RCD GRANT HOLDERS' ANNUAL MEETING 2023

SAMRC Conference Centre, Cape Town
8-9 March 2023

Building research leadership for societal impact

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MESSAGE FROM THE PRESIDENT AND CEO OF SAMRC

Professor Glenda Gray

A very warm welcome to all of you at our Grant Holders Annual Meeting for the year 2023 taking place under the theme of "*Building research leadership for societal impact*". We are excited to have all of you here and look forward to hearing your ideas and perspectives.

As the South African Medical Research Council (SAMRC), through our Division of Research Capacity Development (RCD), we developed funding mechanisms to support emerging research leaders in different areas of health research and institutions across the country for the long-term sustainability of South African health research. The purpose of RCD grant programmes is to create an opportunity to fast-track and transition early-career and mid-career scientists to independent research leaders and ensure the ability to provide better solutions to various health problems. This RCD Grant Holders Annual Meeting is an opportunity for the RCD grant beneficiaries to meet with each other and with the SAMRC leadership and share their research.

Our theme for this year's meeting was carefully chosen because building research leadership for societal impact is essential for the advancement of society. Our work means nothing if it doesn't positively impact society. It is important for us as SAMRC to support, through research grants, individuals who can become effective leaders in their field and contribute to positive societal change.

Research grants are essential for the advancement of knowledge and the development of new ideas. They provide financial support for researchers to pursue their projects and make meaningful contributions to their field. Research grants also provide an opportunity for researchers to gain experience and build their professional networks. By receiving a research grant, emerging researchers can gain access to resources and expertise that would otherwise be unavailable to them. Additionally, research grants can help emerging researchers develop their skills and gain recognition in their field.

This meeting provides a number of opportunities such as the creation of possible collaborations amongst our grant holders. Collaboration is essential for successful research projects. Working with other researchers can help you gain new perspectives and insights into your project. Additionally, collaborating with other researchers can help you develop your skills and knowledge in your field. Finally, collaboration can help you build relationships with other professionals in your field which can be beneficial for future projects.

Of course, collaboration cannot happen without networking. So, another opportunity that this meeting provides is the opportunity of networking. Networking is an important part of any research project. It allows you to connect with other professionals in your field and build relationships that can be beneficial for future projects. Additionally, networking can help you gain access to resources and expertise that would otherwise be unavailable to you. Finally, networking can help you stay up-to-date on the latest developments in your field and provide you with valuable insight into potential opportunities.

In conclusion, this Grant Holders Annual Meeting is an invaluable opportunity to learn from experienced professionals, network with peers, and gain valuable insight into the world of research. We hope that this event will provide you with the tools and resources necessary to succeed in your research projects. We hope that you will gain a better understanding of the importance of research grants, collaboration and networking.

Thank you for joining us and we look forward to hearing your ideas, and perspectives and that you will find this event to be of value to your work.

"Our theme for this year's meeting was carefully chosen because building research leadership for societal impact is essential for the advancement of society. "
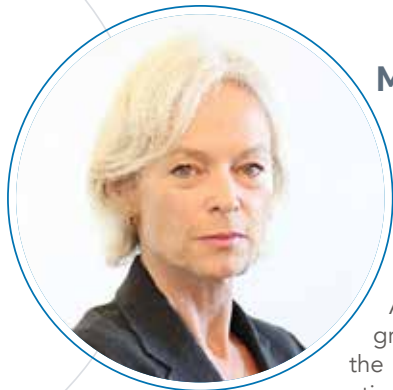
MESSAGE FROM LINE EXECUTIVE

Dr Michelle Mulder

It gives me great pleasure to welcome the SAMRC RCD Grant holders back to an in-person engagement on our campus. The SAMRC's RCD Grant Holders Annual Meeting is an excellent opportunity for RCD grant beneficiaries to meet with each other and with the SAMRC President and share their research. This year's meeting brings together the beneficiaries under the theme of "*Building Research Leadership for Societal Impact*". This theme reflects the growing emphasis on research that directly addresses societal challenges and focuses on delivering and testing new solutions.

Ensuring societal impact from research requires high quality, ethical and innovative research, interdisciplinary collaboration, community engagement, knowledge transfer, and a strong commitment to influencing change. All of this must be underpinned by strong research leadership, gained through targeted skills development, continuous learning, institutional support and years of experience. Research has significant potential to change lives, but this requires substantial effort to convert into new or improved policies, practices, products and services with social, cultural, environmental, and economic benefit.

We need to move towards a broader, more outcome- and impact-focused way of measuring and rewarding success in science, particularly when it comes to health research, where it is the lives saved and quality of life improvements that matter. The COVID-19 pandemic has demonstrated the critical role played by research in addressing a global threat, the importance of collaboration, data sharing and rapid dissemination and, most importantly, the visible impact of this. It has also increased public interest and involvement in the global scientific debates, with activities such as science advocacy, activism and lobbying also coming to the fore. As research leaders, impacting our society requires you to get together across disciplines and departments and foster an environment that encourages sharing of knowledge and expertise and provides opportunities for networking and collaboration. This is one of the key objectives of the GHAM 2023. To be relevant to society, researchers

should leverage every opportunity to engage with all stakeholders to effectively communicate their research results in a way that is understood and trusted by other scientists, policy makers, communities and the public at large.

At this year's GHAM, you will be exposed to various topics, from ethics matters in research and development to innovation and IP, leadership, research translation and indigenous knowledge. I want to encourage all participants to actively engage in the discussions, share their knowledge and experiences, and challenge each other and the other speakers with probing questions to make this a truly interactive and informative event. I hope this meeting will open up new avenues to learn, to explore new ideas and collaborations and to develop your own leadership skills, understanding that it is also your responsibility to train the future research leaders.

I would like to sincerely thank our esteemed invited speakers who have given up their time to share their knowledge and experience with us, the grant holders who will present their research, the organizing committee for their input in organizing the meeting and the Research Capacity Development (RCD) team for their time and efforts in making this year's grant holder meeting a success.

"We need to move towards a broader, more outcome- and impact-focused way of measuring and rewarding success in science "

KEYNOTE SPEAKERS

Prof Glenda Gray

President and CEO of SAMRC

An NRF A1 rated scientist, CEO and President of the South African Medical Research Council (SAMRC), Professor Glenda Gray is a qualified pediatrician and co-founder of the internationally recognized Perinatal HIV Research Unit in Soweto, South Africa. Prior to her appointment at the SAMRC, she was the Executive Director of the Perinatal HIV Research Unit, an affiliate of Wits University. Glenda's global profile includes a role as Co-PI of the HIV Vaccine Trials Network (HVTN), an international collaboration for the development of HIV/AIDS prevention vaccines.

As the COVID-19 pandemic developed, she was among the first to lead public discourse on the issue, and to move quickly to establish COVID-19 vaccine trials in South Africa, utilizing the experience and network developed over the years for the HIV vaccine work. Glenda served as a Protocol Co-Chair of the multi-country Ensemble Study investigating the single-dose Ad26.COV2.S vaccine as an emergency response intervention. When South Africa's national vaccine roll-out faltered, her international stature enabled her to negotiate a donation of 500 000 doses of the Ad26.CoV.2 vaccine before any emergency use authorization was available and conduct a phase 3B open-label study in health care workers, called the Sisonke Study.

She received South Africa's highest honour – the Order of Mapungubwe - for her pioneering research in PMTCT. Other prestigious accolades include the Nelson Mandela Health and Human Rights Award for significant contributions in the field of mother-to-child transmission of HIV. Selected as one of Time's 100 Most Influential People in the World, Forbes top 50 women in Africa, honorary degrees include: DSc (honoris causa Simon Fraser University), DSc (honoris causa Stellenbosch University), and LLD (honoris causa Rhodes University). She is a member of the National Academy of Medicine, the Academy of Science of South Africa, the African Academy of Science and the World Academy of Science. She is fellow of the American Academy of Microbiology. She is a member of the board of GARDP, AAHI and a member of the WHO TB-STAG.

Dr Michelle Mulder

Executive Director of the Grants, Innovation and Product Development Unit

Michelle Mulder is the Executive Director of the Grants, Innovation and Product Development Unit (GIPD) at the South African Medical Research Council (SAMRC). Michelle strategically manages Research & Development (R&D) funding, including SAMRC grant mechanisms and strategic funding partnerships, to enable the SAMRC to fund and support cutting edge research that impacts on the lives of South Africans. This role also focuses on supporting and driving innovation, both within the SAMRC and with external innovation projects aimed at developing new health solutions.

Dr Mulder holds a doctorate in Medical Microbiology from the University of Cape Town and has post-doctoral experience in a start-up biotechnology company emanating from the University of Cambridge (UK). She has previously spent 10 years consulting on technology innovation through her own company and has been involved for the last 17 years in the strategic management and commercialization of the SAMRC's intellectual property and in capacity building in these areas in southern and east Africa.

She has also spent the last 9 years managing grant funding for the SAMRC. She has headed the Technology Transfer Office, the Global Health Innovation Accelerator and the GIPD HIV Programme, and provided oversight of various other grant programs and strategic projects for GIPD. She has also been extensively involved in the SAMRC's funding response to COVID-19.

Dr Mulder was a member of the Executive Committee of the Southern African Research & Innovation Management Association (SARIMA) for 10 years, including 3 years as Vice President: Innovation and Technology Transfer, and 2 years as President. She served previously as Chair of the Board of Acorn Technologies, a life sciences incubator, a Director of the Licensing Executive's Society South Africa, the South Africa Liaison for the Life Sciences Committee of LESI, a member of the Higher Education South Africa (HESA) Strategy Group for Innovation and Technology Transfer and a board member of the Biologicals and Vaccines Institute of SA (Biovac). She currently serves as a board member for two SAMRC linked companies and is a member of the NHLS Research and Innovation Committee

Prof Leslie London

Professor and Head of Division
University of Cape Town

Professor Leslie London is a public health medicine specialist in the School of Public Health at the University at the Cape Town, South Africa. He is Head of the Division of Public Health Medicine and leads the Head of its Health and Human Rights programme as well as leading a research field in the Centre for Environmental and Occupational Health Research. He has published over 170 peer-reviewed journal articles and books or book chapters and supervised to completion over 40 Masters and PhD students. His research and teaching interests span human rights in public health, public health ethics, farm worker health, prevention of alcohol related harms and the health hazards of pesticides. He a Steering Committee member of the Network on Equity in Health in Southern Africa (EQUINET) and coordinates the Learning Network for Health and Human Rights, a collaboration between civil society organisations and university researchers developing best practice for realising the right to health. He has been a member of the Peoples Health Movement South Africa since inception and is active in human rights teaching, research and advocacy, both nationally and internationally. He is active in the Governance and Conflict of Interest in Public Health Network, with a particular interest in research to limit alcohol industry influence over alcohol harm-reduction policies for population health.

Prof Mosa Moshabela

Professor and Head of Division Professor of Public Health and Deputy Vice-Chancellor for Research and Innovation University of KwaZulu-Natal

Professor Mosa Moshabela (MBChB, MMed, MSc, PhD) is a Professor of Public Health and Deputy Vice-Chancellor for Research and Innovation at the University of KwaZulu-Natal. An esteemed academic and clinician scientist, he was awarded PHILA Annual Award (2022) by the Public Health Association of South Africa (PHASA) for his contribution to Public Health in South Africa, and a Ministerial Special Covid-19 Award (2020 - 2021) for Covid-19 Science Communication and Public Engagement.

Prof Moshabela is the Chairperson of the Governing Board at the National Research Foundation (NRF), Member of the Board at the South African Medical Research Council (SAMRC), Chairperson of the Standing Committee on Health in the Academy of Science of South Africa (ASSAf), Health Commissioner to the Premier of KwaZulu-Natal, as one of the seven multi-sector commissioners on the Premier's Provincial Planning Commission.

Currently, he leads the Quality Health Systems and Transformation (QuEST) Center in South Africa, a collaboration with the T.H. Chan School of Public Health, Harvard University, USA, and he is a faculty member in HIV, Infectious Disease and Global Health Research Institute (HIGH IRI) at the University of Washington in St. Louis, USA.

