ABSTRACT BOOK

INVITATION:
14th ANNUAL EARLY CAREER SCIENTIST CONVENTION

Theme:
Adaptability and Resilience: A new norm for researchers

Date: 26 – 27 October 2020

Venue: Virtual/SAMRC Conference Centre

HOSTED BY:
DIVISION OF RESEARCH CAPACITY DEVELOPMENT (RCD)

Developing the next generation of Scientists

saMRC advancinglife

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MESSAGE FROM SAMRC VICE PRESIDENT

Prof Jeffery Mphahlele

Vice President for Research, South African Research Council

"It is my absolute pleasure to welcome you to the 14th annual Early Career Scientist Convention (14th ECSC), taking place for the first time ever on a virtual platform. The conference theme titled "Adaptability and Resilience: A new normal for researchers" couldn't be more fitting and timely considering how the novel coronavirus pandemic has changed the ways in which we live, work, teach and learn. The pandemic has triggered and coerced our connection with the VUCA (Volatility, Uncertainty, Complexity and Ambiguity) world which in turn demands our mental and physical agility. It is for this reason that I am immensely grateful for the Division of Research Capacity Development (RCD) to continue providing an innovative platform for our scholars to connect, share experiences and showcase their research. While we do acknowledge that the virtual conference cannot entirely replicate the in-person conference experience, which normally involves social connections which is in fact important for mental health, we ask you to take this opportunity to connect with your fellow scholars on the virtual platform. We also understand that for some of you this may be a comfort-zone-stretching activity and trust you will accommodate and give each other a grace."

MESSAGE FROM DIVISION MANAGER

Dr Thabi Maitin

"If the theme of the Convention of 2020 talks about adapting and resilience, then this could not have been more keenly felt in the Division in putting together this year's event!

It is for this reason, before I welcome you all, that I must pass my extraordinary thanks and gratitude to the team from various business units of the SAMRC who worked superbly to pull this event off. Thank you to colleagues from Corporate & Marketing Communications, Conference Centre, various Research Units which gave RCD their scientists' time to constitute and work as the Convention's Scientific & Organizing Committee, and last but certainly not least, to the team at RCD led by Dr Ndlandla. You have truly amazed me at how adaptable and resilient you all have remained working under unspeakable pressure. Thank you.

To our priceless human capital investment: the SAMRC -beneficiaries from all six Post Graduate funding programmes. Once again you are RCD's guests today and I warmly welcome you and give you all a big warm virtual embrace. Thank you for participating, but more pointedly, thank you for the commitment to your academic development that you show by submitting your abstracts every single year without fail. Without these abstracts this Convention would not happen, and more seriously, RCD would have no evidence of your sustained performance which guarantees the Division continuous funding. I was pleasantly appraised by the Scientific & Organizing Committee that the abstracts this year were of a very high caliber, with only a handful that needed further attention. This warms my heart and gives our Division renewed strength for the next lap into the following year.

I wish you a successful Convention, and a productive time in what is left of 2020. Further, I wish you and your families health and safety given the challenges of COVID-19 that we and the rest of the world are face with.

CONTRIBUTORS

Keynote Speakers

Dr Tracy Naledi – Deputy Dean of the University of Cape Town (UCT)'s Faculty of Health Sciences
Dr Vukosi Marivate – ABSA-UP Chair of Data Science at the University of Pretoria
Professor Richard Hift – Head of Department: Clinical and professional practice (UKZN)

Scientific Committee

Dr Nadine Harker Burnhams – Alcohol Tobacco and Other Drug Research Unit (SAMRC-Chair)
Dr Jillian Hill – Non-Communicable Disease Research Unit (SAMRC-Deputy Chair)
Dr Ebrahim Samodien – Biomedical Research and Innovation Platform (SAMRC)
Dr Lawrence Mabasa – Biomedical Research and Innovation Platform (SAMRC)
Dr Awelani Mutshembele – TB Platform (SAMRC)
Ms Colleen Van Wyk – RCD Scholarships Administrator (SAMRC)

Facilitators

Dr Jillian Hill – Non-Communicable Diseases Research Unit (SAMRC)
Dr Phiwayinkosi Dludla – Biomedical Research and Innovation Platform (SAMRC)
Dr Lawrence Mabasa – Biomedical Research and Innovation Platform (SAMRC)
Dr Kim Jonas – Health Systems Research Unit (SAMRC)
Dr Ebrahim Samodien – Biomedical Research and Innovation Platform (SAMRC)
Dr Ntevheleni Thovhogi – Biomedical Research and Innovation Platform (SAMRC)
Dr Anelisa Jaca – Cochrane South Africa (SAMRC)
Dr Jenny Coetzee – Gender and Health Research Unit (SAMRC)
Dr Awelani Mutshembele – TB Platform (SAMRC)
Dr Andile Ngwane – Centre for Tuberculosis Research (SUN)
Dr Vundli Ramakolo – Health Systems Research Unit (SAMRC)
Dr Taime Sylvester – Centre for Tuberculosis Research (SUN)
Dr Duduzile Ndwandwe – Cochrane South Africa (SAMRC)
Dr Charissa Naidoo – Centre for Tuberculosis Research (SUN)
Prof Janan Dietrich – Health Systems Research Unit (SAMRC)
Dr Darshini Govindasamy – London school of Hygiene and Tropical Medicine, UK
Dr Kim Nguyen – Non-Communicable Diseases Research Unit (SAMRC)
Dr Kgomotso Poopedi – University of Limpopo
Dr Monique Maqungo – Burden of Diseases Research Unit (SAMRC)
Dr Brendon Pearce – University of the Western Cape
Dr Frederic Nduhirabandi – Research Capacity Development (SAMRC)

With grateful thanks…

Research Capacity Development (RCD) would like to acknowledge the following colleagues who have been contributing to the work of RCD diligently and selflessly over the years. They are indeed the extended RCD team:

NAME & SURNAME	SAMRC PORTFOLIO	CONTRIBUTION AND ROLE AT RCD
Prof Andre Kengne	Director – Non-Communicable Diseases Research Unit (NCDRU)	Chair: RCDs Grants and scholarships Selection Committee (MD. PhD programme)
Ms Sumaya Berhadien	Senior Legal Advisor – SAMRC	Advisor: RCD legal matters, processes, and resources
Mr Brandon Smith	Senior Legal Advisor – SAMRC	Advisor: RCD legal matters, processes, and resources
Ms Noluthando Sikhutshwa	Business Partner: Project Management and Accounting Office SAMRC	Oversight: RCD Financial matters, processes, and budgets

KEYNOTE SPEAKERS

Dr Tracy Naledi

Dr Tracey Naledi is a Deputy Dean of the University of Cape Town (UCT)'s Faculty of Health Sciences. She has over the last two decades held technical and management positions in government and NGO sectors in South Africa and Botswana. Most recently, she was the Chief Director: Health Programmes in the Western Cape Department of Health (WCDOH). Her work has focused on policy development, health system strengthening, addressing health inequity and strengthening systems for health. Some of her career highlights include being part of the team that started the first prevention of mother-to-child transmission (PMTCT) programme in the public sector in South Africa and providing compelling evidence of the feasibility of delivering this programme on the Primary Health Care platform in the public sector. Dr Naledi co-chaired the first Burden of Disease Reduction Project in the Western Cape, a project on social determinants that became seminal to the development of an intersectoral agenda for the WCDOH and the WC Government. She established the first Health Impact Assessment Directorate in the WCDOH where she also developed a structured program for Public Health Registrars. She also set up the first Provincial Health Research Committee with representation from all academic and research institutions in the province. She led the establishment of intersectoral wellness programmes in the province which includes the Western Cape on Wellness (WoW) and the First Thousand Days programmes. She was the Chief of Party for a large USAID funded primary health care project supporting five provinces in South Africa. She is former board member of the Child Safe and the Public Health Association of South Africa (PHASA). Currently, she is a member of the Advisory Board of the Perinatal Mental Health Project; founding Chairperson of Tekano Atlantic Fellows for Health Equity in South Africa and a member of the Council for Public Health Medicine of the Colleges of Medicine of South Africa. She is a senior lecturer in the School of Public Health at the University of Cape Town and she is a fellow in the Desmond and Leah Tutu Legacy Foundation and the Discovery Foundation.

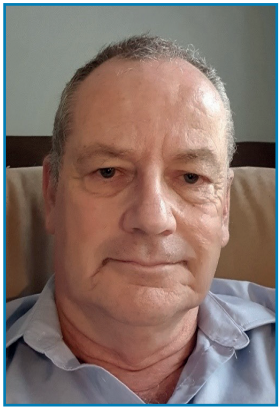
Dr Vukosi Marivate

Dr Vukosi Marivate is the ABSA-UP Chair of Data Science at the University of Pretoria. Vukosi works on developing Machine Learning/Artificial Intelligence methods to extract insights from data. A large part of his work over the last few years has been in the intersection of Machine Learning and Natural Language Processing (due to the abundance of text data and need to extract insights). As part of his vision for the ABSA Data Science chair, Vukosi is interested in Data Science for Social Impact, using local challenges as a springboard for research. In this area, he has worked on projects in science, energy, public safety and utilities. Vukosi is an organiser of the Deep Learning Indaba, the largest Machine Learning/Artificial Intelligence workshop on the African continent, aiming to strengthen African Machine Learning.

He is passionate about developing young talent, supervising MSc and PhD students and mentoring budding Data Scientists. In the past, Vukosi has worked for, amongst others, the Council for Scientific and Industrial Research (CSIR) as a Principal Researcher; Knewton Inc where he was a Data Science Intern and Google as a Machine Learning Intern.

Dr Marivate was listed on this year's Mail & Guardian 200 Young South Africans under "COVID-19 Heroes – Editor's Choice" for his outstanding work on leading the team that first piloted a dashboard with facts about COVID-19 & its impact in SA. When asked about the potential impact of his work Dr Marivate said "What the dashboard and data repository does is provide one place where all the necessary information is available to the public and scientists, and it's continuously updated, which is especially important for those in the health sector who need to make decisions by the hour,"

He adds that without this information, we wouldn't know where we should be putting resources or offering support.



Professor Richard Hift

Professor Richard Hift was born in Durban. He studied Medicine and then specialised in Internal Medicine at the University of Cape Town (UCT), after which he joined the South African Medical Research Council (SAMRC)'s Liver Research Centre where he trained as a clinical hepatologist while completing his PhD with a dissertation titled "Variegate porphyria: molecular aspects and their clinical and biochemical consequences." In 2007 he was appointed Head of the Department of Medicine at the Nelson R Mandela School of Medicine and later in 2012, Dean and Head of the School of Clinical Medicine – a position he held for a five-year term. During his tenure, his priorities included the standardisation and improvement of the undergraduate medical curriculum and undergraduate teaching, development of a decentralised province-wide clinical training platform, formalisation of postgraduate clinical training and the introduction of the MMed degree, inculcation of a research culture among clinicians, accelerated research outputs and transformation amongst medical academics. For two years he chaired the South African Committee of Medical Deans, where he was instrumental in effecting a number of major initiatives, notably, the return of the Nelson Mandela-Fidel Castro medical collaboration students from Cuba and standardisation of the MMed research component nationally. Currently he is directing a formal programme of research development, promotion and support in the College of Health Sciences, including a Doctoral Academy. He recently chaired a working group tasked to develop a new funding model for training of clinician-scientists, an SAMRC funded programme that is aimed at addressing the need for accelerated growth in the number of Clinician Scientists by encouraging the development of integrated clinical/research training programs for clinicians across all South African universities. Throughout his career he has retained a broad interest in clinical medicine, teaching and learning and research. His research interests have included hepatitis, porphyria, the cognitive aspects of learning and expertise in clinical medicine, and the sociological aspects of the return of the South African students trained in Cuba, and academic aspects of postgraduate supervision and the academic and cognitive changes associated with PhD candidacy.

(Photo source: http:www.people.com)

"Education is the most powerful weapon which you can use to change the world."

– Nelson Mandela

RESEARCH CAPACITY DEVELOPMENT (RCD) FUNDING CATEGORIES 2020/21

ADMINISTRATORS	SCHOLARSHIP PROGRAM/ GRANT TYPE	TARGET GROUP	PURPOSE/ IMPORTANCE	VALUE OF SCHOLARSHIP/GRANT
Mr. Thobile Mabuya	SAMRC Clinician Researcher (MD. PhD) Development programme	Post-MBChB/D.D. S studying towards their PhD degree	Response to dearth of MD. PhD cadre within the health research team in SA and Globally	R500K p.a salary contribution x 4 yrs.
Ms. Colleen van Wyk	SAMRC Internship scholarship programme	MSc's and PhDs research training for generic black's scientist	Directly supports transformation. In-house research skills transfer programme.	PhD: R200K p.a x 3yrs. MSc R160K p.a x 2yrs (package incl. tuition)
Ms. Colleen van Wyk	Bongani Mayosi National Health Scholarship Program (BM-NHSP)	Doctoral (and Masters where compelling) Research training Internships for SA young Scientist	Gold standard Public-Private Partnership for PhD development in SA. (Stakeholders: NHRC/NDoH/ PHEF and SAMRC partnership)	Various: equivalent to after-tax take-home package for profession according to SA Government Full-time Cost of Employment figures.
Ms. Colleen van Wyk	Biostatistics Capacity Development Programme	Master's and Doctoral scholarships in the field of Biostatistics at a South African University	Subsistence/cost of living and studying	PhD: R200 000 p.a x 3 years Masters: R160 000 p.a x 2 years (Package incl. tuition)
Ms. Philistia Joshua	SAMRC Research Capacity Development Initiative (RCDI) programme at Selected Universities – Postgraduate programme	Target institutions rather than Individual Researcher Capacity Development: Project leaders in selected under-resourced institutions	Directly support transformation: to develop research capacity and to work towards closing the gap in the rate of generation of knowledge between established research-intensive universities and under-resourced universities	R1ML p.a. per selected university for 5 years
Mr Thobile Mabuya	SAMRC Intramural Postdoctoral Award	Post-Doctoral Award	R250K salary contribution and R100K for project running expenses	R250 000.00 + R100 000.00 = R350 000.00 p. a x 5 years

ADMINISTRATORS	SCHOLARSHIP PROGRAM/ GRANT TYPE	TARGET GROUP	PURPOSE/ IMPORTANCE	VALUE OF SCHOLARSHIP/GRANT
Ms Philistia Joshua	Mid-Career Scientist Programme (MCSP)	Mid-career scientist to facilitate their retention in the public sector in areas of strategic interest to the NDoH and the SAMRC	To establish mid-career scientists to fast track and transition to independent researchers who will become equipped to write their own grants and secure their own salary and research support. Showcasing SAMRC/ Selected Universities partnership	R1 250 000.00 first year and R1 500 000.00 second year of funding
Mr Thobile Mabuya	International Masters in Vaccinology (IMVACC) programme	South African citizens from designated race/ gender individuals with MBChB/MBBCHB background must hold M-Med degree or any speciality discipline (e.g. FCP) recognized by CMSA	This is an e-learning facilitated program with the University of Lausanne funded jointly with the SAMRC	R300 000 per candidate up to the completion of the degree (MSc)
Dr Lindokuhle Ndlandla (Interim)	SAMRC Research Development Grant	Strategic PhDs/ Research Development Grant/ Staff Development Grant	As detailed in motivation and request and as agreed. Once-off last year of PhD	Up to R250 000.00 p. a x 1 year

LIST OF SCHOLARS-EARLY CAREER SCIENTIST CONVENTION 2020

SAMRC CLINICIAN RESEARCHER (M.D PHD) DEVELOPMENT PROGRAMME				
No.	Initials	Surname	University/Research unit	Abstract title
1.	I.	Beesham	University of Witwatersrand	Unpacking the use of oral PrEP as part of the HIV prevention package in clinical trial [abstract 1]
2.	T.	Kootbodien	University of Cape Town	Utilisation of health care services prior to suicidal behaviour in Cape Town. [abstract 2]
3.	E.	Kroon	University of Stellenbosch	Neutrophils in tuberculosis-exposed, HIV-1-infected but persistently TB, tuberculin-and IGRA-negative persons [abstract 3]
4.	L.	Rametse	University of Cape Town	Medical Male Circumcision disciplines the penis: barrier integrity & understanding HIV susceptibility [abstract 4]
5.	T.	Hlongwane	University of Pretoria	The effects of Introducing Basic antenatal care Plus and Umbiflow on antenatal care and perinatal mortality. [abstract 5]
6.	Y.	Moosa	University of KwaZulu-Natal	Microbial transmission in rural KwaZulu-Natal: Integration of classical epidemiology with geospatial data and pathogen genomics. [abstract 6]
7.	F.	Mabena	University of Witwatersrand	Epidemiology of community and hospital-acquired invasive infections in young infants. [abstract 7]
8.	S.	Simelane	University of Cape Town	Strengthening child and adolescent mental health systems in South Africa: a multi-stakeholder implementation science initiative. [abstract 8]
9.	P.	Rose	University of Stellenbosch	Determinants of Liver Disease in HIV-Infected Children in the Era of Early Antiretroviral Therapy [abstract 9]
10.	F.	Mustafa	University of Pretoria	Biomarkers that may predict severe COVID-19 in South Africa. [abstract 10]
11.	C.	Snyders	University of Pretoria	Return to sport guidelines in athletes with selected upper respiratory tract infections, based on clinical criteria and laboratory investigations. [abstract 11]
12.	T	Molefi	University of Pretoria	Profiling Molecular Pathways in Endometrial Cancers (EC) occurring in Black South African Women: Therapeutic Targets. [abstract 12]
13.	S.	Mendelsohn	University of Cape Town	Prospective Validation of a Host-Blood Tuberculosis Transcriptomic Signature in Adults with HIV. [abstract 13]

SAMRC INTERNSHIP SCHOLARSHIP PROGRAMME (ISP)				
No.	Initials	Surname	University/Research unit	Abstract title
14.	W.	Lucas	University of Cape Town	Trends of treatment admissions for alcohol and other drugs among youth and younger adults in South Africa: A descriptive analysis of the South African Community Epidemiology Network on Drug Use project between 2009-2019. [abstract 14]
15.	E.	Oduwole	University of Stellenbosch	Vaccine hesitancy in the Cape Metro: the perception of vaccinators. [abstract 15]
16.	M.	Shaku	University of Witwatersrand	A modified BCG vaccine for enhancing trained innate immunity against Mycobacterium tuberculosis infection. [abstract 16]
17.	C.	Masilela	University of the Western Cape	Cross-sectional study of prevalence and determinants of uncontrolled Hypertension among South African adult residents of Mkhondo Municipality. [abstract 42]
18.	T.	Lopes	University of Stellenbosch	Different definitions of a PBD may affect its association with CVD risk. [abstract 17]
19.	M.	Alaouna	University of Witwatersrand	The effects of indigenous South African plant extracts (Cotyledon orbiculate and Tulbaghia. Violacea) on triple negative breast cancer cells. [abstract 39]
20.	R.	Mbau	University of Cape Town	Whole-genome transposon mutagenesis to elucidate the genetic requirements for vitamin B12 biosynthesis and assimilation in mycobacteria. [abstract 18]
21.	N.	Sangweni	University of Stellenbosch	Prevention of Doxorubicin-induced cardiotoxicity: A mechanistic study. [abstract 43]
22.	L.	Montewa	University of Cape Town	Fostering Ethical dialogues in research: Evaluating the Drama of DNA method for feedback of findings in genomics research in South Africa. [abstract 19]
23.	S.	Mabhida	University of the Western Cape	In Silico evaluation of hypertension-related genes in an African based population. [abstract 40]
24.	S.	Madlala	University of the Western Cape	Adult food choices in association with the local food retail environment and food access in resource poor communities: a systematic scoping review. [abstract 20]
25.	I.	Boshielo	University of Witwatersrand	Changes in cytokine and chemokine responses in plasma during TB treatment. [abstract 38]

26.	R.	Roomaney	University of the Western Cape	Burden of Multimorbidity in South Africa: Implications for health policy and service delivery. [abstract 21]
27.	E.	Ekoka Etouman	University of Witwatersrand	20-hydroxyecdysone (20E) signaling regulates fecundity and immunity in Anopheles arabiensis malaria vectors. [abstract 35]
28.	D.	Ralefeta	University of Cape Town	Investigating the impact of mycobacterial cell-cell heterogeneity on susceptibility to anti-tuberculosis (TB) chemotherapy. [abstract 22]
29.	N.	Mthembu	University of Cape Town	Transcriptomic approach on the early development of severe asthma. [abstract 41]
30.	S.	Poswayo	University of Cape Town	Investigating the role of protein Kinase C zeta during Mycobacterium tuberculosis infection in mice and human macrophages. [abstract 44]
31.	S.	Geyer	University of Cape Town	Investigating host immune responses in astrocytes during central nervous system-tuberculosis infection. [abstract 23]
32.	A.	Walters	University of Cape Town	Investigating Neuronal Immune Responses To Early Central Nervous System Mycobacterium Tuberculosis infection in mice. [abstract 24]
33.	K.	Ziqubu	North West University	Isoorientin ameliorates lipid accumulation by regulating fat browning in palmitate-exposed 3T3-L1 adipocytes. [abstract 25]
34.	M.	Kuali	University of KwaZulu Natal	Effect of endo/exogenous female sex hormones on HIV-1C latent reservoir reactivation. [abstract 26]
35.	S.	Khoza	University of the Western Cape	Identification and expression of cathepsin S inhibitors from South African medicinal plants. [abstract 27]
36.	G.	Ndlangalavu	University of Stellenbosch	Novel sputum and non-sputum based tuberculosis diagnostics in minimally-symptomatic HIV-positive patients initiating ART. [abstract 34]
37.	M.	Manyelo	University of Stellenbosch	Evaluation of host biomarker signatures for early diagnosis of tuberculosis meningitis. [abstract 28]
38.	L.	Moyakhe	University of Cape Town	Genetic and epigenetic contributions to developmental psychopathology in childhood and adolescence. [abstract 29]

39.	K.	Fisher	University of KwaZulu Natal	Understanding the role of NK cells in TB disease progression in the lung. [abstract 30]
40.	M.	Mokoatle	University of Pretoria	Representation Learning for DNA Sequences: An analysis of Men with Advanced prostate cancer in Africa. [abstract 31]
41.	T.	Mabuda	University of Stellenbosch	Effect of green rooibos tea extract (Afriplex GRTTM) on inflammatory and oxidative stress genes in models of NAFLD. [abstract 32]
42.	S.	Mthembu	University of ZuluLand	Antimycin A induced both insulin resistance and mitochondrial dysfunction in skeletal muscle. [abstract 33]
43.	C.	Africa	University of Cape Town	The correlates of sedentary behavior in individuals at risk of developing type 2 diabetes mellitus in Cape Town, South Africa. [abstract 36]
44.	T.	Mulabisano	University of the Western Cape	Dietary cost in relation to diversity and nutrient adequacy in children. [abstract 37]

BONGANI MAYOSI NATIONAL HEALTH SCHOLARSHIP PROGRAMME (BM-NHSP)

