours or days of birth. **Conclusion**This study categorised women by clinical condition at birth and it showed that the neonatal outcome is different for these groups. The data that can be useful for the counselling of women with imminent delivery at a peri-viable gestation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

Case Study: Prenatal Screening, Management Options and Ethical Considerations in a Twin Pregnancy Discordant for Down Syndrome

Amy Strydom (Stellenbosch University)

A woman pregnant with twins was presented with several management options after a 2nd trimester antenatal ultrasound scan revealed that these twins were likely to be discordant for Down syndrome. The management options offered included continued pregnancy, selective termination of the affected twin and non-selective termination of the entire pregnancy. Each management option had various ethical implications with conflicting maternal and fetal interests as a prominent theme. When considering the Choice on Termination of Pregnancy Act of 1996, as well as Tygerberg policy, these issues become even more complex. The mother chose to non-selectively terminate the pregnancy. At first glance, this option seemed ethically unjustifiable, but when considering the mother's disposition towards raising a child with disability, as well as the risks of complications to the unaffected twin should selective termination have been opted for, it became clear that this option was ethically justifiable. This case study and ethical discussion highlights the need for further discussion regarding current termination of pregnancy laws in South Africa and unusual scenarios such as the one presented in this case study.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

Weight-related quality of life in obese, pregnant women in South Africa

Hall DR (Academic hospital), Tisane MA (Academic hospital), Van der Merwe JL (Academic hospital)

The global obesity pandemic includes pregnant women. Obesity may negatively impact quality of life (QOL). A validated, obesity-specific QOL assessment tool was used to assess the impact of obesity on five specific domains. Domains included are, physical function, self-esteem, sexual life, work and public distress. A prospective cohort study was performed at (information omitted to hide identity) hospital in South Africa. Morbid obesity was defined as body mass index (BMI) of 40-49.9kg/square meters and super-obesity as BMI \geq 50kg/square meters, using the first recorded weight during the pregnancy. Pregnant women with BMI of \geq 40 were approached at the high-risk antenatal clinic where written informed consent was taken before recruitment. Using the QOL tool they answered statements about their current experiences. A total of 66 morbidly obese and 46 super obese women were enrolled across an age range of 18-45 years. Physical function and self-esteem were the domains with the lowest QOL scores. When comparing morbid with super obesity, all scores were significantly lower in the latter group except for the domains of self-esteem and sexual life. In conclusion we found that morbid and super-obesity occur across the full spectrum of the adult reproductive period. Physical function and self-esteem are the most affected while QOL is linked to the degree of obesity,

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

Degree of blood pressure elevation is not a differentiating factor in patients with pre-eclampsia presenting with and without pulmonary oedema: Findings from the LV IMPACT study

Anton Doubell (Division of Cardiology, Department of Medicine, Tygerberg Hospital), Bradley Griffiths (Division of Cardiology, Department of Medicine, Tygerberg Hospital), Eduard Langenegger (Department of Obstetrics and Gynaecology, Tygerberg Hospital), Philip Herbst (Division of Cardiology, Department of Medicine, Tygerberg Hospital)

BACKGROUND: The cause of acute pulmonary oedema in patients presenting with pre-eclampsia (PET) is not known, and is likely multifactorial. It has been hypothesised that acute afterload mismatch due to the severity of blood pressure elevation is a significant contributing factor. **METHODS:** Patients presenting to Tygerberg Hospital with PET and pulmonary oedema between February 2016 and February 2017 were prospectively enrolled in the LV IMPACT Study. Pre-existing cardiac disease, chronic hypertension, or an alternative cause for pulmonary oedema were exclusion criteria. Clinical information was gathered as soon as possible after enrolment, including blood pressure at time of enrolment, highest recorded blood pressure from presentation to enrolment, and transthoracic echocardiography. A control cohort of patients presenting with PET without pulmonary oedema was simultaneously enrolled. **RESULTS:** 21 patients were enrolled with PET and pulmonary oedema (cases), and 21 were enrolled with PET without pulmonary oedema (controls). Mean ages for the groups were 28.3 years and 26.7 years respectively (p-value 0.081). Patients were enrolled at a median time of 24 hours post-delivery for cases, and 35 hours post-delivery for controls (p-value for difference 0.241). Mean systolic and diastolic blood pressures at enrolment were 146/81mmHg for cases, and 140/84mmHg for controls (p-values 0.655 [systolic] and 1.00 [diastolic]). Mean highest recorded blood pressures were 177/106mmHg for cases, and 180/114mmHg for controls (p-values 0.200 [systolic] and 0.191 [diastolic]). Cases were more likely to be receiving intravenous nitrates, and controls were more likely to be receiving oral calcium channel blockers. There were no other differences in medication being administered. **CONCLUSIONS:** The degree of blood pressure elevation is not a differentiating factor in patients presenting with pre-eclampsia with or without pulmonary oedema.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

A prospective population-based study of preterm pre-labour rupture of membranes between 24 and 34 weeks of gestation in Cape Town Metro East - measure protocol intervention fidelity and clinical outcome

*Noma Mbungu, Department of Obstetrics and Gynaecology, University of Stellenbosch, S Gebhardt
Department of Obstetrics and Gynaecology, University of Stellenbosch*

BACKGROUND: Preterm premature rupture of membranes (PPROM) complicates 2 to 3% of pregnancies and is associated with significant neonatal mortality and morbidity. Intrauterine infection is the most common cause of PPRM, approximately 50% overall. **OBJECTIVES:** The primary objective of this study was to evaluate the quality of care delivered to women undergoing inpatient management with PPRM compared with a recently instituted hospital protocol. A secondary objective was to investigate the maternal and neonatal outcome of conservative management of PPRM 24-34 weeks in Tygerberg Hospital (TBH), and to determine the impact of the protocol on hospital stay (bed occupancy rate). **METHODS:** A prospective population-based observational study on patients with confirmed PPRM managed conservatively, between 24 and 34 weeks gestation at TBH from 01 February 2014 to 31 January 2015. The charts of all patients (n=353) evaluated for possible PPRM were retrieved from the online TBH records system, Enterprise Content Management (ECM). Ninety-eight patients were eligible for the study. **RESULTS:** The cumulative incidence of PPRM in the drainage region during this study period was 2.86 per 1000. The median gestational age at delivery was 31 weeks and 4 days and most babies were appropriately grown for their gestation with but with 18 babies born below the 10th centile for birth weight according to their gestation. The median birth weight was 1690g. The most identifiable associated risk factor was cigarette smoking (35%). In 90% of patients with PPRM counselling was not done. Clear nursing prescriptions were not given in 90% of patients as per protocol and more than 65% of patients were not given betamethasone at correct intervals. Close to 60% of women were given antibiotics correctly and 86% of patients were checked for signs of chorioamnionitis twice day as per protocol. Most babies were admitted in high care with a median average stay of 8 days, but one stayed a maximum of 188 days and 6 babies died from severe prematurity. Other neonatal complications included neonatal jaundice (60%), respiratory distress (41%), sepsis (7%), necrotising enterocolitis (3%) and patent ductus arteriosus (4%). Total length of stay of mothers in hospital was a median of 6 days and none of the mothers had complications post-delivery. **CONCLUSION:** PPRM is a serious complication of pregnancy and associated with low birth weight, preterm delivery significant perinatal morbidity and mortality. Counselling women with PPRM on what to expect plays an important role in the initial management of PPRM.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

Postpartum haemorrhage managed with free flow pressure controlled uterine balloons (Ellavi UBT) - A case series

Adele de Villiers (Sinapi biomedical (Pty) Ltd, Lelie Road, Stellenbosch), Chris de Villiers (Sinapi biomedical (Pty) Ltd, Lelie Road, Stellenbosch), Gerhard Theron (Department of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg), Nardus Koekemoer (Sinapi biomedical (Pty) Ltd, Lelie Road, Stellenbosch), Nico Smit (Sinapi biomedical (Pty) Ltd, Lelie Road, Stellenbosch)

Introduction Uterine balloon tamponade (UBT) is an accepted method in postpartum haemorrhage (PPH) management. Sinapi biomedical (Pty) Ltd took up the challenge to develop a free flow pressure controlled uterine balloon (Ellavi UBT). Intra-uterine balloon pressure is controlled by adjusting the height of the supply bag and water is allowed to be expelled from the balloon when the uterus contracts. **Methods** Workshops were conducted in 3 district and one central hospital in Cape Town on the use of the Ellavi UBT and devices were made available to these hospitals to be used when indicated. The researcher subsequently visited the hospitals to extract all relevant patient information from medical records and structured interviews were conducted with the physicians that intended to use or used the Ellavi UBT. **Results** The case series included 19 patients with Ellavi UBT insertions. The insertion

of the Ellavi UBT and management of patients following insertion proved to be feasible. Twelve patients were managed in the district hospitals and 7 in the central hospital. Filling the uterine balloon from the supply bag or with intravenous fluid according systolic blood pressure did not pose any problems and the concept was well accepted. The Ellavi UBT stopped the bleeding in 15 patients, reduced the volume of bleeding in 1 and had no effect on the bleeding in 3 patients. The overall success rate was 78.9% (15/19). Excluding 2 patients with uterine tears increased the success rate to 88.2% (15/17). No complications resulted from the use of the Ellavi UBT and all patients included in the case series had a good outcome. Conclusion Using the Ellavi UBT for treatment of PPH due to uterine atony and placental bed bleeding is feasible and successful. Similar case series[™] are planned for midwives working in midwife obstetric units and a rural regional hospital.

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

The Feasibility and Advantages of Laparoscopic Ectopic Pregnancy Surgery at a Secondary Level Public Hospital in South Africa - A Retrospective Study.

Dr Denise Armatas (University of Stellenbosch), Dr Ramon Aronius (Worcester Hospital), Prof Gerhard Theron (University of Stellenbosch)

INTRODUCTION: Ectopic pregnancy is a gynaecological emergency that impacts maternal morbidity worldwide. Laparoscopic surgery remains the preferred method of surgical management for majority of patients. Not only has laparoscopic surgery been proven to improve patient outcomes but also to be cost effective and efficient. **OBJECTIVES:** The primary objective is to show the feasibility of laparoscopic surgery at a secondary level hospital. To determine the rate and several variables of laparoscopic management of surgical treatment of ectopic pregnancy compared to laparotomy. **METHODOLOGY:** A retrospective study design was used. All patients who presented to Worcester Provincial Hospital with suspected ectopic pregnancy and underwent surgical management were included. The sample size was calculated required 81 patients to be included. Data was collected by the principal investigator using online records and theatre reports. Participants were identified and assigned into two cohort groups based on method of surgical management (laparoscopy or laparotomy) the rates and outcomes were compared. **RESULTS:** A total of 84 cases were identified. Of which 48 (57.1%) were managed laparoscopically and 36 (42.9%) managed with laparotomy. Majority of the cases were ruptured (78.57%). The average surgical time was 34.6 mins and 44.9 mins for the laparotomy and laparoscopy group's respectively. Average hospital stay for the laparotomy group was 3.6 days compared to 2.5 days for laparoscopy group. Post-operative analgesia usage was significantly less in the laparoscopy group compared to the laparotomy group. **CONCLUSION** This study shows with the right training programme in place and equipment available, not only can first world laparoscopy treatment rates be achieved, but also shows it is feasible and has significantly better outcomes for the patient. The benefits of laparoscopic surgery make[™] this treatment modality the gold standard, if surgical intervention is required. Less hospital stays and analgesia usage drastically reduces costs for the hospital.

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

EFFECT OF HUMAN MALE PATIENT DIAGNOSIS ON SYNGAMY TIMING AND BLASTULATION RATE USING TIME-LAPSE TECHNOLOGY

Cheyenne Steyn (University of Stellenbosch), Dr. Marie-Lena Windt-De Beer (Tygerberg Fertility Clinic), Lydia Els-Smit (Wijnland Fertility Clinic)

Introduction: Embryo selection for embryo transfer, essential in Assisted Reproductive Technologies, is based on assessment of morphological and kinetic characteristics during embryo development. Syngamy is the merging event of maternal and paternal DNA during fertilization. The functional centrosome within the spermatozoa contributes to DNA alignment and combination, therefore possibly impacting syngamy. Time lapse generated kinetic time points during embryo development can be used to examine the potential effect of male fertility diagnosis on syngamy and blastulation. Aim: Primary

aim: Investigate the possible correlation of three male prognosis groups [good (GP), poor (PP) and very poor (VP)] with syngamy time length and blastulation rate. Secondary aim: Investigate the possible effect of syngamy time length on blastocyst quality scores. Methods: Retrospective study conducted from 2017 to 2018 at Wijnland Fertility on aggregated patient embryo data from 2014 to 2016, sifted according to inclusion and exclusion criteria and submitted for statistical analysis ($p < 0.05$). Results: Results indicated that all three male prognosis groups had similar rates of normal fertilization and blastulation. The GP group showed shorter syngamy time compared to the VP group. Shorter syngamy time correlated with increased blastocyst expansion in all groups. It also correlated with trophectoderm quality scores within and across groups. Specifically, A-grade trophectoderm of the GP group and VP group showed significantly shorter syngamy time compared to B-grade in the VP group. Syngamy time did not show correlations with inner cell mass quality. Conclusion: Results indicated that although fertilization and blastulation rate amongst the prognosis groups were similar, poorer male diagnoses may lead to extended syngamy times and poorer blastocysts, impacting expansion and trophectoderm quality.

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

FIVE-YEAR OVERALL SURVIVAL OUTCOME AMONG HIV-POSITIVE AND HIV-NEGATIVE CERVICAL CANCER PATIENTS IN SOUTH AFRICA

H M Simonds (Division of Clinical and Radiation Oncology; MICO; FMHS Stellenbosch University), M H Botha (Department of Obstetrics and Gynaecology; FMHS Stellenbosch University), FH Van der Merwe (Department of Obstetrics and Gynaecology; FMHS Stellenbosch University), JS Jacobson (Mailman School of Public Health; Columbia University; New York)

Introduction: Cervical carcinoma is the second most common malignancy in women in South Africa. Oncology services in South Africa are considerably more accessible than in many neighbouring countries in sub-Saharan Africa. The additional challenge is the epidemic of Human Immunodeficiency Virus infection (HIV). The aim of this study was to report five-year overall survival in a prospective cohort of HIV-positive and -negative cervix carcinoma patients undergoing radiotherapy, from a single institution in South Africa.

Methods: Prospective cohort study of all locally advanced cervix carcinoma patients attending for radiotherapy from July 2007 to November 2011. Data collected included demographics, clinical characteristics and treatment parameters. Overall survival (OS) was the primary end-point of this study. Results: All patients with the intent to treat of over 40Gy EBRT were included, a total of 492 patients. The cohort included 71 HIV-positive patients (14.4%) and 421 HIV-negative patients (85.6%). In the cohort, 433 were prescribed standard fractionation EBRT of which 384 patients were prescribed concurrent platinum-based chemotherapy (88.7%). Significantly fewer HIV-positive patients were able to complete a minimum of 4 cycles (58.5% vs. 76.1%; $p = 0.007$). HIV-negative patients had an OS of 55.1% and 49.2% at 2- and 5-years. For HIV-positive patients OS was significantly lower at 42.3% and 39.4%, at 2- and 5-years, compared to the HIV-negative patients ($p = 0.02$). Conclusion: This prospective cohort study of nearly 500 patients with locally advanced cervical cancer demonstrates a significant difference in overall survival of HIV-negative compared to HIV-positive patients. Factors affecting outcome include stage of disease, HIV status and the delivery of concurrent chemotherapy.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

ASSISTED REPRODUCTIVE TECHNOLOGY (ART) SUCCESS RATES IN DONOR GAMETE (SPERMATOZOA AND OOCYTE) PROGRAMS AT DRS AEVITAS FERTILITY CLINIC.

Camilla Janke (Stellenbosch University), Dr Marie-Lena Windt De Beer (Stellenbosch University)

Objective: To evaluate the Clinical pregnancy rate [CPR] and live birth rate [LBR] in the oocyte donor program at Aevitas Fertility Clinic for the period 2013-2016 to determine the success rate of this program and to evaluate the CPR and LBR of the donor spermatozoa program at Aevitas Fertility Clinic for the period 2015-2016 to determine the success rate of this program. **Design:** Retrospective Study **Patients:** The sample size for study A was n=289 patients and study B n=262 patients. **Main Outcome Measure(s):** The CPR and LBR of the oocyte donation program to determine the success rate of this program and to measure the effect of the number of ova aspirated, type of fertilization method, age of the female recipient and recipient diagnosis on these outcomes. To measure the CPR and LBR of the spermatozoa donation program to determine the success rate of this program and to measure the effect of female age on these outcomes. **Results:** The CPR and LBR for the donor oocyte program are 59% and 51.48% respectively. The type of fertilization method had no effect on the CPR but it did have an effect on the LBR. The number of ova aspirated, the age of the female recipient and the recipient diagnosis all had no effect on the CPR nor the LBR. The CPR and LBR for the donor spermatozoa program are 18% and 13.82% respectively. The age of the female had no effect on the CPR and LBR but the type of fertilization method had a significant effect. **Conclusion:** This study's results show that the current oocyte and spermatozoa donation programs at Aevitas Fertility Clinic yields high CPRs and LBRs comparable to those reported in the literature and is a very successful treatment option for ART patients attending Aevitas Fertility Clinic.

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Blastocysts Vitrification: Retrospective Analysis of Success at Drs. Aevitas Fertility Clinic â€” 2015-2016.