Globally, he is a member of the international advisory board for the Lancet Healthy Longevity, Lancet commission on synergies between Health Promotion, Universal Healthcare Access and Global Health Security, and the commission of the US National Academies for Science, Engineering and Medicine (NASEM) on the Global Roadmap to Healthy Longevity.

Prof Charles Shey Wiysonge

Senior Director of Cochrane South Africa & the HIV and other Infectious Diseases Research Unit
South African Medical Research Council

Charles Shey Wiysonge is a physician with postgraduate training in epidemiology, evidence-based health care, and vaccinology. He is the Senior Director of Cochrane South Africa & the HIV and other Infectious Diseases Research Unit at the South African Medical Research Council. His previous appointments include Deputy Director of the Centre for Evidence-based Health Care and Professor of Community Health at Stellenbosch University; Manager of the Vaccines for Africa Initiative at the University of Cape Town, South Africa; Chief Research Officer at UNAIDS in Geneva, Switzerland; Deputy Permanent Secretary in the Central Technical Group in charge of the Expanded Programme on Immunisation at the National Ministry of Public Health in Cameroon; Medical Epidemiologist at the Centre Pasteur du Cameroun; and General Physician at the Centre Hospitalier et Universitaire in Yaoundé, Cameroon. Charles is a member of numerous national, continental, and global advisory committees. He has published more than 400 journal articles and his current research interest is vaccination implementation science.

KEYNOTE SPEAKERS

Professor Fhumulani Mavis Mulaudzi

**Chair in the Ubuntu Community Model in Nursing
University of Pretoria**

Prof Fhumulani Mavis Mulaudzi is the South African Research Chair in the Ubuntu Community Model in Nursing. She is a Professor of Nursing at the University of Pretoria with 41 years of professional experience. Prior to her appointment as SARChI, Prof Mulaudzi was the Head of Department of Nursing Science for ten years and the Chair of the School of Health Care Sciences at the University of Pretoria. She has served in many leadership positions. She is currently the first Deputy President of Democratic Nursing Organisation of South Africa (DENOSA) and President of the Global Nurses and Midwives Rotary Club. Prof Mulaudzi is also chief editor of Curationis Journal.

BENEFICIARY ABSTRACTS

No	Abstract Title	University/ Research Unit	Beneficiary
**SAMRC MID CAREER SCIENTISTS PROGRAMME**
1	Current approaches and understanding of the common musculoskeletal soft tissue injuries affecting the lower limb.	UCT	Alison Septemer
2	Investigating Neutrophil-Associated proteins in human TB granulomas as targets for host-directed therapy	UKZN/AHRI	Jackson Marakalala
3	Prevalence and correlates of 30-day suicidal ideation and intent: Results of the South African National Student Mental Health Survey	SUN/SAMRC	Jason Bantjes
4	Harnessing big heterogeneous data to evaluate the potential impact of HIV responses among key populations in South Africa: The Boloka Project	UJ	Refilwe Paswana-Mafuya
5	Women's Surgical Outcomes in Africa	UCT	Salome Maswime
6	Assessing patients' experience of care in four referral hospitals: A Cross-sectional survey of outpatients in two South African rural provinces	WITS	Wezile Chitha
7	Immunology of co-infection: immunomodulation by neglected tropical diseases	UKZN	Zilungile Kwitshana-Mkhize

SAMRC EARLY INVESTIGATORS PROGRAMME			
No	Abstract Title	University/ Research Unit	Beneficiary
1	FAM111B dysregulation promotes malignancy in fibrosarcoma and POIKTMP and a low-cost method for its mutation screening	UCT	Afolake Arowolo
2	Evaluation of anticancer potential of Berberine against cancer cells as monotherapy and combination therapy	UJ	Blassan George
3	Biological aging profiles of neuropsychological function in South African women with HIV	SUN	Jacqueline Womersley
4	Implementing ecological momentary assessments to measure violence and adolescent HIV transmission risk: Lessons from Johannesburg, South Africa	WITS	Janan Dietrich
5	Screening of epigenetic biomarkers as prognostic factors in black South African women diagnosed with breast cancer	UL	Kgomotso Poopedi
6	Establishing expression kinetics and delivery platforms for self-amplifying mRNA vaccines and therapies.	WITS	Kristie Bloom
7	Why Men Rape: Perspectives from Incarcerated Rapists in a KwaZulu-Natal Prison, South Africa	SUN	Lihle Qulu
8	Mental health trajectories in the PURE-SA Cohort	NWU	Lusilda Schutte
9	Exploring the antimalarial potential of recently synthesized novel pyrimidine inspired hybrids	UKZN	Ofentse Pooe
10	The development of a dual vaccine candidate against respiratory diseases in plants	UCT	Sandiswa Mbewana
11	Clinical Genomics in Southern Africa: Lessons from the Undiagnosed Disease Programme	SUN	Shahida Moosa
12	Disease progression promotes changes in adipose tissue signatures in type 2 diabetic (db/db) mice: The potential pathophysiological role of batokines	NWU	Sithandiwe Mazibuko-Mbeje
13	Glycosylation of protein GBS2106 using polysaccharides derived from group B streptococcus serotype III	UCT	Sonwabile Dzanibe

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE			
No	Abstract Title	University/ Research Unit	Beneficiary
1	ADME polymorphism in tuberculosis: Pharmacogenetic analysis of samples from patients in healthcare facilities in the Vhembe District	UNIVEN	Afsatou Traore
2	Process and Outcomes of Spinal Cord Rehabilitation in the Western Cape, South Africa	UWC	Anthea Rhoda
3	Knowledge Translation Platforms for bridging public health and health systems research into Universal Health Coverage related policy and practice in South Africa (KTP-UHC)	UWC	Bey-Marrié Schmidt Maduneni
4	The South African COVID-19 Surgical Outcomes Study (SACSOS) - A prospective observational study of long-term patient-reported outcomes after surgery using a digital health platform	SMU	Hyla-Louise Kluyts
5	Designing neuropharmaceuticals to permeate the blood-brain barrier and combat neurological disorders	UWC	Jacques Joubert
6	Electrochemical chronocoulometric profiling of SARS-CoV-2 nucleocapsid protein at aptamer/quantum dot functionalized disposable electrodes	UWC	Keagan Pokpas
7	Health seeking behaviors amongst guardians of children under the age of five years in the low resource district of Vhembe in the Limpopo province	SMU	Livhuwani Tshvhase
8	Rare Diseases: Enamel Renal Syndrome in South Africa	UWC	Manogari Chetty
9	The physical, physiological and psychological risk factors for non-communicable diseases among adolescents from the Eastern Cape – A situational analysis report	UFH	Maya van Gent
10	SARS-CoV-2 drug discovery using in silico screening and cell-based virus assays to identify novel antiviral compounds	UWC	Megan Shaw
11	Precision medicine: Pharmacogenomics and Development of Individualised Drug Therapy for Diabetes and Hypertension Patients	UWC	Mongi Benjeddou

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE			
No	Abstract Title	University/ Research Unit	Beneficiary
12	Evaluation of the effect of *Warburgia salutaris* extract and its bioactive compounds on the metabolism of anti-diabetic and lip lowering drugs.	UNIZULU	Nokulunga Hlengwa
13	Telerehabilitation: Enabling the Delivery of Healthcare, Rehabilitation, and Self-Management through Community Health Workers.	UWC	Nondwe Mlenzana
14	Integration of metabolomic fingerprinting and molecular docking analysis of secondary metabolites of South African plants: Focus on protease (Mpro) and spike (S) glycoprotein of SARS-CoV-2	SMU	Nqobile Monate Mkolo
15	Risk Factors Attributable to Hypertension among HIV-Infected Patients on Antiretroviral Therapy in Selected Rural Districts of the Eastern Cape Province, South Africa	WSU	Ruffin Apalata
16	Determinants of high neonatal and child mortality rates in the rural areas of Limpopo province, South Africa	UNIVEN	Thivhulawi Malwela
17	Anti-cancer, Anti-diabetic, Anti-obesity and Anti-inflammatory potential of plant extracts/plant-derived compounds	UL	Vusi Mbazima

	SAMRC RCDI-NESTED POST-DOCTORAL PROGRAMME		
No	Abstract Title	University/ Research Unit	Beneficiary
1	Improving the solubility and blood brain permeability of edaravone-benzyl-pyridinium hybrid using solid lipid nanoparticle delivery system	UWC	Ayodeji Egunlusi
2	The Antioxidant, Anti-Cancer, And Anti-Metastatic Effect of *Tarchonanthus Camphoratus* on Metastatic MDA-MB-231 Cells	UL	Bernice Monchusi
3	SARS-CoV-2 drug discovery using in silico screening and cell-based virus assays to identify novel antiviral compounds	UWC	Bianca Gordon
4	Knowledge Translation Platforms for bridging public health and health systems research into Universal Health Coverage related policy and practice in South Africa (KTP-UHC)	UWC	Chanelle Mulopo
5	Discovery of SARS-CoV-2 human angiotensin-converting enzyme 2 (hACE2) and targeting transmembrane serine protease 2 (TMPRSS2) inhibitors from South African plant-based product	SMU	Clarissa Naidoo
6	Prevalence of putative drug resistance mutations in HIV-1 subtype C in Africa: A systematic review and individual sequence level meta-analysis	UNIVEN	Daphney Matume
7	Phytoconstituents analysis of *Cyclopia genistoides* (red honeybush tea kombucha) and its *in vitro* antidiabetic and antioxidant activities	UNIZULU	Freedom Tshabuse
8	Liposomal naringenin exerts radio-sensitizing effects in vitro	UWC	Keenau Pearce
9	Contraceptive failure: Herbal supplements and their effect on the metabolism of an ethinylestradiol based contraceptive	UNIZULU	Kgothatso Machaba
10	Investigating and understanding factors associated with health outcomes and quality of life in people with spinal cord injury in South Africa	UWC	Lucien Bezuidenhout
11	ADME polymorphism in tuberculosis: Pharmacogenetic analysis of samples from patients in healthcare facilities in the Vhembe District	UNIVEN	Mpumelelo Rikhotso
12	In vitro antidiabetic, antioxidant and cytotoxic evaluation of honeybush tea (Cyclopia genistoides) extracts	UNIZULU	Nkosinathi Cele

SAMRC CLINICIAN POST-DOCTORAL PROGRAMME			
No	Abstract Title	University/ Research Unit	Beneficiary
1	The longitudinal impact of air pollution and environmental tobacco smoke exposure on childhood respiratory diseases in an African birth cohort.	UCT	Aneesa Vanker
2	Matching study using health and police datasets for characterising interpersonal violence in the community of Khayelitsha, South Africa 2013–2015	UCT	Ardil Jabar
3	National and regional burden of chronic kidney disease and its risk factors in South Africa: a systematic analysis of the Global Burden of Disease Study 2021	UCT	Noluabalo Unati Nqebelele

SAMRC INTRAMURAL POSTDOCTORAL PROGRAMME			
No	Abstract Title	University/ Research Unit	Beneficiary
1	Developing a long-read sequencing method for identifying and quantifying SARS-CoV-2 variants of concern in wastewater	Genomics	Amsha Viraragavan
2	The Effect of Childhood Trauma Type and Timing on Acute Posttraumatic Response Following Adult Rape Exposure	NCDRU	Jani Nöthling
3	Changing policy through creating an evidence base: HIV, violence and mental illness amongst sex workers	GHRU	Jenny Coetzee
4	An exploration of the associations between total phospholipid Fatty Acid profiles and cardiovascular diseases in the SA-DPP cohort	NCDRU	Kamogelo Lebeko
5	Exposures to abuse in childhood and adulthood are associated with prevalent hypertension in women-the RICE study	NCDRU	Kim Nguyen
6	Screening potential repurposed drugs for antimycobacterial activity	SUN-CTR	Lauren Julius
7	Does a verbal autopsy narrative provide accurate information about treatment defaulting for people who have died from HIV/AIDS?	BODRU	Monique Maqungo
8	Using glucocorticoid hormones in wastewater as biomarkers to assess the health status of a community	EHRU	Nomfundo Mahlangeni
9	Preventing chemotherapy-induced cardiotoxicity	BRIP	Nonhlakanipho Sangweni
10	A study to assess the association between circulating miRNAs and cardiometabolic risk in pregnant women from Cape Town, South Africa	BRIP	Yoonus Abrahams

SAMRC MID-CAREER SCIENTIST PROGRAMME

1. Current Approaches And Understanding of The Common Musculoskeletal Soft Tissue Injuries Affecting The Lower Limb

September AV[1], Laguette MJ[1] and Collins M[1]

[1]Division of Physiological Sciences, Department of Human Biology, Faculty of Health Sciences, University of Cape Town

Globally and nationally, musculoskeletal injury remains one of the most common health problems affecting all populations and prevalence is predicted to increase as physically inactive populations age and with the notable added increase in non-communicable diseases such as diabetes, cardiovascular disease, and cancer. Currently, they are within the top 20 causes of burden of disease in South Africa. Although it is well-established that physical activity is one of the critical components for health and wellness, musculoskeletal soft tissue injuries resulting from participation in leisure time physical activity, as well as activities of daily living and in the workplace are common. The aetiology of musculoskeletal soft tissue injuries remains undefined. Our current understanding is that they are complex phenotypes resulting from both extrinsic and intrinsic factors with a genetic contribution being a strong risk factor.