No.	Initials	Surname	University/Research unit	Abstract title
45.	W.	Barnett	University of Cape Town	Intimate Partner Violence and growth outcomes through infancy: a longitudinal investigation of multiple mediators in a South African birth cohort. [abstract 45]
46.	G.	Barnwell	Nelson Mandela Metro University	Paper Presentation: Mine-affected communities psychological experiences of ecological degradation and resistance in Rustenburg, South African. [abstract 46]
47.	E.	Bröcker	University of Stellenbosch	A Systematic review of internet-based interventions for PTSD and ASD with and without support. [abstract 47]
48.	M.	Burger	University of Stellenbosch	Perinatal Mental Health and Infant Neurodevelopment – Evidence from LMICs. A Systematic Review. [abstract 48]
49.	T.	Glass	University of Cape Town	Viral load turnaround time and monitoring among pregnant and breastfeeding women, a simulation study. [abstract 49]
50.	F.	Scheffler	University of Stellenbosch	Cannabis use and longitudinal clinical outcome in schizophrenia patients. [abstract 50]
51.	A	Damons	University of Stellenbosch	Introducing an arteriovenous fistula pre-cannulation assessment care-bundle to reduce complications in patients with an arteriovenous fistula on haemodialysis. [abstract 61]

52.	L.	Frigati	University of Cape Town	Tuberculosis infection and Disease in HIV-infected Adolescents on ART. [abstract 51]
53.	M.	Osman	University of Stellenbosch	Excess mortality in TB patients diagnosed at hospital vs at primary health care in South Africa. [abstract 52]
54.	M.	Nglazi	University of Cape Town	The intergenerational transmission of socioeconomic inequalities in overweight and obesity from mothers to their offspring in South Africa. [abstract 53]
55.	B.	Carpenter	University of KwaZulu Natal	Understanding why individualized research requires an appropriate design and analysis: simulation study. [abstract 54]
56.	D.	Senthebane	University of Cape Town	Cancer Stem Cells Enhance Chemoresistance and Metastatic Behaviour in human Oesophageal Cancer. [abstract 55]
57.	E.	Mabotha	University of Cape Town	Can biomarkers in scalp hair identify patients at risk of a heart attack. [abstract 56]
58.	J.	du Plessis/ Van Schalkwyk	North West University	Homocysteine and its relationship with cardiovascular health in adolescents from African descents. [abstract 57]
59.	T.	Chetty	University of KwaZulu Natal	An Incremental cost-effectiveness analysis of a quality improvement model for integrated HIV-TB services within rural KZN. [abstract 58]
60.	M.	Hlongwa	University of KwaZulu Natal	Men's perspectives on HIV self-testing in sub-Saharan Africa: a systematic review and meta-synthesis. [abstract 59]
61.	N.	Sematlane	University of the Western Cape	Living with, adapting to and self-managing HIV as a chronic illness: A scoping review protocol. [abstract 60]
62.	A.	Van Zyl	University of Stellenbosch	Late effects of childhood cancer and -treatment in a South African cohort. [abstract 62]
63.	F.	Takalani	University of Witwatersrand	Fabrication of chitosan/alginate nanoparticles stabilized by TPGS1000 for enhanced TDF delivery across the FGT. [abstract 63]
64.	L.	Majara	University of Cape Town	Genome-wide analysis of common and rare variants in the South African Xhosa (SAX) affected by Schizophrenia: a case-control study. [abstract 66]

65.	A.	Ndadza	University of Cape Town	Profiling of pharmacogenetic variants and their influence on warfarin dose variability among Southern Africans. [abstract 65]
66.	C.	Goosen	University of Stellenbosch	Iron in HIV-infected schoolchildren: Nutritional status, fractional absorption, and the gut microbiome. [abstract 64]
67.	ML.	Nhleko	University of Witwatersrand	The cancer mortality among economically active South Africans from 1997-2016): Adopting temporal, spatial and health economic modelling approaches. [abstract 67]
68.	IA.	Basson	University of Cape Town	Novel proteomics biomarkers for acral lentiginous melanoma. [abstract 68]
69.	M.	Kitchin	University of Stellenbosch	The maternal and infant gut microbiome in Foetal Alcohol Spectrum Disorder. [abstract 69]

BIOSTATISTICS CAPACITY DEVELOPMENT PROGRAMME				
No.	Initials	Surname	University/Research unit	Abstract title
70.	M.	De Klerk	University of Pretoria	Generalization of contingency tables for gene expression readings. Joint Modelling of Longitudinal Colony-Forming-Unit Count and Time-To-Event Data from Tuberculosis Trials. [abstract 70]
71.	S.	Nigrini	University of Pretoria	Joint Modelling of Longitudinal Colony-Forming-Unit Count and Time-To-Event Data from Tuberculosis Trials. [abstract 71]

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE (RCDI): POST-GRADUATE PROGRAMME				
No.	Initials	Surname	University/Research unit	Abstract title
72.	K.	Malemela	University of Limpopo	Momordica balsamina methanol extract induces apoptosis and inhibits selected drug metabolizing enzymes. [abstract 72]
73.	K.	Rakau	Sefako Makgatho University	Investigation of mutations within the Fucosyltransferase gene in children suffering from gastroenteritis (preliminary results). [abstract 73]

PROGRAMME

MONDAY, 26 OCTOBER 2020		
Registration/log-in		
10h00 – 10h10	Welcome and Housekeeping	Programme Director: **Dr Nadine Harker**
10h10 – 10h20	Welcome	RCD Division Manager: **Dr Thabi Maitin**
10h20 – 10h30	Welcome address	SAMRC Vice President: **Prof Jefferey Mphahlele**
10h30 – 11h15	**Keynote speaker:** Mental Health "Resilience and Adaptability in research." Dr Tracy Naledi Venue: Auditorium	
	TEA BREAK	
11h30 – 12h30	**Session 1: Non-communicable diseases** **Facilitators: Drs Jillian Hill & Phiwayinkosi Dludla** **Venue: Auditorium** **Mandlakayise Nhleko:** Cancer mortality in South Africa (1997 – 2016): Adopting temporal, spatial and health economic modelling approaches. **[abstract 67]** **Charity Masilela:** Cross-sectional study of prevalence and determinants of uncontrolled Hypertension among South African adult residents of Mkhondo municipality. **[abstract 42]** **Tatum Lopes:** The association of plant-based diet with CVD risk. **[abstract 17]** **Mohammed Alaouna:** The effects of indigenous South African plant extracts *(Cotyledon orbiculate and Tulbaghia. Violecea)* on triple-negative breast cancer cells. **[abstract 39]** **Nonhlakanipho Sangweni:** Prevention of Doxorubicin-induced cardiotoxicity: a mechanistic study. **[abstract 43]** **Anneleen Damons:** Introducing an arteriovenous fistula pre-cannulation assessment care-bundle to reduce complications in patients with an arteriovenous fistula on haemodialysis. **[abstract 61]**	**Session 2: Mental Health/Public Health** **Facilitators: Drs Kim Jonas & Darshini Govindasamy** **Venue: Board room** **Whitney Barnett:** Intimate partner violence and growth outcomes through infancy: a longitudinal investigation of multiple mediators in a South African birth cohort. **[abstract 45]** **Natasha Kitchin:** The maternal and infant gut microbiome in Foetal Alcohol Spectrum Disorder. **[abstract 69]** **Frederika Scheffler:** Cannabis use and longitudinal clinical outcome in schizophrenia patients. **[abstract 50]** **Tahira Kootbodien:** Utilisation of health care services prior to suicidal behaviour in Cape Town. **[abstract 2]** **Erine Bröcker:** A systematic review of internet-based interventions for PTSD and ASD with and without support. **[abstract 47]** **Q&A**

12h30 – 13h30	LUNCH	
13h30 – 14h30	Session 3: Non-communicable diseases Facilitators: Drs Lawrence Mabasa & Ntevheleni Thovhogi Venue: Auditorium **Sihle Mabhida:** In Silico evaluation of hypertension-related genes in an African based population. **[abstract 40]** **Nontobeko Mthembu:** Transcriptomic approach on the early development of severe asthma. **[abstract 41]** **Mpho Mokoatle:** Representation Learning for DNA Sequences: an analysis of men with advanced prostate cancer in Africa. **[abstract 31]** **Arinao Ndadza:** Profiling of pharmacogenetic variants and their influence on warfarin dose variability among Southern Africans. **[abstract 65]** **Thulo Molefi:** Profiling molecular pathways in endometrial cancers occurring in black South African women: therapeutic targets. **[abstract 12]** Q&A	Session 4: Mental Health/Public Health Facilitators: Drs Anelisa Jaca & Jenny Coetzee Venue: Board room **Garret Barnwell:** Paper Presentation: Mine-affected communities' psychological experiences of ecological degradation and resistance in Rustenburg, South Africa. **[abstract 46]** **Marlette Burger:** Perinatal mental health and infant neurodevelopment – evidence from LMICs. a systematic review. **[abstract 48]** **Lihle Moyakhe:** Genetic and epigenetic contributions to developmental psychopathology in childhood and adolescence. **[abstract 29]** **Lerato Majara:** Genome-wide analysis of common and rare variants in the South African Xhosa (SAX) affected by Schizophrenia: a case-control study. **[abstract 66]** **Warren Lucas:** Trends of treatment admissions for alcohol and other drugs among youth and younger adults in South Africa: A descriptive analysis of the South African Community Epidemiology Network on Drug Use project between 2009-2019. **[abstract 14]** Q&A

14h30 – 15h30	Session 5: Communicable diseases Facilitators: Drs Awelani Mutshembele & Andile Ngwane Venue: Auditorium **Elouise Kroon:** Neutrophils in tuberculosis-exposed, HIV-1-infected but persistently TB, tuberculin- and IGRA- negative persons. **[abstract 3]** **Sharday Nigrini:** Joint modelling of longitudinal colony forming unit count and time-to-event data emanating from tuberculosis trials. **[abstract 71]** **Moagi Shaku:** A modified BCG vaccine for enhancing trained innate immunity against Mycobacterium tuberculosis infection. **[abstract 16]** **Rendani Mbau:** Whole genome transposon mutagenesis to elucidate the genetic requirements for vitamin B12 biosynthesis and assimilation in mycobacteria. **[abstract 18]** **Simon Mendelsohn:** Translation and evaluation of parsimonious host-blood tuberculosis transcriptomic signatures for point-of-care testing in HIV-infected and HIV-uninfected individuals. **[abstract 13]** Q&A	Session 6: Mental Health/Public Health Facilitators: Drs Vundli Ramakolo & Taime Sylvester Venue: Board room **Rifqah Roomaney:** Burden of Multimorbidity in South Africa: Implications for health policy and service delivery. **[abstract 21]** **Mbuzeleni Hlongwa:** Men's perspectives on HIV self-testing in sub-Saharan Africa: a systematic review and meta-synthesis. **[abstract 59]** **Bradley Carpenter:** Understanding why individualised research requires an appropriate design and analysis: simulation study. **[abstract 54]** **Lebogang Montewa:** Fostering Ethical dialogues in research: Evaluating the Drama of DNA method for feedback of findings in genomics research in South Africa. **[abstract 19]** **Michelle de Klerk:** Generalisation of contingency tables for gene expression readings. **[abstract 70]** Q&A

15h30 – 16h30	Session 7: Communicable diseases Facilitators: Drs Marissa Klopper & Charissa Naidoo Venue: Auditorium **Fatima Mustafa:** Biomarkers that may predict severe COVID-19 in South Africans. **[abstract 10]** **Penelope Rose:** Determinants of Liver Disease in HIV-Infected Children in the Era of Early Antiretroviral Therapy. **[abstract 9]** **Carolette Snyders:** Return to sport guidelines in athletes with selected upper respiratory tract infections, based on clinical criteria and laboratory investigations. **[abstract 11]** **Yumna Moosa:** Microbial transmission in rural KwaZulu-Natal: Integration of classical epidemiology with geospatial data and pathogen genomics. **[abstract 6]** **Fikile Mabena:** Epidemiology of community and hospital-acquired invasive infections in young infants. **[abstract 7]** Q&A	Session 8: Mental Health/Public Health Facilitators: Drs Janan Deitrich & Darshini Govindasamy Venue: Board room **Taruna Chetty:** An Incremental cost-effectiveness analysis of a quality improvement model for integrated HIV-TB services within rural KZN. **[abstract 58]** **Elizabeth Oduwole:** Vaccine hesitancy in the Cape Metro: the perception of vaccinators. **[abstract 15]** **Simphiwe Simelane:** Strengthening child and adolescent mental health systems in South Africa: a multi-stakeholder implementation science initiative. **[abstract 8]** **Tracy Glass:** Viral load turnaround time and monitoring among pregnant and breastfeeding women, a simulation study. **[abstract 49]** **Tsakane Hlongwane:** The effects of introducing Basic antenatal care Plus and Umbiflow on antenatal care and perinatal mortality. **[abstract 5]** Q&A
	CLOSING	

TUESDAY, 27 OCTOBER 2020		
08h30 – 08h55	Registration/log-in	
08h55 – 09h00	Welcome and Housekeeping – Dr Nadine Harker Venue: Auditorium	
PRE-RECORDED PRESENTATIONS (PARALLEL SESSIONS)		
09h00 – 10h00	Session 9: Non-Communicable Diseases Facilitators: Drs Jillian Hill and Kim Nguyen Venue: Auditorium **Ilana Basson:** Novel proteomics biomarkers for acral lentiginous melanoma. **[abstract 68]** **Kholofelo Malemela:** Momordica balsamina methanol extract induces apoptosis and inhibits selected drug metabolising enzymes. **[abstract 72]** **Elodie Ekoka Etouman:** 20-hydroxyecdysone (20E) signaling regulates fecundity and immunity in Anopheles arabiensis malaria vectors. **[abstract 35]** **Sanele Khoza:** Identification and expression of cathepsin S inhibitors from South African medicinal plants. **[abstract 27]** **Samkelisiwe Madlala:** Adult food choices in association with the local food retail environment and food access in resource poor communities: a systematic scoping review. **[abstract 20]** Q&A	Session 10: communicable diseases Facilitators: Drs Ebrahim Samodien & Kgomotso Poopedi Venue: Board room **Ivana Beesham:** Unpacking the use of oral PrEP as part of the HIV prevention package in a clinical trial **[abstract 1]** **Lerato Cosnet Rametse:** Medical Male Circumcision disciplines the penis: barrier integrity & understanding HIV susceptibility **[abstract 4]** **Charlene Goosen:** Iron in HIV-infected schoolchildren: Nutritional status, fractional absorption, and the gut microbiome. **[abstract 64]** **Neo Sematlane:** Living with, adapting to and self-managing HIV as a chronic illness: A scoping review protocol. **[abstract 60]** **Mamokoena Kuali:** Effect of endo/exogenous female sex hormones on HIV-1C latent reservoir reactivation. **[abstract 26]** **Uvistra Naidoo:** Adaptation and validation of a rapid, point-of-care diagnostic test based on novel, recently developed proteomic signatures as a marker for risk progression to TB disease in children Q&A

10h00 – 10h15	TEA BREAK	
10h15 – 11h00	Plenary Speaker: Maximising the Value of Your Project Prof Richard Hift Venue: Auditorium	
11h00 – 12h00	Session 11: Non-communicable Disease Facilitators: Drs Kim Jonas & Monique Maqungo Venue: Auditorium **Khanyisani Ziqubu:** Isoorientin ameliorates lipid accumulation by regulating fat browning in palmitate-exposed 3T3-L1 adipocytes [abstract 20). **[abstract 25]** **Thendo Mabuda:** Effect of green rooibos tea extract (Afriplex GRTTM) on inflammatory and oxidative stress genes in models of NAFLD. **[abstract 32]** **Chad Africa:** The correlates of sedentary behaviour in individuals at risk of developing type 2 diabetes mellitus in Cape Town, South Africa. **[abstract 36]** **Tshavhuyo Mulabisano:** Dietary cost in relation to dietary diversity and nutrient adequacy in children. **[abstract 37]** **Sinenhlanhla Mthembu:** Antimycin A induces both insulin resistance and mitochondrial dysfunction in skeletal muscle. **[abstract 33]** Q&A	Session 12: Communicable Diseases Facilitators: Dr Marissa Klopper & Dr Brendon Pearce Venue: Board room **Lisa Frigati:** Tuberculosis Infection and Disease In HIV-infected Adolescents on ART. **[abstract 51]** **Muhammad Osman:** Excess mortality in TB patients diagnosed at hospital vs at primary health care in South Africa. **[abstract 52]** **Funanani Takalani:** Fabrication of chitosan/ alginate nanoparticles stabilized by TPGS1000 for enhanced TDF delivery across the FGT. **[abstract 63]** **Masilo Manyelo:** Evaluation of host biomarker signatures for early diagnosis of tuberculous meningitis. **[abstract 28]** **Itumeleng Boshielo:** Changes in cytokine and chemokine responses in plasma during TB treatment. **[abstract 38]** **Kebareng Rakau:** Investigation of mutations within the Fucosyltransferase gene in children suffering from gastroenteritis (preliminary results). **[abstract 73]** Q&A

12h00 – 13h00	LUNCH	
13h00 – 14h00	Session 13: Non-communicable Disease Facilitators: Dr Ebrahim Samodien & Frederic Nduhirabandi Venue: Auditorium **Dimakatso Senthebane:** Cancer stem cells enhance chemoresistance and metastatic behaviour in human oesophageal cancer. **[abstract 55]** **Ernest Mabotha:** Can biomarkers in scalp hair identify patients at risk of a heart attack? **[abstract 56]** **Jacomina (du Plessis) Van Schalkwyk:** Homocysteine and its relationship with cardiovascular health in adolescents from African descent. **[abstract 57]** **Anel Van Zyl:** Late effects of childhood cancer and -treatment in a South African cohort. **[abstract 62]** **Mweete Nglazi:** The intergenerational transmission of socioeconomic inequalities in overweight and obesity from mothers to their offspring in South Africa. **[abstract 53]** **Gcobisa Ndlangalavu:** Novel sputum and non-sputum-based tuberculosis diagnostics in minimally-symptomatic HIV-positive patients initiating ART. **[abstract 34]** Q&A	Session 14: Communicable Diseases Facilitators: Drs Awelani Mutshembele & Andile Ngwane Venue: Board room **Ditshego Ralefeta:** Investigating the impact of mycobacterial cell-cell heterogeneity on susceptibility to anti-tuberculosis (TB) chemotherapy. **[abstract 22]** **Sibongiseni Poswayo:** Investigating the role of Protein Kinase C zeta during Mycobacterium tuberculosis infection in mice and human macrophages. **[abstract 44]** **Sohair Geyer:** Investigating host immune responses in astrocytes during central nervous system-tuberculosis infection. **[abstract 23]** **Avril Walters:** Investigating Neuronal Immune Responses To Early Central Nervous System Mycobacterium Tuberculosis Infection In Mice. **[abstract 24]** Kimone Fisher: Understanding the role of NK cells in TB disease progression in the lung. **[abstract 30]** Q&A
14h00 – 14h45	Plenary Speaker: The Role of Learning Agility in Career Advancement Dr Vukosi Marivate Venue: Auditorium	
14h45 – 15h30	CLOSURE AND AWARD CEREMONY Venue: Auditorium	
	Celebrating the completers Awards & Closing remarks Dr Thabi Maitin Division Manager RCD Vote of Thanks: Dr Lindokuhle Ndlandla RCD Final word: Programme Director Dr Nadine Harker	

SAMRC CLINICIAN RESEARCHER (MD.PHD) DEVELOPMENT PROGRAMME

1. Unpacking the use of oral PrEP as part of the HIV prevention package in a clinical trial

I Beesham[1], S Evans[1], JM Baeten[2], R Heffron[2], J Smit[1], M Beksinska[1], LE Mansoor[3]

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[2] *University of Washington, Seattle, United States*
[3] *Centre for Aids Programme of Research in South Africa (CAPRISA), Durban, South Africa*

BACKGROUND

The ECHO (Evidence for Contraceptive Options and HIV Outcomes) trial, which was conducted at 12 sites in Africa measured HIV incidence among 7829 women randomised to one of three effective contraceptives. Pre-exposure prophylaxis (PrEP) was offered as part of the HIV prevention package throughout the trial, and the trial provided oral PrEP at the Durban, South Africa site part-way through the trial. We present findings below on experiences of women who initiated oral PrEP at the Durban site.

METHODS

All women who initiated oral PrEP on-site at the Durban site were invited to complete an additional structured interviewer-administered questionnaire that probed experiences with using trial-provided PrEP. Women were interviewed approximately three months after initiating PrEP from April to October 2018. Data were entered on REDCap and analysed using Stata. Open-ended questions were coded into categories and descriptively analysed.

RESULTS

In total, 132 (96.4% of 137 women who initiated PrEP on-site) were interviewed. The mean age was 24 years. Twenty-seven (20.5%) women felt they would probably get infected with HIV. Women felt at risk for acquiring HIV due to many reasons including: not knowing their partner's HIV status (24, 18.2%), feeling their partner had other sexual partners (57, 43.2%), not always using a condom when having sex (97, 73.5%) and having had a previous sexually transmitted infection (17, 12.9%). PrEP use was disclosed by 119 (90.2%) women: 46 (38.7%) disclosed to partners, 44 (37.0%) to friends, and 81 (68.1%) to family. In total, 120 (90.9%) women heard about PrEP for the first time from ECHO trial staff. Three-quarters (99, 75.0%) elected to continue using PrEP at study exit. Reasons for stopping PrEP included (n=32): side effects (12, 37.5%), partner or family influence (5, 15.6%), forgetfulness (4, 12.5%) and other reasons (11, 34.4%).

CONCLUSION

Staff were found to be vital in the delivery of oral PrEP and up to 38% of attrition from PrEP was due to side effects. Most clients disclosed PrEP use. Three-quarters of women continued PrEP at study exit. These findings can be used to inform other trials delivering oral PrEP.

#This abstract was submitted to AIDS2020 and accepted for poster presentation.

2. Utilisation of health care services prior to suicidal behaviour in CapeTown

T Kootbodien[1], R Ramesar[2], L London[3], L Martin[4]

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[2] *UCT/MRC Genomic and Precision Medicine Research Unit, Division of Human Genetics, Department of Pathology, Institute for Infectious Diseases and Molecular Medicine, University of Cape Town and Affiliated Hospitals*
[3] *School of Public Health and Community Medicine, University of Cape Town*
[4] *Division of Forensic Medicine, Department of Pathology, University of Cape Town*

BACKGROUND

Mental health care services are underutilised in South Africa. Access and use of health care services is often promoted as an opportunity for suicide prevention strategies. However, suicide completers and attempters have different profiles that may affect their help-seeking behaviour.

METHODS

We linked electronic health records of suicide completers, low-risk suicide attempters and high-risk suicide attempters (n=484). We described the prevalence of mental health diagnoses and type of health care contact. Length of time from last health care visit to date of suicidal behaviour was calculated, and Kaplan Meier curves were used to compare the differences across the three groups. Comparisons were performed using log-rank tests. A Cox proportional hazards model examined covariates.

RESULTS

We found that suicide completers were different from suicide attempters, while high- and low-risk attempters shared characteristics. Majority of participants accessed general health care services, while only 27% had prior mental health contact. Approximately 60% of contacts occurred at hospital outpatient clinics and 29% at primary health care facilities. The median time from last health care contact to suicidal behaviour was 156 days for completed suicides, 95 days for high-risk and 83 days for low-risk suicide attempters. Health care visits for completed suicides were significantly associated with chronic illness and a history of assault. For high-risk suicide attempters, health care visits were associated with depression, chronic illness and HIV and for low-risk suicide attempters, health care visits were associated with depression, chronic illness, substance use disorder and HIV.