Elizabeth Meiring (Stellenbosch University), Marie-Lena Windt-De Beer (Stellenbosch University)

Objective: With the practice of single blastocyst transfer becoming more prevalent in Assisted Reproductive Technology (ART), there is a considerable demand for efficient methods of cryopreservation of surplus blastocysts, such as vitrification. Therefore, the objective of this study was to evaluate the success of the blastocyst vitrification program implemented at Drs. Aevitas Fertility Clinic by comparing outcomes in fresh embryo transfer (ET) cycles and vitrified-warmed ET cycles. **Design:** Retrospective study **Patients:** A population of n=271 patients within the clinic (2015-2016). **Main Outcome Measures:** Post-thaw survival rate and Clinical pregnancy rate (CPR), which is defined as any product of conception 7 weeks post embryo transfer. **Results:** The post-thaw survival rate during the period 2015-2016 was 87.3%. After acknowledging the contributions of various variables (age of female ova, day of embryo vitrification, and assisted hatching (AH), donor oocyte cycles), the overall CPR for patients in the fresh ET cycle group was 46.0%. The CPR for patients in the vitrified-warmed ET cycle group was 31.0%. This difference was not statistically significant ($p > 0.05$). The vitrified-warmed CPR for cycles that included the application of AH was 54.0%, which was 17% higher than the vitrified-warmed CPR for cycles that excluded the application of AH ($p = 0.02$). **Conclusion(s):** This study found that patients were 15% more likely to achieve a clinical pregnancy in fresh ET cycles than in vitrified-warmed ET cycles (46.0% vs 31.0%). Moreover, this study established that the vitrified-warmed CPR was higher when AH was applied. However, this study found no significance with regards to donor oocyte cycles. **Key Words:** Assisted Reproductive Technology (ART), Clinical Pregnancy Rate (CPR), fresh embryo transfer cycle, vitrified-warmed embryo transfer cycle, donor oocyte cycle, assisted hatching (AH), cryopreservation, vitrification.

ABSTRACT NUMBER / ABSTRAKNOMMER: 21

Chronic villitis of unknown etiology: Association with adverse pregnancy outcomes in a consecutive series of 92 cases.

Vicki Pretorius (National Health Laboratory Service)

Objective: Chronic placental villitis is characterized by a chronic inflammatory infiltrate within placental villi. Although some cases have a recognizable infectious etiology, a specific infective organism cannot be identified in the vast majority of cases. Non-infectious cases are designated, by exclusion, as chronic villitis of unknown etiology (CVUE). CVUE is associated with adverse pregnancy outcomes, especially when high grade. Established associations include intra-uterine growth restriction, idiopathic preterm labour, intra-uterine fetal death and perinatal asphyxia. Aim: To investigate associations between CVUE, adverse pregnancy outcomes and clinical parameters. Materials and methods: A retrospective, descriptive study of all cases of chronic villitis during a five year period at Tygerberg Hospital. The pathology database at the Division of Anatomical Pathology, National Health Laboratory Service and Stellenbosch University was searched for the term "villitis" from 1 January 2010 through 31 December 2014, which yielded 250 cases. Cases were reclassified as i.) no villitis (62); ii.) acute villitis (15) or iii.) chronic villitis (173) after histopathological review. 81 cases of chronic villitis with an identifiable infectious cause were excluded. The remaining 92 cases of chronic villitis (53%) were designated as CVUE and were linked to pregnancy outcomes. Results: Upon grading the severity of CVUE, 47 cases (51%) were classified as low grade and 42 (46%) as high grade villitis. 36 (77%) and 30 (71%) cases with low and high grade villitis, respectively were associated with preterm birth. Stillbirth was seen in 14 (31%) and 23 (56%) cases with low and high grade villitis. 50% of cases with low and high grade CVUE were associated with small for gestational age babies. Conclusions: In this study CVUE was associated with adverse pregnancy outcomes, i.e. preterm delivery, small for gestational age babies and stillbirth.

ABSTRACT NUMBER / ABSTRAKNOMMER: 22

Effect of statins on male reproductive parameters

Bongekile Skosana (Medical Physiology), Cebisa Bhadula (Medical Physiology), Derick Van Vuraan (Medical Physiology), Reggie Williams (Anatomy and histology), Stefan du Plessis (Medical Physiology)

The risk of cardiovascular disease (CVD) is prevalent and on the increase globally. Lipid-lowering drugs, such as statins, have been found to reduce CVD. The widespread prophylactic use of statins, especially by men of reproductive age, give rise to concerns regarding the effect thereof on the male reproductive system. To ascertain whether the reduction in cholesterol levels caused by statins have any effects on male reproductive parameters, 60 male Wistar rats were randomly divided in four groups and treated for 16 weeks as follows: Control, Simvastatin (0.5 mg/kg), Fenofibrate (100mg/kg) and Simvastatin+Fenofibrate (S+F). Testicular histology (H&E staining, Zeiss Imaging) anti-oxidant activity and lipid peroxidation (Microplate reader) as well as sperm morphology (CASA) were measured. Both fenofibrate ($p < 0.001$) and S+F ($p < 0.05$) had significantly fewer sperm with normal morphology when compared to control and fenofibrate. Quantification of seminiferous tubule lumen diameter, tubule circumference and epithelial length showed no differences between treatment groups. Similarly, no quantitative histomorphometrical differences were observed in the epididymis of these animals. Qualitative histological analysis revealed that the lumen of the three treatment groups had fewer spermatids compared to control. Catalase activity differed significantly across groups ($p < 0.05$), with the S+F group having significantly higher activity compared to the fenofibrate group. From these results it is evident that short-term exposure to lipid-lowering drugs can alter male reproductive parameters, however more studies using longer treatment regimens are needed.

ABSTRACT NUMBER / ABSTRAKNOMMER: 23

INVESTIGATING IN VITRO EFFECTS OF AQUEOUS ROOT EXTRACT OF *Mondia whitei* IN HUMAN SPERM FUNCTIONALITY OF OLIGOZOOSPEMIC PATIENTS

Aqeel Morris (Department of Medical Biosciences, Andrology laboratory, University of Western Cape South Africa.), Bilinga M Tendwa (Department of Medical Biosciences, Andrology laboratory, University of Western Cape South Africa.), Ralf Henkel (Department of Medical Biosciences, Andrology laboratory, University of Western Cape South Africa.)

The medicinal plant commonly known as "white ginger" spreads from Guinea-Bissau through tropical Africa to Kwa-Zulu Natal province in South Africa, where it is classified as an endangered species. Traditionally, *M. whitei* roots extracts are used as a general tonic and it has been highly appraised in treatment of male infertility in folklore medicine. So far, no studies have been done to investigate the effect of the root extract in oligozoospermic patients. Hence, the aim of this study is to investigate the effect of aqueous root extract of *M. whitei* in oligozoospermia (concentration < 15 million/ml) in vitro. A total of 60 semen samples were collected: 28 of them represented healthy sperm donors and 32 represented infertile patients. Furthermore, oligozoospermic semen samples were identified and analysed separately. Sperm was washed (HTF-BSA) and incubated for 1 hour at 37°C with different concentration of *M. whitei* (0, 0.0185, 0.185, 1.85, 18.5 and 185¼g/ml). A sample without *M. whitei* served as the control. Sperm cell motility, vitality, reactive oxygen species production (ROS), mitochondrial membrane potential (MMP) ($\Delta\psi^m$), capacitation, acrosome reaction and DNA fragmentation was assessed. Results revealed that there was a significant dose-dependent increase in percentage of total motile spermatozoa, MMP-intact spermatozoa, a positive trend on ROS positive spermatozoa and a negative trend in the percentage of DNA fragmented spermatozoa in the oligozoospermic group. Similarly, there was a significant dose-dependent increase in the percentage of MMP-intact spermatozoa and a positive trend in percentage of ROS positive spermatozoa in the normozoospermic group. There was no effect seen in the remaining sperm functional parameters. In conclusion, *M. whitei* increases percentage of total motile and does not induce the production of intrinsic superoxide that leads to DNA fragmentation hence, maintaining the MMP of the spermatozoa. Keywords: *Mondia whitei*, Spermatozoa, infertility, sperm functionality

ABSTRACT NUMBER / ABSTRAKNOMMER: 24

The Effect of the Time Interval Between the Human Chorionic Gonadotropin (hCG) Trigger and Sperm Insemination Time on Assisted Reproductive Technology (ART).

Dr. Marie-Lena de Beer (Tygerberg Hospital Fertility Unit), Dr. Victor Hulme (Drs. Aevitas Fertility Clinic), Dylan Ramsay (Stellenbosch University)

Objective: To determine the optimal time between hCG trigger to analyse if there is a difference on embryo quality and structure. Design: Retrospective study Patients: A population of n=580 and n=79 patients within two clinics (A & B), respectively. Main Outcome Measure(s): Optimal time from hCG trigger (T0) to insemination (Tf) was evaluated: To establish if the time span between HCG trigger and insemination influences: [1] live birth rate (LBR) [2] fertilization rate (FR) and good quality embryos (GQE). Results: Mean time to insemination (Ti) for the total population was 39.26 (SD1.11) hours and for Clinic A and B respectively, 39.26 (SD1.04) and 39.25 (SD1.50). Mean time to aspiration (Ta) for the total population was 33.98 (SD1.21) hours. Mean hours difference between aspiration and insemination (Td) for the total population was 5.16 (SD1.28) hours. Although not statistically significant, mean Ti for the total cohort of patients correlated with LBR was 39.29 (SD 1.140) and 39.19 (SD 1.00) hours respectively. The largest cohort of GQE on Day 3 for the total patient population was found between $\hat{A}\pm 35$ to $\hat{A}\pm 44$ hours post insemination. Clinic B had a stronger correlation than Clinic A as well as the total population. Clinic B had a $Ti = \hat{A}\pm 38$ hours which yielded the most GQE on Day 3 ($p=0.18$; $p<0.05$). Conclusion(s): This study found no significance in terms of FR, number of GQE on Day 3 nor in LBR with regards to Ti. It did show, however, that the consistently superior Ti from this study was $\hat{A}\pm 39$ hours post insemination for FR, GQE on Day 3 and LBR; although none were significant. It also showed that the strongest correlation within this study was between QGE on Day 3 for Clinic B specifically ($Ti = \hat{A}\pm 38$ hours; $p=0.18$).

ABSTRACT NUMBER / ABSTRAKNOMMER: 25

A Description and Highlights of Interventions with Children Prenatally Exposed to Alcohol

Anna-Susan Marais (Stellenbosch University), Marlene de Vries (Stellenbosch University), Philip A. May (University of North Carolina), Soraya Seedat (Stellenbosch University), Wendy Kalberg (University of New Mexico)

Background Fetal alcohol spectrum disorders (FASD) are caused by the deleterious effects of maternal alcohol consumption during pregnancy. FASD are the most common environmentally induced form of mental retardation in the world. Fetal alcohol syndrome (FAS) as the most clinically recognizable form of FASD is characterized by a pattern of minor facial anomalies, prenatal and postnatal growth retardation, and functional or structural central nervous system (CNS) abnormalities. The effects of alcohol on the developing fetus represent a continuum, with FAS the worst affected. The consequences of FASD are life long, and behavioural and learning difficulties often greater than the degree of neurocognitive impairment. Early diagnosis and referral for early intervention services is imperative. Identification and referral within the first few months of life may represent the most crucial time in the affected child's lifespan for initiation of early intervention services. Research aims/objectives Initiate early intervention /remediation research on development through cognitive / behavioural enhancement techniques for children with FASD and controls from 9 months of age. Method Participants, who fitted specific criteria for enrollment, were recruited from the Newborn screening and Bayley Scales of Infant and Toddler Development studies, which followed the development of participants from birth to 18 months. Both alcohol exposed and non-exposed children were recruited into three groups: intervention only, nutritional supplementation only and a combined intervention and nutritional supplementation group for a 12-month intervention. The Heart Start model developed for the interventions, focused on strengthening the relationship between mother and child. The nutritional supplementation given was PediaSure Plus. The combined group received both interventions and nutritional supplementation. Results Early indicators are that both control and study participants and their mothers benefitted from the interventions. Conclusion The need for the development and implementation of a formal early intervention model is undisputable and needs to be explored further.

ABSTRACT NUMBER / ABSTRAKNOMMER: 26

Factors which facilitate or constrain Antiretroviral Therapy adherence in children

Thandiwe Hamana (FAMCRU, Department of Paediatric and Child Health)

Factors which facilitate or constrain Antiretroviral Therapy adherence in children Mrs. T. Hamana & Ms. Riana Diepenaar ^{1,2} Introduction: Antiretroviral therapy (ART) has transformed the HIV/AIDS era by reducing both mortality and morbidity rates, leading to an improved quality of life. However, for ART to be effective, good adherence is very important. Children depend on their caregivers for their ART administration. This puts them in a vulnerable position as they are often not in control of the adherence process. Ineffective adherence can cause health-related complications and weakens the child's immune system. Methods: A qualitative methodology was used to explore the barriers and facilitators to ART adherence in children. Children's medical records were reviewed to acquire information relative to levels of adherence and to purposefully select participants who have either poor or good levels of adherence. 10 caregivers and 12 Health Care Workers were interviewed at the Family Clinical Research Unit (FAMCRU), Tygerberg Hospital. Ethical approval was obtained from the Health Research Ethics Committee at Stellenbosch University. Data were transcribed and analysed using the interpretative content/ thematic analysis. Results: Identified barriers to adherence included: disclosure of HIV status and stigma; medication related factors; maternal depression and family structure. Identified facilitators to adherence included: an efficient transport system to the hospital; support from family and friends; knowledge of medication and the positive relationships with health care workers (staff). The outcomes of the current research revealed that caregiver reports tended to overestimate adherence. Conclusion: A strong correlation between disclosure of HIV status; family support; administration of medicines and quality of health care services exist. Recommendations: To facilitate change, children should be encouraged to play an active role and become more involved in the administration of their medication. It is recommended that caregiver reports should be complemented by children's self-reports whenever possible.

ABSTRACT NUMBER / ABSTRAKNOMMER: 27

HOW DOES NUTRITIONAL INTAKES AFFECT THE BODY COMPOSITION OF HIV-EXPOSED AND HIV-UNEXPOSED PRETERM, VERY-AND EXTREMELY-LOW BIRTH WEIGHT INFANTS?

Daniel Gerhardus Nel (Stellenbosch University), Evette Van Niekerk (Stellenbosch University), Klara Strydom (Stellenbosch University), Muhammad Ali Dhansay (Medical Research Council)

Background: Human breast milk (HBM) is considered inadequate in meeting protein requirements, especially for very low birth weight (VLBW) infants, which could effect the body composition. Objectives: Determining the effect of HBM on body composition of HIV-exposed and unexposed preterm VLBW and extremely low birth weight (ELBW) infants. Furthermore the effect of breast milk fortification, and days nil per os (NPO) has on body composition. Methods: A descriptive cross-sectional study was conducted. Preterm infants with a birth weight of ≤ 1200 g were included. Infant nutritional intakes and body composition measurements were recorded during the 28-day follow-up period. Results: 110 of 113 preterm infants received HBM and 91 infants received fortified HBM. HIV-exposed and unexposed infants receiving fortified HBM displayed differences in fat mass % (FM%) (0.88 vs. 1.36; $p=0.01$) and (0.97 vs. 1.49; $p=0.03$) and fat free mass % (FFM%) (98.98 vs. 98.68 $p=0.03$) and (99.02 vs. 98.49; $p=0.02$), on day 21 and 28, respectively. Infants kept NPO displayed differences in FM% on day 7, 21 and 28 (0.9 vs 1.3; $p=0.03$), (0.99 vs 1.4; $p=0.02$) and (0.9 vs 1.6 $p=0.0004$) as well as differences in FFM% (99.1 vs 98.4 $p=0.0005$) on day 28 of life. Conclusion: There were no significant differences in the body composition of infants who received HBM vs. fortified HBM. However, significant differences in body composition were between HIV exposure groups for infants who received fortified HBM. Infants who were kept NPO were generally smaller, shorter, and had lower FM% and more FFM%.

ABSTRACT NUMBER / ABSTRAKNOMMER: 28

Iron deficiency in children and adolescents with attention deficit hyperactivity disorder: Does the relationship exist?

Luzuko Magula (Stellenbosch University)

Abstract Background: Iron is a cofactor in the production and breakdown of neurotransmitters like dopamine, and is vital for normal brain function. Iron deficiency potentially contributes to development of attention deficit hyperactivity disorder (ADHD) because dopamine imbalances can cause hyperactivity, restlessness and problems with concentration and attention. However, a direct association between iron deficiency ADHD remains to be determined. Objectives: The aim of this study was to investigate the possible correlation between iron deficiency and ADHD in children and adolescents seen at the child psychiatry outpatient service at Tygerberg Hospital, South Africa. Methods: A retrospective chart review was conducted to gather data of all outpatient children and adolescents who had their serum ferritin and/or iron levels tested between February 2011 to January 2016. Relevant demographic and clinical information was extracted from 255 records and statistical methods were used to test for correlations between ADHD and certain variables, including iron deficiency. Results: Out of 255 patients, 88 (34.5%) had iron deficiency, 157 (61.6%) had ADHD and 54 (21%) had both iron deficiency and ADHD. Of those patients with ADHD, 11 (7%) had other psychiatric comorbidities and more males (89%) had this dual diagnosis compared to females (11%). Variables found to be significantly associated with ADHD included gender, age, Ritalin treatment and psychiatric comorbidities, but there was no significant association between ADHD and iron deficiency ($p= 0.150$). Conclusion: There was no relationship between ADHD and iron deficiency in this cohort of children and adolescents. Further studies using a treatment-naïve sample are required.