Genes within key pathways have been highlighted and some mechanisms proposed. Most of the research to date have focused on the candidate gene approach with a few studies starting to exploit next generation sequencing technologies. Our aims are to build on our current research strengths by employing a whole genome sequencing approach so that we can identify key genes and pathways towards positioning of functional mechanisms of injury. These insights would allow us also to improve our understanding of healing and recovery of connective tissue related injuries we commonly note with the increase of non-communicable diseases such as shoulder related injuries in breast cancer survivors to name one.

It remains important to establish large data sets to confirm the potential clinical and biological significance at the population level. In this regard, we have explored some of the key genetic loci in several populations as part of a global consortium such genes include the collagen encoding genes and the angiogenesis association pathways.

2. Investigating Neutrophil-Associated Proteins In Human TB Granulomas As Targets For Host-Directed Therapy

Fisher, K[1,2] and **Marakalala, MJ**[1,2,3]

[1]Africa Health Research Institute, Durban, KZN, SA; [2]School of Laboratory Science and Medical Sciences, College of Health Sciences, UKZN, Durban, SA; [3]Division of Infection and Immunity, University College London, London, UK

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a major global health problem. The disease is aggravated by emergence of drug resistant Mtb strains, which result in high number of treatment refractory patients. There is a dire need for new therapeutic interventions that will augment current treatment protocols. Understanding drivers of TB associated lung pathological damage is vital in identifying targets for host directed therapies (HDTs). NETosis is a neutrophil specific cell death characterized by release of neutrophil extracellular traps (NETs). To understand the role of NETosis in TB pathogenesis, we analyzed human lung TB granuloma samples using a proteomics approach, which revealed enrichment of neutrophil specific proteins in necrotic regions of caseous and cavitary granulomas. Using immunohistochemistry (IHC) we validated the abundance of neutrophil associated proteins, including myeloperoxidase (MPO) and neutrophil cytosol factors in necrotic caseum of human TB granulomas. MPO protein was also more abundant in the plasma of TB patients compared to healthy and LTBI participants. MPO directly correlated with inflammatory disease markers, including IP-10 and a neutrophil chemoattractant, IL-8. In addition, MPO and IP-10 colocalized in caseous granulomas. In-vitro drug inhibition assays were used to investigate potential drivers of NETosis, with pharmaceutical inhibition of neutrophil specific proteins resulting in reduction of Mtb induced NETosis. Using RT-qPCR we analysed the expression of the neutrophil specific genes in the blood of healthy, latent TB infection (LTBI) and TB participants. We found that the neutrophil genes were more upregulated in the TB group. Our data presents new evidence on NETosis association with lung pathological damage in TB and identifies key novel drivers of the neutrophil cell death that can be intercepted as potential HDT targets to reduce neutrophil driven lung pathological damage.

3. Prevalence And Correlates Of 30-Day Suicidal Ideation and Intent: Results Of The South African National Student Mental Health Survey

Bantjes, J[1,2]

[1]Alcohol, Tobacco and Other Drug Research Unit, South African Medical Research Council, Cape Town, South Africa. [2]Institute for Life Course Health Research, Department of Global Health, Stellenbosch University, South Africa.

Background: It is unclear what proportion of university students in South Africa (SA) require urgent indicated interventions for suicidal ideation and what the characteristics are of these students.

Aim: Assess the prevalence and sociodemographic correlates of 30-day suicidal ideation, frequency of ideation, and self-reported intention to act on ideation in the next year among a national sample of SA university students.

Methods: Self-report cross-sectional data were collected online from students (n=28,268) at 17 universities across SA as part of the national student mental health survey. Students reported suicidal ideation in the past 30 days, frequency of ideation, and intention to act on ideation in the next year. Data were weighted within institutions and across universities to correct for response rate discrepancies. Poisson regression was used to investigate associations of sociodemographic characteristics with ideation and intention to act on suicidal ideation.

Results: 30-day prevalence of suicidal ideation was 24.4% (SE=0.3), with 2.1% (SE=0.1) and 4.1% (SE=0.1), respectively, reporting suicidal ideation all/almost all the time, or most of the time. About 1.5% (SE=0.1) of respondents reported being very likely to act on their suicidal ideation, while 3.9% (SE=0.2) were somewhat likely, and 8.7% (0.2) were not very likely. About85.8% (SE=0.5) either reported no suicidal ideation or that they were not at all likely to act on this ideation. Risk of suicidal ideation with high intent in the total sample was elevated among females (RR=1.9, 95%CI=1.3-2.7) and gender non-conforming students (RR=4.3, 95%CI=1.4-13.0) relative to males Black-African students compared to White students (RR=3.6, 95%CI=1.9-7.1), parental education (RR=1.6, 95%CI=1.0-2.5), and sexual minority students compared to heterosexual students (RR=1.9, 95%CI=1.3-2.6).

Conclusion: Scalable suicide prevention interventions are needed to reach the large number of SA students who report suicidal ideation with intent.

Key words: suicide prevention, university students, suicidal ideation, South Africa, suicide intent

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4. Harnessing Big Heterogeneous Data To Evaluate The Potential Impact Of HIV Responses Among Key Populations In South Africa: The Boloka Project

Phaswana-Mafuya RN[1,2], Phalane E[1,2], Journeay KS[3], Sisel HI[3], Siyamayambo C[1,2], Makanzi E[1,2], Sebati B[1,2], Thubeni S[1,2], Rucinski K[3], Rao A[3], Willis K[3], Xiaoming L[4]; Olatosi B[4]; Mishra S[5], Baral SD[3]

[1]South African Medical Research Council/University of Johannesburg (SAMRC/UJ) - Pan African Centre for Epidemics Research (PACER) Extramural Unit, Johannesburg, South Africa, [2]Faculty of Health Sciences, Department of Environmental Health, University of Johannesburg, Johannesburg, South Africa, [3]Key Populations Program, Center for Public Health and Human Rights, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, [4] Health Services Policy and Management, Arnold School of Public Health, University of South Carolina, [5]Division of Infectious Disease, University of Toronto

Background: South Africa (SA)has the largest HIV epidemic in the world with about eight million people living with HIV. Key Populations (KPs), including gay men and other men who have sex with men, female sex workers and their clients, transgender persons, people who use drugs, and incarcerated persons, bear a disproportionately higher burden of HIV compared to adults of a reproductive age. Currently, there is no specific centralized mechanism to gather and monitor KP data for targeted HIV responses in SA.

Objectives: To build a flexible and comprehensive data platform with computational power to handle integrated datasets; collate available HIV-related and relevant auxiliary data for KPs with high variability in SA from 2000 onwards; and align the data to Findable, Accessible, Interoperable, & Reusable principles.

Methods: There will be engagement of a wide range of stakeholders throughout SA to develop meaningful partnerships to acquire data and facilitate the creation of a data platform. Data varying in type, source, and structure including routinely collected HIV programmatic, epidemiologic and auxiliary data will be collated. Data will be screened for relevance and quality. The collated data will be stored in a flexible and updatable data platform called Boloka, which means to "store or keep".

Anticipated results: Meaningful data partnerships established; datasets secured; Postgraduate studies completed using the data; manuscripts published; local and international conference presentations; dissemination meetings; enhanced research capacities, and research reports.

Conclusion: The comprehensive analyses of KPs data will greatly improve our understanding of HIV among KPs and assist in setting programme targets and evaluate SA progress towards SA meeting the objectives of the National Strategic Plan for HIV, STIs and TB and global goal of ending HIV/AIDS as a public health issue.

Key Words: HIV, data platform, heterogeneous data, Key Populations, South Africa

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5. Women's Surgical Outcomes in Africa

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Introduction: Women merit special attention because of their distinctive contribution to society. Obstetric outcomes have received significant focus, however non-obstetric outcomes remain largely unexamined.

Methods: We did a secondary analysis of the African Surgical Outcomes Study and International Surgical Outcomes Study. In our substudy we focussed specifically on the analysis of the female, elective, non-obstetric, non-gynaecological surgical data collected during the two large multicentre studies. The African data were compared

with international outcomes in a risk-adjusted logistic regression analysis using a generalised linear mixed-effects model.

Results: ASOS had recruited 11 422 patients from 247 hospitals, and ISOS recruited 44 814 patients from 474 hospitals. 1698 African participants and 18 449 international participants met the inclusion criteria. Severe complications occurred in 2.9%, and 2.3% of patients in the African and international cohorts, respectively. The in-hospital mortality after severe complications 47.9% in Africa and 18.1% internationally. After adjusting for patient and procedure risk-profile, a woman in Africa has twice the odds (aOR=2.060; 95% CI, 1.173–3.618; P=0.012) of having a severe postoperative complication including in-hospital mortality compared with the international incidence.

Conclusion: Women in Africa have double the odds of having severe complications after non-obstetric non-gynaecological obstetric surgery compared to international rates; suggesting that health system issues could be addressed to improve women's surgical outcomes.

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6. Assessing Patients' Experience of Care In Four Referral Hospitals: A Cross-Sectional Survey of Outpatients In Two South African Rural Provinces

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Introduction: Patients' experience of care surveys have become an important component of performance improvement and clinical effectiveness because they

serve as a good proxy for patient's satisfaction and the quality of care. The purpose of the study was to assess patients' experience of care in four referral hospitals in two of South Africa's rural provinces.

Methods: A cross-sectional study was conducted in four public hospitals in Eastern Cape (Nelson Mandela Academic (NMAH) and St. Elizabeth (SEH)) and Mpumalanga provinces (Rob Ferreira (RF) and Themba) for two weeks in 2022. Systematic random sampling was used to select 662 outpatients. The patient experience of care questionnaire measuring demographics, access to care, availability of medicines, cleanliness, staff attitudes and waiting times was used. The level of statistical significance was p-value ≤0.05. Ethics approval was obtained from the University of the Witwatersrand.

Results: Females accounted for 71.6% (474/662) of participants; the median age was 47 years and 20.2% (133/657) required assistance with a disability. More than 78.5% (518/662) of the patients had received health services from the same facility within the immediate 12-months of the survey. Only 19.0% (31/659) of patients had been turned away from hospital previously; one hospital was reported to not have drinking water; the other was reported to not be clean (68.5%, 111/162); more than two-thirds of Mpumalanga province respondents (223/329, 67.8%) reported absence of drinking water (p-value,0.0001); 68.5% (111/162) of Themba respondents did not think that the hospital was clean compared to NMAH's 82.2% (134/163) who thought it was clean (p-value <0.0001). At least 70% of respondents in each of the hospitals found the health professionals to be respectful towards patients (p-value<0.0001). In all hospitals, at least half of the respondents did not know the processes to be followed when lodging a complaint (p-value=0.002). Waiting times were not acceptable as reported by 72.4% (118/163) and 67.1% (112/167) of Themba and Rob Ferreira hospital respondents respectively (p-value<0.0001)

Conclusion: Whilst hospitals have made some positive efforts in trying to improve patients' experience of care, there are a few concerns such as non-availability of drinking water, lack of knowledge of complaints processes and acceptable waiting times.