CONCLUSION

Opportunities for suicide prevention at health care facilities do exist for low-risk suicide attempters. However, suicide completers and high-risk suicide attempters are more likely to be missed. Future prevention efforts may be most effective at primary care level for those with chronic conditions. Community-based prevention efforts may prove beneficial for the 43% who did not access health care services.

3. Neutrophils as effector cells in resistance to infection by Mycobacterium tuberculosis in HIV-infected persons

EE Kroon[1], M Möller[1], AK Coussens[2-4], A Seeger2, G Walzl[1], RJ Wilkinson[2,5,6], G Tromp[1], E Schurr[7-9], EG Hoal[1]

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8 *McGill International TB Centre, McGill University, Montreal, Canada*
9 *Departments of Medicine and Human Genetics, McGill University, Montreal, Canada*

BACKGROUND

Mycobacterium tuberculosis (*M.tb*) is transmitted by aerosol inhalation. Not all individuals exposed to *M.tb* become infected as inferred by a lack of T cell memory response to *M.tb* specific antigens. These individuals do not develop signs and symptoms suggestive of 'active tuberculosis' and are defined as resisters. Resistance to infection is supported by multiple lines of evidence. The contribution of the innate immune system and the cells involved in resistance remain incompletely elucidated. Neutrophils are some of the first phagocytes recruited from the pulmonary vasculature to the interstitium to control infection and are therefore prime candidates.

METHODS

Samples collected from 60 HIV-infected individuals enrolled in the NIH-funded ResisTB study in Cape Town, Western Cape, South Africa, have been subdivided into four groups based on their IGRA/TST results (positive/negative) and age categories (18-25 years, 35-60 years). Age was used as a surrogate for the cumulative likelihood of exposure in our area of high *M.tb* transmission. We will investigate any significant differences in the effector mechanisms

of neutrophils in response to pathogenic *M.tb* (H37Rv) by comparing responses between innate resisters and infection susceptible individuals. Furthermore, we aim to ascertain if these differences potentially contribute to the innate resister phenotype.

RESULTS

Sampling for the study has been completed, and sample processing and analysis are underway.

CONCLUSION

Understanding the mechanism of innate resistance could aid the development of novel elimination strategies as well as provide urgently required correlates of protection for vaccine evaluation and design.

4. The Effect of Asymptomatic STI's on Male Foreskin Susceptibility to HIV

Lerato Cosnet Rametse[1]

[1] *University of Cape Town*

BACKGROUND

South Africa has high rates of sexually transmitted infections (both HIV and non HIV). There is approximately 13.1% HIV prevalence rate in the South African population, additionally, with nearly 1 million people becoming infected daily with any of four curable sexually transmitted infections (STIs): chlamydia, gonorrhoea, syphilis, and trichomonas (WHO, 2019). Effective control of the HIV epidemic will require a better understanding of how the virus is transmitted and acquired in males. It is known from both empirical data and mathematical modelling that STIs (both symptomatic and asymptomatic) increase the risk of HIV acquisition. My project will investigate the molecular and biological mechanisms underlying this epidemiological finding by measuring the impact of STIs on foreskin integrity and HIV permeability from men electing to undergo voluntary (V) MMC and who have an asymptomatic STI.

METHODS

Foreskins and first pass urine samples are being collected from 200 males (18 35 years) who attend four provincial clinics in and around Cape Town for VMMC. We are assessing foreskin barrier integrity and the impact of asymptomatic non HIV STIs (Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, and Mycoplasma genitalium) on foreskin susceptibility upon in vitro HIV challenge. We are using subtype C HIV that is photoactivated by incident light to identify whether Th17/Th22 cells are HIV targets in the foreskin as well epithelial barrier integrity.

RESULTS

To date, we have identified that 1:4 men in two MMC clinics near Cape Town are infected with asymptomatic STIs (any of the four organisms above) and who then undergo VMMC. We will recruit 200 males to identify the impact of STI's in 50 male foreskins. All STI results have been reported to the clinic for participant treatment.

CONCLUSION

This study will provide insight into viral acquisition and lay the foundation for further critical prevention strategies in males.

5. The Prevalence of abnormal Doppler's in a low risk pregnant population in South Africa

TMAG Hlongwane[1], T Cronje[2], BSS Nkosi[1], RC Pattinson[1]

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[2] *Department of Statistics, University of Pretoria*

BACKGROUND

The assessment of fetal blood flow using Doppler waveform is one of the innovative methods of fetal surveillance- it can be used to identify placental insufficiency. It is a tool to identify fetuses at risk of stillbirth due to fetal growth restriction. In South Africa the largest category of perinatal deaths is 'unexplained intrauterine death'. The majority of the mothers are clinically healthy women and the highest prevalence of stillbirth was between 32 and 38 weeks' gestation. It is hypothesized that many of these deaths are due to undetected placental insufficiency.

METHOD

A descriptive study across 9 sites in 8 provinces of South Africa (Gauteng, North West, Northern Cape, Limpopo, Mpumalanga, KwaZulu Natal, Free State and Eastern Cape) was performed to determine the prevalence of raised resistance indices (RI) of the umbilical artery in women classified as having a low-risk pregnancy. Pregnant women classified as having low risk pregnancies were screened for placental insufficiency using a continuous wave Doppler ultrasound apparatus (UmbiflowTM) between 28 and 34 weeks' gestation. Women with fetuses with a raised resistance index were referred to a high-risk clinic and were managed according to standard protocol. The outcomes of all the deliveries were recorded.

RESULTS

UmbiflowTM screening was performed in 7171 women across 9 sites; 919 (12.8%) fetuses were regarded as high risk. Absent end diastolic flow (AEDF) was found in 88 (1.2%) of fetuses.

CONCLUSION

The prevalence of abnormal Doppler's in this low risk population is 12.8%. The Prevalence of AEDF in this low risk population is about 8-10 times higher than that previously recorded. (Comparable to what other low risk study in Pretoria found). There is a need for an antenatal tool to assess placental function to identify fetuses at risk of dying. Screening a low risk pregnant population may reduce the prevalence of unexplained stillbirths in South Africa.

6. Tuberculosis transmission in rural South Africa: integrating classical, spatial and genomic epidemiology

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[2] *Africa Health Research Institute, Durban, South Africa*

BACKGROUND

Tuberculosis (TB) remains the top infectious killer in the world. Mounting evidence from countries with high TB burdens points to ongoing transmission as the driving force maintaining incidence of TB disease; and this evidence appears to be even more pronounced for drug-resistant forms of tuberculosis. Our ability to break the transmission chain remains hindered by key knowledge gaps about pathogen spread between hosts, especially in HIV-endemic populations. Who transmits? Where does transmission occur?

METHODS

We establish the clinical, epidemiologic and geospatial determinants of prevalent TB (including subclinical TB) in a highly HIV endemic population in rural KwaZulu-Natal. We generate potential transmission clusters using population data (including family and household relationships, geospatial information and migration patterns). We integrate this data with whole genome sequences of 106 active TB cases for whom sputum culture is positive.

RESULTS

Results to follow.

CONCLUSION

The desired outcome of this project is an analytic framework that will integrate the diverse data streams utilized to create a user-friendly pipeline that will facilitate future real-time data analysis as additional TB cases accrue in the population.

7. Epidemiology of community and hospital-acquired invasive infections in young infants

FC Mabena[1,2,3], SA Madhi[1,2], SC Velaphi[1,3]

[1] *University of the Witwatersrand*
[2] *Vaccines and Infectious Diseases Analytics Research Unit (VIDA)*
[3] *Chris Hani Baragwanath Academic hospital*

BACKGROUND

Globally, the under-five childhood mortality rate (per 1,000 live births) decreased by 58%, from 93 in 1990 to 39 in 2017. Although neonatal mortality rate has also declined by 41% (from 37 to 18/ 1000 live births) during the same period, the rate of decline has been slower than observed in children 1 – 59 months old (3.1% vs 4.7%). Consequently, neonatal deaths now constitute a greater percentage (46% in 2017) of all under-five childhood deaths than in 2000 (41%). Sepsis as a cause of neonatal deaths may be difficult to accurately ascertain using verbal autopsy alone, which could lead to an underestimate of the role of sepsis in the causal pathway of neonatal deaths. Recently, it has been observed that ante-mortem sampling may under-estimate the role of infections in the causal pathway to neonatal (and older children) deaths by 2-3-fold. There is paucity of data on pathogen-specific causes of neonatal sepsis in SSA due to limited biological investigation of neonatal and childhood deaths. More data on young infant infection aetiology and antimicrobial resistance (AMR) from SSA is required to inform policies and appropriate management strategies for the region.

METHODS

The first objective of the study is to investigate the epidemiology of culture-confirmed sepsis. A retrospective review of approximately 38,000 mother-newborn dyads days enrolled between July 2014 and December 2016 (V98_28OBTP study) will be performed. The second objective is to study the dynamics of colonization by pathogenic organisms. Prospective surveillance for surface and mucosal colonization by ESKAPE pathogens in newborns hospitalised immediately post-delivery will be performed. Lastly, the role of infections in the causal pathway to death among neonates and young infants will be investigated using post-mortem minimally invasive tissue sampling (MITS) procedure together with microbiological and histopathological examination. The common causative pathogens and their antibiotic susceptibility patterns will be determined.

8. Strengthening child and adolescent mental health systems in South Africa – a multistakeholder implementation science initiative

SRN Simelane[1], PJ de Vries[1,2]

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[2] *Adolescent Health Research Unit (AHRU), Division of Child and Adolescent Psychiatry, University of Cape Town*

BACKGROUND

Mental health disorders represent the greatest burden of disease in young people. South Africa currently has no policies or implementation strategies detailing how child and adolescent mental health (CAMH) services should be delivered. In addition, there is a gap between the formulation of evidence-informed best practices and the rollout or implementation of these practices. This project aims to strengthen CAMH services at the primary care level in the Western Cape by using the Exploration, Preparation, Implementation and Sustainment (EPIS) framework to develop a shared set of priorities with key stakeholders and address these through the implementation of existing evidence based practices for the evaluation and management of CAMH disorders

METHODS

Our study will make use of the EPIS framework which has four phases. The exploration phase is a participatory process involving different stakeholders in the primary care setting i.e. policymakers, primary care facility management, and mental health practitioners, to generate shared priorities and actions based on existing evidence. The preparation phase requires the development of a shared action plan, based on the evidence-based practice identified to best address challenges identified. The next phase is the implementation of the action plan including the provision of any resources and training that may be required. The implementation is then evaluated with strengthening and modifications based on contextual factors to ensure actions for sustainment in primary care settings. Data is collected at each phase using mixed qualitative and quantitative methods.

RESULTS

The study is still ongoing with no results generated with no results generated at this stage.

CONCLUSION

This project will strengthen CAMH services at the primary care level by supporting primary health care workers to allow for the early identification, correct assessment and diagnoses, and early intervention that is key to successful CAMH care services. South Africa is thought to have similar levels of organic CAMH pathology as high-income countries, and this is further compounded by high levels of poverty and trauma. The implementation science approach means that this research is translated into practice in real time. By using existing evidence-based practices and involving policy makers from the initial stages of the project, the rollout of any positive results could potentially be streamlined.

9. High Prevalence of Hepatic Steatosis in Children with Perinatally Acquired HIV Starting Antiretroviral Therapy Beyond Infancy

PC Rose[1], ED Nel[1], M Cotton[1,2], S Innes[2]

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BACKGROUND

Despite the high prevalence of non-alcoholic fatty liver disease (NAFLD) in adults with HIV, little is known about this problem in children. Our aim was to evaluate the prevalence of hepatic steatosis and fibrosis in South African children with perinatally acquired HIV (PHIV) and HIV-uninfected (HU) children, evaluating both traditional and HIV-specific risk factors.

METHODS

This cross-sectional study, conducted from April to December 2019, enrolled well school-aged children participating in an ongoing cohort study. Both PHIV and HU were included. Demographic and clinical data were collected. All children had transient elastography (TE) and controlled attenuation parameter (CAP) performed using the Fibroscan Mini 430 (Echosens, Paris, France) after an overnight fast. Hepatic steatosis was defined as CAP ≥238dB/m and hepatic fibrosis as a liver stiffness ≥7.1kPa. Comparisons of categorical variables used the Chi-square or Fisher's exact test. For parametric and non-parametric continuous variables, the t-test and Wilcoxon test were used as appropriate. Multivariate logistic regression analyses identified predictors for hepatic steatosis. All analyses were two-tailed and $p<0.05$ was considered statistically significant.

RESULTS

138 children were evaluated. The median age was 12.5 years [IQR 11.2-13.5 years], 73 (53%) were female, 43 (31%) were PHIV and 95 (69%) were HU. All PHIV children had been on antiretroviral therapy (ART) since early life. A total of 18 (13%) children had evidence of hepatic steatosis: 1/2 (50%) *obese,* 4/14 (29%) overweight and 13/122 (11%) lean children. There were 3 (3%) HU children and 1 (2%) PHIV with evidence of hepatic fibrosis.

Eight (19%) PHIV children [5/10 (50%) who initiated ART beyond infancy and 3/33 (9%) who started ART during infancy] and ten (11%) HU children had hepatic steatosis (p=0.019). There was no significant difference in HIV stage, ART regimen, CD4 count (absolute or %), viral load or nadir CD4 count (absolute or %) between those with and without hepatic steatosis. There was no significant difference in duration of ART, duration of suppression of HIV viraemia, nadir CD4 count or whether the ART regimen contained a protease inhibitor or non-nucleoside reverse transcriptase inhibitor between PHIV children initiating ART after infancy and those initiating ART during infancy. In multivariable logistic regression analysis, the only significant risk factors for hepatic steatosis were obesity or overweight in HU children (OR 9.6; 95% CI 2.0-45.8) and starting ART beyond infancy in PHIV children (OR 9.9; 95% CI 1.4-68.4).

CONCLUSION

PHIV children starting ART beyond infancy had a much higher prevalence of hepatic steatosis compared to PHIV children starting ART during infancy. Early ART may protect PHIV children from developing NAFLD. Further longitudinal studies are needed to monitor for the development and progression of hepatic steatosis, NASH and hepatic fibrosis in PHIV children and to elucidate the possible mechanisms though which early ART may protect PHIV from developing hepatic steatosis.

10. Biomarkers that may predict South Africans who develop severe COVID-19

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BACKGROUND

Since the first wave of the disease has abated in South Africa, we aim to collect retrospective clinical, haematological, and infectious disease data on patients who test positive for coronavirus SARS-2, in order to better understand early clinical features that may predict hyper-inflammatory consequences.

Study hypothesis: biomarkers can be identified that can be used to predict disease severity in South African children and adolescents.

To investigate haematological, infectious disease and clinical biomarkers that may predict or may be associated with developing severe SARS-CoV-2 infection in children and adolescents, and to assess whether the disease has a different severity profile in South Africans and in particular in high risk groups (including HIV-infected individuals).

METHODS

Inclusion criteria: Patients admitted to hospital facilities meeting the applicable NICD case definition for COVID-19. Clinical, nasopharyngeal specimens for infectious disease PCR, and haematological parameters will be collected. All clinical progress and treatments will be documented. The study is not intended to assess treatment outcomes.

Control group: SARS-CoV-2 positive patients who do not progress to the to MIS-C.

RESULTS

Identify biomarkers to predict severity of disease in children infected with SARS-CoV-2.

CONCLUSION

COVID-19 will continue to dominate the medical landscape in South Africa for some time to come. This PhD proposal aims to identify biomarkers that can be used to predict disease severity for use in managing children and adolescents with COVID-19, in particular those who may be at risk of severe disease and hospitalisation. This could reduce the current morbidity in the South African population. Understanding SARS-CoV-2 in the South African context will be of great benefit to public health as it can aid in curbing the anxiety and apprehension felt by the population.

11. Return to sport guidelines in athletes with acute respiratory infections (including COVID-19)

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BACKGROUND

Athletes are generally considered as healthy individuals with exceptional physical capabilities. They are however, also susceptible to acute illness, and epidemiological studies indicate that acute respiratory infections (ARI) are the most common infection affecting athletes. Many pathogens can cause ARI in athletes but the effects of specific pathogens on selected laboratory investigations, and possible organ or organ system involvement, duration of the illness episode, residual symptoms or prolonged health concerns in athletes are not known. Recently, the emergence of COVID-19, caused by the novel coronavirus (SARS-CoV-2), also threatens athlete wellbeing and health. It is well known that COVID-19, together with other pathogens associated with ARI, can affect multiple organs in the body and in some cases, symptoms can last for weeks to months. Currently there are no data on the health effects of COVID-19 on athletes, the time to recovery and the possible medical complications during physical activity. Clinicians are challenged to provide safe guidance for athletes to full sports participation and competition after a recent respiratory/COVID-19 infection.

This study therefore aims to formulate pathogen-specific return to sport guidelines in athletes with selected acute respiratory infections (ARI), including COVID-19, based on clinical criteria and laboratory investigations. The secondary aim is to determine the incidence and risk factors associated with acute respiratory and COVID-19 infections.

METHODS

The study will comprise of the following three study designs:

1. A prospective cohort study to determine the incidence of ARI (including COVID-19) in competitive athletes (15 years and older), during a 12-month period with a cross-sectional analysis to identify selected risk factors associated with ARI (including COVID-19). Participants of a student athlete cohort will be requested to complete daily monitoring on training load, daily symptoms, well-being, and health status (indicating presence of ARI), captured on an online health monitoring system (Smartabase) over a period of a minimum of 12 months.
2. A prospective cohort, experimental laboratory study with repeated measures and longitudinal follow-up for 6 months, documenting residual symptoms, clinical manifestations, laboratory evidence of multiple organ involvement and exercise performance parameters as athletes (18 – 60 years old) with recent ARI (including COVID-19) return to training and full sports participation. Participants with a confirmed ARI/COVID-19 infection will be assessed clinically and selected laboratory and special investigations will be requested to determine possible multi organ involvement. Participants will be monitored for residual symptoms and health concerns and once medically cleared, return to sport participation will be initiated. Progression to return to sport will be monitored over the 6 month period.
3. A retrospective study of self-reported cases of a recent (last 6 months) ARI, including COVID-19, in athletes with a cross-sectional analysis will be conducted comparing sub-populations of athletes comparing symptom type, severity and duration. Participants will be requested to complete an online questionnaire with personal information, symptoms (type, duration and severity) experienced during recent ARI/COVID-19 infection, general medical and training history prior to infection, and residual health concerns after an acute respiratory or COVID-19 infection.

RESULTS

The study is in the recruitment of participants phase and no preliminary results are available to date.

CONCLUSION

The results of this study will advance the knowledge in the general field of medicine and specifically in Sport and Exercise Medicine. The study addresses a very common and important clinical problem that not only affects high level athletes, but also recreational athletes. It also has practical clinical implications for occupations where physical work is required e.g. mining, construction, and security. The practical clinical decision-making tool could be implemented by health professionals nationally and internationally and would serve as a valuable aid to assist the active individual in returning to physical activity.

The dissemination of the information is of equal importance. Once the results are peer-reviewed and published in national/international journals, the information will be disseminated to athletes and medical staff, coaches, and sports organisations using various strategies including presentations, press releases, social media platforms, and websites. This will enable professionals to provide safe and scientifically based guidelines for the active individual in returning to physical activity and sport participation after an acute respiratory infection.

12. Profiling Molecular Pathways in Endometrial Cancers (EC) occurring in Black South African Women: Therapeutic Targets

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BACKGROUND

In developed countries, endometrial cancer (EC) is the most common gynaecological malignancy and has a higher incidence in white women but black women have a mortality rate up to 80% greater than that of white women. Despite this disproportionate aggressive behaviour, the genomics of EC in black women is largely unexplored.

METHODS

An ambispective study to evaluate the epidemiology of EC in South African women, together with the genomics and bioinformatic analysis of Type II EC in black South African women is being conducted.

RESULTS

This study is aimed at the unique cohort of black South African women and we hope to gain important insights into the pathogenesis of endometrial cancers in this cohort. There is a need to study endometrial cancers in South Africa to ascertain if the aggressive form (Type II EC) is the predominant subtype and explore the molecular mechanisms underlying this potency.

CONCLUSION

This would be the first study of its kind in South Africa and the information gathered, will enhance our understanding of EC's aggressiveness in African patients and also lead to the identification of aberrant molecular pathways and molecules which can be manipulated as future drug targets in an African population and help address EC's racial disparities.

13. Prospective Validation of A Host-Blood Tuberculosis Transcriptomic Signature In Adults With HIV

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BACKGROUND

In 2018, 45% of the estimated 862,000 global incident tuberculosis cases amongst people living with HIV (PLHIV) went undiagnosed or unreported, the so-called "missing millions", with an estimated case fatality rate of 29% in this population. There is an urgent need for earlier tuberculosis diagnosis, using novel non-sputum approaches. We tested diagnostic and prgnostic performance of a host blood transcriptomic signature of tuberculosis (RISK11) for screening of PLHIV in a prospective, community-based cohort.

METHODS

Ambulant adult volunteers living with HIV were enrolled at five South African sites. RISK11 status was assessed at baseline by real-time PCR and was double-blinded. Participants underwent active surveillance for microbiologically-confirmed tuberculosis from enrolment through 15 months. The primary outcomes were prevalence and cumulative incidence of two-sputum-sample positive tuberculosis in RISK11+ versus RISK11- participants.

RESULTS

Among 820 participants with valid RISK11 results, eight (1%) tuberculosis cases were identified at baseline. Risk of prevalent tuberculosis was 13.1-fold (95%CI 2.1-81.6) greater in RISK11+ than RISK11- participants, with tuberculosis prevalence of 2.5% and 0.2%, respectively. RISK11 had diagnostic area under the receiver-operating-characteristic curve (AUC) 88.2%; sensitivity 87.5% and specificity 65.8% at the pre-defined threshold (60%).

Thereafter, eight tuberculosis cases were identified through median 15 months follow-up. Tuberculosis incidence was 2.5 vs 0.2 per 100 person-years in RISK11+ compared to RISK11- participants with cumulative incidence ratio 16.0 (95%CI 2.0-129.5); AUC 80.0%; sensitivity 88.6% and specificity 68.9%. By comparison, QuantiFERON TB Gold-Plus (QFT) had a cumulative incidence ratio of 2.0 (95%CI 0.5-8.4); AUC 70.8%; sensitivity 62.1% and specificity 56.2%.

CONCLUSION

RISK11 identified prevalent tuberculosis and predicted risk of progression to incident tuberculosis within 15 months in ambulant PLHIV. Performance approached the World Health Organization Target Product Profile benchmarks for screening and predictive tests for tuberculosis. QFT performance fell short of the predictive benchmark.