ABSTRACT NUMBER / ABSTRAKNOMMER: 29

Is adrenal suppression in asthmatic children reversible?

Ekkehard Zollner (University Stellenbosch)

AbstractBackground: Six hypocortisolaemic asthmatic children on steroids given at physiological doses were identified during a previous study.Objective: To establish whether hypothalamic-pituitary-adrenal axis suppression (HPAS) could be reversed in hypocortisolaemic asthmatic children treated with steroids without sacrificing asthma control.Methods: All hypocortisolaemic asthmatic children were started on hydrocortisone (HC). Steroid sparing medications were introduced. Subsequently, HC was stopped. Serum cortisol and repeat overnight metyrapone tests (ONMTPTs) were done until HPAS had recovered in all patients. A retrospective folder review was performed and the following extracted: BMI standard deviation score (SDS), asthma score, FEV1, adherence, daily steroid type & dose, treatment modification, serum cortisol, final ONMTPT and time taken until normalization.Results: Median serum cortisol recovered from 50 to 311 nmol/l after 0.9 (median) years. The ONMTPT had normalized by 3.3 (median) years. Steroid load decreased from 9.2 to 5.0 HC equivalent mg/m²/day (medians), while asthma score improved from 1.42 to 0.85 (medians). Number of prednisone courses decreased from 5 to 3 (medians). FEV1, before and after intervention was 79 and 82 % (medians) respectively. The median BMI SDS decreased from -0.08 to -0.16. Poor adherence was noted in two children before and four after treatment modification.Conclusions: Hypocortisolaemia and HPAS could be reversed in asthmatic children treated with physiological doses of steroids by reducing steroid load by 40% and supplementing therapy with steroid sparing medication. Poor adherence may have either contributed to or retarded HPA recovery. Simultaneously asthma control improved.

ABSTRACT NUMBER / ABSTRAKNOMMER: 30

South African Speech-Language Therapists' Assessment and Intervention Practices with Multilingual Children

Anmari Smith (Stellenbosch University), Celeste Lucas (Stellenbosch University), Jerry Harck (Stellenbosch University), Nerinda Bezuidenhout (Stellenbosch University)

Background: In a diverse multilingual and multicultural South Africa, the linguistic profile of South African Speech-Language Therapists (SLTs) are not representative of the country's linguistic and cultural diversity, as the vast majority is only proficient in English and Afrikaans. Objectives: The study aimed to investigate South African SLTs' perspectives and experiences of multilingualism, including their assessment and intervention practices with children from multilingual backgrounds, and adaptations implemented with children who speak languages that the SLTs are not proficient in. Method: A questionnaire was completed by 28 South African SLTs, who work or have worked with multilingual children. A descriptive mixed methods design was followed. Results: Most participants indicated to be only proficient in both English and Afrikaans. In comparison, their caseloads consisted of children who mainly spoke a variety of other African languages. Findings showed that the SLTs mostly conducted assessment and intervention in English only using informal and dynamic assessment methods. Majority of the SLTs noted that they conducted entire assessments by themselves and half of the participants sought additional information about the children's cultural backgrounds. The greater number of participants considered the child and family members as clients during intervention. However, most participants felt that they did not have sufficient resources in order to provide the best services to children from multilingual backgrounds. Conclusion: The mismatch between languages spoken by the SLTs and children on their caseload highlights the need for a diverse group of SLTs, who are adequately trained to work with the multilingual population.

ABSTRACT NUMBER / ABSTRAKNOMMER: 31

The Factors Influencing the Timing of Stroke in Childhood Tuberculous Meningitis

Regan Solomons (Stellenbosch University), Sarel Tielman Nieuwoudt (Stellenbosch University)

Background: Cerebrovascular complications are commonly observed in tuberculous meningitis and are its most menacing complication. Sequelae of stroke include an array of neurological deficits, from focal weakness to seizures, and may also result in death. Research Questions, Hypothesis and Objectives: We postulated that there are clinical factors associated with timing of stroke in childhood TBM. Our hypothesis was that these clinical factors would allow prediction of stroke in childhood TBM. Our objective was to determine clinical factors which can allow us to better understand and improve management of stroke in childhood TBM. Methods: This was a retrospective, analytical cohort study based at Tygerberg Hospital, Cape Town, South Africa. The study population included 354 children between the ages of 3 months and 13 years who were diagnosed with and treated for TBM at Tygerberg Hospital between 1985 and 2015. Results: Patients who have had TBM for 10 days or more before treatment initiation were less likely to acquire a stroke (RR 0.37) showing a 63% protective effect of longer duration of illness (CI 95% [0.17, 0.82]. The p-value is <0.05 and if the chance threshold is set at 5%, this means that there is only 1% chance this finding happened by chance. Patients under the age of 2 years were also at an increased risk of acquiring stroke (RR 1.34) with a 34% increased risk (CI 95% [1.01, 1.78]). Presence of HIV co-infection, malnutrition and a more advanced TB stage show no added risk of stroke complicating TBM. Conclusion: A lower age (<2 years) appears to be a definite risk factor for stroke complicating TBM. Delaying treatment initiation by 10 days after TBM manifests protects patients from stroke complicating their TBM.

ABSTRACT NUMBER / ABSTRAKNOMMER: 32

The Heart Start Early intervention program for children prenatally exposed to alcohol: A case study

Anna-Susan MARAIS (Stellenbosch University), Carisa SIEMENS (Stellenbosch University), Cecile KRIEL (Stellenbosch University), Marlene DE VRIES (Stellenbosch University), Phillip A MAY (University of North Carolina), Soraya SEEDAT (Stellenbosch University), Wendy KALBERG (University of New Mexico)

Background: With the highest recorded prevalence of Fetal Alcohol Spectrum Disorders (FASD) in the world, there is a crucial need for Early Intervention (EI) services for children affected by prenatal alcohol exposure. As the effects of alcohol on the developing fetus are life long, it is imperative to start interventions as early as possible. Objectives: To follow the intervention process of one child prenatally exposed to alcohol and his mother over a 12-month period. Methods: The EI cohort was recruited at age 9 months from an existing Bayley cohort who were recruited as newborns, permitting they fitted specific criteria. Before entering the EI study, they were assessed as newborns and tested at 6 weeks and 9 months using the Bayley Scales of Infant and Toddler Development assessments. The EI study used a relationship-based coaching model, the Heart Start model. It focuses on building and maintaining a relationship between mother and child, whilst creating an environment for constructive interaction that promotes developmental stimulation within the home, means and abilities of the participants. Results: The child in this case study is from a poor household where he is the youngest of multiple children of whom several are alcohol exposed. Although his mother accepted very little responsibility for her other children, she managed to stay the primary caregiver of this child. She attended most sessions and even participated in making toys from recyclable materials for the interventions. Despite slower than average development, the child showed progress and actively participated in the sessions, which he thoroughly enjoyed. Conclusions: A developmental program that promotes a mother-child relationship while creating a safe space for stimulation is utterly important for any child, but even more so for developmentally challenged children. This program holds promise of long-term benefits for both the mothers and their children.

ABSTRACT NUMBER / ABSTRAKNOMMER: 33

The pharmacokinetics of high dose Isoniazid for the prevention or treatment of drug-resistant tuberculosis in HIV-infected and -uninfected children

Anneke Hesselning (Desmond Tutu TB Centre. Stellenbosch), Anthony Garcia-Prats (Desmond Tutu TB Centre. Stellenbosch), Heather Draper (Desmond Tutu TB Centre), Helen McIlleron (Division of Clinical Pharmacology UCT), Hendrik Simon Schaaf (Desmond Tutu TB Centre. Stellenbosch), Jana Louise Winckler (Desmond Tutu TB Centre, Stellenbosch University), Jennifer Norman (Division of Clinical Pharmacology UCT), Louvina van der Laan (Desmond Tutu TB Centre. Stellenbosch), Lubbe Wiesner (Division of Clinical Pharmacology UCT), Peter Donald (Desmond Tutu TB Centre. Stellenbosch)

Background: Treatment options for multidrug-resistant tuberculosis (MDR-TB) in children are limited. High-dose isoniazid (hdINH) may overcome low-grade INH resistance. However, pharmacokinetic data to inform dosing in children is currently absent. The aim of this study was to characterize the pharmacokinetics of hdINH in children. Methods: This prospective observational study in Cape Town, South Africa, included HIV-infected and -uninfected children routinely receiving hdINH for the prevention or treatment of MDR-TB. Pharmacokinetic sampling was performed after a 20mg/kg INH dose (maximum 400mg). Non-compartmental analysis and multivariable regression models were used to determine associations of key covariates with AUC(0- ∞) and C_{max} and to compare to proposed targets. Results: Seventy-seven children were included. In the group < 5 years (n=58), 32 received hdINH for MDR-TB disease and 26 for MDR-TB exposure. All children >5 years (n=19) had MDR-TB disease. Overall, the median (IQR) AUC(0- ∞) was 17.9 $\mu\text{g}\cdot\text{h}/\text{mL}$ (9.9-48.6) and C_{max} was 5.14 $\mu\text{g}/\text{mL}$ (2.69-12.2). In multivariable analysis in children < 5 years old, MDR-TB disease (vs. MDR-TB exposure) was associated with both [GMR=0.19 (95 % CI 0.15-0.26), p< 0.001] and C_{max} [0.20 (0.15-0.26), p< 0.001]. In children with MDR-TB disease, the median (IQR) of 9.9 $\mu\text{g}\cdot\text{h}/\text{mL}$ (6.3-14.3) and C_{max} of 3.4 $\mu\text{g}/\text{mL}$ (2.0-5.1) were well below those in the MDR-TB exposure group [$\mu\text{g}\cdot\text{h}/\text{mL}$ (43.2-102.7), C_{max} 16.0 $\mu\text{g}/\text{mL}$ (12.9-20.5)] and also well below previously reported values in children receiving a 20mg/kg dose of INH for TB meningitis (19.1 $\mu\text{g}/\text{mL}$ at 1-2 hours). INH exposures seen here were below proposed targets for the majority of isolates with low and intermediate level resistance (Table 1). Conclusions: INH concentrations in children treated for MDR-TB disease with hdINH were much lower than expected. However, concentrations in the MDR-TB exposed groups were comparable to previous reports. Further studies are needed to confirm these findings and explore causes including previously undescribed drug-drug interactions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 34

The reliability of estimated glomerular filtration rate in South African children

Anita Brink (University of Cape Town), James Warwick (Stellenbosch University), Jennifer Holness (Stellenbosch University), M. Razeen Davids (Stellenbosch University)

Background: Accurate measurement of kidney function is essential in a subgroup of children with chronic kidney disease and those being treated with nephrotoxic drugs. Glomerular filtration rate (GFR) is widely accepted as the best measure of kidney function, yet it is seldom measured in children. In most cases, GFR is estimated using a creatinine-based equation, however these equations were all developed in predominantly Caucasian populations in North America and Europe. To date, the equations have not been validated in African children. It is hypothesized that, due to differences in pathology and socioeconomic conditions, serum creatinine levels will be lower on average leading to higher GFR estimates. Aim: To determine the reliability of estimated GFR in South African children. Methods: Cross-sectional study of children referred for GFR measurement at the Red Cross Children's Hospital, Cape Town, between February 2014 and November 2017. GFR was measured (mGFR) from the plasma clearance of Cr-51 EDTA using the slope-intercept method. GFR was estimated (eGFR) from a same-day serum creatinine sample using the new bedside Schwartz formula, Gao's quadratic equation, and the FAS equation. The bias, precision and accuracy of each equation was determined, and the agreement between eGFR and mGFR was determined using Bland-Altman analyses. Results: 173 children were included (100 female; median age 9 years; median GFR 91.5 ml/min/1.73m²). The correlation between eGFR and mGFR was poor (r² = 0.40-0.45). All equations over-estimated GFR with median biases of 16.0-26.8 ml/min/1.73m². RMSE values ranged between 14.8 and 34.8 ml/min/1.73m². The accuracy (P30 values) ranged between 43% and 63%. Conclusion: Estimated GFR

cannot replace measured GFR in South African paediatric patients due to extremely poor accuracy. There is a need for development of an estimating equation from local data, as well as increased availability of GFR measurement.

ABSTRACT NUMBER / ABSTRAKNOMMER: 35

The Value of Genetic Diagnosis in Clinical Practice

Ansia van Coller (Stellenbosch University), Brigitte Glanzmann (Stellenbosch University), Caitlin Uren (Stellenbosch University), Craig J. Kinnear (Stellenbosch University), Eileen G. Hoal (Stellenbosch University), Glenda Durrheim (Stellenbosch University), Mardelle Schoeman (Stellenbosch University), Marlo Máñller (Stellenbosch University), Michael Urban (Stellenbosch University), Monika Esser (Stellenbosch University), Paul D. van Helden (Stellenbosch University), Richar Glashoff (Stellenbosch University), Rina Nortje (Stellenbosch University)

For patients suffering from rare diseases an accurate genetic diagnosis is vital. In addition to providing an "answer", an accurate diagnosis often guides targeted medical therapy, and is useful toward understanding the chance of recurrence in other family members and for antenatal counselling. However, the large number of rare disorders are a great challenge to diagnose: (in the order of 7,000) as this means that the distinguishing features of a particular condition may be unfamiliar to the treating physicians, or the condition may not be particularly distinct from similar genetic or acquired disorders. New developments in genome sequencing have transformed diagnostic testing for genetic diseases, and are exemplified by the use of whole exome sequencing (WES) for rare diseases. We report the molecular results of the Primary Immunodeficiency Genomics Research Group (PIDGEN) as an example of the value of using genetic diagnosis in clinical practice. PIDs comprise over 300 different heritable disorders which are caused by inborn errors of the immune system that results in increased susceptibility to infection, autoimmunity, autoinflammation, allergy, and occasionally tumours. As with rare diseases more generally, PIDs are difficult to diagnose because of their variable clinical presentations and PIDGEN was able to assist in achieving a definitive diagnosis through WES. To date, 227 individuals have been enrolled of which 85 are patients and 192 are family members. Molecular analyses were completed for 35 affected individuals and 73 family members. Molecular diagnoses have been obtained for 23 (66,7%) of these patients. All patients received genetic counselling and in selected patients our findings directly impacted on clinical management and treatment.

ABSTRACT NUMBER / ABSTRAKNOMMER: 36

Use of chest radiographs in a phase 3 randomised controlled efficacy trial for treatment shortening of non-severe drug-susceptible TB in children (the SHINE Trial)

Aarti Kinikar (BJ Medical College, Pune), Angela Crook (MRC Clinical Trials Unit, University College London (UCL), London), Anneke Hesselning (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University, South Africa), Dhanaraj Baskaran (National Institute for Research in Tuberculosis, Chetpet), Margaret Thomason (MRC Clinical Trials Unit, University College London (UCL), London), Megan Palmer (Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University, South Africa), Robert Mboizi (Makerere University - John Hopkins University Research Collaboration (MUJHU), Uganda), Veronica Mulenga (University Teaching Hospital, University of Zambia, Lusaka)

Background: Chest x-ray (CXR) is an important diagnostic tool for paediatric pulmonary tuberculosis (PTB). SHINE is a randomised open-label multicentre non-inferiority trial comparing 4 versus 6 months of standard first-line TB treatment in 1200 children with non-severe PTB and/or peripheral TB lymphadenitis. Eligibility depends on local site clinicians' assessment of TB disease status and severity. We describe clinician assessment of baseline CXR features across countries. Methods: Children <16 years, with non-severe TB, were enrolled at 5 sites in Zambia, South Africa, Uganda and India.

Workup included symptom screen, TB contact history, CXR, clinical assessment, HIV testing and bacteriology (smear, Xpert MTB/Rif and culture). Children with smear+ PTB or clinical or radiological features of severe TB were ineligible (not described here). Clinicians were trained on reading CXRs and completed standard CXR reporting forms; CXRs were classified as 'typical' or 'not typical' of TB and by severity of radiological features. Results: Baseline CXR data were analysed for 881 children enrolled: 47% female; median age 3.3 years (IQR 1.4, 6.8); HIV prevalence was 13%. Overall, 90/719 (13%) children had culture-confirmation of Mycobacterium tuberculosis. 351/881 (40%) CXRs were classified as 'not typical of TB' (Table). The commonest radiological pattern in the 'typical TB' spectrum was 'uncomplicated lymph node disease' (511/530, 97%) and in the 'not typical TB' was perihilar infiltrates. Variability in CXR reporting across countries was minimal. Conclusions: Despite challenges in interpreting CXRs for PTB in young children, acceptable quality CXRs were performed and reported at all sites, with minimal variability. Appropriate training, standard reporting forms and well-defined approaches for classifying radiological abnormalities were essential. 40% of children with non-severe PTB had CXRs reported as 'not typical' of TB. Independent retrospective blinded expert reading of CXRs is ongoing, and will provide information to an independent committee adjudicating TB disease status and trial endpoints.