7. Immunology Of Co-Infection: Immunomodulation By Neglected Tropical Diseases

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Background: Helminth infections (part of neglected tropical diseases) are highly prevalent and have a geographic overlap with malnutrition and other infectious/non-infectious diseases of poverty. Helminths downmodulate the immune response for their protracted survival in the host, resulting in deleterious bystander effects on the host's ability to control and/or eliminate other viral and bacterial infections, while concurrent malnutrition exacerbates this lethal combination of pathogenesis.

Aim: To investigate the interaction between microbiome, nutritional and immunological effects of coinfection with helminths and HIV/TB.

Methods: Adult participants recruited in 6 peri-urban Primary Healthcare clinics, south of Durban, KwaZulu-Natal donated stool samples for parasite coproscopic diagnosis and microbiome profiling, and blood samples for macronutrients/micronutrients and immune profiling during HIV-helminth coinfection. TB and helminth coinfected individuals' and an in vitro model of TB-helminth coinfection (monocytic THP-1 and lymphocytic Jurkat cells stimulated with Mycobacterium tuberculosis H37Rv strain and Ascaris lumbricoides antigens) were analysed for immune profiling of cytokine gene expression.

Results: HIV-helminth coinfection: Of the 414 adults, 33% were helminth singly infected while 15% were coinfected. Coinfection was associated with older age ($p=0.0006$), low income ($p=0.0358$) and poor toilet use ($p=0.0007$). Around 17% of coinfected individuals were anaemic and displayed lower vitamin A ($p=0.040$), calcium ($p=0.003$) and albumin ($p=0.001$) levels, and higher proinflammatory cytokines [TNF-α ($p=0.036$), IL-2 ($p=0.008$) and IL-17 ($p=0.001$)] levels compared to HIV-helminth uninfected controls. TB-helminth coinfection: Coinfected cells had decreased Th1 proinflammatory (IFN-γ, TNF-α, perforin and granzyme B) and higher anti-inflammatory (IL-4) and regulatory (TGF-β and IL-10) cytokine levels compared to TB stimulated-only cells ($p<0.0001$). Similarly, coinfected individuals had significantly reduced Th1 proinflammatory and increased Th2/Treg cytokine genes. Microbiome

profiling: Helminth-infected individuals had higher proportions of Bacteroides fragilis (p=0.0003) and Bacteroides spp. (p=0.03), and lower levels of Lactobacilli spp. (p=0.035) (lower Firmicutes: Bacteroides ratio), Prevotella spp. (p=0.01) and Bifidobacterium spp. (p=0.012) compared to helminth-uninfected controls.

Conclusion: HIV-helminth coinfection causes micronutrient deficiency and anaemia. Helminths dampens HIV and TB immune responses during coinfection and associated with dysbiosis suggestive of increased susceptibility to inflammatory bowel disease (low Firmicutes: Bacteroides ratio).

SAMRC EARLY INVESTIGATORS PROGRAMME

1. FAM111B Dysregulation Promotes Malignancy in Fibrosarcoma And POIKTMP And A Low-Cost Method For Its Mutation Screening

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Introduction: Fibrosis is a significant health and economic concern as the common pathway to the failure of many organs and the high burden of this disorder. Mutations in the human *FAM111B* gene are associated with Hereditary fibrosing poikiloderma with tendon contractures, myopathy and pulmonary fibrosis (abbreviated to POIKTMP), a rare multi-organ fibrosing disease. Recent studies have also reported the overexpression of FAM111B in specific cancers. However, it's physiological role or how its mutations contribute to these diseases needs better delineation. Moreover, mutation screening for this gene may prove expensive in under-resourced facilities. This study, therefore, investigated its cellular expression, function and dysfunction using POIKTMP-patient-derived fibroblasts and fibrosarcoma (HT1080) cells. Additionally, this study described an inexpensive mutation screening method.

FAM111B gene expression was assessed *in silico* and validated *in vitro* in cell lines and primary skin fibroblasts from a South African POIKTMP-patient with the

heterozygous *FAM111B* gene mutation: NM_198947.4: c.1861T>G (p. Tyr621Asp or Y621D) by qPCR and western blot. The cellular function of FAM111B was studied in HT1080 using various cell-based functional assays, and PCR-RFLP genotyped the Y621D mutation.

Expression studies showed upregulated FAM111B mRNA and protein in the cancer cells. High FAM111B expression with robust nuclear localization occurred in HT1080. The expression data and cell-based assays indicated that FAM111B led to the upregulation of cell migration, decreased cell apoptosis, and modulatory effects on cell proliferation. Y621D mutation showed similar effects on cell migration but minimal impact on cell apoptosis. FAM111B mRNA and protein expression were markedly downregulated ($p \leq 0.05$) in the POIKTMP patient's fibroblasts. The PCR-RFLP method successfully genotyped the Y621D gene mutation.

FAM111B modulation by mutations or overexpression may contribute to the malignancy of cancers and POIKTMP/fibrosis and poor clinical outcomes and represents a viable prognostic marker or therapeutic target. Furthermore, the PCR-RFLP method could prove a valuable tool for *FAM111B* gene mutation validation or screening in resource-constrained laboratories.

2. Evaluation of Anticancer Potential of Berberine Against Cancer Cells As Monotherapy And Combination Therapy

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Berberine (BBR) is a potent phytochemical that has been used in traditional medicine, however its clinical application is limited due to its poor solubility, bioavailability, and membrane permeability. Therefore, combination of BBR with other therapies can be an effective option. This study focuses on evaluation of chemo-toxic efficacy of free form of BBR against MCF-7 breast cancer and A549 lung cancer cells and effectiveness of green synthesized silver nanoparticles (AgNPs) in enhancing the antiproliferative effect of BBR. Synthesis of AgNPs was carried out using Dicoma anomala plant extract. The cytotoxicity of BBR and AgNPs alone or combinations was measured by MTT assay, ATP proliferation, cellular morphological changes

and fluorescence staining. Results showed BBR induced dose and time dependent decrease in cell viability. The IC50 concentration of ~144 mM was obtained at 24 h which is decreased to 57 mM at 48 h incubation. Morphological analysis and Live dead fluorescence imaging showed induction of non-conventional mode of cell death which warrants further investigation. The evaluation of phototoxic potential of BBR against MCF-7 cells with different sublethal concentration and light doses are on-going. Treatment with 160 mM of BBR and 10 mg/mL AgNPs for 24 h resulted into ~52% and ~ 61% decrease in cell viability in A549 cells. The IC50 dose was determined to be ~144 mM and ~7.6 mg/ml for BBR and AgNPs. In comparison to monotherapy, the combination of 160 mM of BBR and 6 mg/mL AgNPs resulted ~ 80% loss in cell viability. Morphological analysis also showed significant cell damage, which was further confirmed by Acridine orange/Ethidium Bromide fluorescence imaging, whereby large population of cells showed cell death in combination therapy. These results suggested the potential of BBR against breast cancer cells at higher concentration, thus combination of different treatment strategies holds potential for augmenting the anticancer property.

3. Biological Aging Profiles of Neuropsychological Function in South African Women With HIV

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Introduction: Childhood maltreatment is a risk factor for neurocognitive impairment (NI) and depression in people with HIV. Biological aging, the progressive decline in function that occurs over and above that due to chronological age, has been linked to both morbidity and mortality, and can be investigated in relation to specific phenotypes.

Methods: We will use data and biospecimens collected as part of an ongoing longitudinal investigation of biological endophenotypes of HIV in South African women. Participants provided blood, underwent structural magnetic resonance imaging (sMRI), and completed the HIV Neurobehavioral Research Centre

Neuropsychological battery, Centre for Epidemiologic Studies Depression Scale and Childhood Trauma Questionnaire to provide measures of cognitive function, depressive symptomology, and CM, respectively. This study will assess four measures of biological aging in participants with clinical, neuropsychological and sMRI data at baseline (N_{Total} = 152, N_{HIV} = 76), one (N_{Total} = 136, N_{HIV} = 68) and five (N_{Total} = 80, N_{HIV} = 40) years. Absolute telomere length and mitochondrial DNA copy number will be determined using quantitative polymerase chain reaction. Genome-wide methylation data will be submitted to an online portal for calculation of Horvath, Hannum and DNAm PhenoAge epigenetic clock estimates. Machine learning will be used to generate a brain-predicted age by comparing participant grey matter volumes to those in an independent training dataset. The association of biological aging metrics, alone and in combination with CM, with baseline and follow-up cognitive and depression data will be assessed using regression and linear mixed models.

Expected outcomes: This research will investigate and compare the impact of HIV and CM on four biological aging measures and examine their relationship with baseline and longitudinal cognitive function and depressive symptomology. The results will provide insight into underlying pathophysiological mechanisms and determine the longitudinal predictive value of these biological correlates for NI and depression.

4. Implementing Ecological Momentary Assessments to Measure Violence And Adolescent HIV Transmission Risk: Lessons From Johannesburg, South Africa

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Background: Ecological Momentary Assessment (EMA) is an important methodology to understand risky behaviour and holds promise for HIV research. EMA is still novel in sub-Saharan Africa. We describe challenges and lessons learned on a novel study implementing mobile phone EMAs with adolescent boys in South Africa.

Methods The Tsamaisano study is an ongoing longitudinal study, started in 2020 to recruit perinatally HIV infected and uninfected male adolescents aged 15-19 years. Participants completed 52 weekly mobile phone surveys on emotional state, exposure to and perpetration of violence, and sexual risk behaviour. Surveys were delivered using a random algorithm to choose the day. We incorporated mechanisms to assess challenges and optimize survey completion: weekly team meetings with youth representation and real-time data monitoring. Additionally, 20 frequent vs infrequent survey submitters participated in qualitative interviews about barriers and recommendations.

Results Real-time monitoring indicated low survey completion in the first months of study implementation. To ensure that both the adolescent participant and their caregiver understood the commitment required for successful EMA, we created and implemented a guided discussion around mobile phone access during the enrolment visit. We identified a need for increased and ongoing technical support; addressed by creating technical guides, implementing a standard two-week check-in call after enrolment, adding an automated request button for call-back assistance, creating a WhatsApp messaging stream, and reaching out to all participants failing to submit two sequential surveys. Entry-level smartphones, including those initially distributed by the study, did not have capacity for certain updates and had to be replaced with more expensive models. Participants struggled with randomly allocated survey days; completion improved with set completion days and targeted reminder messages. Together, these steps improved survey completion from 40% in December 2020 to 65% in April 2022.

Conclusions The key lessons learned through the ongoing Tsamaisano are important to inform future study designs with EMA utilizing mobile phone, electronic data collection among adolescent boys in low-and-middle-income settings.

5. Screening Of Epigenetic Biomarkers as Prognostic Factors in Black South African Women Diagnosed With Breast Cancer

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Background: A majority of cancer-related deaths are a result of metastasis. Traditional and molecular clinical prognostic factors that have been used in determining the ability of the tumour to metastasise have limited predictive power and poor generalisation ability (Abraham et al., 2010). Therefore, this study aims to evaluate the prognostic significance of epigenetic biomarkers in breast cancer patients.