SAMRC INTERNSHIP SCHOLARSHIP PROGRAMME (ISP)

14. Trends of treatment admissions for alcohol and other drugs among youth and younger adults in South Africa: A descriptive analysis of the South African Community Epidemiology Network on Drug Use project between 2009-2019

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BACKGROUND

South African youth are often described as being the healthiest in the population but do face a variety of health risks. The use of psychoactive substances by youth and young people globally and in South Africa is of major concern, particularly given young people's increased access to legal and illegal substances. The increased use of certain drugs may be resultant unintentional and intentional injuries, crime, violence and other social and health problems such as developing a substance use disorder. Treatment for substance use disorders (SUDs) in South Africa boasts one of the most developed substance abuse treatment systems on the African continent, however, it is reported that the demand for substance use treatment continues to exceed the supply. Among youth, up to 86% return to substance use behaviour within 12 months following SUD treatment, which places increasing pressure on SUD treatment facilities as first-time SUD treatment admissions appear to make up the majority of total admissions in South Africa. The purpose of this study is to describe the sociodemographic characteristics and the primary substances of use upon admission to treatment among a sample of South African youth over the last 11 years. Results may assist with guiding policy-makers and other relevant stakeholders in the planning of substance use treatment services in South Africa.

METHODS

This study adopted a quantitative approach for the descriptive secondary data analysis of a raw dataset; to determine the trends of alcohol and other drug use among youth between the ages of 15 to 34 years old, who have accessed specialist AOD treatment services in South Africa between 2009-2019. Secondary data analysis of previously collected data allows for methodological advances and the generation of new knowledge. The raw dataset identified for secondary data analysis is the *South African Community Epidemiology Network on Drug Use* (SACENDU).

RESULTS

Descriptive statistical results revealed that the mean age of patients in this sample was 23.60 years old (SD=5.610) between 2009-2019. Of all admissions (n=139994), gender differences revealed that 83.2% (n=116409) were male and 16.8% (23585) were female. Majority of admitted patients indicated that they had high school level of education (70.6%; n=98832). Most admissions were of youth aged 15-19 years (n=42240) who presented most frequently with Cannabis (61.3%) as their primary substance of abuse. Majority of the 20-24-year group (n=35565) also presented with cannabis (30%) as the most frequent substance of abuse, with heroin (20.5%) following in as the second most frequent substance of abuse for this age group. Among youth aged 25-29 years old (n=36170), cannabis (20.4%), alcohol (20%), methamphetamine (19.6%) and heroin (19.2%) were similar in proportion. Among youth aged 30-34 years old (n=26192), more frequent admissions were seen for alcohol (30.7%) and methamphetamine (18%) as the second most frequent substance of abuse for this age cohort. Of all treatment episodes seen in this period (n=139994), 19.5% of youth in this study (n=26007) reported having previous SUD treatment experiences in the past.

CONCLUSION

The majority of youth admitted to SUD treatment presented with cannabis-, alcohol-, methamphetamine- and heroin-related use as their primary substances of abuse. While readmission formed one fifth of treatment intake over the 11-year period, results suggest that further exploration may be required to understand youth needs for SUD treatment in order to reduce patient readmission rates. The design of youth-centred substance use disorder interventions that take into account youth needs may serve to improve individual substance use treatment outcomes.

15. Vaccine hesitancy in the Cape Metro: the perception of vaccinators

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BACKGROUND

Despite the remarkable advantages of vaccination, coverage still remains suboptimal in many parts of the world, especially in low- and middle-income countries including South Africa. Vaccine hesitancy, a major factor responsible for low vaccination uptake in many parts of the world, is suspect in the suboptimal vaccination coverage in the Western Cape Province. This study provides empirical evidence of vaccine hesitancy in the Cape Metro, by conducting a context-specific qualitative enquiry into the drivers of vaccine hesitancy as perceived by point-of-care vaccinators in the Metro.

METHODS

Key informant interviews were conducted in 16 purposively selected health care facilities in the Cape Metro between September and November 2019. The interviews were transcribed verbatim and the transcripts coded both manually and electronically using ATLAS.ti QDA software version 8.4.24. The data were thematically analysed using Braun and Clarkes' (2006) prescribed method for thematic analysis.

RESULTS

Of the 19 point-of-care vaccinators interviewed, 11 reported having encountered vaccine hesitant individuals at some point in their careers. Reasons given for this hesitancy ranged from concern over causing pain to the child to deep-rooted religious beliefs. The influence of the internet was also a prominent factor mentioned. Though the demography of vaccine hesitant individuals seemed to cut across race and class, specific communities in the Cape Metro were directly indicted as being vaccine hesitant. Overall, four overarching themes and three sub-themes were extracted from the data and discussed.

CONCLUSION

Vaccine hesitancy is present in the Cape Metro. Continuous health education in the clinics and communities, as well as stakeholder engagements are some of the remedial actions proffered by the point-of-care vaccinators to mitigate against vaccine hesitancy in the Cape Metro. Focused qualitative and quantitative lenses are to be trained on indicted communities.

16. A modified BCG vaccine for enhancing trained innate immunity against Mycobacterium tuberculosis infection

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BACKGROUND

The BCG vaccine is the only licensed Tuberculosis (TB) vaccine. However, BCG only protects against disseminated TB disease in infants and does not protect against TB in adults. Recent BCG revaccination studies in TB negative adults provides only 45% protection against TB infection. Modified BCG strains with reduced peptidoglycan amidation properties (a phenotype allowing mycobacterial immune recognition) are attractive candidates to enhance protection against TB infection.

METHODS

CRISPR-dCas9 gene silencing was used to create a modified BCG strain (BCG-ΔMurT-GatD) which does not amidate peptidoglycan (PG). PG labelling with fluorescent reporter peptides was used to assess PG amidation in BCG-ΔMurT-GatD. Lack of PG amidation in BCG-ΔMurT-GatD is proposed to enhance innate immune training against mycobacterial infection through introduction of epigenetic modifications in host cells. Monocytes will be trained with the BCG-ΔMurT-GatD and epigenetic modifications and cytokine responses upon challenge with *Mycobacterium tuberculosis (Mtb)* will be assessed. Firstly, chromatin immunoprecipiation and analysis of epigenetic modifications (H3K4me3 – associated with increased gene transcription) at the genes nod1 and nod2 (required for detection of *Mtb* during infection) will be performed with the use of a H3K4me3 targeting antibody. Secondly, ELISAs and qPCR will be used for analysis of the cytokine response of BCG or BCG-ΔMurT-GatD trained macrophages during *Mtb* infection. Specifically, increased expression of the IL-1ß-PGE2 cytokine axis which has been demonstrated to provide early anti-mycobacterial responses during infection of host cells will be analysed.

RESULTS

CRISPR-dCas9 mediated knockdown of MurT-GatD in BCG reduced PG amidation, characterized by changes in cell growth rates and cell wall staining profile with PG amidation detection fluorescent probes. To this end monocytes are being prepared for training experiments to assess whether training with BCG-ΔMurT-GatD causes increased cytokine expression.

CONCLUSION

The BCG-ΔMurT-GatD vaccine is an attractive candidate to enter pre-clinical studies as a future TB vaccine

17. Different definitions of a PBD may affect its association with CVD risk

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BACKGROUND

Plant-based diets (PBDs) are dietary patterns that encourage the intake of healthy plant foods and limit the intake of unhealthy plant and animal foods. The Mediterranean and Dietary Approaches to Stop Hypertension diets are common examples of a PBD. There is a growing literature on the inverse associations between PBD status, i.e. the exposure to a PBD, and cardiovascular disease (CVD) outcome. However, there are numerous ways to define PBD status across studies.

METHODS

The review will focus on studies published globally that investigate PBD status in relation with CVD risk to; determine how PBDs are defined across studies, assess to what extent the differences in the PBD definitions affect the distribution of PBD status within a study population, and how different definitions of a PBD affect the associations of PBD status with CVD risk. PubMed-Medline, Scopus and EBSCOhost will be searched up to July 2020, using relevant key words. Two reviewers will independently screen the identified records and review the full texts for inclusion. Discrepancies will be resolved by consensus or through discussion with a third reviewer. Appropriate meta-analysis will be performed where possible and consistency of the findings checked through subgroup analysis. Heterogeneity across studies will be assessed and quantified, and publication bias investigated. Relevant sensitivity analysis will be performed to substantiate the robustness of the study findings.

RESULTS

(Not applicable)

CONCLUSION

This systematic review aims to scrutinize the consistency of definitions used to derive a PBD status across published studies. To determine to what extent the differences in defining exposure to a PBD consistently rank participants and how these differences affect the association of PBD with CVD risk. This could potentially improve the worldwide uptake of their findings for policy and practice purposes. The resulting findings will be published in peer-reviewed journals, presented at relevant conferences, and submitted as part of a PhD thesis at the University of Stellenbosch, South Africa.

18. Whole-genome transposon mutagenesis to elucidate the genetic requirements for vitamin B12 biosynthesis and assimilation in mycobacteria

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BACKGROUND

Resolving the full gene complement involved in the complex, multi-step pathways for co-enzyme B_{12} biosynthesis, assimilation, and salvage in different mycobacterial species is enormously challenging. To address this problem, we have adopted a genome-scale approach to yield detailed genetic maps of *de novo* vitamin B_{12} biosynthesis in *M. smegmatis*, a non-pathogenic saprophyte.

METHODS

A combination of whole-genome transposon (Tn) mutagenesis and next generation sequencing (Tn-seq) was applied in *M. smegmatis* Δ*metE*, a gene-deletion mutant in which the B12-independent methionine synthase has been inactivated, thus rendering the B^{12}-dependent isoform, MetH, essential for viability. Following growth of the *metE* mutant in rich laboratory medium, genomic DNA was extracted, amplified by PCR, and subjected to high-throughput sequencing to quantify all Tn junctions. Thereafter, the library was cultivated in defined minimal medium to enable identification of conditionally essential genes – including those required for *de novo* B_{12} biosynthesis.

RESULTS

A Δ*metE* library comprising 400,000 individual Tn insertion mutants (cfu/ml) was generated. Of the predicted 6,716 genes in the *M. smegmatis* genome, 213 genes were identified as essential for growth on rich (LB) agar while 356, 301, and 337 genes were identified as essential in unsupplemented, B_{12}-supplemented and cobalt-supplemented Sauton's minimal medium, respectively. Utilizing targeted depletion via CRISPR interference, a number of candidate B_{12} genes has subsequently been validated, providing functional evidence of their essentiality for *metE* survival in minimal medium.

CONCLUSION

On average, predicted B_{12} pathway genes were associated with a very small number of Tn insertions and read counts, indicating the likely essentiality of these genes during growth in minimal medium. Notably, definitive elucidation of B_{12} biosynthetic and assimilatory genes required the analysis of libraries exposed to B_{12}-unsupplemented minimal media for extended durations, probably to ensure exhaustion of the organism's capacity for co-factor storage and recycling. Elucidating the genetic requirements for optimal growth under specific conditions can inform our basic understanding of mycobacterial physiology and pathogenicity, identifying potential vulnerabilities for novel anti-TB therapeutics.

19. Fostering Ethical dialogues in research: Evaluating the Drama of DNA method for feedback of findings in genomics research in South Africa

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BACKGROUND

Community Engagement (CE) practices are becoming increasingly popular with the expansion of genomics research in Africa. However little attention has been paid to exploring their utility in fostering ethical dialogues about the science that is proposed. Recognising CE as a growing entity and an ethical requirement, equally important consideration is how African research participants can be empowered to engage in ethical dialogues about research.

This study seeks to explore and investigate the utility of Drama as an effective engagement tool to foster ethical dialogues within the context of returning individual genetic research results.

METHODS

The study adopts mixed methods to collect ethnographic data using a questionnaire, public engagement forums, focus group discussions and in-depth interviews.

ANTICIPATED RESULTS

Given the documented unique advantages of drama to disseminate research findings in novel and potentially influential ways and its value in engaging complex questions in health research, it is anticipated that Drama of DNA (DoD) method which was specifically created for genomics research will be an effective tool to engage South African audiences in the ethical questions raised by genomics research, and in considering issues relating to feedback of findings in genomics research.

CONCLUSION

Given the increasing investment in genomics research for Africa, this research study recognises the gaps in the limited strategies used to engage communities in a way that supports and enhances the ethical conduct of genomics research. This study therefore seeks to identify the value of drama and to narrow the gaps by exploring innovative dissemination techniques to reach broader audiences, particularly research participants and their communities as a platform to foster ethical dialogues in genomics research.

20. Adult food choices in association with the local food retail environment and food access in resource poor communities: a systematic scoping review

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BACKGROUND

Literature suggests that the local food retail environment influences dietary patterns and food choices. The lack of access to healthy food within this environment may result in unhealthy food choices which may lead to obesity and development of non-communicable diseases (NCDs) such as cancers, cardiovascular disease and type 2 diabetes mellitus. A systematic scoping review will be conducted with the aim to provide an overview of evidence on adult food choices in association with the local retail food environment and food access in resource poor communities.

METHODS

A systematic scoping review of literature will be conducted following a five-step framework process. These five steps include identifying the research question, identifying relevant studies, study selection, charting the data and collating, summarising and reporting the results. Published studies from January 2011 to January 2021 will be searched and screened. Keywords and medical subject headings (MeSH) terms will be used to search multidisciplinary electronic databases such as PubMed/MEDLINE, EBSCOhost, Green FILE, PsycARTICLES, Social Science Research Network, Scopus and Web of Science. The reference list of bibliographies of studies found will be checked for additional sources. Two independent reviewers will firstly screen identified articles by title, abstract and keywords; secondly full-text articles will be assessed for eligibility using inclusion and exclusion criteria. A third reviewer will be consulted to reach consensus on any disagreements between reviewers. Data will be extracted using the Preferred Reporting Items for Systematic reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) checklist.

RESULTS

(Not Applicable)

CONCLUSION

The scoping review findings will provide evidence that may assist public health policy makers in developing interventions to improve access to healthy foods in local food retail environments in resource poor communities, with the aim to enable healthier food choices and reduce the risk for NCDs.

21. Burden of Multimorbidity in South Africa: Implications for health policy and service delivery

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BACKGROUND

The number of people that are living with more than one disease condition (defined as multimorbidity), is thought to be increasing. Multimorbidity challenges the way the health system is organised as it traverses different spheres of service delivery. It is also difficult to plan for as the contemporary evidence base on multimorbidity is fragmented. This study aims to determine the epidemiology of multimorbidity in South Africa and describe health policy and system responses to addressing multimorbidities in service delivery.

METHODS

A sequential mixed-methods and multi-phase research design will be used. In Phase 1 (Year 1), a systematic review of prevalence studies on multimorbidity in South Africa will be conducted. In Phase 2 (Year 2), multiple datasets of South African surveys conducted between 1998 – 2019 and reported multimorbidity, will be analysed to determine the prevalence of multimorbidity and disease clusters, through the application of cluster analysis and multivariate logistic regression. Phase 3 (Year 3) constitutes a desktop review of health policies pertaining to multimorbidity, and followed up with qualitative interviews with purposively programme managers from Western Cape Government Department of Health. Qualitative data will be subjected to content analysis to describe policy, implementation and gaps related to addressing multimorbidity.

RESULTS

The PhD proposal has been accepted by the university and received ethics approval. In Phase 1 (Year 1: 2020), the multimorbidity systematic review protocol was registered with PROSPERO. In total, 1078 records were screened after de-duplication. Thirty-eight full-text articles were assessed for eligibility and 13 were included in a synthesis. The data is currently being analysed to produce a coherent evidence-base, and report critical evidence gaps. Phase 2 (Year 2) will develop a systematic method with which to analyse multimorbidity in national survey datasets and generate estimates of multimorbidity and disease clustering. A literature review has been conducted to identify suitable study methodologies and survey metadata has been reviewed. Phase 3 (Year 3) will identify barriers and opportunities in service delivery related to multimorbidity.

CONCLUSION

The current study has potential to influence health policy formulation and the implementation of comprehensive, integrated primary health care in South Africa.

22. Investigating the impact of mycobacterial cell-cell heterogeneity on susceptibility to anti-tuberculosis (TB) chemotherapy

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BACKGROUND

As an agent of tuberculosis (TB), *Mycobacterium tuberculosis* is the leading infectious cause of death globally, surpassing HIV and malaria. The success of *M. tuberculosis* as human pathogen derives in part from its ability to survive host-mediated antibacterial defenses, as well as clinical interventions including extended duration combination chemotherapy. Understanding the molecular mechanisms underpinning these characteristics is essential to the development of novel approaches to improved anti-TB interventions. The mycobacterial mutasome is a DNA damage-inducible complex that has been implicated in SOS-induced mutagenesis and the emergence of drug-resistance during antibiotic therapy. In prior work, we observed that mutasome induction is not uniform in a population of clonal bacilli exposed to the same exogenous genotoxic stress. By elucidating a mechanism for generating heterogeneity under applied stress, our aim is to identify targets for novel interventions aimed at curbing the evolution of drug resistance.

METHODS

This study comprises applying a panel of transcriptional reporter mutants in combination with single-cell time-lapse fluorescence microscopy, fluorescence-activated cell sorting, transcriptomics and proteomics to investigate the possibility that a sub-population of "SOS-active" cells might give rise to drug resistance.

RESULTS

Flow cytometry data and microscopic analysis of antibiotic stressed transcriptional reporter mutants revealed that mutasome induction is heterogenous, wherein two distinct sub-populations were observed. These sub-populations were either "SOS" active or unresponsive.

CONCLUSION

Collectively, the data point to an important role of the mutasome in driving mycobacterial evolution and highlights this pathway as novel drug target for TB disease.

23. Investigating host immune responses in astrocytes during central nervous system-tuberculosis infection

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BACKGROUND

Tuberculosis (TB) is a major health concern causing 1,2 million deaths in 2018 worldwide. Dissemination of *Mycobacterium tuberculosis (Mtb)* to the central nervous system (CNS-TB) is the severest clinical extra-pulmonary manifestation of the disease which constitutes approximately 1% of global TB cases. Substantial complications present in survivors include neurological sequelae, motor impairment, optic atrophy, ophthalmoplegia and hearing impairment. Although microglia are the prime resident immune-effector cells in the CNS, increasing evidence indicates that astrocytes regulate innate and adaptive immunity in CNS disease and injury. This study therefore evaluates the potential immunological role of astrocytes in CNS-TB by exploring their interactions and regulation of CNS inflammation following *Mtb* challenge.

METHODS

To investigate the direct interaction between astrocytes and *Mtb*, primary astroglial cultures will be inoculated with virulent H37Rv and attenuated BCG bacilli and analyzed by immunocytochemistry. The immune regulatory role of astrocytes will be assessed through microarray analysis, flow cytometry and ELISA. To validate this in an animal model, flow cytometry analysis and immunohistochemistry will be performed on mouse brains following H37Rv intracerebral infection.

RESULTS

Orthogonal views of confocal fluorescent images demonstrate that astrocytes can internalize *Mtb ex vivo*. Bacterial uptake by astrocytes was further supported by Colony-forming unit (CFU) enumeration. The transcriptomic analysis indicates that astrocytes induce and modulate cytokine and chemokine responses *ex vivo*. In intracerebrally infected mice, flow cytometry analysis of astrocytes showed an upregulation of interleukin-1β (IL-1β) and interleukin-10 (IL-10), compared to saline controls.

CONCLUSION

Our data supports the regulatory role of astrocytes to maintain a delicate balance through promoting cellular responses whilst limiting inflammation during CNS-TB infection. Characterizing *Mtb* infection of astrocytes and identifying mechanisms that are associated with neurological complications offer the potential to improve diagnostics and therapeutic strategies, leading to better prognosis.

24. Investigating Neuronal Immune Responses To Early Central Nervous System Mycobacterium Tuberculosis Infection In Mice

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BACKGROUND

Central nervous system tuberculosis (CNS-TB) is one of the most severe forms of extra-pulmonary tuberculosis and is most prevalent in children and immunocompromised individuals. The CNS has always been regarded as immune-privileged. However, studies have shown that *Mycobacterium tuberculosis (M.tb)* can infect various cell types in the brain including neurons and activate an immune response in the CNS. The contribution of neurons to the immune regulation in CNS-TB is not known therefore warrants further investigating.

METHODS

The immune properties of neurons will be investigated using *in vitro* and *in vivo* models. RNA extraction, microarray analysis, flow cytometry, ELISA and immunocytochemistry will be performed in primary neuronal cultures. The in vivo component will comprise of intracerebral infection, flow cytometry analysis and immunohistochemistry in the mouse brains.

RESULTS

Intracerebral infections showed a significant increase in MHC-I presentation, IL1B and TNF-a pro-inflammatory cytokines in the neurons of infected mice by 14 days post infection. Peripheral cellular recruitment did not reveal any significant differences in the recruitment of neutrophils, monocytes/macrophages and dendritic cells, but MHC-II presentation was significantly upregulated in all these innate immune cells. The percentage of CD4+ and CD8+ lymphocytes recruited to the brain were not significantly different at these early time points but there was however a significant increase in TBet expression in both CD4+ and CD8+ T cells.

CONCLUSION

Our data suggests neurons are capable of initiating an immune response against M.tb infection. For future study we will be assessing the neuronal transcriptome for molecular changes during M.tb infection. Furthermore, we will set up co-cultures to investigate the immune regulatory role of neurons. A better understanding of neuronal immunity will improve therapeutic strategy in CNS-TB.

25. Isoorientin ameliorates lipid accumulation by regulating fat browning in palmitate-exposed 3T3-L1 adipocytes

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BACKGROUND
Stimulation of fat browning using natural bioactive products is regarded as one of the promising approaches to treat obesity and insulin resistance. Here, we investigated the physiological effects of isoorientin on glucose uptake and lipid accumulation in insulin resistant 3T3-L1 adipocytes.

METHODS
To achieve our aim, 3T3-L1 adipocytes were exposed to 0.75 mM palmitate for 24 h, to induce insulin resistance, before treatment with 10 µM isoorientin or the comparative controls such as CL-316,243 (10 µM), pioglitazone (10 µM) and compound C (1 µM) for 4 h. Relevant bioassays and Western blot analysis were conducted on these insulin resistant adipocytes.

RESULTS
Our results showed that palmitate exposure could induce insulin resistance and mitochondrial dysfunction as measured by reduction in glucose uptake and impaired mitochondrial bioenergetics parameters. However, treatment with isoorientin reversed these effects by improving glucose uptake, blocking lipid accumulation, and modulating the process of mitochondrial respiration. Mechanistically, isoorientin could mediate lipid metabolism by activating 50 AMP-activated protein kinase (AMPK), while also effectively modulating the expression of genes involved in fat browning such as peroxisome proliferator-activated receptor gamma (PPAR)g/a and uncoupling protein 1 (UCP1).

CONCLUSION
Isoorientin impacts insulin resistance in vitro by improving glucose uptake and mitochondrial function, consistent to modulating the expression of genes involved in energy metabolism and fat browning.

26. Effect of endo/exogenous female sex hormones on HIV-1C latent reservoir reactivation

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BACKGROUND

The persistent latent reservoir is the major drawback to developing an HIV cure. The maintenance of viral latency has been attributed to clonal expansion and methylation of the provirus 5' long terminal repeat (LTR). However, the mechanisms that govern viral latency are not fully elucidated. Numerous factors may contribute to latent reservoir size and reactivation potential. A recent study demonstrated that the estrogen receptor-1 (ESR-1) is a key factor regulating HIV-1 subtype B (HIV-1B) latency. Women are disproportionally affected by HIV-1 and account for more than 50% of new infections. However, the role of endogenous and exogenous hormones on HIV-1C reservoir size and activation potential remain to be determined.