ABSTRACT NUMBER / ABSTRAKNOMMER: 37

Clinical presentation and treatment outcomes of infants with tuberculosis in Cape Town, South Africa

A Bekker (Paediatrics and Child Health, Stellenbosch University), A Dramowski (Paediatrics and Child Health, Stellenbosch University), AC Hesseling (Desmond Tutu TB Centre, Paediatrics and Child Health, Stellenbosch University), HS Schaaf (Paediatrics and Child Health, Stellenbosch University), L van der Laan (Desmond Tutu TB Centre, Paediatrics and Child Health, Stellenbosch University), R Aryao (Paediatrics and Child Health, Stellenbosch University)

Introduction: Limited data are available on infants (<12 months of age) with tuberculosis. We describe the clinical presentation, course and outcome of infants initiated on first-line antituberculosis drugs. Methods: Infants with tuberculosis admitted to Tygerberg, Khayelitsha District and Brooklyn Chest Hospitals (March 2014 - March 2015) were enrolled. Antituberculosis treatment was administered in hospital or at local clinics. In addition, study evaluations took place at entry, 3 and 6 months post-initiation of antituberculosis treatment. Results: Of 39 infants treated for tuberculosis, 33 (85%) had pulmonary, 1 (2%) had extrapulmonary and 5 (13%) had both pulmonary and extrapulmonary tuberculosis. The median age was 6 months (IQR: 3-7) and median weight 6.1 kg (IQR: 5-7.3) at tuberculosis diagnosis. Of the 22/39 (56%) of HIV-exposed infants, 5 (13%) were HIV-infected. Tuberculosis was culture-confirmed in 14/39 (36%), 22 (56%) infants had probable tuberculosis and 3 (8%) had possible tuberculosis using international consensus criteria. Common presenting symptoms were failure to thrive (24; 62%), weight loss (14; 36%), lethargy (14; 36%) and persistent cough (13; 33%). Nine infants (23%) had bronchoscopy for lymph nodes causing severe airway obstruction; 3 required surgical lymph node decompression. A tuberculosis source case was identified in 21/39 (54%) infants; the mother was the source case in 11/21 (52%). Only 4/21 (19%) infants were started on isoniazid preventive therapy prior to tuberculosis diagnosis. Tuberculosis treatment outcomes were favourable in 33 (85%) infants (4 cured; 29 completed treatment) and 6 (15%) had unfavourable outcomes (4 interrupted treatment for >2 months but were re-initiated and completed treatment, 2 were lost to follow-up). Conclusions: Failure to thrive was common in infants with tuberculosis. In infants with pulmonary tuberculosis, almost a quarter required bronchoscopy for severe airway compression. Good treatment outcomes were observed in this cohort with additional study follow-up.

ABSTRACT NUMBER / ABSTRAKNOMMER: 38

Clinical Trials and Emotional Labour: The Role of the Research Nurse in Paediatric MDR TB Studies

Anneke Hesseling (University Stellenbosch DTTC), Klassina Zimri (University Stellenbosch DTTC), Lario Viljoen (University Stellenbosch DTTC)

BACKGROUND: Nurses are employed in paediatric clinical studies to recruit participants and administer novel treatments while adhering to research protocols. While studies have explored the emotional labour in 'traditional' clinic-based nurses, the experiences of research nurses remains under-explored. We explore the clinical research nurse's role, present a personal account of experiences and reflect on emotional labour. **METHODS:** During a paediatric clinical trial, a research nurse (first author) documented her experiences working on the paediatric study. Her role was distinct from that of the 'traditional' nurse. The author worked in hospitals for 25 years and as a research nurse on clinical studies for the past 8 years. By using field notes, we provide a critical reflection informed by the theory of emotional labour. **RESULTS:** The paediatric research nurse's role involves providing care and adhering to research protocols, but also several unofficial responsibilities. Responsibilities fall within the characteristic of emotional labour: 1) Contact with public: Paediatric studies can be distressing for parents of participants and research nurses often unofficially avail themselves for concerned parents after hours. 2) Producing an emotional state: Nurses are present during consultations, support and re-insure concerned parents about their child's health and help parents to 'interpret' doctor's messages. 3) Control over emotional activities: Nurses are expected to appear calm even when parents receive discouraging news about their child's health. Parents often react emotionally and the research nurse must provide support. These duties often take a personal toll on the nurse who is expected to facilitate the success of the study. **CONCLUSIONS:** Paediatric research nursing duties involve emotional labour. Duties extend beyond the scope of the traditional nurse and their unofficial contribution should be acknowledged and supported.

ABSTRACT NUMBER / ABSTRAKNOMMER: 39

Evaluating impact of Early Childhood Development Education on nutrition using a theory-based Program Impact Pathway.

Busie Maziya-Dixon (International Institute of Tropical Agriculture), Dieter Von Fintel (Dept of Economics, Stellenbosch University), Oluchi Ezekannagha (Division of Human Nutrition, Stellenbosch University), Scott Drimie (Division of Human Nutrition, Stellenbosch University), Xikombiso Mbhenyane (Division of Human Nutrition, Stellenbosch University)

Background: Evaluating impact of programs can be rigorous and in some situations, impact (or lack of) does not provide explicit explanation on reasons why impact was or was not made. **Objective:** This presentation illustrates how process evaluation assessment of impact of Early Childhood Development Education on nutrition has been executed using theory-based program impact pathway. **Methods:** A program theory was hypothesized, developed and used for the evaluation. Key Informant interviews with program implementers (n = 10), program beneficiaries (n = 4), observation of program delivery (n = 2) were conducted to assess the delivery and subsequent utilization of the program impact pathway hypothesized. **Results:** Four pathways were hypothesized through which early childhood development education impacts on nutrition. While the program itself was implemented as planned numerous components that were necessary for maximum impact were impact. These include a gap in human and infrastructural resource, poor delivery of in-service training and poor student's recruitments. **Conclusion:** The PIP analysis was key for identifying strengths and weaknesses of the Early Childhood Development program, in addition to also identifying key processes and indicators that must be improved on for adequate impact on nutrition.

ABSTRACT NUMBER / ABSTRAKNOMMER: 40

Neurodevelopmental and behavioural outcome of HIV-exposed uninfected infants from the Mother and Infant Health study Cape Town at a 2 year follow-up visit.

A Slogrove (Paediatrics and Child Health, Stellenbosch University), CD Molteno (Psychiatry, University of Cape Town), JA Bettinger (University of British Columbia), M Kidd (Centre for Statistical Consultation, Stellenbosch University), M Kruger (Paediatrics and Child Health, Stellenbosch University), M Zunza (Epidemiology and Biostatistics, Stellenbosch University), MM Esser (Head of NHLS Immunology Unit Tygerberg, Stellenbosch University), PE Springer (Paediatrics and Child Health, Stellenbosch University), R Barnard (Paediatrics and Child Health, Stellenbosch University)

Background: With the success of Prevention of Mother to Child Transmission Programmes (PMTCT) consideration of long- term developmental outcomes of HIV-exposed uninfected (HEU) infants is now required. In 2012 the Western Cape was using WHO Option A as a PMTCT strategy; only HIV-infected pregnant women with a CD4 count $\geq 350/\mu\text{ml}$ or WHO stage 3 or 4 disease received triple drug antiretroviral therapy while the rest received zidovudine monotherapy from 14 weeks gestation. We primarily aimed to compare neurodevelopmental and behavioural outcomes of HEU pre-school children with that of HIV-unexposed uninfected (HUU) children. Methods: This neurodevelopmental study was nested in a prospective cohort study comparing infectious morbidity in HEU and HUU infants. HIV-infected and HIV-uninfected women and their HIV-uninfected infants were enrolled within three days of birth from a single low-risk, peri-urban obstetric unit in Cape Town, South Africa. Mother-infant pairs aged between 30 and 42 months were invited for neurodevelopmental assessment from July 2015 to September 2016. Development was assessed using the Peabody Picture Vocabulary Test Fourth Edition (PPVT-4), cognitive, language and motor scales of the Bayley scales of Infant Development III (BSID) and behaviour by means of the Strengths and Difficulties questionnaire (SDQ). Results: Thirty two HEU and 27 HUU children and their mothers were included. HEU children performed as well as HUU children on PPVT-4 ($p=0.49$) and BSIDIII cognitive ($p=0.61$), language ($p=0.82$) and motor ($p=0.73$) domains. The HEU mothers reported less externalising behaviours ($p=0.04$) and conduct disorders ($p=0.02$) on the SDQ. Four HEU (12.5%) children had macrocephaly but no neurological deficit. Conclusions: Young pre-school HEU children performed as well as HUU children on developmental assessment and mothers reported fewer behavioural problems. The increased macrocephaly was unexplained.

ABSTRACT NUMBER / ABSTRAKNOMMER: 41

Pharmacokinetics of intracellular stavudine-triphosphate in children after reduced-dose: can we improve stavudine's safety profile?

Louvina van der Laan (Desmond Tutu TB Centre and University of Cape Town), Mark Cotton (Family Clinical Research Unit), Paolo Denti (University of Cape Town), Peter Anderson (University of Denver), Steve Innes (Family Clinical Research Unit)

Introduction Stavudine remains an important replacement option for HIV+ children in sub-Saharan Africa. WHO reduced the adult dose to 30mg twice-daily, which maintains efficacy and lowers mitochondrial toxicity. We compared intracellular stavudine-triphosphate levels in children receiving a reduced dose of 0.5-0.75mg/kg twice-daily to investigate whether this provides a similar reduction in exposure. Methods A population pharmacokinetic model was developed to describe the pharmacokinetics of stavudine-triphosphate in 23 HIV+ children and 24 HIV+ adults who received stavudine at 0.5mg/kg and 20mg twice-daily for 7 days, respectively. Simulations were employed to optimise the paediatric dosing regimen targeting the exposure in adults receiving the current WHO-recommended dose of 30mg twice-daily. Results A bi-phasic disposition model with first-order appearance and disappearance described the pharmacokinetics of stavudine-triphosphate. The use of allometric scaling with fat-free mass characterised well the pharmacokinetics in both adults and children, and no other significant effect could be detected. Simulations of 30mg twice-daily in adults predicted median (interquartile range) stavudine-triphosphate C_{min} and C_{max} values of 14(9-19) and 45(38-53)fmol/10⁶ cells, respectively. Targeting this exposure, simulations in HIV+ children were used to identify a suitable weight-band dosing approach (0.5-0.75mg/kg), which was predicted to achieve C_{min} and C_{max} of 14(10-21) and 58(50-68)fmol/10⁶ cells, respectively. Conclusion Weight-band dosing using a stavudine dose of 0.5-0.75mg/kg is proposed and it shows comparable exposures to adults receiving the current WHO recommended dose of 30mg twice-daily. Our pharmacokinetic results

suggest that the decreased stavudine dose in children >7kg would have a reduced toxic effect while maintaining viral suppression.

Theme 6 / Tema 6
Perioperative Sciences /
Perioperatiewe Wetenskappe

Oral Presentations/ Referate

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

Expediting red blood cell transfusions by syringing causes significant hemolysis

Adriaan Albertus Murray (University of Stellenbosch), Andrew Ian Levin (University of Stellenbosch), Willem Lambertus de Villiers (University of Stellenbosch)

BACKGROUND: Techniques commonly used to expedite blood transfusions include pneumatically pressurizing red blood cell (RBC) bags or manual syringing its contents. We compared these techniques on RBC hemolysis using a simulated transfusion model. **STUDY DESIGN AND METHODS:** Fifteen warmed RBC units that were 12.3 (95% confidence interval [CI], 10.1-14.5) days old were each subjected to two experimental rapid transfusion techniques. RBCs from each technique were directed through 18- and 22-gauge cannulas attached to blood administration sets. One technique involved RBC bag pressurization to 300 mmHg. The other employed a 20-mL syringe to effect forceful, manual aspiration from the RBC bag followed by forceful, manual RBC injection. The control group was gravity driven without cannulas. Free hemoglobin (Hb) concentrations were measured and percent hemolysis was calculated. **RESULTS:** Free Hb concentrations and percent hemolysis (median [95% CI]) were similar in the control (0.05 [0.03-0.08] g/dL and 0.13% [0.09%-0.17%], respectively) and pressurized experiments (0.06 [0.05- 0.09] g/dL; 0.14% [0.12%-0.22%]), respectively. Syringing resulted in 10-fold higher free Hb concentrations (0.55 [0.38-0.92] g/dL) and percent hemolysis (1.28% [1.03%-2.15%]) than when employing the control ($p < 0.0001$) or pressurization ($p < 0.0001$) techniques. Cannula sizes studied did not affect hemolysis. **CONCLUSION:** Forceful manual syringing caused significant hemolysis and high free Hb concentrations. Pressurizing RBC bags induced no more hemolysis than after gravity-facilitated transfusions. Syringing to expedite RBC transfusions should be avoided in favor of pneumatic RBC bag pressurization.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

Efficacy Of Periarticular Local Anaesthetic Blocks In Total Knee Arthroplasty- A Move Towards The Simplification And Standardization Of Peri-Articular Infiltration.

Marcus van Heukelum (Stellenbosch University dept. of orthopaedics)

Title: Efficacy Of Periarticular Local Anaesthetic Blocks In Total Knee Arthroplasty- A Move Towards The Simplification And Standardization Of Peri-Articular Infiltration. **Marcus van Heukelum, Craig Blake, Graeme Gobetz, Theo Franken, Nando Ferreira, Marilize Burger** Stellenbosch University, Tygerberg Medical Campus, Cape Town, South Africa **Keywords:** Standardization Peri-Articular Infiltration, Multimodal, Pre-Emptive Analgesia **Background** Peri-articular injections (PAI) in total knee arthroplasty offer affective analgesia, are cost effective, safe and easy to perform. Currently there is no prescribed technique in performing the infiltration; this is highlighted by the significant heterogeneity in the literature surrounding PAI. **Objectives** This study aims to investigate the effectiveness of the technique and contribute towards the simplification and standardization of PAI. **Study Design & Methods** A double blind randomized control trial compared the effectiveness of PAI with a simple anaesthetic solution (bupivacaine and adrenalin) to a normal saline control group. Infiltration volumes were calculated at 1ml/kg and the infiltration technique followed a specific protocol. Post-operative outcomes included Visual Analogue Scores, ambulation scores, morphine use, knee range of motion and time to discharge. **Results** Two comparable groups of 26 patients each were included (intervention: 80.7% female, mean age 64.73 $\hat{\pm}$ 8.80 years vs control: 65.38% female, mean age 67.03 $\hat{\pm}$ 7.60 years). No difference of VAS scores was noted at 24 and 72 hours. Mean VAS scores at 48 hours were significantly lower in the intervention group. (VAS score 3.0 $\hat{\pm}$ 1.60 vs 4.14 $\hat{\pm}$ 1.23, $p=0.013$). The other parameters measured strongly favoured the intervention group but did not prove to be significant. **Conclusions** A simplified dose per kilogram peri-articular injection protocol provides a significant reduction in VAS scores at 48h

hours after total knee arthroplasty. This study contributes towards the simplification and standardization of the peri-articular infiltration technique

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

Cardiac magnetic resonance imaging vs trans-oesophageal echocardiography to detect left atrial thrombi before percutaneous balloon mitral valvotomy for mitral stenosis – A pilot study

Christiaan Kotze (, Faculty of Medicine and Health Sciences, Stellenbosch University), Dr Alfonso Pecoraro (Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerb), Dr Anne-Marie Du Plessis (Department of Radiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital), Dr Christelle Ackermann (Department of Radiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital), Dr Hellmuth Weich (Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerb), Dr Philip Herbst (Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerb), Prof Anton Doubell (Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerb)

Introduction:Detection of left atrial (LA) and LA appendage (LAA) thrombus prior to percutaneous balloon mitral valvotomy (PBMV) is critical to prevent thrombo-embolism. Trans-oesophageal echocardiography (TOE) is the gold standard for detecting atrial thrombi, but its interpretation remains challenging in some cases. Cardiac Magnetic Resonance Imaging (CMRI) is considered the gold standard modality for tissue characterization, including thrombus identification, elsewhere in the heart. However, it is poorly studied in the setting of LAA thrombus detection and particularly so in the setting of mitral stenosis pre-PBMV. **Methods:**Prior to PBMV, patients underwent both TOE and CMRI within 48h of each other, assessing for the presence or absence of LA/LAA thrombus. TOE was performed in accordance with the British Society of Echocardiography guideline for a comprehensive study. All patients received CMRI at 1.5 Tesla utilizing sequences appropriate for detecting thrombi, incorporating systematic thin slices taken through the LAA in 3 image planes. All results were independently reported by the respective operators. **Results:**21 patients have been included to date. TOE reported presence of thrombus in 7 cases, absence of thrombus in 11 cases and suspected thrombus in 3 cases. CMRI reported presence of thrombus in 9 cases and absence of thrombus in 12 cases. In 16 cases, there was agreement between TOE and CMRI. 5 cases of discrepancy were reviewed by the investigators and consensus reached (‘‘gold standard’’). In 3 cases where TOE reported suspected thrombus, CMRI confirmed the presence of thrombus. Both TOE and CMRI reported only 1 case each differing from the consensus opinion. All patients in whom thrombus was excluded underwent successful PBMV without thrombo-embolic events. **Conclusions:**Both TOE and CMRI identify or exclude thrombus with a high degree of certainty. CMRI offers a safe, non-invasive adjunct to TOE, adding value in difficult TOE cases.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Relationship between functional mobility and lower extremity muscle strength in adults with cerebral palsy; 30 years post orthopaedic interventions

A Graham Fieggen (Division of Neurosurgery, University of Cape Town), BE Nienke Veerbeek (Division of Neurosurgery, University of Cape Town), Jacques du Toit (Division of Orthopaedic Surgery, Stellenbosch University), Maaïke M Eken (Division of Orthopaedic Surgery, Stellenbosch University), Nelleke G Langerak (Division of Neurosurgery, University of Cape Town), Robert P Lamberts (Institute of Sport and Exercise Medicine, Stellenbosch University), Susanne Koschnick (Institute of Sport and Preventive Medicine, Saarland University)