Methods: This is a longitudinal cohort study and ethical approval for the study has been acquired. A total of 188 black South African women, stratified into two groups; breast cancer of all stages (n=128) and age-matched healthy volunteers (n=60), between the age of 23 – 75 will be recruited from March 2023 to March 2024 at the Mankweng hospital and Pietersburg Provincial hospital. Blood will be collected once pre-chemotherapy treatment and every 2 months for 12 months after breast surgery from the same participants receiving adjuvant chemotherapy. DNA will be extracted from plasma using a QIAamp DNA mini blood kit. The expression of breast cancer-associated genes known to be regulated by differential methylation will be analysed using the Human Breast Cancer RT[2] Profiler PCR Array kit. Bisulfite modification of DNA will be performed using the EpiTect bisulfite kit. Methylation specific PCR amplification will be performed to detect the presence of hypermethylation within the promoter CpG islands of selected epigenetic genes, identified from the PCR array.

Results: The expectation is for the aberrant methylated genes in plasma DNA to be associated with tumour-related symptoms. It is also envisaged that aberrant methylated genes would result in higher specificity and sensitivity compared to the classical tumour marker CA 15.3.

Conclusion: The findings of the study will suggest that epigenetic biomarkers in plasma have clinical applicability in defining breast cancer prognostic measures.

6. Establishing Expression Kinetics and Delivery Platforms For Self-Amplifying mRNA Vaccines And Therapies

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Synthetic mRNA technologies have gained prominence following the successful implementation of the COVID-19 vaccines. One major advantage of this vaccination approach is the activation of both humoral and cell-mediated immune responses. Using self-amplifying mRNA (saRNA) we aim to develop prophylactic, and possibly therapeutic, vaccinations for chronic infectious diseases including HBV. Unlike conventional mRNA, alphavirus-derived saRNAs are large transcripts capable of in situ self-propagation, leading to improved antigen expression with lower doses. These exogenous RNAs possess the inherent ability to trigger innate immune responses that enhance immunogenicity. However, this self-adjuvant effect must be balanced, as it could also lead to translation inhibition. Establishing saRNA kinetics, innate immunity, and non-viral delivery is important for turning these designs into clinically viable drug products. To this end we have begun optimizing the chemical synthesis, characterizing the in-situ translation kinetics, and establishing lipid nanoparticle (LNP) formulations of synthetic saRNA encoding reporters (eGFP/Fluc) or vaccine antigens. In vitro kinetic analysis of saRNA encoding eGFP showed prolonged expression of the reporter (up to 15 days) when compared to conventional mRNA. The ability of saRNA to trigger interferon responses was examined by measuring the fold change in the expression levels of interferon β and interferon-inducible genes in cell cultures. saRNA transcripts encoding antigens showed upregulation of interferon and interferon-inducible genes, whereas reporters were less immunogenic. Although innate immune responses were triggered, it did not impede in situ translation of these antigens. To facilitate the delivery of large saRNAs, different methods of encapsulation were investigated. Traditional lipid film hydration and microfluidics-based approaches were prioritized, and both cationic and ionizable lipids at different N:P ratios were evaluated. Formulations demonstrating monodisperse size, high

encapsulation efficiency, and efficient in vitro delivery have been selected for further characterization. These preliminary results will help to develop and optimize saRNA vaccine strategies for HBV.

7. Why Men Rape: Perspectives From Incarcerated Rapists in a KwaZulu-Natal Prison, South Africa

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Sexual offending is a global problem but is particularly prevalent on the African continent and in South Africa. Childhood experiences related to abuse, alcohol use, and criminal activities in the household and community has been associated with an increased risk for violence perpetration in adulthood. Less is known about sexual violence perpetration, especially in the South African context. In this study, the experiences of incarcerated male perpetrators of rape in South Africa are investigated along with the collective social context and individual childhood experiences that potentially contribute to rape perpetration. Eighteen male perpetrators of rape who were inmates at Westville Correctional Services in KwaZulu Natal, South Africa, were interviewed. The semi structured in-depth qualitative interviews were transcribed, coded and annotated using an interpretive paradigm and thematic analysis approach. Five main themes emerged from the research and included (1) childhood trauma and adverse events, (2) understanding rape, (3) substance abuse, (4) gender roles and avoiding responsibility and (5) recidivism. The findings revealed that all rape perpetrators were exposed to at least one childhood trauma type. Family

and community violence and criminality was common. Most participants avoided taking responsibility for their actions and blamed the victim and recidivism/prior convictions were often reported. The findings demonstrate the complex personality dynamic involved in the cycle of abuse and the evolution of criminal behaviour, starting as a victim and ending as a perpetrator. The findings also highlight the need for interventions aimed at reducing childhood trauma exposure and improving the social and relational context of those at risk for childhood neglect and abuse.

Keywords: incarcerated rapist men, childhood trauma and adversity, rapist behaviour, rape, recidivism

8. Mental Health Trajectories in The PURE-SA Cohort

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Mental health poses a persistent challenge for individuals, families, and communities, and creates a major economic burden for countries, particularly in low resource settings. To understand the development and impact of mental (ill-) health over the lifespan and to develop strategically targeted prevention strategies, insight into the trajectories, determinants, and correlates of mental health in low resource settings must be gained through interdisciplinary longitudinal epidemiological studies. To this end, the overarching aim of this project is to examine the mental health (from mental illness to psychosocial well-being) of ageing adults in low resource South African settings in terms of prevalence, trajectories, social determinants, and physical health correlates. Specifically, this project adds a mental health leg to the South African (SA) cohort of the multi-country, longitudinal Prospective Urban and Rural Epidemiology (PURE) study that started in 2005. Adult participants from each site in PURE-SA (two urban: Ikageng, Northwest and Langa, Western Cape; two rural: Ganyesa, North West and Mount Frere, Eastern Cape) respond to questionnaires on facets such as stress, depression, anxiety, and psychosocial well-being. At the same time, data are gathered in the core PURE-SA project on various social and economic determinants and physical health. At the two North West sites, some mental health data have been gathered since 2005, which are also combined with the current data. Preliminary findings show high prevalence of depression in the target communities,

but, at the same time, also high prevalence of flourishing. Scores varied across different localities (urban vs rural) and time points. The study shows that many older adults in low resource settings suffer in terms of mental health, suggesting that the necessary support and health care services must be available to serve this population. At the same time, many older adults show resilience amidst challenging circumstances, and understanding pathways to resilience may inform preventative and promotive interventions.

9. Exploring The Antimalarial Potential of Recently Synthesized Novel Pyrimidine Inspired Hybrids

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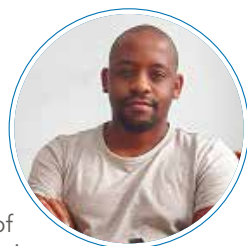
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Recently, the emergence of antimalarial resistance by Plasmodium sp. has enhanced the need for the development of new novel drug targets. Using a molecular hybridization approach, we report the design and synthesis of an unique class of antiprotozoal agents; (E)-1-(4-(4,6-diphenylpyrimidin-2-yl)piperazin-1-yl)-3-phenyl prop-2-en-1-one derivatives (8a-n). In vitro inhibitory activity for the compounds were evaluated against the NF54 chloroquine-sensitive strain of Plasmodium falciparum (P. falciparum). From the antiprotozoal screening, three compounds displayed propitious activity with IC50 (0.18-0.21μM), using quinine and chloroquine as standard drugs. Compounds 8o and 8l emerged as the most potent candidates with IC50 values of 0.18 ± 0.02 μM and 0.21 ±0.001 μM with an associated good safety index of 18.59 and 16.75 to human kidney epithelial (HEK293) cells, respectively. Furthermore, we investigated the binding affinities of the compounds against two purified P. falciparum heat shock protein 70 homologues; PfHsp70-1 and

PfHsp70-z. Compound 8l exhibited the highest binding affinity for both PfHsp70s. In silico molecular docking data validated the high binding ability between PfHsp70-1 and 8l and 8o, with the highest binding affinity of 10.5kcal/mol and 10.1kcal/mol, respectively. Therefore, it could be speculated that PfHsp70-1 is one of the targets of these inhibitors.

10. The Development Of A Dual Vaccine Candidate Against Respiratory Diseases In Plants

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The current COVID-19 pandemic and seasonal influenza represent looming global health challenges. Efficacious and safe vaccines remain the frontline tools for mitigating both severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus-induced diseases. These viruses can realistically be expected to co-circulate for the foreseeable future, leading to the requirement for universal long-term public health measures to simultaneously manage both respiratory infections.

The aim of this study is to develop dual COVID-19 and universal influenza vaccine candidates by displaying the SARS-CoV2 receptor binding domain (RBD) and Influenza A matrix ectodomain (M2e) on a trimerized chimeric influenza B HA stem. The influenza M2e has been identified as a universal influenza vaccine target while RBD has been shown to have high neutralization and protection against viral infection. These antigens are very small and poorly immunogenic on their own, therefore, will be presented on virus-like particles (VLPs) that can be rapidly and cheaply produced in plants. We speculate that linking antigens to the influenza B HA stem will allow for optimal display, thus increasing immunogenicity for broad cross-protection. The dual vaccine will achieve a holistic approach to the global public health measures needed to deal with the combined threat of influenza and COVID-19.

The expected outcome is a potential dual vaccine against SARS-CoV-2 and influenza that can confer protection against emerging and re-emerging strains. The potential candidate vaccine will provide a broad immune response against different SARS-CoV-2 and influenza strains and aid in preventing zoonotic transmission of the disease.

11. Clinical Genomics in Southern Africa: Lessons from the Undiagnosed Disease Programme

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Rare diseases (RDs) collectively affect about 6% of the population. The vast majority of RDs have a genetic basis. In southern Africa, the many millions of patients, and families with RDs have remained undiagnosed and left on their so-called "diagnostic odyssey" indefinitely, as there has been limited access to the genomic technology, testing and expertise needed to provide definitive diagnoses. We established southern Africa's first Undiagnosed Disease Programme (UDP) to begin to address this gap. To date, more than 600 individuals with undiagnosed rare genetic disorders have been recruited and almost half of them have undergone genomic testing through the UDP. We used whole exome sequencing as a first line test on individuals with a wide variety of different disorders, who presented with clinical features which made them ideal candidates for exome sequencing. The study cohort included patients from all population groups in South Africa, who are understudied and under-represented in genomics globally. With a diagnostic rate of over 50%, we provide first evidence that exome sequencing is a valuable tool in this African population. Furthermore, exome sequencing has proven useful for novel variant and novel candidate gene identification in this population. We also set the stage for what we believe is needed to optimize clinical genomics in Africa, especially with respect to capacity building, clinical bioinformatics, variant interpretation and the value of data sharing. The experiences from the UDP thus far will be invaluable to researchers and clinicians working in this and other resource-constrained environments and with populations who are understudied. Here, we present the myths encountered and refuted, the challenges faced and overcome, and the triumphs already achieved through the UDP.

12. Disease Progression Promotes Changes in Adipose Tissue Signatures in Type 2 diabetic (db/db) Mice: The Potential Pathophysiological Role Of Batokines

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Unlike white adipose tissue (WAT), which mainly stores excess energy as fat, brown adipose tissue (BAT) has become physiologically important and therapeutically relevant for its prominent role in regulating energy metabolism. The current study uses an established animal model of type 2 diabetes (T2D) db/db mice to determine the effect of the disease progression on adipose tissue morphology and gene regulatory signatures. Results showed that WAT and BAT from db/db mice display a hypertrophied phenotype that is consistent with increased expression of the pro-inflammatory cytokine, tumor necrosis factor-alpha (Tnf-α). Moreover, BAT from both db/db and non-diabetic db/+ control mice displayed an age-related impairment in glucose homeostasis, inflammatory profile, and thermogenic regulation, as demonstrated by reduced expression of genes like glucose transporter (Glut-4), adiponectin (AdipoQ), and uncoupling protein 1 (Ucp-1). Notably, gene expression of the batokines regulating sympathetic neurite outgrowth and vascularization, including bone morphogenic protein 8b (Bmp8b), fibroblast growth factor 21 (Fgf-21), neuregulin 4 (Nrg-4), were altered in BAT from db/db mice. Likewise, gene expression of meteorin-like (Metrnl), growth differentiation factor 15 (Gdt-15), and C-X-C motif chemokine-14 (Cxcl-14) regulating pro- and anti-inflammation were altered. This data provides some new insights into the pathophysiological mechanisms involved in BAT hypertrophy (or whitening) and the disturbances of batokines during the development and progression of T2D. However, these are only preliminary results, as additional experiments are necessary to confirm these findings in other experimental models of T2D.