METHODS

CD4+ T cells will be isolated from PBMCs by negative magnetic selection. Thereafter, total RNA will be extracted from CD4+ T cells using miRNeasy Mini kit and used for cDNA synthesis using the Iscript cDNA kit. ESR-1, androgen receptor (AR) and cytokine mRNA levels will be determined by real-time (RT) PCR assay, SYBR Green chemistry using the LightCycler 480. Aromatase activity will be determined by the Human Aromatase enzyme-linked immunosorbent assay (ELISA) kit. The viral reservoir will be characterised by measuring total HIV-1 DNA and cell associated RNA levels using the DNA qPCR kit (Diatheva, Fano, Italy) and the two step rt qPCR respectively, together with the C-TILDA method. Correlation of HIV-1 reservoir size to the mRNA expression levels of AR, ESR-1 and cytokines together with age and menopausal state will be done on Graph pad. CD4+ Tcells will lastly be treated with hormone and the reactivation potential determined after treating with latency reversing agents.

CONCLUSION

The study will provide insight regarding the effect of endogenous and exogenous hormones on the reservoir size and reactivation potential in pre- and post-menopausal WLHIV on suppressive cART in South Africa.

27. Identification and expression of cathepsin S inhibitors from South African medicinal plants

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BACKGROUND

Cardiovascular disease (CVD) is the leading cause of disability and death worldwide. An important physiological process which is common in a plethora of CVD is the dysfunctional remodeling of the extracellular matrix (ECM). Research efforts have been directed towards discovering new potential targets for the treatment or prevention of CVDs based on the remodeling of ECM. One such recent discovery is the involvement of cathepsin S and its activity that has been directly linked to the dyfunsctional remodelling of ECM, and identified as a good target to unlock possibilities of treating CVD based on the remodelling of ECM. This study aims to identify compounds that inhibit cathepsin S activity from South African medicinal plants using *in silico*, *in vitro* and *in vivo* models.

METHODS

Computational modelling using molecular operating environment would be used to identify plant-based compounds with affinity for cathepsin S enzyme. Plants containing identified compounds would be assayed for enzyme inhibition using a fluorescence-based enzyme assay, and commercially compound that are available would be tested for cathepsin S inhibition. Plants identified to possess significant enzyme inhibition would be subjected to a bioassay-guided fractionation process to isolate active compound(s). Isolated or purchased compounds with significant *in vitro* cathepsin S inhibition would then be subjected to *in vivo* evaluation to determine their effect on enzyme expression and activity in captive-bred Vervet monkeys *(Chlorocebus aethiops)*.

CONCLUSION

Identifying the compounds that can inhibit cathepsin S and serve as lead compounds for the development of new CVD drug entities will contribute extensively to pharmacological intervention of medicinal plants. Since the proposed study will utilize an animal model that is phylogenetically close to humans, the research data generated in this project is anticipated to have valuable translational outputs with a high potential of providing relevant health information that might benefit the public.

28. Evaluation of host biomarker signatures for early diagnosis of tuberculous meningitis

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BACKGROUND

Tuberculous meningitis (TBM) is the most severe form of tuberculosis (TB), causing substantial mortality and long-term disability. Early diagnosis is fundamental to improving clinical outcome. Limitations in the existing diagnostic approaches underscore need for improved tools. In my PhD studies, we aim to 1) refine and validate host cerebrospinal fluid (CSF) and blood-based inflammatory biomarkers that we recently identified in previous studies as candidate tools for diagnosis of TBM, 2) evaluate the performance of different published TB mRNA transcriptomic biosignatures for diagnosis of TBM, 3) characterise the immune cells in CSF and peripheral blood samples from children with different forms of meningitis, to enhance our understanding of disease mechanisms and pathology.

METHODS

We will collect CSF and blood samples from children admitted at Tygerberg Hospital on suspicion of TBM. The concentrations of biomarkers in CSF and serum samples shall be measured using the Luminex multiplex platform and Enzyme linked immunosorbent assays. We will use quantitative reverse-transcription PCR to measure the expression of selected genes in whole blood collected in PAXgene blood RNA tubes as diagnostic candidates for childhood TBM. The characteristics of different immune cells at the site of disease and periphery will be investigated using flow cytometry.

RESULTS

The project has been approved by the Doctoral Committee, and Health Research Ethics Committee at Stellenbosch University. We have stored CSF and serum samples from 113 children for the proposed experiments with further sample collection ongoing. We have isolated RNA from blood samples for the training (discovery) arm of the gene expression work, with RT-PCR being planned.

CONCLUSION

Data obtained from this project will contribute to the development of improved point-of-care tests for early diagnosis and timely initiation of treatment in TBM and provide information about the immunopathology of TBM in children.

29. Genetic and epigenetic contributions to developmental psychopathology in childhood and adolescence

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BACKGROUND

There is growing interest in delineating the biological underpinnings of developmental outcomes in childhood and adolescence. However, there remains a relative paucity of data emerging from low- and middle-income countries (LMICs), in which the majority of the global juvenile population resides. To address the gap in the current literature, we propose to explore potential genetic and epigenetic influences on developmental psychopathology in childhood and adolescence.

METHODS

First, we plan to undertake systematic reviews of the existing evidence on the contribution of genetic risk (including polygenic risk) and of epigenetic age (EA) deviation on the outcomes of interest. Second, we shall examine the contributions of these genetic and epigenetic variations on developmental psychopathology in childhood and adolescence in the Drakenstein Child Health Study (DCHS), an ongoing South African birth cohort study. Finally, we plan to investigate potential methylation risk conferred in our study sample.

The DCHS is a well-established, multidisciplinary birth cohort study investigating maternal and child health longitudinally in a peri-urban sub-district in the Western Cape, South Africa. For the proposed study, secondary data analyses will be undertaken and will be supported by the existing infrastructure and resources of the larger study. The systematic reviews will adhere to PRISMA guidelines. To investigate

30. Understanding the role of NK cells in TB disease progression in the lung

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BACKGROUND

Tuberculosis (TB) remains the leading cause of death by a single infectious agent worldwide, with approximately 1.5 million deaths reported in 2018. Understanding lung immunity in the context of TB infection and the role innate immune cells play in disease progression is

important in identifying biomarkers of TB infection. During initial TB infection, an immune structure known as a granuloma forms to control and prevent the spread of Mycobacterium TB. The granuloma is a highly organized immune structure composed of macrophages at the centre, surrounded by a layer of epithelioid cells and multinucleated giant cells, with lymphocytes at the cuff. Whether, NK cells form part of the cuff remains a gap in our knowledge. In active TB infection the formation of caseums within the granuloma causes severe damage to lung tissue when infected macrophages undergo necrosis. Understanding the immune cell mechanisms that hinder or exacerbate this process is important in identifying potential targets for effective vaccine design. Natural killer cells are innate immune cells that form a bridge between the innate and adaptive immune system. NK cells are cytolytic and kill invading pathogens and damaged or infected cells through recognition of various receptors. NK cells are an important source of IFN-□, which is well known to control TB. We hypothesis that NK cells are present at the cuff of granuloma's and may aid in controlling TB by preventing bacteria from disseminating to other parts of the lung. In addition to their cytolytic activity, NK cells exhibit memory like phenotypes expanding and contracting upon re-exposure to viral antigens, which may be true for prior TB exposure. These diverse characteristics of NK cells suggest that they may play a crucial role in controlling TB infection due to their enhanced cytolytic activities, a benefit of exhibiting memory. NK cells are well known to be circulating cells which would enable us to study them in detail using blood from various clinical stages of TB infection. Recent studies have also shown that NK cells are tissue resident cells that express markers of mature cytolytic activity to control tumour growth in mice.

METHOD

Our study aims to resolve three major questions regarding the role of NK cells in TB disease progression: 1) to investigate the role of NK cells as tissue resident cells in the lung by studying lung pathological damage at the tissue level using immunohistochemistry staining procedures. 2) to determine the association of resident NK cells with disease severity by studying the expression of NK cells in cellular, caseating and cavitary granulomas and then spatially characterize their colocalization with pathological progression; 3) to determine the potential role of NK cells as latent TB biomarkers, by investigating NK cell dynamics in the blood from healthy, latent TB infected and active TB patients from a Durban based cohort at AHRI. We will be using specific intracellular cytokine-based NK cell assays and flow cytometry to determine cytotoxic activities.

HYPOTHESES

We hypothesize that there are unique NK cell phenotypes associated with latent TB that may be used as a biomarker of infection. These findings may provide more information on potential targets for TB vaccine design.

31. Representation Learning for DNA Sequences: An analysis of Men with Advanced prostate cancer in Africa

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BACKGROUND

African-American men are at a higher predisposition to die from prostate cancer than any other racial cohort. A study from the South African Prostate Cancer Society (SAPCS) determined a 1.8-fold increase in somatic aberrations in African-men than men of European ancestry. This work will serve as an extension of the work that has been done by the SAPCS by looking at representation learning for raw DNA sequences in the BRAC1/2 gene of advanced prostate cancer patients. The *word2vec* algorithm has been used to learn embeddings using raw DNA sequences. However, *word2vec* leads to an explosion of data, as tokens of size 4^k are generated. This algorithm also leads to sparse matrices since tokens first need to be one-hot encoded. Recurrent Neural Networks (RNNs) and their variants have been used to learn the interactions between word embedding tokens; however, these still lack the ability to capture long-term dependencies in sequences.

METHODS

Character-level Convolutional Neural Networks (Char-CNNs) with the extension of positional information will be used to learn embeddings of raw DNA sequences. These embeddings will then be fed as input to a Character-level Transformer model. Instead of predicting the next character in a sequence as in the Character-level Transformer, this process will be substituted by learning a target function that best maps the input sequences (x) to an output variable (y).

CONCLUSION

This work aims to provide early and correct detection of deleterious health outcomes in prostate cancer patients. Early detection of these health outcomes holds the ability to guide the decision-making process by selecting therapies that would yield optimum results

32. Effect of green rooibos tea extract (Afriplex GRTTM) on inflammatory and oxidative stress genes in models of NAFLD.

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BACKGROUND

Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) has been associated with the rise in liver dysfunction. Inflammation and oxidative stress are key mediators in NAFLD development. Current therapeutics used to treat NAFLD include insulin sensitizers and vitamin E. Afriplex GRT™ previously showed to decrease inflammation and oxidative stress in cardiac cells. The study aimed to assess if Afriplex GRT™ extract and pioglitazone could protect against hepatic oxidative stress, apoptosis and inflammation in *in vitro* and *in vivo* NAFLD models.

METHODS

Liver steatosis *in vitro* was induced by exposing HepG2/C3A human liver cells to 1 mM oleic acid for 24 hours. Anti-steatotic effects of Afriplex GRT™ [1, 10 and 100 µg/ml] and/or pioglitazone [30 µM] were determined in mono- and co-treatments for 24 hours post steatosis induction. Liver samples from a previous study that used Afriplex GRT™ [74 and 740 mg/kg] and pioglitazone [10 mg/kg] in C57BLKS mice treated for ten weeks as approved by Stellenbosch University Ethics Committee (ACU-2020-14382). The 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium (MTT) assay was conducted to confirm cell metabolic activity and viability. Expression of genes and proteins associated with the development of NAFLD (AKT, AMPK-α, TNF-α, SOD2, IRS1, PPAR-α, SREBF1, ChREBP and FASN) were analyzed in both models by quantitative real-time polymerase chain reaction (qRT-PCR) and Western blot.

RESULTS

In vitro oleic acid induced steatosis in C3A cells ($p < 0,01$). Afriplex GRTTM treated cells showed a reduction in fat accumulation in a dose-dependent manner. Furthermore, co-treatment with pioglitazone was shown to be effective at the lowest Afriplex GRTTM concentration ($p < 0,05$). MTT assay confirmed cell viability across all treatments, over the treatment period. Genes involved in carbohydrate and lipid metabolism (*SREBF1*, *ChREBP* and *FASN*) were differentially expressed in both models, contributing to reduced lipid content by Afriplex GRT™. Improved insulin signaling was also identified as a mechanism of action whereby Afriplex GRT™ ameliorated hepatic steatosis. Afriplex GRT™ action also showed to reduce oxidative stress (SOD2) and inflammatory cytokine (TNF-α).

CONCLUSION

Afriplex GRTTM reduces hepatic steatosis in C3A cells and C57BLKS mouse liver used in this study by modulating *SREBF1*, *ChREBP* and *FASN* gene expression. The extract also protects against oxidative stress damage and inflammation in both models, through the reduced expression of oxidative stress (SOD2) and inflammation (TNF-α) genes suggesting that Afriplex GRT™ has potential as a therapeutic for NAFLD.

33. Antimycin A induces both insulin resistance and mitochondrial dysfunction in skeletal muscle

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BACKGROUND

Mitochondrial dysfunction and insulin resistance (IR) are major risk factors for the development of type 2 diabetes mellitus (T2DM). The identification of cellular processes and gene networks that are associated with an impairment of insulin action and mitochondrial dysfunction in target tissues, might be crucial for the development of new drugs and therapeutic strategies for T2DM. However, there is sparse information on the relationship between the development of IR and mitochondrial dysfunction in skeletal muscle. Accordingly, we have established a model that can be used to induce both IR and mitochondrial dysfunction in C2C12 skeletal muscle cells.

METHODS

Mitochondrial dysfunction was induced in C2C12 myotubes by treating cells with different concentrations of Antimycin A (AA) (3.125, 6.25, 12.5, 25, and 50 μM) for 12 hours. Thereafter, mitochondrial activity, ROS production, glucose uptake, Seahorse XF Real-time ATP and Mito Stress assays were conducted. Subsequently, molecular mechanisms of AA's ability to induce both IR and mitochondrial dysfunction were assessed using the real-time polymerase chain reaction (RT-PCR) and Western blot analysis.

RESULTS

This study demonstrated that AA induces both mitochondrial dysfunction and IR, culminating in a significant decrease in mitochondrial respiration and downregulation of genes involved in mitochondrial bioenergetics including those involved in insulin signalling pathway (AKT). This was further confirmed by a significant decrease in insulin stimulated glucose uptake in C2C12 myotubes.

CONCLUSION

This study provides evidence that mitochondrial dysfunction is associated with development of IR, which suggests that therapeutics targeting Insulin resistance can improve mitochondrial function as well.

34. Novel sputum and non-sputum-based tuberculosis diagnostics in minimally-symptomatic HIV-positive patients initiating ART

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BACKGROUND

People living with HIV (PLHIV) have high tuberculosis (TB) risk. Many PLHIV cannot produce sputum, and those initiating antiretroviral therapy (ART) often have early TB disease and minimal symptoms. Symptom screening is the first step to diagnosing TB, however, it is subjective, has suboptimal specificity and is susceptible to poor implementation. C-reactive protein (CRP), for which point-of-care tests exist, meets the minimum World Health Organization criteria for triaging testing in HIV-positives, but data in ART-initiators is limited, especially in patients not pre-selected based on symptoms. We tested ART initiators, many of whom cannot naturally produce sputum, irrespective of their symptom status. We evaluated the diagnostic accuracy of CRP vs. symptoms, sputum-Xpert MTB/RIF Ultra (Ultra, done after induction), concentrated urine-Ultra and the urine-lateral flow lipoarabinomannan assay (LF-LAM).

METHODS

20-40µl fingerprick blood was collected for point-of-care CRP done by a minimally trained health worker. 25-100ml urine (20ml for concentrated urine Ultra, 60µL for LF-LAM), and three induced sputa were collected [two for MGIT960 culture (reference standard), one for Ultra].

RESULTS

Of the 897 patients recruited, 107 had TB. The sensitivity and specificity of symptoms were 76% (95% confidence interval 66, 85) and 49% (45, 53), whereas CRP were 80% (70,87; p=0.595) and 60% (56, 64; p<0.001). Sputum Ultra had 71% (62, 80) sensitivity and 96% (95, 98)) specificity. Concentrated urine-Ultra and LF-LAM has similar sensitivities (25% and 15%), however, urine-Ultra detected 10 more culture-positives missed by LF-LAM.

CONCLUSION

POC CRP should replace symptom screening in this population. It would reduce unnecessary expensive downstream testing by ~10%. Sputum-Ultra detected 7/10 culture-positives, of which 48% of them are asymptomatic and would ordinarily be missed if symptoms use. Urine Ultra detected cases missed by LF-LAM and sputum-Ultra. This work can be used for policy making, particularly changing diagnostic algorithms.

35. 20-hydroxyecdysone (20E) pathway regulates fecundity and immunity in Anopheles arabiensis malaria vectors

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BACKGROUND

Anopheles arabiensis, the primary malaria vector in South Africa, is currently poorly controlled because of its increasing level of resistance to the insecticides used locally. Thus, enhanced insecticides are being developed, including those that target mosquito fecundity and immunity. The former process regulates the number of mosquitoes available to transmit malaria, while the latter regulates the ability of mosquitoes to destroy malaria parasites within them before biting another subject. Previous studies revealed that the 20-hydroxyecdysone (20E) pathway regulates both fecundity and *anti-Plasmodium* immune responses in Anopheles gambiae, another important malaria vector. In this project, we sought to determine whether the 20E pathway plays similar roles in *An. arabiensis*, as a first step towards validating the use of "20E pathway-targeting insecticides" to control An. *arabiensis* in South Africa.

METHODS

We either over-activated or under-activated *An. arabiensis* 20E pathway by injecting mosquitoes with 20E or using RNA interference to silence the 20E receptor (EcR), respectively. The effect of these manipulations on key components of *An. arabiensis* fecundity (e.g. vitellogenesis, egg clutch size) and anti-*Plasmodium* immunity (e.g. gut microbiota, expression of immune genes) were recorded.

RESULTS

Regarding fecundity, EcR expression was induced during egg yolk formation (vitellogenesis), while EcR silencing decreased the expression of egg yolk proteins, and the egg clutch size. With respect to immunity, we found that 20E injection induces the expression of several immune genes involved in *Plasmodium* melanization and phagocytosis, while EcR silencing decreases not only the expression of these immune genes, but also the abundance of the gut microbiota (which plays a major role in regulating the development of *Plasmodium* inside the mosquitoes). In addition, EcR expression was induced by pathogen challenge.

CONCLUSION

Altogether, these findings support our hypothesis that the 20E pathway regulates both *An. arabiensis* fecundity and immunity. Therefore, "20E pathway-targeting insecticides" such as methoxyfenozide or halofenozide are worth investigating against *An. arabiensis* in South Africa. Not only are these two chemicals already showing promising results

against related mosquito species, but previous reports also suggest that resistance to methoxyfenozide is unstable, due to the fitness costs it induces in the insect.

36. The correlates of sedentary behaviour in individuals at risk of developing type 2 diabetes mellitus in Cape Town, South Africa

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BACKGROUND

The prevalence of type 2 diabetes mellitus (T2DM) is on the rise globally. According to the most recent statistics, 12.7% of adults in South Africa had T2DM in 2019, which is a 137% increase from 2017. Sedentary behaviour (SB), which is defined as behaviours involving sitting and/or reclining positions and low levels of energy expenditure (≤1.5 metabolic equivalents) during waking hours, is considered an independent risk factor for T2DM. Therefore, the aim of this study is to identify the correlates of SB among adults with T2DM and those at risk of developing T2DM in 16 low-income communities in Cape Town, South Africa. Specific objectives include: (1) determining the prevalence of SB in this population, grouping these according to specific types/domains of SB and (2) evaluating the relationship between SB and the risk of developing T2DM.

METHODS

This cross-sectional study used data, collected between August 2017 and March 2018, of 1051 individuals, aged >18 years, of black and mixed ancestry, who participated in the South African Diabetes Prevention Programme (SADPP) study. The SADPP study is a cluster randomized control trial. Participants were screened using a brief questionnaire to ascertain basic demographic information. The Global Physical Activity Questionnaire was used to determine physical activity and SB. Standardized anthropometric and blood pressure measurements were taken to estimate risk of T2DM using the African Diabetes Risk Score. T2DM was classified based on an oral glucose tolerance test.

RESULTS

(Not applicable)

CONCLUSION

Knowledge of the correlates of SB will give us an idea of how much SB people are engaging in and reasons why people are engaging in these behaviours. This knowledge could aid intervention development aimed at reducing SB and ultimately decrease the risk of developing T2DM. Also, transferring this knowledge to the community will empower them to make better decisions regarding SBs.

37. Dietary cost in relation to dietary diversity and nutrient adequacy in children

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BACKGROUND

Children less than 2 years of age have high nutrient needs to support growth and development, and therefore need nutrient dense foods. It has been documented that a diverse diet is significantly associated with micronutrient adequacy in young children. The aim of the study is to determine the association of dietary cost with dietary diversity and nutrient adequacy in breastfeeding and non-breastfeeding children aged 12 to 24 months in resource poor settings.

METHODS

This study will use an existing dataset consisting of pooled previously collected 24-hour dietary recalls for babies 12-24 months old (n = 1751). The 24-hour recalls were recoded to ensure that coding was standardized; food intake data was converted to nutrients using the 2017 South African Food Composition Database, which includes an updated section on infant foods. Food prices for various food items were entered into the dataset. Cost of the diet will be calculated. A dietary diversity score will be calculated. The mean nutrient adequacy ratio will be calculated as an average of the nutrient adequacy ratios of the individual nutrients of interest. Associations of diet cost with dietary diversity and nutrient adequacy will be determined using correlation analysis for breastfed and non-breastfed babies aged 12- 24 months respectively.

RESULTS

Results are not yet available. My results will indicate association of cost of diet with dietary diversity and nutrient adequacy

CONCLUSION

My research will contribute towards developing guidelines and tools to assist mothers/caregivers from resource poor communities to plan a varied and nutritionally adequate diet for their children at the lowest possible cost. Improving dietary intake of children during the first two years of life will contribute towards the fight against the burden of malnutrition in South Africa. Ultimately, government will be spending less in plight to fight child malnutrition and realizing the achievement of Sustainable Development Goal 2.

38. Changes in cytokine and chemokine responses in plasma during TB treatment

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BACKGROUND

Tuberculosis (TB) is a chronic disease caused by Mycobacterium tuberculosis (Mtb)). The immunological host response against Mtb is a complex interaction between innate and adaptive immune responses. Mtb infection activates protective cell-mediated immune responses and innate immune cells such as dendritic cells, alveolar macrophages and natural killer cells, which secrete several inflammatory cytokines. This study aimed to identify biomarkers that predict an effective response to TB treatment by evaluating the differences in plasma cytokine abundance between three TB treatment responsive groups.

METHODS

Participants included those that were able to clear differentially culturable bacteria within the first two weeks of treatment (treatment-responsive), those with delayed ability to clear these organisms (delayed-responsive) and those whose TB bacterial counts persisted during treatment (non-responsive). We used a Luminex Bead Array Multiplex Immunoassay, to quantify cytokines and chemokines in plasma from these groups. Statistically significant differences between these groups were analysed using the Kruskal-Wallis test with Dunn's multiple comparisons and $p<0.05$ was considered statistically significant. GraphPad Prism 6 software was used to perform these analyses.

RESULTS

We observed that when bacterial burdens are actively being reduced in treatment-responsive as compared to non-responsive patients, pro-inflammatory cytokines (IL-3, IL-4, IL-15, IL-20, IL-2 and M-CSF) were significantly increased as early as 2 weeks after treatment initiation. After 4 weeks of treatment, HGF, IL-2, SCF and Tweak displayed a significant reduction in plasma levels of the treatment-responsive patients. The non-responsive patients showed a significant increase in the levels of SDF-1α and IL-18, IL-22, LIF, TNF-RII during the first 2 weeks of treatment as compared to the treatment and delayed-responsive patients, respectively.