Background: Individuals with cerebral palsy (CP) are prone to experience life-long limitations in mobility. Maintaining locomotion/mobility is however crucial for individuals' independence when aging. To improve and/or maintain locomotion, orthopaedic interventions are commonly performed during childhood. Studies have shown that functional mobility related to muscle strength in children with CP. It is however unknown what the level of functional mobility is in adults with CP who received an orthopaedic intervention during childhood, and whether the relationship between functional mobility and strength continues to exist when they grow into adulthood. Objective: To investigate the relationship between functional mobility and lower extremity muscle strength in adults with CP long-term after their initial orthopaedic intervention. Methods: Adults with CP and spastic diplegia who received their initial orthopaedic intervention 30 years ago and were able to walk with or without assistive devices (GMFCS level I-III) were included. The Functional Mobility Scale (FMS) was used to classify subjects' level of mobility for three different distances, 5m, 50, and 500m taken into account the use of an assistive device. Lower limb muscle strength was assessed using hand held dynamometry (HHD) and normalized to bodyweight. Results: Twenty-eight adults with CP (12male; age: mean (SD) = 39.2yr (7.9yr)) were included in the study. The majority of subjects was able to walk 5m (87%), 50m (64%) and 500m (63%) independently. Negative associations between FMS and lower limb muscle strength were observed. Discussion: Results showed that in adults with CP who received orthopaedic interventions more than 30 years ago reduced lower limb muscle strength was related to more limitations in functional mobility. Clinicians are therefore suggested to focus on strength training of lower extremities in adults with CP. These long-term outcomes may help individuals with CP and their families in setting realistic expectations and support clinicians in optimizing interventions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Gait status of adults with cerebral palsy 15 to 39 years after their first orthopaedic intervention

A. Graham Fieggen (Division of Neurosurgery, Faculty of Health Sciences, University of Cape Town, South Africa), Jacques du Toit (Division of Orthopaedic Surgery & Division of Community Health, Stellenbosch University, South Africa), Nelleke G Langerak (Division of Neurosurgery & Division of Physiotherapy, Faculty of Health Sciences, University of Cape Town, South Africa), Nicholas Tam (Division of Exercise Science and Sport Medicine, University of Cape Town, South Africa), Robert P. Lamberts (Division of Orthopaedic Surgery, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa)

Background: Although gait patterns are frequently described in children with Cerebral Palsy (CP), less is known about the gait patterns of the adult CP population. In order to determine the long-term effectiveness of new treatment regimes, such as the Single Event Multilevel Surgery approach, over the yearly interventional treatment approach, it is important to document the gait patterns of adults with CP. The aim of this study was therefore to describe the gait patterns of adults who had received their first orthopaedic intervention more than 15 years ago. Methods: Thirty adults with CP and bilateral lower limb spasticity participated in this study (Gross Motor Function Classification System levels I: n=15; II: n=11; and III: n=4). Three-dimensional gait analysis was performed on all the adults. Background information, based on detailed clinical records and an in-depth questionnaire, was recorded. Findings: The median age at initial surgery was 4.6 years (interquartile range: 3.6 – 7.3), while the median follow-up period was 27.7 years (21.6 – 33.7). The gait pattern of the adult with CP is characterised by an increased anterior pelvic tilt, decreased extension of the hip during the stance phase, decreased knee flexion during the swing phase and slower (non-dimensional) walking speed. The overall gait deviation index (GDI) score at follow-up was 68.2 ± 14.0, compared to 100 ± 10.0 in typically developed adults. Interpretation: Although all adults with CP were still ambulant more than 15 years after their first orthopaedic intervention, their gait pattern differed significantly to that of typically developed adults.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

SPINAL DEFORMITIES AND PAIN IN ADULTS WITH CEREBRAL PALSY AND SPASTIC DIPLEGIA MORE THAN 15 YEARS AFTER THE FIRST ORTHOPAEDI INTERVENTION

A Graham Fieggen (Division of Neurosurgery Surgery, University of Cape Town, South Africa), Elsabe Britz (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa), Nelleke G. Langerak (Division of Neurosurgery Surgery, University of Cape Town, South Africa), Robert P. Lamberts (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa), Steven I Dix-Peek (Division of Orthopaedic Surgery, University of Cape Town, South Africa)

Purpose: The aim of this study was to determine the incidence of spinal deformities (scoliosis, hyperkyphosis, hyperlordosis and spondylolisthesis), pain (location, frequency and influence on daily life) and the physical status of the lower extremities in adults with spastic diplegic Cerebral Palsy (CP), who had multiple orthopaedic surgeries, with the first surgery more than 15 years before. **Methods:** Thirty adults (18 females) with spastic diplegic CP were recruited for this study (HREC no: N10/05/181). All participants were assessed by an orthopaedic surgeon (SD) and a physiotherapist (NL). In addition to the consult and physical exam, spinal X-rays were taken and participants completed the Oswestry Disability Index (ODI) questionnaire. **Results:** The median time after the first orthopaedic intervention was 27 years (IQR: 21-33 years). X-rays revealed that 31% (28% mild; 3% severe) of the participants had a scoliosis, 7% had a thoracic hyperkyphosis, 17% had a lumbar hyperlordosis, while in 3% of the patients a spondylolisthesis was found. Three-quarters of the patients reported back pain, however, based on the ODI, 77% indicated that this led to only "minimal disability", while 6% reported "moderate disability" and 3% "severe disability". The physical examination showed limited range of motion in mainly hip and knee extension and dorsal flexion of the foot. Strength was most commonly reduced in hip abduction (in 60% of participants), hip and knee flexion (43% and 48% resp.). Increased muscle tone was mainly seen in knee extension (83%), while selectivity overall was pretty good. **Conclusion:** A relatively high number of adults with CP have spinal deformities with mild scoliosis being most common. Although this and the fact that most adults reported some level of back-pain, did not lead to moderate or severe disability in most participants.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

DISPARITIES IN BREAST CANCER: PRIVATE PATIENTS HAVE BETTER OUTCOMES THAN PUBLIC PATIENTS.

W COETZEE (Division of General Surgery, Stellenbosch University), JPA APPFELSTAEDT (Division of General Surgery, Stellenbosch University), M DU PLESSIS (Appfelstaedt & Associates, Panorama, Cape Town), TV ZEEMAN (Mediclinic Constantiaberg & Milnerton, Cape Town)*

Introduction: Different outcomes in breast cancer have been reported for low and high socio-economic groups. We present data quantifying disparities between South African public and private patients. **Methods:** Records of 240 consecutive patients treated in 2008 in a public versus 97 patients in a private health facility were reviewed for demographic and oncologic data. **Results:** The average of patients was 56.2 versus 51.9 years ($p=0.032$). Stage at presentation was 0 in 0.83 versus 25.8%, I in 4.5 versus 15.5%, II in 41.3 versus 37.1%, III in 37.1 versus 18.6% and IV in 16.3 versus 3.1% public versus private patients. Seventy-three percent of patients were symptomatic versus 57.7%. Of patients with stage 0–III disease, 17.9 versus 20% had simple tumour excision and 7.5 versus 14%, oncoplastic tumour excision. The mastectomy rate was similar (52 vs. 60%), but immediate reconstruction was performed in 10 versus 63%. Public patients were less likely to have radiotherapy. The pathology was similar, 27.2 versus 20, 54 versus 52, 87 versus 61% of patients with stage I, II and III disease, respectively, had chemotherapy. Hormonal therapy for premenopausal patients in private was a LHRH agonist in 9.3%, ovarian ablation/BSO in 11.7% of public patients; biologicals were given in 7.2 versus 0% of patients. Overall survival for public versus private was 66 versus 80% ($p<0.001$) months. Better per stage survival of private patients 100 versus 100, 72.7 versus 93.3, 84.8 versus 88.9, 57.3 versus 77.8 and 33 versus 33% for stages 0, I, II, III and IV, did not reach statistical significance. **Conclusion:**

The greatest impact on outcome was stage at presentation, but more aggressive therapy for each stage resulted in a trend to better outcome for private patients. *Ethics approval number: S15/10/240*

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

TREATMENT OF PERIPROSTHETIC JOINT INFECTION: WHAT WE CAN LEARN FROM WORK IN BONE-DERIVED STEM CELLS

E BOOYSEN (Department of Microbiology, Stellenbosch University), H SADIE-VAN-GIJSN (Division of Medical Physiology, Stellenbosch University), S DAENE (Department of Microbiology, Stellenbosch University), M RAUTENBACH (Department of Biochemistry, Stellenbosch University), W FERRIS (Division of Endocrinology, Stellenbosch University), L DICKS (Department of Microbiology, Stellenbosch University)*

Background: The majority of periprosthetic joint infections (PJIs) are caused by biofilm-forming bacteria that are resistant to most commercially available antibiotics. It is thus imperative to identify and develop novel antibiotics. Treatment of PJI often involves the removal of the arthroplasty prosthesis and flushing of the infected area with antibiotics, but the effect of these directly applied antibiotics on the surrounding bone tissue has not been investigated on a cellular level. **Objective:** To investigate the effect of the conventional antibiotic vancomycin and a novel antibiotic, rhabdin, isolated from the entomopathogenic bacterium *Xenorhabdus khoisanus*, on the in vitro viability and osteogenic differentiation of rat primary bone-derived mesenchymal stem cells (MSCs). **Methods:** Primary bone-derived MSCs were isolated from bone marrow and from the proximal end of the femur (bmMSCs and pfMSCs, respectively), with differential capacity for osteogenesis (bone formation). Cultured MSCs were treated with increasing concentrations of vancomycin and rhabdin, and cytotoxicity and osteogenic differentiation were assessed. **Results:** Minimum inhibitory concentrations (MICs) for vancomycin and rhabdin were determined against both methicillin-sensitive and -resistant *Staphylococcus aureus* strains. The viability of bmMSCs and pfMSCs was not affected by vancomycin, even at 4x MIC. Vancomycin also had no effect on the osteogenic differentiation of bmMSCs, but partially inhibited osteogenesis in pfMSCs. In contrast, rhabdin was cytotoxic in both cell-types at MIC. **Conclusions:** These findings suggest that direct application of rhabdin to infected bone tissue is likely to result in tissue damage, which may be irreparable, due to the loss of the resident stem cell population. Direct application of excessive doses of vancomycin in the femur region may possibly result in mild bone loss, which should be reversible upon cessation of antibiotics exposure, due to the survival of the resident stem cell population. Preservation of the bone stem cell population should also aid osseointegration post-surgery. *Ethics approval number: SU-ACUD15-00012*

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

METABOLIC SURGERY IN SOUTH AFRICA - AN INITIAL ACADEMIC HOSPITAL EXPERIENCE

A Potgieter (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University), A Webner (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University), AVV Lambrechts (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University), CE Cooper (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University), J Lubbe (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University), WJ Odendaal (Department of Surgery; Tygerberg Academic Hospital and Stellenbosch University)

Introduction: In South Africa, 42% of adult females, and 13.5% of adult males are classified as obese, the highest recorded numbers in Sub-Saharan Africa. Metabolic surgery has been proven to be a safe and effective treatment, yet due to demand on government resources has only been performed to a limited extent in public hospitals. **Aim(s):** The aim of this study was to describe the experience with metabolic surgery at a single academic hospital. **Methods:** This was a single center retrospective

review of all metabolic surgery procedures performed from October 2011 to September 2017. Ethics approval by the Stellenbosch University Health Research Ethics Committee. Results: A total of 57 patients underwent laparoscopic metabolic surgery, 56 (89%) Roux and Y gastric bypass, and 1 (2%) sleeve gastrectomy. The follow-up rate at 1 year was 97%. Mean preoperative BMI was 59 kg/m², and comorbidities included Type 2 Diabetes Mellitus (42%), hypertension (60%), and dyslipidemia (37%). There were no conversions to open surgery and at one year mean percentage total weight loss was 27.62±8 and mean percentage excess body mass index loss was 50.4±15.78. Overall morbidity was 14%, with 3 (5%) classified as major and 5 (9%) as minor. Conclusion/Recommendations: This study confirms that metabolic surgery can be performed safely in an academic hospital in South Africa. As outcomes are closely related to both surgeon and center volume, as well as long-term patient compliance, and taking into account both the socio-demographic index and the increased obesity numbers in South Africa, the role of metabolic surgery remains to be determined. Larger scale studies, and cost analyses are needed to answer these questions.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

Ethnic and gender specific incidence rates for hip fractures in South Africa – A Multicentre study

Asgar Kalla (UCT), Bilkish Cassim (UKZN), Farhanah Paruk (UKZN), Koos Jordaan (US), Mac Lukhele (WITS), Magda Conradie (US), Sapna Dela (UKZN)

Purpose: To determine ethnic and gender specific incidence rates of hip fractures in South Africa (SA) and to understand the burden of the disease in our multi-ethnic population. The secondary purpose is to develop a FRAX® base model for SA. **Methods:** A prospective, multi-centre, observational study was conducted in Gauteng, KwaZulu-Natal and the Western Cape. All patients ≥40 years presenting with an osteoporotic hip fracture to both public and private sector hospitals within the defined geographic areas were captured between April 2017 to December 2017 by trained fieldworkers. Traumatic and pathological fractures were excluded. (HREC N15/09/085) **Results:** A total of 2115 patients (n=682 male; n=1433 female) were included of African (n=563, 26.6%); Coloured (n=384, 18.2%); Indian (n=284, 13.4%) and White (n=882, 41.7%) ethnicity. Women were significantly older than men in the total and each ethnic group (p<0.001). Additionally, White subjects were significantly older (p<0.001) and Africans significantly younger (p<0.001) than other groups. Differences in the gender- and ethnic-specific, age-adjusted incidence rates were observed: in women, the highest incidence rate was noted in Whites (164.8 per 100 000), followed by Indians (128.7 per 100 000) with the lowest rates in Coloured and African women (61 and 36.7 per 100 000, respectively). A similar pattern was seen in men albeit at lower rates, with the highest rate in White men (73.1 per 100 000). An increase in the relative risk with increased age in the i) total cohort, ii) in women, and iii) in White, Indian and Coloured women was observed. **Conclusion:** Hip fractures occur in all ethnic groups at higher rates than previously thought. Differences in the ethnic specific incidence rates suggest that ethnic specific FRAX® models are required for South Africa.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

THE PREVALENCE AND SENSITIVITY PROFILE OF POSITIVE BACTERIAL AND FUNGAL CULTURES DURING PANCREATICOUDODENECTOMY AT TYGERBERG ACADEMIC HOSPITAL

Izak Loftus (University of Stellenbosch)

Introduction Pancreatico-duodenectomy (PD) is a complex procedure associated with major post-operative morbidity in 30-50% of cases, of which infectious complications are the most significant. Pre-operative biliary stenting has the potential to contaminate the biliary tree and is associated with a higher rate of infectious complications. Administration of an effective prophylactic antibiotic may

mitigate against this risk. Aim To describe the range of positive bile cultures and antibiotic sensitivity in patients undergoing PD at Tygerberg Academic Hospital. Methods A retrospective study involving all patients who underwent PD at Tygerberg Academic Hospital since the inception of the hepato-pancreatico-biliary unit in 2014. The total prevalence of positive bile cultures, the prevalence of different species and the sensitivity profiles were recorded and compared. The data were compared for patients who underwent pre-operative biliary stenting and those who did not. Results Thirty-seven patients underwent PD during the study period, of which 17(46%) were male and 20(54%) female. The median age was 52 years. Twenty-eight patients had bile cultures performed of which 29% and 32% grew a single organism and multiple organisms respectively. Klebsiella and Enterobacter species were the most commonly cultured organisms. Antibiotic resistance was common, especially to recommended and commonly used prophylactic antibiotics. Conclusions Most patients undergoing PD have contaminated bile, often with resistant organisms. The prophylactic antibiotic regimen at Tygerberg Academic Hospital requires adjustment.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

THE ANATOMY OF THE INTRA MEDULLARY CANAL OF THE DISTAL FIBULA

Etienne Joubert (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa), Hilgard MÅ¼ller (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa), Ignatius P.S. Terblanche (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa), Robert P Lamberts (Division of Orthopaedic Surgery, Stellenbosch University, Tygerberg campus, South Africa)

Purpose: Detailed anatomical descriptions of the ankle joint and more specifically the distal fibula is lacking. Insight into this anatomy can further improve the treatment of ankle fractures and design of distal ankle fixation methods and devices. Therefore the aim of this study was to determine the anatomical variability in intra-medullary measurements of the distal part of the fibula. Methods: A 158 patients (113 male) who received a Computer Tomography (CT) scan of their lower limbs at Tygerberg Hospital were included in the study (HREC no. S13/10/224). The anatomical profile of the last 50 mm of the fibula was studied in the antero-posterior and medial-lateral plane. Intramedullary diameters as well as the thickness of the anterior, posterior, medial, and lateral cortex were captured. Results: Two hundred and ninety-two ankle joint computer tomography (CT) scans were studied. No anatomical differences were between the right and left ankle fibula measurements. Average thickness medially (1.1 to 2.0 mm), laterally (1.1 to 2.0 mm) and posteriorly (1.0 - 2.0 mm) tended to become more with moving more distally. The average medial-lateral intramedullary diameter ranged from 6.2 to 15.5 mm, while the anterior posterior intramedullary diameter ranged from 11.0 to 22.8 mm. No correlations were found between the measurements and the age, gender and side. Conclusion: No differences in cortex thickness and intramedullary diameters were found between gender, side and age. The reported anatomical variation provides important clinical insight and potentially can assist manufacturers to further improve the designs of intramedullary nails.