13. Glycosylation Of Protein GBS2106 Using Polysaccharides Derived from Group B Streptococcus Serotype III

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Group B streptococcus (GBS) is the leading cause of neonatal sepsis and colonization with serotype III accounting for the majority of GBS cases in infants. Currently, there is no licensed vaccine available for protection against GBS disease. Well conserved GBS surface proteins are a promising target for vaccine development that could confer serotype-independent protection against invasive GBS disease in infants. In this study we aim to develop a serotype-III glycosylated GBS protein as a candidate GBS vaccine.

GBS2106 is a highly immunogenic GBS protein that was previously identified to be expressed on the surface of all GBS serotypes. Using recombinant vectors, protein glycan coupling technology will be employed to synthesize a recombinant GBS2106 protein glycosylated with capsular polysaccharides (CPS) derived from GBS serotype III. The synthesized glycopeptide will be purified using affinity chromatography and characterised using liquid-chromatography and mass spectrometry. Antibody seroprevalence of the recombinant glycopeptide will be measured using GBS colonised motherinfant pairs compared to non-colonized controls.

A chimeric GBS2106 protein bearing at the C-terminal a sequence motif for glycosylation by oligosaccharyltransferase (OST) and a polyhistidine tag for protein purification was designed in silico. Structural computation of the chimeric protein showed good structural preservation of the native GBS2106 protein. Next, we plan to recombinantly clone plasmid vectors expressing gbs2106, cpsIII and ots genes within E.coli for synthesis of the glycopeptide GBS2106-III. We expect that the novel GBS glycopeptide will be capable of inducing serotype independent antibody responses in asymptomatically GBS colonized mother-infant pairs. We further anticipate efficient trans-placental transfer of antiGBS2106 antibodies from colonized mothers to provide protection against invasive GBS disease to their respective infants. These findings will provide evidence for further testing of GBS2106-III glycopeptide as a suitable universal GBS vaccine candidate.

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE

Principal Investigators

1. ADME Polymorphism in Tuberculosis: Pharmacogenetic Analysis Of Samples From Patients In Healthcare Facilities In The Vhembe District

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Background: Tuberculosis is caused by Mycobacterium tuberculosis and is categorised into multidrug-resistant (MDR) and extensively drug-resistant (XDR). Resistance to at least isoniazid and rifampicin is known as MDR TB. XDR TB is resistance to isoniazid and rifampicin and fluoroquinolones, including capreomycin, kanamycin, amikacin. Several studies on drug-resistant tuberculosis have been conducted in South Africa; however, there are limited studies that have reported on the prevalence of DR-TB among patients receiving treatment in the northern region of South Africa.

Materials and methods: In total, 61 patients receiving treatment were enrolled in the study since September 2022 (61 samples each for sputum and blood). After pre-treatment with NALC-NaOH, DNA was isolated from sputum samples and Genomic DNA extraction was done using QIAamp® DNA Mini Kit. Detection of resistance was done using the Allplex™ MTB/MDR/XDRe PCR assay. A questionnaire was administered to identify the risk factors associated with TB. NGS was performed and still in progress.

Results: From the 61 patients enrolled in the study, 48% were male, 28% of patients were still TB positive while 3,3% had resistance TB; 21% of the patients had bacterial co-infection and 56% of them were HIV positive. Several risks factors were identified.

Conclusion: The study found a 3,3% prevalence of resistance in the patients and correlation between risk factor and TB was observed. More studies investigating the prevalence are required in the study region, Limpopo province (SA).

2. Process and Outcomes of Spinal Cord Rehabilitation in the Western Cape, South Africa

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The RCDI funded project explored rehabilitation process and outcome of patients with Spinal Cord Injuries living primarily in the Western Cape. The outcome data was compared with a cohort with the same condition living in Sweden. Our outcome investigation explored physical activity, other functional activities and participation factors, including environmental challenges experienced by the individuals. The specific significance of this study was determining the physical activity levels using an objective process namely the application of accelerometers as a measurement tool. Determining cut points for accelerometer measurement is a significant outcome of this study. With regards to process matters the study explored the process of care of individuals with spinal cord injuries who were found in both in-patient settings and community-based settings. Both qualitative and quantitative research methodologies were used to collect the data. Sensitivity tests were applied to predict mortality in this group of patients, information that will make a valuable contribution to the management of patients with a spinal cord injury managed in acute settings. The findings revealed that modifiable as well as non-modifiable factors contributed to mortality. The majority of patients were engaging in sedentary lifestyles. Assault was the major cause of injury in the South African cohort while falls were the major cause of injury in the Swedish cohort.

3. Knowledge Translation Platforms for Bridging Public Health And Health Systems Research Into Universal Health Coverage Related Policy And Practice In South Africa (KTP-UHC)

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Background: Knowledge Translation Platforms (KTPs) can support evidence-informed decision-making by providing relevant and timely research evidence and they can bridge the gap between research, policy and practice. There are several KTPs in South Africa (that self-identify as such or not), however, there is a need to explore their full potential as interventions that can support NHI related decisions. The aim of this study is to understand and strengthen KTPs in supporting NHI related decisions in South Africa.

Methods: A multi-method study, including a scoping review and formative qualitative research.

Preliminary findings: Our findings are from the (1) scoping review and (2) formative qualitative research.

(1) The scoping review revealed a clear challenge in defining and conceptualizing a KTP, which raised methodological issues around screening and extracting data from the literature. Additionally, most of the KPTs identified were located in a high-income setting, which speaks to the limited research on KTPs in low- and middle-income settings, similar to South Africa.

(2) Our formative qualitative research comprised of a mapping exercise and interviews with research cluster heads at a KTP in South Africa of the knowledge translation (KT) activities and processes being planned and implemented. We organised the mapping and interview results according to the six KT themes described in the Cochrane KT Framework (prioritization and co-production; sustainable infrastructure; engaging with audiences; packaging, communication, and dissemination; building audience capacity; and advocacy). Packaging, communication, and dissemination was identified as the weakest KT theme by researchers at the KTP.

Discussion and conclusion: The ongoing scoping review and formative qualitative research are contributing to an understanding of KTPs, in terms of their conceptualisation and characteristics. The next step in the project will involve enhancing an existing framework for KTPs or developing a new one for identifying and evaluating KTPs if necessary and relevant.

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4. The South African COVID-19 Surgical Outcomes Study (SACSOS) - A Prospective Observational Study of Long-Term Patient-Reported Outcomes After Surgery Using A Digital Health Platform

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Background: The impact that the COVID-19 pandemic has had in disrupting surgical services, and uncertainty about the longer-term outcome in patients receiving surgical care during the pandemic, served as the rationale for the study. The primary objective is to describe the relationship between patient comorbidities, surgical characteristics, and long term (6 months and 1 year) postoperative patient-reported outcome. Outcome measures can best be captured using a digital health platform designed to enable patients to share perioperative information with their healthcare practitioners (surgeons and anaesthetists).

Method: The study is a prospective observational cohort study aiming to recruit patients 18 years and older presenting for any surgical procedure. De-identified data will be extracted from the database and made available to the principal investigator for analysis.

Limitations: The number of case records is not yet sufficient to enable data analysis. Contributing factors are being investigated and addressed. The registration of the surgeon and his/her anaesthetic team is required before patients can be introduced to the study using the digital health platform. Patients are requested to participate by the surgeon when surgery is planned during the consultation, but the processes and workflow in surgical practices proved a barrier to patient recruitment. Patients may be lost to postoperative follow up.

Mitigation: The benefits of using the digital health platform are being promoted among clinicians, to encourage them to introduce the platform to patients. Webinars were organised to introduce the platform and the study. A research assistant visits practices to ensure visibility of study material and practice staff support. A study to optimize the platform for scalability is being conducted. Both email and short message notification systems are enabled to notify patients of data forms requiring completion.

Conclusion: The work required to ensure a successful study has encouraged collaboration and therefore capacity building.

5. Designing Neuropharmaceuticals to Permeate the Blood-Brain Barrier And Combat Neurological Disorders

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Our group is working on developing a solution for the growing global problem of dementia, with Alzheimer's Disease (AD) being the most prevalent form. To address this issue, we have developed edaravone-based pyridinium derivatives (EBPDs) which have shown promising results as potential neuroprotective agents. We have established that these EBPDs have a range of in vitro biological activities such as inhibiting acetylcholinesterase, scavenging free radicals, modulating amyloid-β plaque formation, inhibiting the β-secretase enzyme, and protecting neuronal cells and Zebrafish larvae from neurotoxicity. However, despite these promising results, there is a concern of the formation of EBPD radical adducts in biological

media, which may impact the ability of EBPDs to reach the CNS. To address this issue, we have developed solid-lipid nanoparticle delivery systems to improve the absorption, stability, and penetration of EBPDs across the blood-brain barrier (BBB). An oil in water emulsion technique was used to form polycaprolactone PCL-EBPD nanoparticles, which were subsequently coated with chitosan (CS). The PCL-EBPD-CS nanoparticles were characterised using a Zeta analyser. As expected, positively charged PCL-EBPD-CS nanoparticles were obtained. This suggest that PCL-EBPD-CS is a cationic polyelectrolyte, which could potentially form anionic biological interactions with the BBB and increase BBB permeability. At present, we are validating our in vitro findings through in vivo studies in rodents. Specifically, we are conducting behavioral toxicity studies to determine the safety and potential side effects of the EBPDs. Furthermore, we are planning to evaluate the therapeutic potential of EBPDs for AD by using the 3xTg-AD mouse model, which is a genetically engineered mouse model that develops Alzheimer's-like symptoms. Overall, our research aims to develop a safe and effective treatment for dementia, with a focus on AD, using EBPDs delivered into the CNS through solid-lipid nanoparticle systems.

6. Electrochemical Chronocoulometric Profiling Of SARS-CoV-2 Nucleocapsid Protein At Aptamer/ Quantum Dot Functionalized Disposable Electrodes

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The Covid-19 pandemic has wreaked havoc on the world. Spreading at an alarming rate with 150 million infections and over 3 million deaths worldwide, it has placed a great deal of strain on the health sectors to find effective monitoring, vaccination, and treatment approaches. With this in mind, the development of accurate, inexpensive, portable, reliable, and simple devices for remote sensing applications is pivotal for early detection, limiting exposure, and the prevention of adverse side effects, particularly in areas where access to skilled laboratories is lacking. For the first time, novel quantum dots (MSA-WTe3-QDs) are used in conjunction with aminated single-stranded DNA aptamer to selectively target the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) via nucleocapsid (N) protein in human serum.

Herein, amine-modified anti-SARS-Cov-2 aptamers are covalently bound to novel carboxylic acid-enriched QDs a label-free electrochemical aptasensor at disposable screen printed carbon electrodes and applied to the detection of SARS-Cov-2 N proteins via dual voltammetric and chronocoulometric electrochemical techniques. The QD/aptamer platform offered enhanced sensitivity, specificity, and signal amplification over existing sensing strategies through highly efficient biomarker recognition. Spherical, 3 nm QDs improved the aptasensor active surface area for increased detection capabilities. The work demonstrated the first chronocoulometric detection of the N-protein under optimized conditions, with short immobilisation times of 120 seconds. Linear responses were achieved in the low pg.mL^{-1}, yielding a lower detection limit of 0.08 pg.mL^{-1}. The proposed aptasensor demonstrated good selectivity to the N-protein in the presence of various interferents and was successfully applied in human plasma with good recovery percentages.