CONCLUSION

Our results indicate that some inflammatory markers are elevated in individuals that respond to TB treatment and may contribute to the development of potential diagnostic tests that are important for monitoring the efficacy of TB treatment.

39. The effects of indigenous South African plant extracts (Cotyledon orbiculata and Tulbaghia. Violacea) on triple negative breast cancer cells

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BACKGROUND

Triple-negative breast cancer (TNBC) cells are deficient in estrogen, progesterone, and ERBB2-receptor expression. These tumours are particularly challenging to treat due to their highly invasive nature and relative high low resistance to conventional therapy. In South Africa, TNBC mainly affects younger black women. The purpose of this study was to assess the potential of extracts from two native South African plants, Tulbaghia violacea and Cotyledon orbiculate on TNBC cell lines in vitro.

METHODS

Aqueous and methanol soluble extracts of T. violacea and C. Orbiculata have been effectively prepared. These plant extracts demonstrated cytotoxic activity against the TNBC cell line (MDA-MB-231). The IC50 of crude extracts was determined using cytotoxicity assays. Followed by Fourier Infrared Transformer (FTIR) Spectrophotometer analyzes

RESULTS

The IC50 determined for water abd methanol soluble T. violacea extracts was 70 µg/mL and 110 µg/mL respectively. The IC50 determined for water and methanol soluble C. Orbiculate extracts was 68 µg/mL and 102 µg/mL respectively. Fourier transformer infrared (FTIR) Spectrophotometer of the water and methanol crude extracts revealed the existence of various functional groups, Cotyledon orbiculate methanol extracts contain phytochemicals with hydroxyl, alkyl, ether, ester and halogen groups.

CONCLUSION

Cotyledon orbiculate water extract contains phytochemicals with hydroxyl, alkyl, carbonyls, aromatic, nitro, amine and sulphur derivative groups. Tulbachia violacea water extract ontains phytochemicals with alkyl, methyl, nitro, sulphur derivative and amine groups. These results confirm the presence of secondary plant metabolites, such as alkaloids, saponins, tannins, flavonoids, antioxidants, terpenoids, polyphenols and cardiac glycosides in the leaves of Tulbachia violacea and Cotyledon orbiculate

40. Prevalence of Hypertension and associated risk factors in a rural black population of Mthatha town, South Africa

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BACKGROUND

Globally, 1.39 billion individuals have hypertension, with a prevalence of 31.1%. In Sub-Sharan Africa, South Africa has the heaviest burden of disease with an estimated prevalence between 27-58%. However, a paucity of data exists pertaining to hypertension prevalence in the rural parts of South Africa. This study aims to assess the prevalence and associated risk factors of hypertension amongst rural black population of Mthatha town, Eastern Cape.

METHODS

The present cross-sectional study included black African individuals aged ≥18 years (576 subjects). Sociodemographic information, anthropometric measurements, such as body weight, height and three independent blood pressure measurements were taken using World Health Organization STEPwise questionnaire. Diagnosis of high blood pressure (BP)/hypertension was done in accordance with guidelines provided by American Heart Association (2018). Statistical package for social sciences (SPSS) windows version 16.0 (SPSS, Inc., Chicago, IL., USA) was used to analyse the data. Univariate and multivariate logistic regression analysis was utilized to investigate the associated factors with hypertension.

RESULTS

The mean age of the participants was 46.8 ± 14.5 years. The results demonstrated that 73.4% of subjects had BP in high BP/hypertensive range. In a univariate analysis, of all the participants, male gender, age, western diet, education as well as income status, and overweight/obese status were associated with the BP scores in hypertensive range. However, in the multivariate regression analysis, the only variables that remained significantly associated with hypertensive status were age, BMI, and westernized diet.

CONCLUSION

Prevalence of HTN was high among the black African population of Mthatha town and age, BMI, westernized diet were the most important determinants of hypertension among black African population of Mthatha, South Africa. Male sex and beliefs about HTN were associated with higher odds of being untreated. Moreover, being female, aged and overweight/obese reduces the risks of being untreated.

41. Transcriptomic approach on the early development of severe asthma

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BACKGROUND

Asthma is a chronic inflammatory condition of the airways, with global morbidity estimated at over 300 million and a mortality rate of over 80% in developing countries. The majority of cases are reported to occur within the first 6 years of life. Asthma is principally a Th2-mediated disease which can be controlled using corticosteroids. However, over the years evidence has emerged showing asthma to be a disease of complex nature presenting with multiple endotypes and some of these endotypes often do not respond to standard steroid therapy and their manifestation is poorly understood. Therefore, it is critical to understand, through research, the early events that determine asthma severity development that ultimately result in poor lung growth and function in adults.

METHODS

To study whether childhood exposure to environmental allergens determine asthma severity development, we will model these events in a mouse model of severe asthma. Following exposure of young mice to either house dust mite (HDM) alone or a combination of HDM and lipopolysaccharide (LPS) or ß-glucans, inflammatory responses and pathology will be assessed through flow cytometry, ELISA assay and histology. RNA sequencing will be applied to identify new genes associated with severe asthma. Lastly, TNF-α-deficient mice will be used to elucidate the role of TNF-α as it is one of the cytokines implicated in asthma exacerbation through its function as a chemoattractant for neutrophils and monocytes.

RESULTS

We hypothesize that allergen exposure of young mice at an early lung developmental stage will promote poor lung function and the manifestation of steroid-resistant asthma. TNF-α deficiency will render mice steroid responsive.

CONCLUSION

Our project will provide insight into early development of steroid resistant asthma. Furthermore, new diagnostic tools or treatment strategies that we will be uncovered will likely affect policies related to management of severe asthma in clinics

42. Cross-sectional study of prevalence and determinants of uncontrolled Hypertension among South African adult residents of Mkhondo municipality

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BACKGROUND

Achieving optimal blood pressure in individuals on hypertension treatment is a serious global health challenge. The actual burden of uncontrolled hypertension is poorly understood, especially in developing countries. Therefore, this study examined the rate and factors associated with uncontrolled hypertension in individuals receiving care at primary healthcare facilities in the rural areas of Mkhondo Municipality in the Mpumalanga Province, South Africa.

METHODS

In this cross-sectional study, individuals attending care? for hypertension were recruited from January 2019 to June 2019 at three primary healthcare centres, namely, Piet Retief hospital, Mkhondo town clinic and Thandukukhanya community health centre. Uncontrolled hypertension was defined as systolic blood pressure ≥ 140mmHg and diastolic blood pressure ≥ 90mmHg in accordance with the South African Hypertension Society guideline (2014). Multivariate logistic regression (Forward LR method) analysis was used to identify the significant determinants of uncontrolled hypertension.

RESULTS

The majority of participants were; 55 years old and above (69.0%), Zulus (81.2%), non-smokers (84.19%) and had been diagnosed with hypertension for more than a year prior to the study (72.64%). The overall prevalence of uncontrolled hypertension was 56.83% (n=187) with no significant difference between sexes; 57.38% males versus 56.88% females, respectively. In the multivariate logistic regression model analysis, after adjusting for confounding variables, obesity (AOR=2.90; 95% CI 1.66-5.05), physical activity (AOR=4.79; 95% CI 2.15-10.65) and HDL-Cholesterol (AOR=5.66; 95% CI 3.33-9.60) were the significant and independent determinants of uncontrolled hypertension in this cohort.

CONCLUSION

The high rate of uncontrolled hypertension in this study setting can largely be attributed to obesity, physical activity and dyslipidaemia. Treatment will require the collaborative efforts of individuals, clinicians and health authorities. These determinants should be addressed decisively to achieve the blood pressure treatment targets in this study population.

43. Prevention of Doxorubicin-induced cardiotoxicity: A mechanistic study

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BACKGROUND

In a recent study, we demonstrated the prophylactic effect of Pinocembrin (Pin) against Doxorubicin (Dox)-induced cardiotoxicity. However, literature indicates that during chemotherapy, distinct bioenergetics dysfunction in cancer mitochondrial subpopulations may be reversed by the co-administrative use of cardioprotective agents. To address this, the degree of impaired mitochondrial function associated with the combined use of Dox plus Pin, using an MCF-7 breast cancer cell model was studied.

METHODS

To mimic a clinical setting of chronic Dox administration, MCF-7 cells were treated with 0.5μM of Dox for 6 days. The effect of Pin on Dox-induced mitochondrial damage was assessed by co-treating the cancer cells with Dox (0.5μM) plus Pin (1μM) for the same treatment duration. Untreated cells served as the vehicle control and cells treated with Pin (1μM) alone were used to establish the compounds anti-cancer properties. On day 7 mitochondrial bioenergetics was quantified using the Seahorse XF Cell Mito Stress Test Kit.

RESULTS

Co-treatment with Dox plus Pin enhanced the basal and spare respiratory capacity of the MCF-7 cells, suggesting the compounds' ability to compensate the cells energy demands. However, no significant difference in the cells maximal respiratory capacity or rate of ATP turnover was observed. Furthermore, the cancer cells co-treated with Pin presented with impaired coupling efficiency, respiratory control ratio and state apparent which were comparable with that detected in cells treated with Dox alone. Despite previous reports, Pin displayed no anti-cancer properties, at the tested concentration, as demonstrated by the preserved bioenergetics of the MCF-7 cells.

CONCLUSION

Although Pin, as an adjunct to Dox, influenced the respiratory parameters of the cancer cells, this effect was insufficient to ameliorate the cells mitochondrial function as determined by the reduced mitochondrial flux ratios.

44. Investigating the role of Protein Kinase C zeta during Mycobacterium tuberculosis infection in mice and human macrophages

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BACKGROUND

Protein kinase C zeta (PKCζ) is a member of the PKC of the serine/threonine kinases family which play various roles in cellular responses such as proliferation, differentiation, and secretion. It has been demonstrated that PKCζ activates MAPK and NF-kB signalling pathways which are crucial in regulation of host responses against danger signals. We conducted a pilot study where we infected human monocyte-derived macrophages with Mycobacterium tuberculosis (Mtb) and measure mRNA expression of PKCζ. We observed that PKCζ was significantly upregulated post Mtb infection. This suggest that PKCζ might be playing a role during Mtb infection and disease progression. We, therefore, aim to elucidate the role of PKCζ during Mtb infection in mice and human macrophages.

METHODS

To determine whether deletion of PKCζ has any effect on mice homeostasis, we will characterize the global knockout of PKCζ and macrophage specific deletion of PKCζ in mice at naïve state compared to their littermate control mice. We will then determine the role of this PKC isoform during Mtb infection in vivo. We will also evaluate the effect of PKCζ specific-peptide inhibitor (ZIP) and knockdown in human monocyte-derived macrophages during Mtb infection. We will also determine the direct role of PKCζ by over-expressing using lentivirus particles in macrophages during Mtb infection.

RESULTS

The results obtained from this study will give us a better understanding of the role PKCζ at macrophage level in TB and whether it can be used a therapeutic target for adjunctive TB treatment.

CONCLUSION

Targeting the host immune responses offers an advantage in reducing the emergence of the drug resistant strains of Mtb. This study will uncover whether macrophage-specific PKCζ play a host detrimental or protective role during TB infection. This has a potential for the development of vaccines and new drug treatments to prevent burden of TB.

BONGANI MAYOSI NATIONAL HEALTH SCHOLARSHIP PROGRAMME (BM – NHSP)

45. Intimate Partner Violence and growth outcomes through infancy: a longitudinal investigation of multiple mediators in a South African birth cohort

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BACKGROUND

Growth faltering during early childhood represents a significant barrier to health. Research has shown an association between maternal intimate partner violence (IPV) and infant growth. However, this relationship isn't well understood. We investigated longitudinal postnatal IPV and infant growth as well as whether maternal depression, tobacco use, alcohol use or infant hospital admission mediated these relationships.

METHODS

Mothers were enrolled into the Drakenstein Child Health Study (DCHS) antenatally and mother-infant pairs followed from pregnancy until 12 months of age. Comprehensive psychosocial data at 10 weeks and 6 months and nutritional and clinical data at 14 weeks, 6, 9 and 12 months were included. Linear mixed effects models were used to predict longitudinal postnatal growth through infancy and linear mixed effects mediation models were used to investigate mediation.

RESULTS

Among 856 mother-infant pairs, contributing 2,265 observations through 12 months, emotional IPV was associated with reduced length-for-age z-scores (LFAZ) through 12 months. No IPV sub-types were associated with weight-for-age z-scores or weight-for-length z-scores. In mediation analyses, postnatal tobacco use mediated the relationship between emotional IPV and LFAZ (proportion mediated = 20%; direct effect p-value=0.144, 95% CI -0.05, 0.01; tobacco indirect effect p-value <0.001, 95% CI -0.01, 0.00).

CONCLUSION

These findings contribute to a growing body of evidence showing that IPV may be detrimental to infant growth. Our study highlights the potential role of emotional IPV as a risk factor for compromised infant growth; further it reveals the potentially important role of tobacco exposure as a mediator in this relationship.

46. Paper Presentation: Mine-affected communities' psychological experiences of ecological degradation and resistance in Rustenburg, South Africa

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BACKGROUND

Extractive industries have a deleterious impact on social ecologies. Mining is one of South Africa's main industries, and communities resistance takes place in these extractive zones. Radical ecopsychology postulates that meaning is co-created through dialogical interaction between Society, Nature and Psyche, and that an injury to one domain influences others. This qualitative case study aims to explore and describe the psychological impact of ecological degradation in the extractive mining context of Rustenburg, North West province, South Africa.

METHODS

Data collection took place in August 2019. Individual semi-structured interviews were conducted with 10 participants, of which four were also interviewed as part of a focus group. English and Setswana interviews were conducted. NVIVO qualitative data analysis software was used to conduct the thematic analysis. Radical ecopsychology served as a theoretical framework and liberation psychology was integrated to allow for further interpretation.

RESULTS

All participants reported psychological distress related to social ecological changes. Place severing was described as a novel psychological distressful process that occurs when the dialogical relationship to place is hindered, distorted or damaged.

CONCLUSION

The interpretation of these findings contributes to radical ecopsychology and liberation theories. Further research is warranted to assist in documenting and overcoming the structural dynamics that perpetuate psychological distress within extractive zones. However, community psychologists must also grapple with the practical and ethical dilemmas of working within these contexts.

47. A systematic review of internet-based interventions for PTSD and ASD with and without support

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BACKGROUND

Posttraumatic stress disorder (PTSD) is a prevalent and impairing mental health condition in the general population and if left untreated, it can have substantial negative effects on both social and relational functioning. Increased global internet access creates a favourable landscape for the use of internet-based interventions to assist with management of mental health challenges

OBJECTIVE

In this systematic review, we aim to answer the research question of whether there is a difference in treatment outcome between supported and unsupported internet-based interventions for PTSD and Acute Stress Disorder (ASD). We further aim to determine whether there is a difference in treatment outcome depending on the qualification of the e-coaches/provider of support.

METHODS

We will perform a systematic review of the scientific literature including all studies that fulfil our inclusion criteria. Independent reviewers will conduct searches in the following electronic databases: Pubmed, Embasse, PsychINFO, PTSDPlus, and Google Scholar. Reference lists of scrutinised studies will be searched to identify relevant studies the reviewers may have missed during the electronic searches, and we will also e-mail corresponding authors to ask them to share unpublished data. Articles we do not have full access to will be marked, and these articles will be requested from the Stellenbosch University library. Two reviewers will independently conduct standardised screening, eligibility assessments, data extraction and quality assessments. We will then undertake a qualitative synthesis of the benefits, harmful effects, mechanisms of change, and predictors of outcome. The review will include studies of internet-based interventions for PTSD/ASD which we will separate according the whether or not support was provided.

RESULTS

Prior research on internet-based interventions differ in their procedures in terms of self-help alone or supported interventions. Some research suggests that technology-based self-help interventions that were supplemented with clinician support increased treatment utilization and effectiveness. We expect a difference in treatment outcomes according to the presence or absence of support, and the qualification of the support provider.

CONCLUSION

This systematic review will contribute to a better understanding of whether internet-based interventions are more effective when supplemented with support, and whether the type of support and qualification of the type of support provider affects outcomes.

48. Perinatal Mental Health and Infant Neurodevelopment – Evidence from LMICs. A Systematic Review

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BACKGROUND

There is an extensive lack of awareness of maternal mental health and its impact on child development in low- and middle income countries (LMICs). The aim of this systematic review was to analyze evidence for various maternal perinatal mental health disorders and their association with different domains of infant and toddler neurodevelopment during the first two postnatal years in LMICs.

METHODS

A comprehensive literature search was conducted within six databases from Jan 1990 – April 2019. Meta-analysis could not be conducted due to the variability in the reported maternal mental health disorders and the different times of assessment of exposures and outcomes. All included studies were narratively synthesized.

RESULTS

A total number of 3771 initial hits were found; of these, 122 studies were conducted in LMICs. Twenty-four studies, nine cross-sectional and 15 longitudinal cohort studies, were included. Three studies were conducted in low-income, 11 in lower-middle-income and ten in upper-middle-income countries. The majority of studies (22 out of 24 studies) assessed maternal mental health postnatally and 14 of these 22 studies found a significant association between maternal mental health disorders and infant and toddler neurodevelopment. Five of the ten studies reporting on exposure to prenatal mental health found a significant association. The most common maternal mental health disorder studied was depression, while the main neurodevelopmental outcomes assessed were motor, cognitive and language development.

CONCLUSION

Maternal perinatal mental health disorders and their association with different domains of neurodevelopment in LMICs is still inconclusive due to a limited number of papers. Mother-infant dyads in LMICs are exposed to multiple and cumulative risk factors and causal pathways between maternal mental health and infant neurodevelopment are still poorly understood. A better understanding of these causal pathways, especially modifiable factors, is of utmost importance for identifying and managing mothers with mental health disorders and the wellbeing of their offspring. Routine maternal mental health screening as a component of obstetric care and well-baby clinic visits should be a public health priority in LMICs.

49. Viral load turnaround time and monitoring among pregnant and breastfeeding women, a simulation study

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BACKGROUND

Routine viral load (VL) testing is the gold standard for monitoring response to antiretroviral therapy (ART) in people living with Human immunodeficiency virus (HIV). Compared to alternatives, VL monitoring ensures timely identification of treatment failure and ART non-adherence, thus improving health outcomes of HIV patients and reducing the risk of HIV transmission, particularly in the case of mother-to-child-transmission (MTCT). However, these benefits of VL monitoring can only be realised once the test results are returned to the patients. The aim of this study is to investigate the impact delays in test return have on VL monitoring predictive performance during pregnancy and breastfeeding.

METHODS

A search for literature on the current turnaround times reported in sub-Saharan Africa (SSA) was conducted in PubMed using the following search terms; HIV, viral load, turnaround time/ delay and SSA. The extracted estimates were applied to an existing VL mathematical model that simulates ART adherence and maternal VL, during the periods of pregnancy and breastfeeding. The VL monitoring strategies evaluated included a variety of current guidelines, from both developed and developing countries.

RESULTS

The search yielded a total of 43 articles of which 8 were included in the review and estimates/ parameter sourced. A wide variety of VL turnaround times were reported in SSA. The following mean VL turnaround times were reported in 2016; Cote d'Ivoire 50 days (66% VL<1000 copies/ml), Kenya 36 days (81% VL<1000 copies/ml), Malawi 42 days (89% VL<1000 copies/ml), Namibia 4 days (87% VL<1000 copies/ml), South Africa 3 days (83%) and Uganda 28 days (92% VL<1000 copies/ml). Analysis of the VL sim model still to be completed.

CONCLUSION

This is the first study to evaluate the impact of VL turnaround times on a variety of potential VL monitoring strategies for pregnant and breastfeeding woman. Long delays in return of VL tests results have considerable impact on the utility of VL testing especially during pregnancy and where late gestation VL tests are recommended.

50. Cannabis use and longitudinal clinical outcome in schizophrenia patients

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BACKGROUND

Cannabis use is associated with an unfavourable course of illness in schizophrenia, although several factors may confound this association. In this longitudinal study, we explored the influence of cannabis use on clinical and treatment outcomes in 98 patients with first-episode schizophrenia spectrum disorders treated with a long acting injectable antipsychotic over 24 months.

METHODS

Using mixed models for repeated measures, we compared visit-wise changes in psychopathology, social and occupational functioning and quality of life between recent/current cannabis users (n=45) and non-users (n=53).

RESULTS

There were no significant group by time interactions for any of our outcomes, and with the exception of poorer functionality in cannabis users at baseline, no significant differences in these domains at baseline or month 24 in the MMRM models. However, more cannabis users met our operationally defined relapse criteria compared to non-users, and more frequent cannabis use over the course of treatment, as assessed by positive urine toxicology testing, predicted relapse.

CONCLUSION

Our results suggest that, when treatment adherence is assured, cannabis use does not have a substantial effect on outcome in the domains of psychopathology, functionality and quality of life, although risk of relapse is increased. Cannabis use may directly reduce the threshold for psychotic breakthrough, in addition to a mediating role for non-adherence.

51. Tuberculosis Infection and Disease In HIV-infected Adolescents on ART

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BACKGROUND

There are limited data on tuberculosis (TB) in adolescents living with perinatally-acquired HIV (PHIV+) in high burden settings. We examined the incidence and determinants of TB infection and TB disease in the Cape Town Adolescent Antiretroviral Cohort.

METHODS

PHIV+ adolescents between 9-14y, on ART for more than 6 months in routine public sector care and age-matched HIV-uninfected children were enrolled between 2013-2015 and followed 6-monthly until end of 2018. Symptomatic screening (including history of having a TB contact and or being on Isoniazid prophylaxis) for TB, chest radiograph, sputum for Xpert MTB/RIF, microscopy and culture, viral load and CD4 count were performed at enrolment and annually. QuantiFERON (QFT, Qiagen, South Africa), a measure of TB infection, was done at enrollment and then annually if prior QFT was negative. TB infection was defined by a QFT of >0.35 IU/ml in the absence of signs and symptoms of TB. TB diagnosis was defined as definite (culture-confirmed) or probable (clinical case definition). Time to event analyses were used to describe the incidence and determinants of TB infection and TB disease.

RESULTS

485 PHIV+ and 95 HIV- participants (median age 12 years [IQR:10.6-13.3]; 50% male) had QFT results at enrolment. PHIV+ had a median CD4 of 715 cell/μL (IQR:564-959) and 365 (75%) had viral load <40 cps/ml. 61% of PHIV+ had a history of TB disease before enrolment (vs 3% in HIV-, $p<0.01$) and 27% were on INH prophylaxis (vs 4% in HIV-) but with no difference in QFT positivity at enrolment (33% vs 28%, $p=0.34$). Over 3 years of follow-up, HIV+ participants had a similar rate of QFT conversion compared to HIV- [7.4 (5.9-9.4) vs 8.7 (CI:5.6-13.7) per 100- person years (PY), $p= 0.31$]. HIV+ participants had a higher rate of TB [2.2 (CI:1.6-3.1) vs 0.3 (0.00-2.2) per 100- PY, $p= 0.07$]. Forty-six percent of HIV+ participants with TB were QFT+, although not all HIV+ participants had a QFT close to their TB diagnosis.