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

Prevalence of a post-operative troponin leak in patients with cardiac risk factors undergoing knee and hip arthroplasty in a South African Population

Dr Koos Jordaan (Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Tygerberg), Dr Marilize Burger (Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Tygerberg), Dr Rainhard van Zyl (Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Tygerberg)

Purpose of the study: Determining the prevalence of a post-operative troponin leak in patients with different cardiac risk factors undergoing hip- or knee arthroplasty and investigating differences in

Troponin T levels between co-morbidities and different types of arthroplasty i.e. Total Hip Replacement (THR), Total Knee Replacement (TKR), and Neck of Femur Fracture Hip Replacement (NOFHR) Methods: A prospective, cross-sectional study of patients with ≥ 1 cardiac risk factor, undergoing replacement surgery and treated at a Tertiary Academic Hospital in South Africa from October 2017 to April 2018 conducted. Troponin T levels of all included patients were recorded on day one and three post-surgery using a Roche, 4th generation Elecsys highly sensitive cardiac Troponin T assay (cTnT-hs). A Troponin T level of $> 15\text{ng/L}$ is considered abnormal and termed Positive Troponin leak and $>100\text{ng/l}$ is suspected in Acute Coronary Syndrome (A.C.S.) (SUN HREC S17/02/042) Summary of Results: One-hundred-and-sixty-two patients ($n=68$ THR; $n=55$ NOFHR; $n=39$ TKR) were included. Sixty-eight patients (42%) recorded a positive Troponin Leak of which six cases had a suspected A.C.S. The highest prevalence was recorded in NOFHR (62%) followed by TKR (46%) and THR (24%) Conclusion Many patients undergoing arthroplasty surgery have multiple co-morbidities putting them at risk for Myocardial Injury after non-cardiac surgery (MINS). MINS is often a silent event estimated at 40% internationally which, with a 4-times raised morbidity and mortality risk, carries a poor prognosis at 30-days, 6-months and 1-year post-surgery. Post-operative Troponin testing, a cost effective measure, is imperative to diagnose MINS, subsequently increasing early detection, medical optimisation referral and prevention strategies. There is currently no published data on MINS prevalence in orthopaedic specific patients in South Africa. Our finding of 42% positive Troponin leaks raises awareness and we recommend routine post-operative Troponin T testing for arthroplasty units in South Africa.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

Large goitres and perioperative airway management

Dr Lydia Cairncross (UCT), Dr Revyl Haylett (UCT), Prof Mike James (UCT), Tarryn Moore (Tygerberg Hospital)

It is widely assumed in the literature that large goitres pose a significant risk to the airway perioperatively. Anaesthetic concerns include potential difficulty with intubation, ventilation and tracheomalacia. Surgical concerns include the risk of difficult dissection, haemorrhage, laryngeal nerve injury and tracheomalacia. The study involved a retrospective review of the folders of all patients who had thyroidectomies performed at Groote Schuur Hospital between January 2010 and June 2016 for large, non-malignant goitres, in order to assess their impact on perioperative and postoperative management. An attempt was also made to identify possible predictive markers associated with difficult intubation. 206 patients were identified as having large, non-malignant goitres, of which ten had missing data and were excluded. There were seven documented difficult intubations and only one case of failed intubation. This patient was subsequently intubated using a rigid fiberoptic bronchoscope on cardiopulmonary bypass. Four cases were intubated using a fiberoptic bronchoscope, eight with a videolaryngoscope, and six with a bougie. All other patients underwent uneventful tracheal intubation via direct laryngoscopy. All glands were removed via a collar incision with no requirement for sternotomy. One patient required blood intraoperatively and only four reported cases of postoperative haematomas. There were no instances of tracheomalacia. Two patients suffered long term recurrent laryngeal nerve injury with voice changes. The data shows that even massive goitres seldom cause insurmountable airway problems. Laryngotracheal oral intubation seldom fails, supporting previous publications that the standard anaesthetic of choice is intravenous induction with laryngotracheal intubation rather than fiberoptic intubation. No incidence of tracheomalacia was reported in our study.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

The reliability of physical examination per anatomic area to detect vascular injury in penetrating trauma to extremities.

Gian du Preez (Department of Orthopaedics, Tygerberg Hospital, University of Stellenbosch), Johannes Abraham le Roux (Department of Orthopaedics, Tygerberg Hospital, University of Stellenbosch),

Marilize Burger (Department of Orthopaedics, Tygerberg Hospital, University of Stellenbosch), Nando Ferreira (Department of Orthopaedics, Tygerberg Hospital, University of Stellenbosch)

PurposeThe purpose of this study was to determine the specificity and sensitivity of physical examination alone in detecting arterial injury in penetrating injuries to extremities (PTE), versus CT Angiography (CTA). Secondary aims were to determine whether the result is similar across all anatomic regions, and with different types of penetrating trauma.

Description of methodsA retrospective review included 353 extremity CTA's performed between 1-June-2016 to 30-June-2017. Presence of arterial injuries were noted, together with the specific anatomic area injured: upper arm, cubital fossa, forearm, thigh, popliteal fossa, lower leg, or multiple zones. Medical notes were reviewed to screen whether pulse deficit/hard signs of arterial bleeding were reported upon admission. (HREC #S16/07/119)

Summary of ResultsA total of 352 CT angiograms were included: 326 (92.4%) male, 27 (7.6%) female. Of these, 220 were lower limbs and 133 upper limbs. The mean age of included patients were 28.9 years (range: 11 - 68 years). The sensitivity of physical examination in detecting an arterial injury when considering all patients, compared to the gold standard CTA, was 92.1% (95% CI 84.5 - 96.8%) with the specificity 93.5% (89.9 - 96.2%). The thigh had the highest specificity of 96.38% (91.75-98.81%), followed by lower leg: 91.75% (78.09-98.3%), upper arm: 89.23% (79.06-95.56%) and forearm: 77.78% (39.99-97.19%). When considering gunshots the specificity was 91.49% (79.62-97.63%) whilst for stab wounds the specificity was 86.79% (74.66-94.52%). The numbers for the other subgroups were too small to interpret.

ConclusionThis study is in agreement with the literature which indicates that physical examination has a high specificity in detecting arterial injury in the setting of penetrating trauma of the extremities (PTE). It does however show that the specificity is not equal for all anatomic regions or mechanisms of injury. This new finding should be considered individually for patients presenting PTE.

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

Water wise hand preparation: The true impact of our practice

Ajmal Ikram (SU), Maarten Potgieter (SU), Marilize Burger (SU)

The Western Cape is experiencing the worst drought in decades. Considering the low dam levels and very little rain fall, every possible method of water saving must be applied. We investigated water usage during scrubbing for surgical procedures and possible interventions to reduce water consumption.

Aim: To determine water consumption during scrubbing procedures and the effect of easy-to-implement, cost effective yet efficient ways to reduce water usage during scrubbing. Secondary aims include: gaining insight into the surgeons' knowledge of water use/saving methods and their experience of water saving strategies.

Method: a two-phase observational study was performed on Orthopaedic theatre personnel scrubbing for theatre cases at our institution. Phase one evaluated standard practice and establish a control group. Phase two implemented three water reducing strategies. Group A) adjusted tap levers to allow surgeon to open and close taps easier; Group B) an assistant to close tap after hands were soaked/rinsed; and Group C) soap wash at the start of the day followed by alcohol-only-preparation between cases. Total water usage and time at basin was recorded for each scrub. Participants completed a questionnaire at the end of the list to establish their experience of the various preparation techniques. Necessary approval was obtained from our Hospital and Ethical Board.

Results: The control group (N=36 scrubs) used 5,2ltr/scrub and spent 2min43seconds washing their hands at a water flow rate of 2.19ltr/min. Total water usage per scrub and lower flow rates (1.93ltrs @ 0.73l/min; 2.29ltrs @ 1.36l/min and 2.96 ltrs@1,57l/min) respectively were recorded for Groups A (N=12), B(N=13) and C(N=18) with no significant difference in scrub time compared to the control group.

Conclusion: Water consumption during scrubbing for surgical cases can be significantly reduced by implementing simple cost effective measures. This study strongly recommends intermittent tap closure or alcohol based scrubs for hand preparation.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 17**A Study of the Preoperative Fasting Duration of Elective Cesarean Section Patients, at Tygerberg Hospital, and The Incidence of Fasting Hypoglycemia & Ketonuria**

Kim Ablort-Morgan (tygerberg Hospital Anaesthesia)

Background: Fasting prior to elective surgery is intended to prevent aspiration of gastric contents. However, a prolonged fasting duration could possibly cause harm. We wondered whether fasting durations in TBH elective caesarean patients was excessive. The first hypothesis was that fasting duration was compliant with international recommendations (6 hours for solids). The second hypothesis was that fasting duration was not associated with hypoglycaemia (whole blood glucose < 3.9 mmol/L) and/or significant (≥ 4.0 mmol/L, $\geq 2+$) ketonuria immediately prior to anaesthesia. Methods: A power analysis indicated that 25 patients would provide an 80% power, to determine a difference in fasting times. 56 patients were enrolled. Patients were questioned about fasting durations, while glucose and ketonuria were measured using an Accu-chek glucometer (Roche, Mannheim, Germany) and RightSign Urinalysis (Hangzhou Biotech, Hangzhou, China), respectively. Results: 1. Overnight fasting was (mean \pm standard deviation (range)) 14.2 \pm 5.7 (3 to 38) hours, clinically and statistically significantly longer than recommended ($p < 0.0001$). 2. Hypoglycaemia and ketonuria occurred in 39,3 and 51% of study parturients, respectively. The median fasting time of the hypoglycaemic patients was 17 (IQR 15 to 18) hours and significantly different to the median duration of the normoglycaemic patients, of 12.3 (IQR 11 to 15) hours ($p < 0.0001$). 3. There was a significant association between fasting duration, and both hypoglycaemia and ketonuria (both $p < 0.0001$). 4. Interestingly, 32% of parturients were subjected to repeated fasting episodes prior to elective caesarean section, with a median fasting time of 31.5 (IQR 21.25- 54.7)(range 17 to 121) hours. Conclusion: Fasting durations were excessive, with an unacceptable number of parturients being hypoglycaemic and ketotic, which is potentially harmful to both mother and foetus. These findings require urgent logistic intervention. Keywords Fasting, obstetric, caesarean section, hypoglycaemia, ketonuria

ABSTRACT NUMBER / ABSTRAKNOMMER: 18**Erector Spinae Plane Block: sensory distribution in breast surgery**

Francois Retief (Department of anaesthesia and critical care), Katrina Wiid (Department of anaesthesia and critical care)

Background: The recently described Erector Spinae Block has been shown in case studies to provide analgesia for thoracic and abdominal surgery. Cephalocaudal spread of local anaesthetic between the transverse processes and erector spinae muscles is believed to block multiple spinal levels. The primary aim of this study was to describe the sensory distribution of the erector spinae block. Secondary objectives were to determine onset time and duration of the block. Method: This was a prospective, descriptive study of 40 patients. After informed consent, erector spinae blocks were performed with 20 millilitres of 0.5% bupivacaine at the level of the third transverse process, for patients booked for breast surgery at Tygerberg Hospital. Sensory distribution was assessed on the anterior, posterior and lateral thorax at 10-minute intervals until no further spread was noticed. Follow-up was at 3 and 6 hours postoperatively. Results: Forty patients were enrolled in the study. Age was (median \pm SD) 57.1 \pm 12 years; weight 75 \pm 16 kilogram and height 165.7 \pm 6 centimetres. All blocks reached maximum distribution by 30 minutes. The median (25th; 75th percentile) number of dermatomes with no sensation were 4 (2; 5), 2 (0; 2) and 6 (5; 7) on the anterior, lateral and posterior surface of the thorax, respectively. The corresponding results for decreased sensation were 12 (10; 13), 4 (3; 5) and 12 (11; 13). Pain scores at 3 hours did not differ from preoperative scores, but at 6 hours the Numeric Rating Scale significantly exceeded that at both other time points. Conclusion: Erector Spinae Plane Block is a novel, promising, and effective analgesic technique, the spread of which was sufficient to provide intra- and immediate postoperative analgesia for breast surgery.

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Reassessment of acute postoperative pain in a resource-limited burns unit after the implementation of an analgesic management plan.

Adriaan Johann Greyling (University of Stellenbosch), Albertus Adriaan Murray (University of Stellenbosch), Annemarie Senekal (University of Stellenbosch)

Reassessment of acute postoperative pain in a resource-limited burns unit after the implementation of an analgesic management plan. Tygerberg Academic Hospital is the referral centre for all major burn wounds in adult patients in the Western Cape. A 2012 Tygerberg Academic Hospital audit identified post-surgical burns patients as having a high incidence of moderate to severe postoperative pain. In an attempt to reduce postoperative pain in burns patients, the Department of Anaesthesiology and Critical Care at Tygerberg Academic Hospital introduced a standardized postoperative analgesia protocol in November 2016. This standardized protocol included pain scores being introduced as part of nursing's routine vital sign observations. A five-month protocol introductory period was allowed before a repeat pain experience audit was performed. The audit comprised a sample of 64 patients that underwent burns related surgery. Using a visual analogue scale (VAS), patients indicated the worst pain experienced in the first 24 hours postoperatively, as well as the amount of pain experienced at the time of the interview 24 hours postoperatively. This data was compared to that collected during the 2012 audit. We considered that a ≥ 18 mm reduction in median VAS scores to be a significant improvement in pain compared to historical controls. Only 34 (53%) of the 64 patients had postoperative pain scores recorded and of those, there were only 24 patients who had more than 1 documented pain score. A reduction of 6mm was found in the median VAS scores for worst pain experienced and a reduction of 3.5mm for the pain experienced at the time of the interview 24h postoperatively. These values were not statistically significant. The poor compliance to the protocol precludes the investigators from confidently concluding that the new protocol is truly ineffective.

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

Access to health care for osteoporotic hip fracture patients in South Africa – Part of FRAX Multicenter study

Asgar Kalla (UCT), Bilkish Cassim (UKZN), Farhanah Paruk (UKZN), Koos Jordaan (US), Mac Lukhele (Wits), Magda Conradie (US), Sapna Dela (UKZN)

Purpose of study: The larger study aim is to determine the ethnic and gender specific incidence of hip fractures in South Africa and to understand the burden of the disease in our multi-ethnic population. The specific purpose of this study was to document the access to health care for this specific population group and to document time between injury, admission and surgical treatment. **Methods:** A prospective multi-center observational study was conducted in Gauteng, KwaZulu-Natal and the Western Cape. All patients ≥ 40 years presenting with an osteoporotic hip fracture to both public and private sector hospitals within the defined geographic areas were captured by trained fieldworkers. Traumatic and pathological fractures were excluded. Data were recorded from April 2017 – December 2017. Additional data captured include time of fall, time of admission and time of surgery. **Results:** Total of 2115 patients (n=682 male; n=1433 female) were included. KZN n=826, Gauteng n=426 and WC n=863 patients. Of these, 1412 (66.7%) were treated in public hospitals and 701 (33.2%) in private hospitals. Median time from fall to admission to hospital was 15 h, whilst the median time from admission to surgery was 95.4 h (nearly 4 days). Finally, median time from fall to surgery was 124 h (>5 days). These times were significantly longer in the public sector compared to private hospitals. **Conclusion:** Morbidity and mortality for osteoporotic hip fractures are known to be very high and international data suggests the biggest modifiable risk factor to reduce this morbidity and mortality to be the time between fractures to surgery. Public health care hospitals have different barriers to

surgery then private health care hospitals in SA to address the delays but this study nonetheless highlights areas to be improved. This is the largest and most representative data on incidence of osteoporotic hip fractures in SA.

Theme 7 / Tema 7
**Violence, Injuries, Trauma and
Rehabilitation/
Geweld, Beserings, Trauma en
Rehabilitasie**

Oral Presentations/ Referate

ABSTRACT NUMBER / ABSTRAKNOMMER: 1

The Effect of Ischemic Compression versus Electrotherapy on Pain and Range of Motion in Patients with Myofascial Trigger Points in the Trapezius Muscle: A Systematic Review

Alexis Partridge (Stellenbosch University), Daniella Pazda (Stellenbosch University), Dayle McLoughlin (Stellenbosch University), Eugenie Lamprecht (Stellenbosch University), Gakeemah Inglis-Jassiem (Stellenbosch University), Georgina Frost (Stellenbosch University), Jatan Patel (Stellenbosch University), Thakeerah Khan (Stellenbosch University)

Introduction: Myofascial trigger points (MTrPs) are clinically identified hyperirritable nodules in a taut band of skeletal muscle causing a decrease in cervical active range of motion (AROM) and an increase in pain, among other symptoms, affecting the function of the muscle. Ischemic compression (IC) and electrotherapy (ET) are often used to treat MTrPs in the trapezius muscle. The aim of this systematic review was to identify, clinically appraise and evaluate available evidence for the effectiveness of IC on increasing cervical AROM and decreasing pain in adults presenting with MTrPs in the trapezius muscle compared to ET modalities. Methods: Eight computerized bibliographical databases accessed from inception to April 2018 through the Stellenbosch University library including; Cochrane, EBSCO Host: CINAHL, EBSCO Host: SPORTDiscus, Google Scholar, PEDRO, Pubmed, Science Direct and Scopus were searched. Studies were included if participants were between the ages of 18 and 65 with palpable MTrPs. The PEDro scale was used to appraise methodological quality. Acquiring ethical approval and participant consent was not necessary as this was secondary research. Results: Modalities evaluated were IC and ET (ultrasound, Laser and TENS). Overall, the results indicated an improvement with both interventions but ET was more effective in increasing cervical AROM and decreasing pain. ET was the most effective treatment, in two out of the three studies, when measuring cervical AROM. IC was statistically significant in increasing cervical AROM in the remaining study. Two of the four studies assessed pain intensity and ET was found again to be more effective than IC. Conclusion: Level II evidence used in this systematic review supports the use of ET over IC in increasing cervical AROM and decreasing pain in participants with MTrPs in the trapezius muscle. Physiotherapists are advised to use the preferred treatment of ET, but in low socio-economic clinical settings IC remains an applicable and feasible treatment option.