7. Health Seeking Behaviours Amongst Guardians Of Children Under The Age Of Five Years In The Low Resource District Of Vhembe In The Limpopo Province

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Background: Health seeking behavior is a tool for investigating individuals' or a population's interaction with the health system. Sub-Saharan Africa continues to be the region with the highest under-five mortality rate in the world with 74 deaths per 1000 live birth. In 2020, one in 13 children in Sub-Saharan Africa died before reaching their fifth birthday which is 15 times higher than the risk for children born in high-income countries. Children are continually dying from preventable diseases due to delays in seeking help from the health care facilities.

Objective: The study aims to identify reasons and delays of seeking healthcare among guardians of children under the age of five years in the primary health care facilities of Vhembe district in Limpopo province.

Method: A quantitative descriptive cross-sectional study design was followed in this

study. Data was collected from 201 guardians of under-five children through face-to-face survey interview using a structured questionnaire. Data were analyzed using Stata Corp, Texas USA 17.0.

Results: Approximately 70% of guardians would seek help from the facility when the child has fever, unable to feed, having convulsions, developed rash all over the body, vomiting, oedema of the feet, weight loss, diarrhea, and cough. About 30% viewed the distance from the facility, financial constraints, lack of believe in the severity and the danger of the illness and knowing that the health facility is always full as the reasons for the delay to seeking health care from the health facilities.

Conclusion: To reduce the childhood morbidity and mortality caused by delays in seeking help, it is necessary to develop and implement interventions for improving household income, establishing healthcare facilities within five-kilometer radius of all communities, and educating the guardians about danger signs and severity of the childhood diseases.

Keywords: Children under-five, guardians, health seeking behavior, primary health care

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8. Rare Diseases: Enamel Renal Syndrome in South Africa

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Enamel Renal Syndrome (ERS) is a rare genetic disorder with a largely unknown prevalence due to limited awareness and frequent misdiagnosis. ERS has a major impact on the quality of life of those affected and is associated with potentially life-threatening renal complications.

Since dentists are often the first to encounter these patients, it is important that they can identify patients with ERS, have sufficient information available to understand the risks associated with the condition and manage patients in a way that ensures that they have access to appropriate healthcare.

A multidisciplinary study was registered at the Faculty of Dentistry at the University of the Western Cape (UWC) with the aim of documenting the ERS-related craniofacial and oro-dental phenotypes, investigating the genetic/genomic basis of ERS in a South African cohort, and to propose guidelines for dental practitioners to manage those who are affected.

Five patients with the pathognomonic oral profile of ERS were identified. Currently, four patients have received the initial dental and craniofacial management, genetic testing, and renal assessment.

The lack of awareness has led to affected patients' renal status often being overlooked resulting in an underestimation of the actual disease prevalence. It is important that rare-disease research, particularly in Africa, be promoted and supported to uphold the ethical principles of justice and provide care to those who need it. This is true for ERS, which has a significant impact on the quality of life of those affected and where early diagnosis, oral health interventions and renal monitoring may greatly improve patient outcomes.

9. The physical, physiological and psychological risk factors for non-communicable diseases among adolescents from the Eastern Cape – A situational analysis report

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Introduction: The World Health Organisation (WHO) has projected that by 2030 non-communicable diseases (NCDs) will have become the largest single cause of mortality on the African continent (Alwan, 2011). In 2018, 72% of South African adolescents and children suffer from one or more NCD (Kamkuemah et al., 2022). The mental health and well-being of adolescents is another global concern (AGOG, 2017), as adolescents account for 16% of reports of instances of mental illness throughout the world (WHO, 2019).

Aim: The aim of this presentation is to report on the prevalence of physical, physiological, and psychological risk factors associated with NCD among a group of adolescents.

Methods: The total sample consist of 15-18 year old adolescents (n=266) from (Buffalo City Metropolitan Municipality, Amatole district) in the Eastern Cape. A Quantitative cross-sectional design was implemented while a descriptive statistic is used to report the prevalence of each risk factor in the population according to sex.

Results: Anthropometrical components (BMI, Fat%, H:W) presented most adolescents at no risk. Blood pressure reported 45% of males and 43.9% of females at risk. Nutritional risk indicated daily consumption of sugar (72.8% males; 76.9% females and cake (41% males and 48% females). Fruit and vegetable daily indicate was also poor (60.8% males; 40.7% females). The majority of the adolescents did achieve enough physical activity. In total the sample at risk , 84.4% presented with behavioural risk factors, while 48.6% presented with metabolic risk factors. Considering overall risk factors, and alarming 77% presented with two or more overall risk factors.

Conclusion: Proportion of overall risk factors indicates that approximately 70.6% of the adolescents present one to three risk factors that are associated with NCDs. It is imperative that these risk factors be reduced during adolescents before they manifest further into adulthood.

10. SARS-CoV-2 drug discovery using in silico screening and cell-based virus assays to identify novel antiviral compounds

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The COVID-19 pandemic pathogen, SARS-CoV-2, is the 3rd highly pathogenic coronavirus (CoV) to emerge in the human population in the last 20 years - with

devastating global implications. Currently there are 2 approved anti-SARS-CoV-2 drugs available, although the efficacy of these is unclear. As pathogenic human CoV species are likely to emerge again, there is a need for novel therapeutics. In this study, *in-silico* modelling was used to identify compounds in a zinc database that are predicted to interact with SARS-CoV-2 non-structural proteins - RNA-dependent RNA polymerase (nsp12) and guanine N7-methyl transferase (nsp14). Selected compounds were purchased and their antiviral activity was examined in SARS-CoV-2 infected cells. To quantify SARS-CoV-2 inhibition in our VeroE6 cell model, an immunodetection assay was developed to establish infectious virus titres. Based on antibody-binding to a specific viral protein and the formation of infection foci, this method is less time-consuming than the traditional plaque assay and has been adapted here to be performed in a 96-well microplate format; allowing more compounds to be processed per batch. Additionally, a CPE-based $TCID_{50}$ assay was optimised to titre virus. The concentration of viral genomic RNA copies present in samples was determined using qPCR. A hit compound was defined as one that exhibits over 90% SARS-CoV-2 inhibition. Characterised antivirals remdesivir and nirmatrelvir were used to validate our assays and the level of viral inhibition was reproducible for both compounds. To date, 14 novel compounds have been tested in our system. Single-point screening revealed cytotoxicity from 2 compounds, with >50% cell death at a concentration of 10μM. Against live SARS-CoV-2 infection, no viral inhibition was observed at the same concentration - virus titres in treated samples were similar to that of the untreated control. Compound identification is ongoing and our optimised protocol enables more efficient screening going forward.

11. Precision medicine: Pharmacogenomics and Development of Individualised Drug Therapy for Diabetes and Hypertension Patients

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Type 2 diabetes mellitus (T2DM) and hypertension represent two common conditions worldwide. They frequently occur in the same individuals in clinical practice. The presence of hypertension does increase the risk of new-onset of diabetes, as well as diabetes does promote development of hypertension. Comorbid hypertension and diabetes mellitus are associated with high rates of macrovascular and microvascular

complications. T2DM is commonly accompanied by other cardiovascular disease (CVD) risk factors, such as hypertension, obesity, and dyslipidemia. CVDs are the most common cause of death in people with T2DM. Due to the frequent association with cardiovascular diseases, the management of hypertensive patients with T2DM is an important clinical priority.

Metformin is often the first drug used to treat newly diagnosed type 2 diabetic patients, and it is widely prescribed worldwide. Metformin is effective as monotherapy and in combination with nearly every other therapy for type 2 diabetes, and its utility is supported by data from a large number of clinical trials. However, despite its exceptional efficacy and safety profile, about 40% of type 2 diabetes patients who have taken metformin failed to reach target fasting glucose level. Recent studies suggest that interpatient variability in response to metformin therapy could be related to polymorphisms in the organic cation transporter (OCT) genes and/or the multidrug and toxin extrusion (MATE) genes.

In the case of hypertension, several genetic biomarkers for antihypertensive drug response have been also identified, which might be used in treatment selection and optimization for hypertension. Research in the field has also enhanced our understanding of hypertension and the mechanisms by which the various drugs produce efficacy. There are several examples of genes in the literature and databases with relatively strong data on associations of genetic polymorphisms with antihypertensive response; the data on ADRB1, CACNB2, and NEDD4L are detailed as examples.

In this talk, we will present the main findings of a 12-year precision medicine project in South Africa with a special focus on admixed and indigenous Sub-Saharan African populations, as well as the main challenges and future directions for the project. The contribution of this project towards the development of an individualised drug therapy for patients with diabetes and hypertension will be highlighted.

12. Evaluation of the effect of Warburgia salutaris extract and its bioactive compounds on the metabolism of anti-diabetic and lip lowering drugs.

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Background: The use of herbal medicines continues to increase precipitously across the world, with many people now resorting to these products for treatment of various health conditions. About 80% of people worldwide utilize herbal medicines alongside mainstream pharmaceuticals. Herbal treatments have numerous bioactive components, and little is known about how they interact with each other and with conventional pharmaceutical drugs, thus increasing the possibility of adverse herb-drug interactions. In chronic medication adverse, herb-drug interactions interfere with normal drug pharmacokinetics and pharmacodynamics, either reducing their efficacy or inducing drug toxicity. To ensure safe and effective use, herbal medication pharmacokinetic and pharmacodynamic studies are necessary. This study will investigate the potential for herb-drug interaction *Warburgia salutaris* extract and compounds with commonly prescribed oral anti-diabetic medications and a lipid lowering statin.

Objectives: To investigate the effects of *Warburgia salutaris* extract and compounds on cytochrome P450 mediated metabolism of selected anti-diabetic and lipid lowering statin using Vivid assay and S9 liver fractions and human liver microsomes.

Methods: The vivid assay will be used for the initial one-point screening, which will be performed for CYP2C9, CYP2C8, CYP1A2, CYP2D6, CYP2B6, CYP2E1, CYP2C19, and CYP3A4 using *Warburgia salutaris* extract and its compounds to determine possible inhibitory effects. Human liver microsomes and S9 liver fractions will be used to determine the effects of *Warburgia salutaris* extract and its bioactive compounds on the clearance of the anti-diabetic and lipid lowering statin drugs.

Results: The changes in the pharmacokinetic profile of the anti-diabetic medications, lipid lowering statin due to the co-administration with the herbal products may reduce therapeutic plasma concentrations ultimately resulting in reduced efficacy.

Conclusion: Assessing the effect of *Warburgia salutaris* extract and compounds will establish the potential risk of co-administrated with the respective drugs which potentially could lead loss of efficacy

13. Telerehabilitation: Enabling the Delivery of Healthcare, Rehabilitation, and Self-Management through Community Health Workers

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This project aims to design and develop a self-management program, delivered by telerehabilitation (TR), to address the problem of the increased prevalence of chronic diseases of lifestyle. By 2030, CDLs will account for five times as many deaths as chronic diseases of lifestyle in low- and middle-income countries. Addressing the chronic diseases of lifestyle (CDL) epidemic is critical to a cycle of improved public health outcomes and better economic growth. Using self-management as a preventative method for non-communicable diseases is well documented and it helps combat related complications for CDLS. However, it would be important to explore how telerehabilitation can be used to promote self-management interventions for CDLS. Our goal is to develop a telerehabilitation program that would engage patients in self-management skills to manage non-communicable diseases. Development of the telerehabilitation programme will involve a structured process to establish content for the program using intervention mapping as a framework. The feasibility of the implementation will be tested by experts in the field and end-users. It is the intention that community health workers can implement and monitor the program.

Keywords: Telerehabilitation, self-management, community health workers, chronic diseases of lifestyles, intervention mapping.

14. Unraveling Of Anti-COVID-19 Biomarkers of South African Plants using UPLC-MS/MS coupled to chemometric analysis.

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Introduction: Some public members have raised direct questions and claims about the possibilities of South African medicinal plants as potential treatment agents for SARS-CoV-2. These questions have not received a simple solution so far. Thus, the aim of this study was to perform a comprehensive study of South African medicinal plants for the discovery of biomarkers that are related to anti- SARS-CoV-2 activities.