CONCLUSION

In this high TB burden setting, the rate of QFT conversion did not differ between PHIV + and HIV- adolescents, but PHIV+ have a higher incidence of TB disease despite ART. INH prophylaxis, ensuring adequate viral suppression and other interventions are needed to reduce TB incidence during the adolescent period.

52. Excess mortality in TB patients diagnosed at hospital vs at primary health care in South Africa

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BACKGROUND

In South Africa, low tuberculosis (TB) case detection and high overall case fatality remain important challenges. In the Western Cape Province, patients diagnosed with TB at hospital level may start TB treatment but must typically attend a primary health care facility (PHC) for TB registration, and for treatment to be continued. We aimed to evaluate mortality in patients routinely diagnosed with TB at a hospital and PHC in Cape Town, South Africa.

METHODS

Retrospective analysis of all routine TB data from the integrated provincial health data centre which harmonises all electronic health data sources. All patients with a laboratory or clinical diagnosis of TB at PHC, district or tertiary hospitals in 2 sub-districts of Cape Town, were identified between October 2018 and February 2020. Logistic regression was used to investigate predictors of mortality and a Kaplan Meier survival curve described survival over time.

RESULTS

Of 16,075 TB patients, 3,574 (22%) were diagnosed at hospital and 12,501 at PHC; 15,112 (94%) initiated TB treatment, and 14,057 (88%) linked to PHC for ongoing TB treatment. A total of 977 (6.1%) patients died, including 195 (20.3%) pre-treatment. Multivariable analysis suggested that age >25 years, HIV infection with and without ART, extrapulmonary TB, drug-resistant TB, failing to start TB treatment and hospital-based diagnosis were independently associated with higher mortality. Of TB patients diagnosed at hospitals who did not start TB treatment, 70% died within 2 weeks of their diagnosis.

CONCLUSIONS

Individuals diagnosed with TB in hospitals contribute significantly to TB-associated mortality. A TB diagnosis made at hospital level reflects more severe and advanced TB disease with possibly additional risk factors and higher mortality risk. TB patients diagnosed at hospital present an opportunity to identify those at high risk of early and overall mortality, where appropriate treatment should be rapidly initiated.

53. The intergenerational transmission of socioeconomic inequalities in overweight and obesity from mothers to their offspring in South Africa

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BACKGROUND

Overweight and obesity impact the health capital of parents and offspring. In South Africa,13% of children were overweight; and 27% and 41% of women aged 15 years and above were overweight and obese, respectively in 2016. This study estimates and decomposes the socioeconomic inequality in the intergenerational transmission of overweight and obesity in South Africa.

METHODS

Data were drawn from the 2017 National Income Dynamic Study, which collected anthropometric and socioeconomic information. Non-pregnant mothers aged between 15 and 49 years and their offspring 0 -14 years were included in the analysis. Dependent variables used in this study was the intergenerational transmission of overweight and obesity. The concentration index was used to assess socioeconomic inequality. A positive index means that intergenerational transmission of overweight and obesity from mothers to their offspring is more likely among the richer while a negative index signifies the opposite. This index was decomposed to understand the drivers (i.e. contributions of the determinants) of socioeconomic inequalities in intergenerational transmission of overweight and obesity from mothers to their offspring. Analyses were stratified by offspring sex.

RESULTS

The concentration indices for the intergenerational transmission of overweight were consistently positive for both sexes (0.13 and 0.17 for boys and girls, respectively). Similarly, the concentration indices for the intergenerational transmission of obesity were consistently positive for both sexes (0.27 and 0.21 respectively for boys and girls). Maternal socioeconomic status and/or those who self-identified as Black African, relative to other population groups, are central determinants of socioeconomic inequality in intergenerational transmission of overweight and obesity for boys and girls. A mother's lack of exercise (26.4%) is also a significant determinant of the intergenerational transmission of obesity for boys.

CONCLUSION

Socioeconomic inequality in the intergenerational transmission of overweight and obesity is concentrated among the rich for both boys and girls. Interventions targeting the rich and mothers who self-identified as Black African are one of the ways to reduce pro-poor

socioeconomic inequality in the intergenerational transmission in overweight and obesity for boys and girls. In addition, incentives to counteract poor exercise habits are likely to reduce pro-poor socioeconomic inequality in the intergenerational transmission of obesity for boys.

54. Understanding why individualised research requires an appropriate design and analysis: simulation study

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BACKGROUND

When designing research, most researchers tend to focus only on preventing type I errors and not on appropriately powering the study. Due to this, many studies lack sufficient power to detect the effects they are studying. This is further exacerbated by inappropriate choices of design and analysis. While this is a problem within research more generally, it is even more problematic for individualised research. This is because investigating individualised effects significantly reduces the power of the analysis compared to a conventional approach. This study serves to illustrate these problems and provides suggestions on how to avoid the most common pitfalls.

METHODS

Data were simulated 10,000 times for each of three different scenarios, namely: 1) no differential treatment effect, 2) differential treatment effects in the same direction, and 3) differential treatment effects in opposite directions. These simulations were repeated for four different effect sizes, namely: a) no effect, b) small effect (d=0.2), c) medium effect (d=0.5), and d) large effect (d=0.8). The data were analysed using a standard regression model, and effects were considered significant if they were under the 5% level.

RESULTS

Examining the three scenarios using a medium effect size; 98.9%, 65.1%, and 5.8% of the simulations had significant overall treatment effects under scenarios 1, 2, and 3, respectively. However, introducing an interaction effect to the model for scenarios 2 and 3 to account for differential treatment effects increased the proportion of significant regressions to 77.7% and 97.7%, respectively. Thus, failing to account for the differential treatment effects can have a profound impact on the results of a study and may lead to treatments being wrongly discarded.

CONCLUSION

This study, together with previous work, highlights the importance of improving the design and analysis of research involving individualisation and provides recommendations for how this can be done.

55. Cancer Stem Cells Enhance Chemoresistance and Metastatic Behaviour in Human oesophageal cancer

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BACKGROUND

Although oesophageal squamous cell carcinoma (OSCC), causes significant deaths throughout the world, especially in the developing world, it is one of the least studied cancers. Despite great advances having been made in OSCC diagnosis and treatment, current therapies fail to prevent therapy resistance, relapse and metastasis. Chief among the culprits causing therapy resistance and relapse is cancer stem cells (CSCs). CSCs have been proposed to self-renew and among the main drivers of cancer the initiation and progression. Thus, CSC may have prognostic value. The coupling of classic therapies such as chemotherapy with those targeting CSCs may provide effective and durable treatment against chemo-resistant disease.

METHODS

We evaluated the expression of CSC markers in clinicopathological-confirmed OSCC tissues versus normal tissues and performed *in vitro* biochemical analysis to ascertain the prognostic value of CSCs in oesophageal cancer. CSC markers were evaluated by using antibodies against ALDH1A1, CD44 and CD133. *In vitro* sphere-formation, migration, colony formation, drug response and the expression of CSC and self-renewal markers were used to compare parental OSCC cancer cells versus isolated CSCs.

RESULTS

Clinical OSCC biopsies stained strongly for the CSC markers, CD44 and ALDH1A1, and the proliferation marker, Ki67, demonstrating the presence of CSCs in tumours. FACS isolated side population cells exhibited high levels of CSC markers, self-renewal markers and drug resistance proteins. FACS-sorted side population cells exhibited increased chemotherapeutic drug resistance, colony formation, migration and invasion *in vitro* versus parental cancer cells. Increase in stemness and drug resistance is correlated with activation of survival pathways.

CONCLUSION

Our data show that OSCC CSCs may be contributing to chemoresistance, relapse and metastasis and that CSC marker expression may serve as a valuable predictive indicator for poor prognosis in OSCC cancer patients.

56. Can biomarkers in scalp hair identify patients at risk of a heart attack?

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BACKGROUND

The incidence of acute myocardial infarction (MI) is increasing in South Africa where psychosocial stress in the general population is known to be high. Biomarkers for stress (cortisol, dehydroepiandrosterone), alcohol abuse (ethyl glucuronide) and those associated with an increased risk of MI (high-density lipoprotein cholesterol, triglycerides, glucose) can potentially be measured in hair. Hair testing could help identify at-risk patients and potentially offer opportunities for stress and other biomarker modifications to reduce MI's.

METHODS

This pilot study was designed to compare concentrations of biomarkers in 3cm scalp hair between 30 acute MI patients and 30 age-matched healthy controls. Cases are patients admitted to Groote Schuur Hospital cardiology wards, and controls are people visiting the hospital with no history of heart disease. Hair samples were collected 3-5 days after an MI, to compare 1) cortisol:dehydroepiandrosterone ratio; 2) ethyl glucuronide; 3) hair lipids (high-density lipoprotein cholesterol and triglycerides) and 4) hair glycation. Biomarkers will be measured using emerging mass spectrometric techniques (GC-MS/MS, LC-MS/MS) as well as thin layer chromatography coupled to flame ionization detector (TLC-FID), enzyme-linked immunosorbent assay (ELISA), and Fourier-transform infrared (FTIR) spectroscopy.

RESULTS

All 30 MI patients have been recruited (i.e.,15 ST elevation and 15 non-ST elevation). FTIR spectrum data of hair samples from these participants have been collected. The ELISA method for cortisol has been developed, validated and cortisol data for the 30 cases collected. Data analysis has started for future comparison with that from controls, which are yet to be recruited. Regarding other assays, the TLC-FID for triglycerides and GC-MS/MS for cholesterol have been developed and currently been validated. Cortisol determined by LCMS as a secondary validation technique is currently under development. Finally, assays for glycation and ethyl glucuronide by LC-MS/MS have not begun.

CONCLUSION

Identifying suitable biomarkers for the risk of MI would prove useful for disease prevention, especially as point of care tools.

57. Homocysteine and its relationship with cardiovascular health in adolescents from African descent

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BACKGROUND

Blood pressure (BP) and haemostasis are major risk factors for stroke and have been associated with homocysteine (Hcy) mainly in European populations. Young South Africans, many burdened by stunted growth, could already be at risk for changes in cardiovascular function and have increased haemostatic risk profiles. To better understand early contributing factors for stroke and cardiovascular risk in people of African descent, we determined Hcy associations with detailed cardiovascular risk markers.

METHODS

During the PhysicaL Activity in Youth study, circulating Hcy, anthropometric–, cardiovascular– and coagulation factors, were measured in adolescents (13 to <18 years) (n=255). Partial Spearman correlations adjusted for age and body fat percentage (BF%) and general linear models (GLMs) were used.

RESULTS

Hcy correlated positively with muscle mass ($r=0.28$, $p<0.001$), stroke volume (SV) ($r=0.20$, $p=0.02$) and arterial compliance (CWK) ($r=0.21$, $p=0.01$), but negatively with; BF% ($r=–0.28$, $p<0.01$), fibrinogen concentrations ($r=–0.20$, $p=0.01$) and aortic impedance (ZAO) ($r=–0.29$, $p<0.001$). GLMs with *post hoc* tests revealed fasting glucose was lowest in the first and highest in the fourth Hcy quartile ($p=0.01$). ZAO decreased, whereas CWK increased over Hcy quartiles ($p<0.01$; $p=0.04$). Already, 25% of adolescents were hypertensive, of which 39% fell in the 4th Hcy quartile ($p=0.01$). Regression analysis indicated a strong glucose-Hcy relationship. Stunted adolescents (23%) had unfavourable cardiovascular markers for the entire group (fibrinogen, SV, cardiac output, total peripheral resistance (TPR), ZAO and CWK) and between genders (factor VIII coagulant activity percentage and insulin resistance in boys and fibrinogen, TPR and ZAO for girls) than non-stunted (all $p<0.05$).

CONCLUSION

Adolescence is a critical window for optimising health and well-being. Associations between Hcy and cardiovascular markers were detected, while stunted growth already placed some individuals at a possible increased haemostatic/cardiovascular risk. Manipulation of Hcy, glucose levels and prevention of stunting through diet may be beneficial in preventing cardiovascular outcomes in adulthood.

58. An Incremental cost-effectiveness analysis of a quality improvement model for integrated HIV-TB services within rural KZN

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BACKGROUND

Despite policies and guidelines that are supportive of offering integrated TB and HIV services, gaps in the HIV/TB care cascade remain. Quality improvement (QI) methods are widely recommended as an approach to improve TB/HIV healthcare delivery, however, little is known of the associated costs and cost-effectiveness. This sub-study aimed to evaluate the incremental cost-effectiveness of implementing a QI model on integrated HIV-TB services in two rural districts of KZN, based on a cluster randomised controlled trial (RCT) with a phased QI approach undertaken by CAPRISA.

METHODS

Cost and clinical HIV-TB outcome data were collected from the RCT over the six-month "intensive" phase, July 2017– December 2017. The study estimated costs from a provider perspective in 2017 Rands, using a mixed methodology approach to identify, measure and value the resources utilised within the RCT. To allocate and apportion costs accurately, a time-in-motion analysis was conducted to record the activities of study-appointed QI mentors and a Data Management team. Using the outcome data from the RCT, these costs were then used to calculate incremental cost effectiveness ratios (ICERs) for the specific process outcome measures for the QI intervention arm compared to the standard of care arm.

RESULTS

The total cost of implementing QI in both districts over the intensive phase amounted to R2136227, 40% of which was attributed to staff costs at R824110. Travel amounted to roughly 20% of total cost over this period and capital costs, 30%. The cost per additional patient screened for TB, or tested for HIV amounted to R2 and R12, respectively and the cost per additional patient initiated on IPT, R93, while each additional HIV/TB co-infected patient diagnosed cost R459.

CONCLUSION

Ranking the ICERs in terms of their respective values demonstrates that using QI methods to improve TB screening is the most cost-effective relative to its use on other clinic indicators, while trying to improve the number of HIV-TB co-infected diagnoses using QI was the least cost-effective. These results can inform policy makers of the value for money when designing a national QI intervention.

59. Men's Perspectives on HIV Self Testing in sub Saharan Africa: A Systematic Review and Meta Synthesis

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BACKGROUND

Despite the many HIV testing models implemented in Africa, the level of HIV testing uptake remains relatively poor, especially among men. The HIV self testing (HIVST) model offers an additional model for attracting men. This study aims to compile evidence on men's perspectives on HIVST in sub Saharan Africa.

METHODS

The databases we searched include PubMed/MEDLINE; American Doctoral Dissertations via EBSCO host; Union Catalogue of Theses and Dissertations; SA ePublications via SABINET Online; World Cat Dissertations; Theses via OCLC; ERIC; CINAH; PsychInfo; Embase, Sociological Abstract, Scopus and Google Scholar. We search World Health Organization and The Joint United Nations Programme on HIV and AIDS. We extracted only qualitative information from the included studies, despite the research method used (qualitative or mixed methods). We used the Preferred Reporting Items for Systematic Reviews and Meta Analysis. The Mixed Method Appraisal Tool version 2018 was used to determine the methodological quality of the included studies. NVivo version 11 was used for thematic analysis.

RESULTS

A total of 2053 articles were identified by our initial search criteria. After following different screening stages and adhering to the inclusion criteria, only 12 studies were included to data extraction and quality assessment stage. Results of this study revealed that men's knowledge of HIVST remain low in SSA, despite the high acceptability. The following key themes emerged from the meta synthesis of the included studies: acceptability of HIVST; need for HIVST counselling; confidentiality of HIVST; convenience of HIVST; and accuracy of HIVST. The study shows that while HIVST provides men with an alternative confidentiality

secured and convenient testing model, the potential psychological and physical harm arising from the lack of pre and post HIV counselling aimed at addressing reactions to HIV test positive outcomes, remain a challenge. Due to the confirmatory HIV test required after the initial HIVST, the trust in the accuracy of HIVST results remain low

CONCLUSION

The introduction of HIVST strategy has a potential of improving men's uptake to HIV testing services, thereby contributing towards addressing the first cascade of the 90 90 90 strategy. While HIVST is aimed at addressing many men's barriers to attending clinic settings, such as, confidentiality and convenience, it hardly addresses the HIVST counselling and accuracy concerns. Empirical evidence on the risk benefit analysis associated with HIVST testing strategy is still required, especially among men in Africa.

60. Living with, adapting to and self-managing HIV as a chronic illness: A scoping review protocol

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BACKGROUND

The experience of living with a chronic illness from the chronically ill individual's perspective, adaptation, is a well-researched phenomenon for many common chronic illnesses, including diabetes mellitus and rheumatoid arthritis, among others. Within its definition, the concept embeds the notion of self-management. Self-management, in turn, may also be perceived as an outcome of adaptation. Fundamentally, adaptation is an important concept in understanding the trajectory and eventual outcomes of living with a chronic illness. Application of these two concepts, adaptation and self-management, to HIV as a chronic illness, however, is limited. Specifically, the process of adaptation to living with HIV as a chronic illness and how the processes effect and affect self-management by adults living with HIV are not well understood. In this paper, we describe a protocol for our scoping review of adaptation to living with HIV as a chronic illness, we first interrogate concepts that have been studied and we then trace the link between the concept of adaptation and any of the patient self-management aspects.

METHODS

This scoping review protocol will follow the scoping review methods proposed by the Johanna Briggs Institute. In addition, our protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for scoping reviews (PRISMA-ScR) and was registered with the Open Science Framework on 2 August 2020 (osf.io/3zv4f). Embase,

MEDLINE, Web of Science Core Collection, and Google Scholar databases will be searched, as the combination has been proposed to yield optimal results. For comprehensiveness, CINHAL and PubMed will also be searched. A search in Social Science Research Network (SSRN) eLibrary and Open Access Theses and Dissertations will gather grey literature and reference lists of included sources will also be screened. The study selection process will involve two phases: (1) a title and abstract review and (2) full text review. In the initial phase, two researchers independently will review the citations retrieved from the search to determine eligibility based on the defined inclusion and exclusion criteria. Related articles will be included if they are empirical studies that address the experience of living with HIV as a chronic illness.

RESULTS

At a broader level, the review work will build on a growing body of literature that examines the concept of adaptation to living with a chronic illness, specifically in our case, HIV, and its influence over patient outcomes. A unique aspect of the current scoping review is that it not only explores literature on concepts of living with HIV as a chronic illness but also attempts to map and document the links between adaptation and self-management, for HIV. Evaluating whether chronically ill individuals successfully adapt to living with chronic illness and their attempts at attaining the ideal of positive living in their illness trajectory, particularly for HIV, is an area within chronic illness care that is relatively unexplored. Exploring and expanding knowledge on these concepts therefore may strengthen HIV chronic care.

CONCLUSION

At a practical level, this work may inform an approach to HIV chronic care by healthcare professionals that recognises the critical role of HIV illness adaptation and its impact on patient outcomes. Furthermore, knowledge gathered from the study may contribute towards a framework that could guide healthcare professionals and significant others in facilitating and assisting PLHIV to successfully adapt to living with HIV, with the aim of assuring better outcomes for the patient.

61. Introducing an arteriovenous fistula pre-cannulation assessment care-bundle to reduce complications in patients with an arteriovenous fistula on haemodialysis

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BACKGROUND

The prevalence of diabetes in sub-Saharan countries is a specific concern, with 9.4 million people living with diabetes in Africa, which is expected to increase to 12.7 million by 2025. Thus, an estimated 6–16% of the sub-Saharan population will be diagnosed with diabetic nephropathy resulting in end-stage kidney disease (ESKD) and requiring renal replacement therapy. In South Africa, for a patient to gain access to treatment on a renal replacement programme, a selection committee reviews each case. Patients diagnosed with ESKD receiving dialysis therapy are at an increased risk of infection because of open vascular access, which is regarded as their lifeline during dialysis therapy. The early detection of arteriovenous fistulae (AVF) complications can benefit the patient because of early diagnosis and treatment. Therefore, it is critically important for staff working in dialysis units to detect AVF complications before initiation of haemodialysis to prevent infection, which may lead to death or prolonged stay in hospitals.

METHODS

This study fits the intervention research model and follows the first four of the six phases of intervention as described by Rothman and Thomas in 1994. The study has been approved by the ethics committee of Stellenbosch University.

RESULTS

The study entered phase 4 in January 2020 as data collected in December 2019 had to be verified, captured and analysed. Results obtained in phase1 of the study assisted the researcher to develop a draft pre-assessment prototype AVF care bundle in phase 2 utilising a nominal group technique before pilot testing. In phase 1 the following major concerns were recorded during the observation phase namely; handwashing, wearing of personal protecting equipment and the use of a glove as a tourniquet.

CONCLUSION

By detecting infection from the AVF early, or determining the incidence of complications relating to AVF failure and infection, we anticipate reducing these complications in patients on haemodialysis in the long-term. With the current Covid-19 situation in the Western Cape the development of a Standing Operating Procedure regarding the pre-cannulation assessment of an arteriovenous fistulae (AVF) may assist the nursing staff reducing vascular access infection.

62. Late Effects Of Childhood Cancer And -Treatment In A South African Cohort

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BACKGROUND AND AIM

Childhood cancer survivors experience late effects following treatment. We documented late effects in a South African cohort.

METHODS

Childhood cancer survivors treated at Tygerberg hospital paediatric oncology unit between 1983 and 2012 were recruited. Appropriate special investigations were done according to the Children's Oncology Group Long-term follow-up guidelines (2013). Data collection included demographic data, socioeconomic status, diagnosis, treatment received and long term effects, graded using the Common Terminology Criteria for adverse events (CTCAE) (2010).

RESULTS

The study included 120 survivors (male:female ratio 1:0.9), mean age at diagnosis of 5 years (median 4.2 years; range 0.5-14.9 years) and at study visit 14.8 years (median 13.4; 6.1 – 37.4 years). The diagnoses were leukaemia (48/120; 40%), renal tumours (20/120; 17%), lymphoma (18/120; 15%), brain tumours (9/120; 8%), rhabdomyosarcoma (6/120; 5%) and other (10/120; 15%).

Treatment modalities included chemotherapy (115/120; 96%), surgery (52/120; 43%), radiotherapy (22/120; 18%) and other (4/120; 3%). A total of 556 clinical abnormalities were detected (mean 4.6/survivor), of which 377 (68%) were cancer-related late effects. These were classified as CTCAE grade 1 (287; 76%), grade 2 (63; 17%), grade 3 (18; 5%) and grade 4 (9; 2%). More than half (210; 56%) (1.8/survivor) were deemed significant. The most common late effects included dental abnormalities (39%), growth retardation (39%), various cytopaenias (22%), anaemia (10%) and obesity (12%). Leukaemia survivors experienced the most late effects (110/377; 29%), followed by brain tumour survivors (63/377; 17%). Survivors with low socio-economic status at diagnosis (80/120;67%) experienced the most late effects (274/377;73%). Almost half (53/120;44%) had poor scholastic performance.

CONCLUSION

Late effects were significant in more than half of this South African cohort, demonstrating the importance of long-term follow-up to improve quality of life. Of note was the increased number of late effects in the low socio-economic group.