ABSTRACT NUMBER / ABSTRAKNOMMER: 2

The complications, outcomes and management strategies of non-missile penetrating head injuries

Adriaan Vlok (Stellenbosch University), Armin Gretschel (Stellenbosch University), Bradley Harrington (Stellenbosch University)

The complications, outcomes and management strategies of non-missile penetrating head injuries
AbstractIntroduction:Non-missile penetrating head injuries (NMPHI) involve low velocity penetrating head injuries for example a knife stab. They differ from injuries caused by axes or machetes in that their mechanism is mainly penetrating, not crushing. Only a few significant NMPHI series have been published and none since the development of endovascular treatment. The literature recommends removal of retained objects by craniotomy. At our institution we have moved away from this practice in favour of in-line removal without craniotomy – using the bone as a guide to limit further intracranial injury.This research investigates the complications (infective, vascular and iatrogenic) of NMPHIs. It also describes the management algorithm employed at Tygerberg Hospital and evaluates its outcomes. Methods: A retrospective review of prospectively collected patient data was carried out for patients having sustained a NMPHI. The study period was 1 August 2007 to 30 April 2018.Results: A total of 180 patients were enrolled. 35 presented with retained blades. Overall mortality was 6%. Intracranial infective complications were seen in 13%. Infection rate following antibiotic prophylaxis was 9% vs

19% without and more common if a mucosal surface involved (30% vs 10%). Vascular complications were seen in 10% of cases. These were more common when the object penetrated transorbitally 40% vs 7%. Other high-risk groups were those where the tract crossed the Sylvian fissure or circle of Willis – 17% each. Together these high-risk groups accounted for 69% of vascular injuries. Conclusion: Outcomes following our management algorithm were favourable when compared to the literature. No deaths occurred following removal of retained blades or following infective complications. Only two patients who presented with retained blades did not reach a Glasgow Outcome Score of 5.

ABSTRACT NUMBER / ABSTRAKNOMMER: 3

Biomechanical analysis of motor impairments contributing to early functional decline in adults living with HIV-1-infection: Sub-study to the EndoAfrica study

John Cockcroft (Stellenbosch University), Karina Berner (Stellenbosch University), Linzette Morris (Stellenbosch University), Quinette Louw (Stellenbosch University)

Background: People living with HIV/AIDS (PLHIV) can nowadays achieve a normal lifespan, but neuromotor impairments remain prevalent. Poor understanding exists of how gait and balance is objectively affected in PLHIV. This project aims to provide biomechanical information about movement impairments of PLHIV, and to correlate clinical test performance to 3D motion analysis, self-reported function, and falls. Methods: Phase I includes a systematic review describing objective locomotor impairments in PLHIV. This is followed by two agreement, correlation and repeated-measures studies, aimed at ascertaining the repeatability of gait measurements using a portable inertial motion capture system (PIMCS) and validity of PIMCS gait-measurements versus optical motion capture in healthy volunteers, community controls and PLHIV. Phase II comprises a cross-sectional field study with an analytical component. The PIMCS was implemented in a clinical setting to measure 3D movement in 50 PLHIV and 50 seronegative participants. Clinical functional test performance, self-reported function and fall history was also recorded. These data will be correlated to investigate associations. Results: The systematic review revealed that locomotor impairments exist in PLHIV, resembling fall-associated parameters in the elderly; although no instrumented gait data currently exists in PLHIV. Study One of psychometric testing indicated that the PIMCS's output was not directly comparable to the reference, but good repeatability and high correlation implied that PIMCS gait data are comparable within, and possibly between, participants when using the same system. Following completion of data analysis, Study Two results will extend these findings, using a community sample of PLHIV and controls. Findings from Phase II will answer the overall project aim and data analysis is currently underway. Conclusions: The project is the first to describe 3D biomechanics in PLHIV. The comprehensive dataset will allow identification of appropriate clinical test(s) for early screening of functional decline in PLHIV at community level.

ABSTRACT NUMBER / ABSTRAKNOMMER: 4

Function and exercise performance of transtibial amputees during a 6 minute walk test and obstacle course using a novel mechanically powered ankle/foot prosthesis: a randomised controlled trial

Phoebe Runciman (Institute of Sport and Exercise Medicine, Dept Surgery, Stellenbosch University)

Objectives: This study describes the functional capacity and exercise performance of a group of South African transtibial amputees using a novel ESAR foot prosthesis, compared with the gold standard ESAR foot, and conventional SACH foot. Methods: Ten participants with unilateral TTA performed a standardized protocol utilizing three different foot prostheses (SACH, gold standard ESAR, novel ESAR), separated by two weeks in a cross-over design. Functional capacity was assessed using the standardized 6-minute walk test, and custom-designed obstacle course, the main outcomes were performance, heart rate and ratings of perceived exertion. Ethics: N16/08/032 Results: More distance

was covered from the first minute during the 6-minute walk test when using the novel ESAR foot compared to the gold standard ESAR and SACH feet ($p < 0.05$). Similar heart rate values were recorded for all three feet, however there was a lower rating of perceived exertion when using the novel ESAR foot. The obstacle course, which comprised six challenges, was completed in the fastest time when utilising the novel ESAR foot. Furthermore, there were fewer mistakes made (task completeness) when utilising this foot. Again, heart rates obtained during the obstacle course were similar between the feet. Conclusion: The current study is the first to investigate the effect of a novel mechanically powered ESAR foot prosthesis on functional exercise performance as it relates to health, in a sample of South African transtibial amputees. It was shown that the novel ESAR foot had improved functional and exercise performance. These findings are hypothesized to have a significant effect on the health parameters and degenerative changes associated with amputation.

ABSTRACT NUMBER / ABSTRAKNOMMER: 5

Spinal trauma: the burden and clinical profile at a major tertiary hospital in the Western Cape

Danie Krynauw (Stellenbosch University), Sanesh Miseer (Stellenbosch University), Theresa Mann (Stellenbosch University)

Background Spinal orthopaedic trauma continues to be an important cause of morbidity, often affecting young and healthy individuals. This severe form of injury typically requires specialist care and anecdotal evidence suggests that spinal trauma contributes significantly to the burden on the Spinal Unit at Tygerberg Hospital. However this has never been formally investigated. Therefore, the aim of this study was to describe the burden, clinical profile and resource use associated with spinal orthopaedic trauma admissions to Tygerberg Hospital. **Methods** All patients admitted to the Tygerberg Hospital Spinal Unit between the 1st of October 2016 and the 30th of September 2017 for spinal orthopaedic trauma were included in the study. Clinical and demographic information such as age, gender, residential district, mechanism of injury, region of spinal trauma, advanced radiological investigations, operating time and length of hospital stay was extracted from medical records and presented using descriptive analyses. **Results** Overall burden was comprised of 180 patients and 192 admissions, including re-admissions. Most patients were male ($n=121$, 67%) and from the Cape Town Metro ($n=120$, 60%). Spine trauma to the cervical spine ($n=85$, 47%) and thoracolumbar spine ($n=41$, 23%) accounted for the majority of cases with motor vehicle accidents ($n=87$, 49%) and falls ($n=46$, 26%) identified as the most common mechanisms of injury. Almost all patients ($n=165$, 92%) required advanced imaging and 41% received operative management. The median hospital stay was 15 days with an interquartile range of 9 to 27 days. **Conclusion** There was a significant burden of spinal trauma over the study period, of which the majority could be considered preventable. Furthermore, management of spinal trauma was very resource-intensive in terms of imaging, theatre time and hospital days. These findings highlight the need for prevention strategies aimed at reducing the burden of these injuries within our resource-limited setting.

ABSTRACT NUMBER / ABSTRAKNOMMER: 6

The effectiveness of Schroth exercises in adolescents with idiopathic scoliosis in decreasing the Cobb angle compared to non-surgical management: A Systematic Review

Chanté van Rooyen (Stellenbosch University Physiotherapy division), Elzanne Myburgh (Stellenbosch University Physiotherapy division), Francois Joubert (Stellenbosch University Physiotherapy division), Larissa Geldenhuys (Stellenbosch University Physiotherapy division), Lenka du Plessis (Stellenbosch University Physiotherapy division), Nicol Vermeulen (Stellenbosch University Physiotherapy division), Wilna Coetzee (Stellenbosch University Physiotherapy division)

Background: Adolescent idiopathic scoliosis (AIS) is one of the most common structural spinal deformities and becomes apparent in generally healthy children around the time of puberty. The Schroth method of exercise is a scoliosis-specific modality used to treat idiopathic scoliosis in young adolescents to reduce the progression of the scoliotic deformity and to delay or avoid the need of wearing a brace. Objective: To identify, critically appraise, evaluate and establish best available evidence for the effectiveness of Schroth exercises in comparison to non-surgical management (including observation or conservative management) in adolescents with idiopathic scoliosis to decrease the Cobb angle. Results: Four randomised control trials with an average PEDro score of 6.75/10 were included in this study. Results indicated that Schroth exercises had a significant effect in decreasing the Cobb angle ($p < 0.05$) and in improving quality of life (QoL) in comparison to non-surgical management. The pooled effect of the intervention on QoL showed a significant result in favour of Schroth exercises at 12 weeks ($p < 0.002$) and at 24 weeks ($p < 0.0004$). Conclusion: Level II evidence suggests that Schroth exercises have a significant effect on reducing the Cobb angle and improving QoL in adolescents with idiopathic scoliosis when compared to non-surgical management. The minimum duration of the intervention should span across 12 weeks to have an effect on both these outcomes, but the treatment programme should last at least six months or longer to optimise results. Physiotherapists are encouraged to combine supervised Schroth exercises with conventional physiotherapy care and also include a supervised home exercise program to reach more favourable outcomes. Further research is needed to determine the long-term effects of Schroth exercises as well as to establish the effect on the respective domains of QoL, such as pain, function and self-image.

ABSTRACT NUMBER / ABSTRAKNOMMER: 7

Unstable ankle fractures – Is there a difference between using a locked intramedullary fixation compared to anatomically contoured plating.

De la Rey Badenhorst (Tygerberg orthopaedic department), Naas Terblanche (Tygerberg orthopaedic department)

Ankle fractures represents a major proportion of orthopaedic trauma workload. The gold standard treatment is open-reduction-internal-fixation with plate-and-screws but skin complications are reported to be as high as 30%. Fibular nails are a potential alternative technique for fixation of the lateral malleolus. The aim of the study was to evaluate whether the fibula nail can be used to effectively maintain reduction of an unstable Weber B and C ankle fracture and cause less soft tissue complications. All ankle fractures presenting to a tertiary referral centre were randomised into two groups: i) patients receiving plate-and-screw fixation (PG, $n=26$) or ii) patients receiving intramedullary nail fixation (NG, $n=37$). Post-operatively, patients were followed-up at 2-weeks, 6-weeks, 3-months, 6-months and 1-year recording measurements and functional scores. (SUN HREC S13/10/202) General characteristics between groups were similar ($p > 0.05$). The PG consisted of 84.6% (52.4% unstable syndesmosis) Weber B and 7.7% (4% unstable) Weber C vs the NG which had 56.8% (52.4% unstable) Weber B and 37.8% (81.8% unstable) Weber C fractures. The posterior malleolus were involved in 76.6% of the PG and 75.7% of the NG. The scar sizes of the PG and NG were 10cm and 1.5cm whilst operating time was 51.7 ± 9.2 min and 46.8 ± 14.3 min, respectively. Screening time for PG and NG 0.4min and 0.6min, respectively. A single deep infection required plate removal after union in the PG. Using the Olarud-Molander scoring system, a significant difference ($p < 0.001$) at 6-months post-operative with the NG having increased range-of-motion was observed. There was an improved cosmetic outcome when comparing plating and nailing. Additionally, at 6-months post-operatively the functional outcome of the NG was significantly better than the PG. The nail proved to reduce and maintain unstable ankle fractures as well as plating does with minimal risk of post-operative infection.

ABSTRACT NUMBER / ABSTRAKNOMMER: 8

Mobility Transition in Older Adults in Worcester using an Occupational Lens

Asisipho Tsotsa (Rural Clinical School, Occupational Therapy), Isolde Burger (Rural Clinical School, Occupational Therapy), Kay De Villiers (Rural Clinical School, Occupational Therapy), Marianne Breytenbach (Rural Clinical School, Occupational Therapy), Retha-Mari Smith (Rural Clinical School, Occupational Therapy), Sharlotte Sehlapelo (Rural Clinical School, Occupational Therapy), Tamsin Ballantyne (Rural Clinical School, Occupational Therapy)

Introduction: This study was conducted within a rural setting in Worcester, Western Cape, with the target population being able-bodied and sensory-impaired older adults aged 65 years and older. The objectives were to gather data on the places of interest among the older adult participants, the modes of transport they use to arrive at these places of occupation and the satisfaction they derived from their occupational engagement in these out-of-home occupations. **Methods:** Quantitative study design with 59 participants recruited by means of convenience sampling from Kaleidoscope, National Institute for the Deaf (NID) and the Worcester Community Day Centre. The WHODAS 2.0 and the Mobility of Older Adult and Satisfaction questionnaire were used. Data relating to forms of transport, places of interest, meaning and satisfaction derived from engagement in out-of-home occupations were obtained. Data analysis were done using the SPSS version 24 and STATA version 15. **Results:** Findings concluded that walking is the most frequently used mode of transportation for older adults in this population, followed by transportation opportunities from friends. Participants housed at NID and Kaleidoscope were primarily dependent on the institution transport to get to their places of occupation. The places of interest that the older adults visited most frequently were grocery stores, places of worship, the hospital, clothing stores and friends. In general, the levels of satisfaction with all forms of transport were relatively high. **Conclusion:** Mobility transition within this population has displayed a minor change in trajectory, since walking has been recorded as the most frequently used mode of transport. What has changed, however, is the physical demands expected for this activity as a result of the wear and tear of the human body. Overall, the environmental barriers experienced by the participants contributed greatly to the participants' occupational engagement and thus, their satisfaction with their modes of transport.

ABSTRACT NUMBER / ABSTRAKNOMMER: 9

The Development and Validation of the Stellenbosch University On-road Assessment for Fitness to Drive

Lizette Swanepoel (Stellenbosch University)

Background: Internationally, occupational therapists are called upon to assess fitness to drive. Fitness to drive is assessed through a comprehensive driving evaluation consisting of a clinical battery of tests and an on-road assessment. The on-road assessment is the criterion standard for assessing fitness to drive. Such an assessment has not yet been developed or validated in the South African context. **Purpose:** For this study, the researcher (a) developed the first on-road assessment for fitness to drive and, (b) quantified the face, content and construct validity of the Stellenbosch University on-road assessment. **Methods:** The researcher developed an on-road assessment for fitness to drive through literature review. Validity was established: (1) face validity using feedback from peer reviewers, (2) content validity using ratings of expert reviewers, and (3) construct validity by assessing between group differences in young drivers who drove the road-course. **Results:** Peer review indicated acceptable face validity. Expert reviewers had an average rater agreement percentage of 94%, indicating favourable content validity. One (of two) on-road outcome measures, the Global Rating Score, discriminated between two groups of drivers, indicating construct validity. **Conclusion:** This study introduced the first empirical on-road assessment in the South African context.

ABSTRACT NUMBER / ABSTRAKNOMMER: 10

Unique clinical effects of minor adder envenoming

Cherylynn A Wium (Division Clinical Pharmacology), Gert J Muller (Division Clinical Pharmacology), Johann M van Zyl (Division Clinical Pharmacology)

It is known that the venom of the berg adder (*Bitis atropos*) is both cytotoxic and neurotoxic. The bites of other southern African minor adders have thus far not been associated with neurotoxicity. This is a first report of five cases of minor adder bites, other than berg adder, causing unique neurotoxic effects. Three of the five cases were bitten by *Bitis xeropaga* (36, 21 and 3½ years old, all male), and two by *Bitis peringueyi* (9 year old male and 5 year old female). All the cases presented with local cytotoxic effects and they all developed external ophthalmoplegia with prominent mydriasis. The two older patients in the *B. xeropaga* group complained of changes in their sense of taste and smell (common feature of berg adder envenoming). They also experienced difficulty in walking. The youngest patient had difficulty in breathing and was ventilated. This patient presented with convulsions due to a low serum sodium on day two. Hyponatremia is a common complication of berg adder bite. It has, however, never been documented in other minor adder bites. The cause of the hyponatremia is probably due to the presence of a natriuretic polypeptide in the venom. Both patients in the *B. peringueyi* group had an unsteady gait, but experienced no abnormalities of taste and smell. It took four weeks for the 9 year old patient's eye symptoms and signs to resolve, but the 5 year old female's pupils continued to be dilated two years after the bite. In previous studies it was found that the neurotoxic effects of berg adder venom resides in polypeptides with phospholipase A2 activity. Based on the above findings, it is suspected also to be present in the venoms of the other minor adders, such as *B.xeropaga* and *B. peringueyi*.

ABSTRACT NUMBER / ABSTRAKNOMMER: 11

Designing a longitudinal study to improve the welfare and performance of the 10,000 Maties athletes: a protocol article

James Brown (Stellenbosch University), Lindsay Starling (Stellenbosch University), Pierre Viviers (Stellenbosch University), Sean Surmon (Stellenbosch University), Wayne Derman (Stellenbosch University)

Introduction Sports governing bodies are responsible for their athletes' welfare. South African universities contribute significantly to the country's total athletic population. Stellenbosch University (Maties) alone has about 10,000 athletes. The purpose of this protocol article is to outline the design of a health and wellness surveillance system of this university sport population. Methods The 1,100 members of the Stellenbosch Rugby Football Club (SRFC) were the study pilot group. The SRFC is comprised of players from recreational to semi-professional level. Using a knowledge translation strategy, the end-users were identified as the players, coaches and medical/support staff. General wellness and training load information can be entered by players using an athlete monitoring phone Application. Injury and illness information is captured by the university's medical staff and reconciled with the relevant users' profile. Results The key stakeholders identified their prerequisites of the surveillance system: 1) collected information is stored securely, 2) low data entry burden, 3) data summaries regularly available in a presentable manner. The specific wellness questions were derived from established subjective surveys, which are most sensitive to detecting psychological disturbances. The questions are predominantly closed-ended with branching logic functionality, reducing the athlete burden and standardising data for analyses. Injury and illness forms were based on the WHO, Sports Medicine Australia and consensus statements. Match exposure information is obtained from the university website and cross-checked with the training load data entered by athletes. Discussion This protocol article describes the development of a scalable surveillance system for all levels of athlete, recreational to semi-professional, within the 10,000 Stellenbosch University athletes. Data forms were informed by extant literature and end-user input ensuring the information collected satisfies both science and practice. Ultimately, these data can enhance the wellbeing and performance of Maties athletes, while contributing to the scientific literature in an under-studied population.

ABSTRACT NUMBER / ABSTRAKNOMMER: 12

The effect of pre-exercise low-level laser therapy compared to placebo on exercise induced muscle damage of the knee extensors in 18-35-year-old males

Ernest Nel (Stellenbosch University), Gerda Carstens (Stellenbosch University), Lauren Goliath (Stellenbosch University), Mark Andrianatos (Stellenbosch University), Stephani le Roux (Stellenbosch University), Wilmien Esterhuyzen (Stellenbosch University)

ABSTRACTBACKGROUND: Muscle stiffness and swelling is experienced after eccentric muscle contraction due to inflammatory processes. Low level laser therapy is an effective treatment to reduce inflammation, which causes exercise induced muscle damage (EIMD) and pain. **OBJECTIVES:** To systematically review the evidence on the effect of pre-exercise low-level laser therapy compared to placebo intervention in decreasing (EIMD), specifically MVC and pain, in males aged 18-35.**METHODOLOGY:** Seven computerised databases were used to conduct the searches for randomised controlled trials: PubMed, Cochrane Library, PEDro, Scopus, EBSCO Host, ScienceDirect, OTSeeker . The search terms included: Low Level Laser Therapy, Phototherapy, Electrical Stimulation Therapy, Quadriceps, Muscle Damage. The articles were appraised using the PEDro Scoring Scale and results were tabulated and described.**RESULTS:** Six trials were included with PEDro scores ranging from 6/10 to 10/10. Majority of the studies indicated that pre-exercise LLLT restored muscle power and decreased pain as opposed to placebo pre-exercise LLLT . **CONCLUSION:** The study concluded that pre-exercise LLLT significantly decreases pain ($p \times 0.0009$) and restores muscle power ($p < 0.0001$). LLLT treatment before knee extensor eccentric protocol exercise was effective in lowering the damaging effects of exercise on muscle function measured using VAS and MVC. Physiotherapists are therefore encouraged to make use of pre-exercise LLLT to decrease pain (VAS) and restore muscle power (MVC).**KEYWORDS**â€œLow Level Laser Therapyâ€œ, â€œMVCâ€œ, â€œVASâ€œ and â€œknee extensorsâ€œ, â€œExercise-induced Muscle Damageâ€œ

ABSTRACT NUMBER / ABSTRAKNOMMER: 13

Cross-cultural adaptation of the Disabilities of the Arm, Shoulder and Hand (DASH) Questionnaire: Aspects to consider.

Christina Jerosch-Herold (University of East Anglia), Helen Buchanan (University of Cape Town), Lana van Niekerk (Stellenbosch University), Susan de Klerk (Stellenbosch University)

This abstract was presented at the recent World Federation of Occupational Therapy conference held in Cape Town, May 2018.**Introduction**The Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH) is an evaluative and discriminative region specific patient rated outcome measure (PROM) used by occupational therapists in the field of therapy to the upper limb. The DASH measures symptoms, and aspects of activity and participation as outlined in the nine domains of the International Classification of Functioning, Disability and Health, in patients with upper limb musculoskeletal conditions. This well researched instrument was developed in English in the developed context of Canada. The Institute for Work and Health provide clear guidelines for the process of cross-cultural translation and adaptation. **Objectives**The objectives of this oral presentation are: 1) to outline the process of cross-cultural translation and adaptation of the DASH and; 2) to highlight important consideration when cross-culturally translating and adapting PROMs such as the DASH.**Method**The process of forward and backward translation, as well as the practice of cognitive interviewing in questionnaire design will be discussed. **Aspects of semantic, idiomatic, experiential and conceptual equivalence will be considered.****Results and Conclusion**The DASH (and any PROM), has to be cross-culturally translated and adapted prior to use and psychometric testing thereof in a different culture and context to the one in which it was developed. By cross-culturally adapting PROMs such as the DASH, the instrument can continue to investigate the construct(s) of interest in the new culture and context. This creates measures that are equivalent, irrespective of country, culture, language and occupations.

ABSTRACT NUMBER / ABSTRAKNOMMER: 14

Retrospective review of closed reduction of cervical spine facet dislocations

De la Rey Badenhorst (Tygerberg orthopaedic department), Johan Davis (Tygerberg orthopaedic department)

Evaluation of the success rate of closed reductions of cervical facet dislocations; comparison between the conventional weight-and-pulley system technique and a novel closed system reduction table. Cervical facet dislocations require urgent intervention, especially when associated with spinal cord compromise. The South African Constitutional court mandates reduction within 4 hours. Historical data shows limited success and lengthy delays using standard techniques (weights and pulley). This prompted development of a controlled, closed-system traction table to assist with reduction of cervical facet dislocations. This retrospective review compares outcomes of closed reduction of cervical facet dislocations using the purpose built traction table to the standard technique. Closed reduction of cervical dislocation injuries at Tygerberg Hospital between November 2008 and March 2016 were reviewed. Patients presenting before March 2015 were treated using the traditional method of reduction whereas patients presenting after March 2015 were treated using a novel closed system traction table. Clinical and demographic data was extracted to evaluate (i) reduction success rate and (ii) time to reduction using the different approaches. Sixty-nine patients with cervical spine dislocations were included in this study; 47 were treated using the traditional method (39 men, 8 women, mean age 38 years, range 16-65 years), 14 were treated with the traction table (12 men, 2 women, mean age 38 years, range 23-54 years) and 8 did not receive a reduction attempt. The success rate was 74% (n=35/47) using the traditional method and 100% (n=14/14) using the traction table. Median time to successful reduction was 54 min (range 10-300 min) using the traditional method and 45 min (range 12-87 min) using the traction table. These findings suggest that use of a purpose-built closed system traction table is an effective means of reducing cervical dislocation injuries.

ABSTRACT NUMBER / ABSTRAKNOMMER: 15

Workplace-based rehabilitation for upper limb conditions: A Systematic Review

Marlette Burger (Stellenbosch University), Munira Hoosain (Stellenbosch University), Susan de Klerk (Stellenbosch University)

Background: Upper limb conditions are a common and growing cause of ill health and disability in the workplace. There is a growing trend international to situate rehabilitation services at the workplace, while South African work rehabilitation services tend to be centralised at hospitals and clinics. Objective: To determine the effectiveness of workplace-based rehabilitative interventions in workers with upper limb conditions. Methods: We searched 9 databases for clinical trials with the following inclusion criteria: i) Participants 18 years or older who are actively employed, with a pre-existing upper limb condition or upper limb pain; ii) Rehabilitation programs based at least partly at the workplace, including occupational health clinics. Studies were critically appraised using the Institute for Work and Health Risk of Bias tool. Results: The initial literature search located 1071 articles, of which 80 were full text reviewed. Seventeen original studies were included, across 28 articles, reporting on various outcomes. Studies were sorted into intervention categories: Ergonomic controls (n=3), ergonomic training and workstation adjustments (n=4), exercise and resistance training (n=6), clinic-based versus workplace-based work hardening (n=1), nurse case manager training (n=1), physiotherapy versus Feldenkrais (n=1), and ambulant myofeedback training (n=1). The largest body of evidence supported workplace exercise programs, with positive effects for ergonomic training and workstation adjustments, and mixed effects for ergonomic controls. Ambulant myofeedback training had no effect. The remaining three categories had positive effects in the single study on each intervention. Conclusion and Recommendations: There is substantial evidence supporting workplace exercise programs. Further research needs to be conducted on the remaining intervention categories. Researchers are encouraged to collaborate with clinicians to enable more high quality research in "real-life" rehabilitation

contexts. Clinicians should build partnerships with the Department of Labour and stakeholders at workplaces, in order to develop rehabilitation resources in work environments.

POSTER PRESENTATIONS / PLAKKAATAANBIEDINGS

ABSTRACT NUMBER / ABSTRAKNOMMER: 16

The Availability, Utilization and Relevance of Therapeutic Apparatus in South African Occupational Therapy Clinical Practices

Alicia Swart (Rural Clinical School, Occupational Therapy), Annes Rodrigues (Rural Clinical School, Occupational Therapy), Kelly Slater (Rural Clinical School, Occupational Therapy), Lidia-Marie Olivier (Rural Clinical School, Occupational Therapy)

Introduction: Occupational therapists use various approaches as well as assistive devices to rehabilitate, support and/or strengthen the health as well as the well-being of their patients. The assistive devices used include rehabilitation technology, support technology as well as therapeutic apparatus (T.A.). All of which allow the patient to engage in functional as well as purposeful activities. While most academic institutions in the country offer both theoretical and practical training on therapeutic apparatus the applicability of the training remains to be evaluated. Subsequently, this study aims to assess the relevance, availability and utilisation of T.A. in South African (SA) occupational therapy clinical practise. To achieve this a qualitative study design was used. Methods:Checkbox, an online Stellenbosch University survey platform was used to design and distribute the survey to the 4473 HPCSA registered occupational therapists throughout South Africa. To recruit more eligible participants the survey was also marketed through several social media platforms including the Occupational Therapy Association of South Africa newsletter and Facebook. The data was recorded, cleaned and analysed using SPSS for various measures of central tendency. Results:A total of 949 responses were recorded however, only 784 were valid. A large majority of the participants had 3-10 yearsâ€™ experience in the field and primarily provided services pertaining to mental and physical health. 98% of the population considered T.A. to be beneficial however, only 74% of them found it applicable to their current clinical setting. Only 59.5% of participants had access to functional T.A. in their setting of which 83.6% utilise it. Conclusion: This study provides evidence that T.A. is relevant and utilised in SA occupational therapy clinical practice however, there is a need to upscale the access to functional T.A. and to introduce more T.A. that is applicable to the diverse clinical settings in the country.

ABSTRACT NUMBER / ABSTRAKNOMMER: 17

Why are athletes bringing injuries into the Games? The risk profiles associated with the high pre-competition period injury rate at the Rio 2016 Paralympic Games: a multivariate analysis of 51,198 athlete days

Phoebe Runciman (Institute of Sport and Exercise Medicine, Dept Surgery, Stellenbosch University)

Objectives: The present study constitutes an analysis of several variables identified as risk factors related to injury at the Rio 2016 Paralympic Games. The variables include 1) period of Games when the athlete was injured, 2) sex of the athlete, 3) age group of the athlete and 4) chronicity of the injury. Methods: A total of 3657 athletes from 78 countries, representing 83.4% of all athletes at the Games, were monitored on the web-based injury and illness surveillance system over 51,198 athlete days during the Rio 2016 Summer Paralympic Games. Injury data were obtained daily from teams with their own medical support. Ethics: N16/05/067Results: A total of 141 injuries were reported during the 3 day pre-competition period, with an injury incidence rate (IR) of 12.9 (95% CI 10.9 to 15.2) injuries per 1000 athlete days. There were 369 injuries recorded for 365 athletes (IR of 9.2 (95% CI 8.3 to 10.2) during the 11 day competition period ($p < 0.01$). For female athletes, both acute and chronic overuse injuries

were more prevalent in the pre-competition period, compared with the competition period. For male athletes, only chronic overuse injuries were more prevalent during the pre-competition period. For younger athletes (<35yrs), chronic overuse injuries were more prevalent in the pre-competition period compared with the competition period, whereas for the older athletes (>35yrs), acute injuries were more prevalent in the pre-competition period ($p<0.01$). Conclusion: The data from this sub-analysis indicate that there are certain groups more at risk for injury during the pre-competition period of the Rio 2016 Paralympic Games. Specifically, chronic overuse injuries and injuries to female and young athletes were more frequent in the pre-competition period. These data can be used to inform sports medicine practitioners in their preparation for major international Para competition, as well as inform injury prevention programs.

ABSTRACT NUMBER / ABSTRAKNOMMER: 18

A Descriptive Analysis Of Scorpion Envenomation As Reported To A Poison Centre In South Africa Over A 12 Year Period

Carine Marks (Stellenbosch University)

ABSTRACT NUMBER / ABSTRAKNOMMER: 19

Outcomes of Open Reduction Internal Fixation of Femoral Neck Fractures: A three year audit at Central Academic Hospital

Gerhard Pienaar (Orthopaedic Surgery), Koos Jordaan (Orthopaedic Surgery), Marilize Burger (Orthopaedic Surgery)

Purpose of study Femoral neck fractures, resulting from low or high-energy trauma, are common in patients of all ages. Open reduction and internal fixation (ORIF) is the treatment of choice for younger patients. In elderly patients, ORIF is only considered in stable fracture patterns. The primary purpose of our audit is to evaluate the cohort of femoral neck fractures treated with an ORIF at our hospital and compare our outcomes and complications with what is available in the literature. Methods A retrospective audit was done of all adult patients with femoral neck fractures treated with an ORIF at a single academic hospital from January 2015 to December 2017. Data captured was: demographics, mechanism of injury, time to admission and surgery, type of fixation constructs, complications and re-operation rate. Ethics Reference #: N18/03/029 Results A total of 108 patients (69 males and 39 females), with a mean age of 53 years (range 19-95) were included. Of these, 45 patients (42%) sustained a high velocity injury, with 63 (58%) sustaining low velocity injuries. Average time from injury to admission was 58 hours, with average time to surgery being 81 hours. Cannulated hip screws were used in 41 patients (38%), with Dynamic Hip Screws in 65 patients (60%) and 2 (2%) Cephalomedullary nails. A total of 56 patients (52%) achieved union, 17 patients (16%) complicated by failure and 35 patients (32%) were lost to follow up. Conclusions There are no published studies describing the burden of femoral neck fractures and the outcomes of treatment in South Africa. Multiple surgical fixation techniques were used to treat different age group patients and pathology and subsequently, treatment protocols and modalities varies substantially. We report a high rate of complications in our patients, but it remains comparable with international data

ABSTRACT NUMBER / ABSTRAKNOMMER: 20

The incidence of injury and illness at the Pyeongchang 2018 Paralympic Winter Games: an analysis of 6,804 athlete days

Wayne Derman (Institute of Sport and Exercise Medicine, Dept Surgery, Stellenbosch University)

Objectives: The present study described the incidence of injury and illness during the 12 day Games period of the Pyeongchang 2018 Paralympic Winter Games. **Methods:** A total of 567 athletes from 49 countries were monitored on the web-based injury and illness surveillance system over 6,804 athlete days during the Pyeongchang 2018 Paralympic Winter Games. Injury and illness data were collected from teams with their own medical support (WEB-IISS) and athletes who used the local polyclinic medical facilities. **Ethics:** N16/05/067 **Results:** A total of 153 injuries and 99 illnesses were reported during the 3 day pre-competition and 9 day competition period. The injury incidence rate (IR) was 22.5 injuries per 1000 athlete days. The sport with the highest number of injuries was Para Alpine Skiing ($n=46$, $p < 0.05$), the anatomical area most affected by injury was shoulder joint ($p < 0.05$), and the IR for acute traumatic injuries was significantly higher than other types of injury onset ($p < 0.05$). There were 99 illnesses reported during the Games period (IR of 13.8), with significantly more illnesses reported within the pre-competition period ($p < 0.05$), The respiratory system was the physiological system most affected by illness ($n=29$, $p < 0.05$). **Conclusion:** This study is the continuation of a longitudinal injury and illness surveillance study and constitutes the second Paralympic Winter Games dataset. Para alpine skiing was again highlighted as high risk for injury, and the respiratory system for illness. These data can be used to inform sports medicine practitioners in their preparation for major international Para competition, as well as inform injury and illness prevention programs.