63. Fabrication of chitosan/alginate nanoparticles for enhanced TDF delivery across the FGT.

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BACKGROUND & OBJECTIVES

Penetration of antiretroviral (ARV) drugs into the female genital tract (FGT) has been shown to be difficult to predict due to the permeability-glycoprotein (P-gp) transporter. P-gp, also known as MDR1 (multidrug resistance protein 1), plays a major role of transporting drugs in humans. This transporter acts as a physiological barrier to remove toxins from the cell whilst protecting susceptible organs. However, overexpression of P-gp causes efflux of most ARV drugs that are P-gp substrates. This has been observed mostly in the female genital tract, specifically in the placenta, vagina and cervix where P-gp is highly expressed. Tenofovir disoproxil fumarate (TDF), amongst other ARV drugs, is a P-gp substrate and can be effluxed by this transporter. Therefore, we aim to develop a novel nanoparticulate system comprising of TDF and P-gp inhibitors (chitosan and alginate) to enhance TDF drug absorption in the FGT. Nanoparticles were prepared by ionotropic pre-gelation of alginate core with calcium chloride followed by chitosan cross-linking. Then they were characterised by several techniques such as particle size and zeta-potential measurements. The designed formulation had an average size of ± 160 nm and a zeta potential of -23 ± 1.50 mV. These results show that TDF loaded chitosan-alginate NPs could have the potential to improve TDF drug penetration and absorption in the FGT.

64. Iron in HIV-infected schoolchildren: Nutritional status, fractional absorption, and the gut microbiome.

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BACKGROUND

Anaemia is a common co-morbidity of HIV-infection and predicts disease progression and mortality. There is an interplay between iron and inflammation in the causal pathway of anaemia in HIV. Iron supplementation in the presence of chronic infection is debated. In the last decade, the focus shifted to the potential adverse effects of unabsorbed iron on the gut microbiome where it stimulates the growth and virulence of bacterial pathogens. This study aims to compare nutritional status, fractional iron absorption, and the effect of oral iron supplementation on the gut microbiome between HIV-infected and uninfected schoolchildren.

METHODS

We enrolled 8 to 13-year old virally suppressed HIV-infected and uninfected children from similar low-income areas in Cape Town, South Africa. At baseline, we assessed nutritional status using a cross-sectional descriptive design. We performed a randomised case-crossover trial to investigate fractional iron absorption from maize meal, a lipid-based nutrient supplement and oral iron supplements using a stable isotope method. Lastly, we conducted a controlled trial to investigate the effect of oral iron supplementation on the gut microbiome in iron deficient children.

RESULTS

The nutritional status study included 84 HIV-infected and 90 uninfected children. The absorption study included 41 HIV-infected and 42 uninfected children. The effect study included 33 HIV-infected and 31 uninfected iron deficient children. Data analysis is currently underway.

CONCLUSION

This study will add to the paucity of nutritional status data in virally suppressed HIV-infected schoolchildren. It will quantify fractional iron absorption using a gold standard method free of confounding. Ultimately, it offers the potential to inform policy makers of the safety of routine oral iron supplementation interventions in iron deficient, HIV-infected children from a gut microbial perspective. Findings may lead to tailored intervention approaches and policy changes to support safe treatment strategies of iron deficiency anaemia in HIV-infected individuals.

65. Profiling of pharmacogenetic variants and their influence on warfarin dose variability among Southern Africans

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BACKGROUND

Warfarin is the most widely prescribed anticoagulant for the prevention and treatment of thromboembolic diseases. However, warfarin use is complicated by its narrow therapeutic range and inter-individual variability in the starting dose required to achieve a stable international normalised ratio (INR). Genetic and non-genetic factors have been shown to contribute to the observed inter-individual variability in warfarin response, particularly the starting dose needed to achieve INR. Several warfarin dosing algorithms incorporating genetic variants have been proposed, however, they lack inclusion of African populations. Therefore, we set out to determine genetic predictors of warfarin dose in Southern African populations.

METHODS

Genomic characterization was carried out on 462 Southern Africans (i.e. 211 black Africans and 251 mixed ancestry) undergoing warfarin treatment, using the iPLEX PGx74 Mass Genotyping Array. Statistical analysis was performed using STATA for windows taking a 5% significance level.

RESULTS

We report on significant differences in warfarin dose requirements and genetic variants that affect warfarin response between black Africans and the mixed ancestry group. CYP2C9*8, CYP2C9*11, CYP2C rs12777823G>A, CYP2C8*2 and CYP3A5*6 were significantly correlated with maintenance dose distribution among black Africans, whilst among the mixed ancestry, CYP2C9*2, VKORC1 g.–1639G>A and VKORC1 g.9041G>A were the important variants. We report on a cumulative influence of genetic variants explaining 16% and 20% warfarin dose variability among black Africans and mixed ancestry, respectively.

CONCLUSION

We show inter-ethnicity variation in genetic markers important for warfarin variability. We recommend inclusion of African populations in pharmacogenetics-based warfarin dosing algorithms. Furthermore, we report on pharmacogenetic variants that are important to achieve appropriate warfarin starting doses for southern black Africans and mixed ancestry populations.

66. Genome-wide analysis of common and rare variants in the South African Xhosa (SAX) affected by Schizophrenia: a case-control study

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BACKGROUND

Schizophrenia is a disabling mental disorder with a substantial genetic contribution. Both rare and common genetic loci have been associated with the disorder and account for up to 30% of the genetic heritability. 'Missing' heritability may be attributed to various factors, including environmental exposures such as childhood trauma. Most schizophrenia genomics research has been conducted in populations of European ancestry; therefore, little is known about the genetics of schizophrenia in other populations, including Africans.

METHODS

We investigated the contribution of common and rare variants to the risk of schizophrenia among 1100 schizophrenia cases and 1100 controls Xhosa individuals from South Africa. The association of common variants was testing through three exploratory genome-wide association (GWAS) testing: (i) GWAS controlling only for population structure in the form of principal components (PCs); (ii) GWAS controlling for PCs and childhood trauma and (iii) GWAS stratified by sex. Rare variant analysis (allele frequency < 1%) was done using the sequence kernel association test (SKAT). The contribution of copy number variants (CNVs) was assessed through burden and association testing.

RESULTS

The first GWAS yielded a single SNP, rs35172303 (P = 4.74e-08, OR = 0.6004, 95%CI: [0.499,0.721]), in ZFP3 that was significantly associated with schizophrenia beyond the accepted genome-wide significance (gws) threshold of P < 5e-08. After controlling for childhood trauma, four additional SNPs in ZFP3 were associated with schizophrenia beyond gws. Sex-stratified GWAS indicated sex-specific risk loci. The rare variant analysis identified 24 genes that were significantly associated with schizophrenia. CNV burden testing showed that cases have a higher proportion of large CNV losses than controls. CNV association did not implicate the microdeletions at 22q11.2 — the strongest genetic risk factor for schizophrenia.

CONCLUSION

Our results suggest that there may be population-specific risk loci for schizophrenia and highlight the importance of including more diverse samples in psychiatric genomics research.

67. The cancer mortality among economically active South Africans from 1997-2016): Adopting temporal, spatial and health economic modelling approaches

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BACKGROUND

Worldwide, cancer possesses the highest economic impact from premature death and disability when compared to all causes of death. In South Africa (SA), an increasing life expectancy results in a rise of chronic diseases such as cancer. SA has no population-based occupational health surveillance system (OHSS). This study investigated the cancer mortality amongst economically active individuals from 1997-2016 to determine if the South African mortality data can be used as an alternative for OHSS.

METHODS

Secondary analyses were done based on a case-control study design. Deaths due to cancer were identified, and mortality odds ratios (MORs) calculated for economically active individuals using univariate and multiple logistic regression stratified by sex.

RESULTS

Professional men (MORs = 1.6; 95% CI: 1.5 – 1.7) had an increased likelihood of CM. The managerial position was a stronger risk factor for CM among women (MORs = 1.8; 95% CI: 1.6 – 2.0) relative to the unemployed. There was a significant interaction of occupation and the racial group as they acted synergistically to increase the likelihood of CM among white managers, (MORs = 3.5; 95% CI: 2.3 – 5.3) in males and (MORs = 4.4; 95% CI: 2.9 – 6.5) in females. The likelihood of CM increased with age to a greater magnitude in employed individuals than unemployed. However, the women (MORs = 10.3; 95% CI: 8.8 – 12.0) with the age of 60 to 64 years had the higher likelihood of CM than men (MORs = 8.4; 95% CI: 7.4 – 9.7).

CONCLUSION

The CM in the economically active individuals has increased in SA, and such increase may have a negative economic impact. OHSS in SA could have substantial economic and societal benefits.

68. Novel proteomics biomarkers for acral lentiginous melanoma

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BACKGROUND

Acral lentiginous melanoma (ALM) is a subtype of melanoma that is reported to be more prevalent in pigmented skin. We conducted an audit of 7 year-data to 2019 of biopsies from the Combined Melanoma Clinic at Groote Schuur Hospital and identified 252 cases: 30.6% nodular melanoma and 5.2% ALM (proportions per ethnic group: Caucasians: 30.3% and 1.6%, Mixed-Ancestry: 25.6% and 18.6%, Indigenous-Africans: 41.7% and 8.3% respectively). These data confirmed ALM as relatively more common in brown/black skin and presenting with advanced malignancy (Clark level III, IV and V). Targeting BRAF inhibitors improves the overall survival of patients with advanced nodular melanoma by 63%. No clinically effective biomarker-targeting treatment for ALM has been identified to date. This study may allow us to identify potential proteomic biomarkers that can serve as specific targets for therapy and monitoring disease progression.

METHODS

To explore possible disease progression, in vitro treatment resistant models were developed using 4 cell lines [melanoma (UCT-Mel1, A375), malignant fibroblast (HT1080) and normal keratinocyte (HaCat)], all treated with 0.625-10mM of dacarbazine (DTIC), a common melanoma treatment. Proteins from these treated cell lines were subjected to label-free shotgun proteomics. Resulting raw data was pre-processed and subjected to various qualitative and quantitative bioinformatics pipelines. Functional pathway analysis was further performed to evaluate biological process perturbations.

RESULTS

Two heat-shock (housekeeping) proteins were found to be stably expressed in all 4 cell lines. We also discovered three additional proteins, one was associated with tumour formation, another with pathogenic states and the third was a potential molecular target for early diagnosis and therapeutic monitoring of cancer. Pathway enrichment was identified for differentially expressed proteins.

CONCLUSION

These preliminary findings are initial steps toward identification of predictive biomarkers of disease pathogenesis in ALM. Future workplan includes investigation of differentially expressed proteins in formalin-fixed paraffin-embedded clinical samples.

69. The maternal and infant gut microbiome in Foetal Alcohol Spectrum Disorder

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BACKGROUND

Prenatal alcohol exposure (PAE) is the most preventable cause of birth defects, developmental disorders and mental retardation, yet the prevalence of Foetal Alcohol Spectrum Disorder (FASD) in the Western Cape is 20%-28%, significantly higher than the global prevalence of 0.77%. Excessive alcohol intake can result in alterations in gut microbial composition. An altered maternal gut microbiome may translate into abnormal infant gut colonisation, thereby resulting in altered gut microbiota functioning, which may result in increased susceptibility to disease. This study compared the gut microbial composition of pregnant women who have an infant with FASD, and those who do not have an infant with FASD as well as infants who are diagnosed with FASD, and those who are not diagnosed with FASD.

METHODS

A total of 207 pregnant women (139 drinkers and 68 controls) recruited from antenatal clinics in Robertson and Wellington provided stool samples. Stool was collected from 211 infants (142 with PAE and 69 without PAE) born to these women. Each infant was assessed for FASD by triangulating data from infant dysmorphology examinations, neurodevelopmental assessments, and maternal interviews.

16S rRNA V1-V2 region sequencing was performed on microbial DNA extracted from the stool samples. The dada2 pipeline will be used to pre-process the fastq sequencing files, create an amplicon sequence variant table, and assign taxonomy. Differential compositional analyses will be performed using PhyloSeq, while R will be used to compute the statistical analyses of microbial composition and calculate alpha- and beta-diversity.

RESULTS

At 9 months of age, 101 infants (47.87%) had FASD and 110 infants (52.13%) did not have FASD. The gut microbiome results will be discussed pending the release of the 16S rRNA data in July 2020 and subsequent analyses later in 2020.

CONCLUSION

To date, the microbiome has not been studied in the context of FASD. Understanding the association of the maternal and infant gut microbiome with FASD may suggest possible pathways whereby altered microbial profiles could contribute to FASD outcomes.

BIOSTATISTICS HUMAN CAPACITY DEVELOPMENT

70. Generalisation of contingency tables for gene expression readings

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BACKGROUND

The focus of this study is statistical theoretical with the objective to contribute in techniques which can be used in a variety of fields including application in identifying differentially expressed genes. The design of genome experiments typically follow a block design structure (contingency table for read counts), which are reflected via the linear predictor specification. The linear predictor could also include continuous covariates. As the random component allows for a variety of distributions for the response variable, many experimental setups can be accommodated. Following a non/semi-parametric modelling approach, a broader class of members from the exponential family can be accommodated. This generalised experimental design can accommodate gene expression data as the readings can differ vastly depending on the technology used. If microarray technology is used, hybridisation results in an expression intensity which is continuous and if RNA-Seq is used, sequencing results in discrete read counts.

METHODS

The generalisation of the contingency table will be towards the broad class of exponential family distributions, including mixtures of such distributions. Genes which show a similar pattern of expression, under a subset of experimental conditions, can be clustered together using a finite mixture model. Biclustering highlights the potential association between subsets of genes and subsets of experimental conditions by simultaneously clustering genes and experimental conditions. This is opposed to just identifying differentially expressed genes or experimental conditions separately.

RESULTS

The objective of the final results is to present an updated technique which will allow for a more flexible model. This updated technique will make less assumptions than existing techniques used to identify differentially expressed genes by adding a non/semi-parametric extension. The proposed semi-parametric extension addresses caveats of parametric mixture models by accessing non closeform members from the exponential family. Short term results include applying parametric mixture models to microarray and RNA-Seq data to identify differentially expressed, with a future focus of adding a non/semi-parametric expansion.

CONCLUSION

Analysing gene expression readings through this method will present a new approach to clustering genes. The suggested approach will add to the understanding of transcriptome profiling and potentially identifying different underlying mechanisms.

71. Joint Modelling of Longitudinal Colony-Forming-Unit Count and Time-To-Event Data from Tuberculosis Trials

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BACKGROUND

According to the World Health Organization (WHO), tuberculosis (TB) is one of the top ten infectious diseases in Africa that kills most people. The main objective is to find the appropriate medication that can cure such patients and also prevent people from contracting this disease. One of the main challenges in developing new and effective drugs for the treatment of TB is to identify the combinations of drugs that provide a positive impact on patients when subsequent testing in pivotal clinical trials are performed. Current separate statistical models for the assessment of the efficacy of anti-TB drugs include: nonlinear mixed models for colony-forming unit (CFU) counts collected over time, nonlinear mixed models for time-to-positivity (TTP) over time and models for time to sputum culture conversion, based on Kaplan-Meier and Cox proportional hazard models. A combination of the above will be performed using joint modelling, which will link the predictor of survival endpoints with random effects. A comparison will also be made to determine whether the accuracy of estimating parameters improves when using joint models compared with independent models. Joint modelling may lead to an improvement in the efficiency of statistical inferences and reduces bias in efficacy estimates.

METHODS

The methodology is motivated by and applied to CFU counts in bactericidal activity TB trials. A multivariate joint model comprising of longitudinal and time-to-event models will be linked using an association structure that quantifies the relationship between the clinical outcomes of interest. Sensitivity analysis will also be performed to determine the appropriateness and accuracy of the statistical results. We will undertake a literature review of methodological studies that involved joint modelling of longitudinal and time-to-event data. Study characteristic will be extracted, and the relationship between the longitudinal and time-to-event parameters will be investigated.

RESULTS:

Work in progress.

CONCLUSION:

Work in progress.

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE (RCDI): POST-GRADUATE PROGRAMME

72. Momordica balsamina methanol extract induces apoptosis and inhibits selected drug metabolising enzymes

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BACKGROUND

Momordica balsamina, a plant rich in phytochemicals, possesses a wide spectrum of medicinal values. Its leaves are used in many African countries as traditional medicine, typically for treatment of diabetes and malaria. Momordica species are known to possess *in-vitro* antitumor activities. Since conventional medicine has not yet provided cures for several prevalent chronic illnesses; cancer and diabetes, medicinal plants are promising alternatives. Although *M. balsamina* is widely used, scientific evidence regarding its safety and medicinal properties is scarce. This study was aimed at investigating potential anticancer activity of *M. balsamina* and its interaction with drug metabolising enzymes.

METHODS

Effect of the extract and 5-Fluorouracil (as a control) on colon HT-29 and muscle C2C12 cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide (MTT) assay after 24 and 72 hours. Mode of HT-29 cell death was assessed by microscopy using the 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimi-dazolylcarbocyanine iodide (JC-1) dye and acridine orange and propidium iodide (AO/PI) staining and quantified by flow cytometry using annexin-V/PI. Effect on drug metabolising enzymes, (CYP)1A2, 2A6, 2C8 and 2C9 were assessed using Vivid CYP-450 screening kits.

RESULTS

The extract exhibited significant toxicity against colon HT-29 cells (IC50 267 µg/ml) without significant reduction in viability of muscle C2C12 cells, which were used as a model for normal cells, after a 24-hour treatment. 5-Fluorouracil induced cell death (IC50 3.2 µg/ml) after the 72-hour treatment. Moreover, the extract and 5-Fluorouracil induced apoptosis as shown by the AO/PI and Annexin-V/PI assays, in cells after the 24-hour treatment. The extract further significantly inhibited the activity of CYP2C8 and CYP2C9 with an IC50 of 14 µg/ml and 26 µg/ml, respectively.

CONCLUSION

The extract possesses pro-apoptotic activities against colon HT-29 cancer cells and shows potential as candidate for further drug development. However, its interaction with CYP-450 enzymes needs further exploration as it might have unintended consequences for drug use.

73. Investigation of mutations within the Fucosyltransferase gene in children suffering from gastroenteritis (preliminary results)

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BACKGROUND

The *Fucosyltransferase* 2 *(FUT2)* gene synthesizes H type 1 antigens in epithelial mucosa and biological secretions. When *FUT2* is functional, the Fucα1-2Gal-chain can be detected in saliva of individuals termed 'secretors' and not in 'non-secretors'. The *FUT2* gene is associated with susceptibility to acute rotavirus diarrhoea. Rotavirus is the leading cause of diarrhoea in children under five years especially in developing countries. Since the *FUT2* gene controls the expression of H type 1 antigens in secretions, any mutation in the gene could affect susceptibility to rotavirus infection. Our study aimed to investigate the mutations within *FUT2* gene and how these mutations are related to rotavirus diarrhoea.

METHODS

A total of 254 saliva samples were collected from children younger than five years suffering from diarrhoea, seeking medical attention at Oukasie Primary HealthCare and Dr George Mukhari Academic Hospital. Fucα1-2Gal-chain was detected using lectin-based Enzyme immune assay. Total DNA was extracted from 86 randomly selected saliva using QIAamp DNA Mini Kit. Conventional PCR was then performed using the extracted DNA targeting the *FUT2* gene Sanger DNA sequencing was performed and chromatograms edited using ChromasPro. Conservation plot was constructed and compared with known *FUT2* SNPs.

RESULTS

Common missense mutations A73G, C98A, C146T, C390T/G, G514A, G577A/T and G804A were detected in the *FUT2* gene. Nonsense mutation G461A resulted in the lack of Fucα1-2Gal-chain in saliva. Additionally, novel mutations A204G, C249T and G814T were detected in our study.

CONCLUSION

Mutations within the *FUT2* gene are known to be ethnically specific. The new mutations reported in our study need to be investigated for their ethnic preference globally. Furthermore, nonsense mutations other than the common G428A may be conferring non-secretor status in Africans. The investigation on the association of the detected mutations in the 86 children with rotavirus infection is ongoing in our laboratory.

SAMRC SCHOLARSHIP BENEFICIARIES WHO HAVE COMPLETED THEIR DEGREES (MASTERS/DOCTORATE) IN THE PAST 12 MONTHS: BY PROGRAMME

SAMRC CLINICIAN RESEARCHER M.D PHD DEVELOPMENT PROGRAMME			
Name & Surname	Institution	Research Topic	Supervisor
1. Dr Lynnsay Dickson	University of Witwatersrand	Screening and diagnosis of gestational diabetes mellitus in an urban primary health clinic in South Africa	Prof. Shane Norris/ Prof. Eckhart Buchmann
SAMRC INTERNSHIP SCHOLARSHIP PROGRAMME (ISP)			
2. Dr Yonela Ntamo	University of Zululand	The Role of Beta Secretase in Aging Pancreatic Beta cells: A potential Role for Rooibos	Prof Christo Muller/Dr Nireshni Chellan/ Prof Abidemi Paul Kappo
3. Dr Hygon Mutavhatsindi	University of Stellenbosch	"Evaluation of host biosignatures for targeted screening for tuberculosis at the point of care, and monitoring of the response to TB treatment"	Dr Novel Chegou
4. Dr Nokulunga Hlengwa	University of Zululand	Influence of Echinacea purpurea and Lessertia frutescens on the bioavailability and metabolism of ethinylestradiol based contraceptives"	Dr Sandra Bowles/ Prof Christo Muller
5. Ms Noluxabiso Mangwana	Cape Peninsula University of Technology	The in vitro faecal evaluation of prebiotic effects of rooibos phenolic compounds on the gut microbiota of the Vervet monkeys (Chlorocebus pygerythrus)	Prof Christo Muller/ Dr Nthevheleni Thovhogi
6. Mr Mabule Lucas Raphela	University of Cape Town	Targeted depletion of RibF, a putative bifunctional FAD synthetase/ flavokinase in Mycobacterium smegmatis using CRISPR interference.	Prof. Digby F. Warner/ Dr. Melissa Chengalroyen

BONGANI MAYOSI NATIONAL HEALTH SCHOLARSHIP PROGRAMME (BM-NHSP)			
7. Dr Annelene Govindsamy	University of KwaZulu Natal	Neonatal cardiac insulin signaling in a diet-induced diabetes model	Dr Marlon Cerf/ Dr Strini Naidoo
8. Dr Darshini Govindasamy	London school of Hygiene and Tropical Medicine, UK	Wellbeing among adolescents and young adults in sub-Saharan Africa: a mixed methods study of their wellbeing construct, its health correlates and association with access to HIV treatment"	Dr Giulia Ferrari/ Dr Catherine Mathews
9. Dr Njabulo Mbanda	University of Pretoria	The effects of visual aids on the understanding of Human Immunodefiency virus (HIV) health information in persons with low literacy	Prof Shakila Dada/ Prof RW Schlosser
10. Dr Karlien Malan	University of Stellenbosch	"Diversity and Ecology of Astroviruses in South African bats"	Prof Wolfgang Presier/ Dr Stacey Schultz-Cherry/ Dr Ndaphewa Ithete
11. Dr Andrea Papadopoulos	University of Witwatersrand	"Characterisation of M23-domain activators of peptidoglycan degrading amidases in Mycobacterium tuberculosis"	Prof Bavesh Kana
12. Dr Hlengiwe Gwebu	University of Kwa-Zulu Natal	Schistosomiasis and soil-transmitted helminthiasis prevalence and risk factors among preschool children aged (1-5 years) in rural KwaZulu-Natal	Prof Moses Chimbari
13. Mr Brian Thabane Rambau	University of Cape Town	"Identifying and quantifying organism interaction in longitudinal child health studies"	Dr Maria Lesosky

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