Materials and methods: Cytotoxicity of *Lippia_javanica* (leaves) and *Acorus calamus* (roots) against human normal lung fibroblasts MCR-5 and HEL-299 cell lines was done. Chemical profiling of these plants was accomplished via UPLC-MS/MS. Ions from both ESI- or ESI+ were merged and imported into the SIMCA-P program (version 14.1) for multivariate analysis. Supervised regression modeling was performed on the data set by the use of Partial Least Squares Discriminant Analysis (PLS-DA) and Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) to identify the potential anti- SARS-CoV-2 biomarkers. The biomarkers were filtered and confirmed by combining the results of the VIP values (VIP > 1.5) and t-test ($p < 0.05$). Correlation network diagram based on the KEGG databases and MetaboAnalyst was done to investigate the latent relationships of the plant metabolites. Moreover, identified biomarkers from OPLS analysis were docked into targets pockets of protease (Mpro) and spike (S) glycoprotein of SARS-CoV-2 using Schrodinger® suite.

Results: UPLC-MS/MS analysis of the leaves of *Lippia_javanica* vs. roots of *Acorus calamus* yielded 139 and 227 metabolites for negative and positive ionization mode, respectively. Most of them were triterpenoids and flavonoids. This was incremented by OPLS analysis that related their promising COVID-19 inhibitory activities to the presence of 93 biomarkers for both -/+ ionization mode. In general, data with VIP>1.5, p<0.05 and FC>2 were considered to meet the requirements of

differential metabolite. The highest biomarkers were Flurbiprofen glucuronide (VIP= 2.13, FC=14), Isoyatein (VIP=2,05, FC=13) and Forsythoside B (VIP= 2.06, FC=13.3) for negative ionization mode. All significant metabolites were used to obtain the annotated pathways. The annotated pathways for this negative ionization mode were cysteine and methionine metabolism, Arginine and proline metabolism, Purine metabolism and Steroid hormone biosynthesis. Moreover, the highest biomarkers for positive ionization mode were Tetramethylquercetin 3-rutinoside (VIP=2.41, FC= 11,68), 6b-Hydroxymethandienone (VIP=2.31. FC= 10,74), Isopropyl beta-glucoside (VIP=2.33, FC=10,83). The tested extracts showed 20% cytotoxicity (CC_{50}) at concentrations more than 30 µg/mL indicating their safety on these cells. The annotated pathways for this positive ionization mode were Purine metabolism, alpha-Linolenic acid metabolism and Pantothenate and CoA biosynthesis. Subsequently, in silico molecular docking studies of the identified plant compounds (biomarkers) predicted potential anti- SARS-CoV-2 properties.

Conclusion: This study may provide a more rational phytotherapeutic choice to SARS-CoV-2 with the focus on protease (Mpro) and spike (S) glycoprotein of SARS-CoV-2.

15. Risk Factors Attributable to Hypertension among HIV-Infected Patients on Antiretroviral Therapy in Selected Rural Districts of the Eastern Cape Province, South Africa

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Background: Antiretroviral therapy has improved HIV patients' quality of life and life expectancy. However, complications have emerged in the form of hypertension. In the rural Eastern Cape, there is minimal information about HIV-infected people. The current study intended to evaluate the factors associated with hypertension in HIV-infected individuals receiving antiretroviral therapy in rural areas of South Africa's Eastern Cape.

Methods: For this cohort study, HIV-positive people taking antiretroviral therapy aged 15 and up were recruited at random from several rural locations in the Eastern Cape. Using Cox univariate and multivariate analyses, the key predictors of hypertension were found.

Results: Of the total participants (n = 361), 53% of individuals had hypertension. In the Cox multivariate model, patients that had hypertension heredity, BMI ≥ 25 kg/m2, eGFR < 60 mL/min/1.73 m2, advanced and severe CD4 counts, 1TFE and 1T3E regimens, and the male gender were found to be at greater risk of hypertension.

Conclusions: The findings of this study indicate that hypertension is a prevalent concern among HIV patients receiving antiretroviral therapy. HIV patients should have their blood pressure checked regularly, and they should be screened for high blood pressure and given treatment for it.

16. Determinants Of High Neonatal and Child Mortality Rates In The Rural Areas of Limpopo Province, South Africa

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Neonatal mortality accounts for almost 47 percent of under-five child mortality, globally (UNICEF, 2018e). An understanding of the factors related to neonatal mortality is important to guide the development of focused and evidence-based health interventions to prevent neonatal deaths. There is a gap in information in Limpopo about the improvements in neonatal and child mortality. The proposed study explores and assesses the determinants of high neonatal and child mortality and metabolomic profiles among pregnant women's peripheral blood and infant cord blood. Serum metabolomic profiles will be examined using gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry. A mixed method will be used; qualitative participatory action research and quantitative non-experimental design will be used. The population will include midwives and operational managers from selected hospitals, child age-bearing women (pregnant and non-pregnant) as well as community members. Non-probability purposive and probability sampling will be used. Focus group discussions, field notes reflection and questionnaires will be used to collect data, and laboratory tests using Serum metabolomic profiles will be done using gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry to identify and validate the determinants of neonatal will be through Qualitative data will be analyzed through interpretive phenomenological analysis and this will allow the researcher to identify emergent themes from the phrases. Quantitative data will be analyzed using SPSS version 26.0 assisted by a professional Statistician. The aspect of trustworthiness will be ensured through credibility, authenticity, dependability, transferability, and confirmability, and the validity and reliability of the instrument in the quantitative strand will be ensured. Ethical principles will be applied. Dissemination of the results will be done through perinatal mortality meetings, community forums, and workshop presentations. Articles will be published in peer-reviewed/accredited journals.

17. Anti-Cancer, Anti-Diabetic, Anti-Obesity and Anti-Inflammatory Potential Of Plant Extracts/Plant-Derived Compounds

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Chronic inflammation plays a crucial role in the development of diabetes as well as in the promotion of cancer metastasis by enhancing tumour cell invasiveness and migration. However, there is limited research on natural compounds for the use and development of treatment strategies for diseases that are fuelled by inflammation. Exploratory preliminary data from our lab revealed that Ozoroa paniculosa acetone extract has promising anti-inflammatory properties while the Momordica balsamina methanol extract (MBME) was found to have promising anti-inflammatory and anticancer properties. Thus, this study investigated the anti-migratory and anti-invasive effects of Momordica balsamina methanol extract in IL-6-activated MDA-MB-231 cells as well as O. paniculosa acetone extract's ability to disrupt the crosstalk between RAW 264.7 macrophages and 3T3-L1 adipocytes within the adipose microenvironment. Adipose tissue dysregulation and infiltration by immune cells leads to increased production of pro-inflammatory cytokines and adipokines, persistent inflammation as well as insulin resistance and diabetes. The effect of the acetone extract of O. paniculosa on the viability of the RAW 264.7 macrophages and 3T3-L1 adipocytes was assessed using 3-(4, 5- dimethylthiazol)-2, 5-diphenyltetrazolium bromide (MTT) assay. The expression profile of adipokines and cytokines in extract-treated co-culture of RAW264.7 macrophages and 3T3-L1 adipocytes was assessed using mouse adipokine and cytokine proteome profilers. MDA-MB-231 cells are aggressive breast cancer cells whose invasiveness and migratory capability are enhanced in the presence of high amounts of pro-inflammatory molecules such as IL-6 in the breast tumour microenvironment. The effect of MBME on MDA-MB-231 and HEK-293 kidney cells (in vitro kidney toxicology model) was assessed using the Muse® Count and Viability assay. The anti-migratory and anti-invasive effects of MBME on the IL-6- activated MDA-MB-231 cells were investigated using wound healing and trans-well cell invasion assays. Furthermore, western blotting and gelatin-zymography were used to assess the effect of MBME on MMP-2 and MMP-9 protein expression and activity, respectively. The findings revealed that O. paniculosa

extract did not have an effect on RAW 264.7 macrophages and 3T3 L1 adipocytes viability. It was further observed the O. paniculosa extract significantly decreased the expression profiles of pro-inflammatory adipokines and cytokines in the co-culture system. Treatment with MBME did not have an effect on MDA-MB-231 viability at concentrations below 125 µg/ml while a reduction in HEK-293 cell viability was observed at concentrations above 100 µg/ml of the extract. In addition, MBME significantly inhibited IL-6-induced MDA-MB-231 cell migration and invasiveness via a significant downregulation of MMP-2 and MMP-9 protein expression and activity. This suggests that the O. paniculosa acetone extract and the Mormodica balsamina methanol extracts contain compounds that may be useful in the alleviation of insulin resistance or diabetes as well as tumour cell invasiveness and migration fuelled by persistent inflammation.

SAMRC RESEARCH CAPACITY DEVELOPMENT INITIATIVE-NESTED POSTDOCTORAL PROGRAMME

1. Improving The Solubility and Blood Brain Permeability of Edaravone-Benzyl-Pyridinium Hybrid Using Solid Lipid Nanoparticle Delivery System.

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Alzheimer's disease (AD) is characterised by progressive loss and dysfunction in neuronal cells. Owing to its multifaceted nature, available treatments only offer symptomatic relief, and multifunctional agents could be beneficial. A series of edaravone-benzyl-pyridinium hybrids (EBPD), with neuroprotective potential, have been synthesised by our group. However, blood brain barrier (BBB) permeability in vivo study showed radical adduct formation with this group of compounds, rendering them impermeable. We have designed, synthesised and characterised a series of EBPD loaded solid lipid nanoparticles for the purpose of circumventing this problem. Using the hot homogenisation method, drug loaded nanoparticles including stearic acid/poloxamer 188 (SP188), SP188 coated with chitosan or polysorbate 80 were synthesised. An average size of 165 nm (PDI: 0.4203; zeta potential: -18.9) was

obtained for SP188. However, loading SP188 with EBPD led to an increase in size (615.1 nm) and a positive zeta potential (14.2). Similar trends were seen in SP188 coated with polysorbate 80 as the size increase from 242 nm to 450 nm upon loading the EPBD, and the zeta potential changed from –22 to 3.8, respectively. In contrast, no significant change in size and charge between empty chitosan-coated-SP188 shell (504 nm) and chitosan-coated-EBPD-SP188 (541.6 nm), and both displayed positive zeta potentials. Nano-EBPDs were found to be evenly distributed (size) and stable as indicated by the PDI and zeta potential, respectively. This cationic property is highly desirable as it could potentially aid biological interaction with anionic cellular barrier like BBB to improve permeability. The proposed solid lipid nanoparticles were successfully synthesised and characterised. Albeit further studies such as loading efficiency or capacity, solubility, release profile, stability in biological medium and scanning electron microscope (SEM) are necessary to fully characterise these nanoparticles. We hope these nano-formulations will improve the druggable properties of EBPD necessary for the potential treatment of AD.

2. The Antioxidant, Anti-Cancer, And Anti-Metastatic Effect of Tarchonanthus Camphoratus on Metastatic MDA-MB-231 Cells

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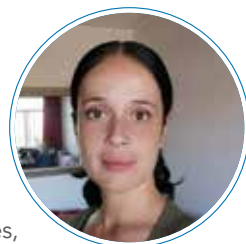
Despite the progress made with conventional anticancer treatments, toxicity and cancer metastasis complication remains a major problem. Moreover, oxidative stress is associated with nucleic acid, lipid, and protein damage which increases the risk of degenerative diseases such as cancer. Medicinal plants have become a suitable alternative due to their minimal toxicity, affordability and abundance. Thus, the aim of this study was to investigate the antioxidant, anticancer and anti-metastatic properties of the acetone extract of *Tarchonanthus camphoratus* leaves on metastatic MDA-MB-231 cells. The antioxidant activities of the acetone extract were assessed by the ferric reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) assays. The cytotoxicity of the acetone extract was tested against metastatic MDA-MB-231 cells and Vero normal kidney cells using the MTT cytotoxicity assay. Furthermore, the effects of the extracts were assessed on their inhibitory potential

of cell adhesion, migration and invasion using the adhesion, wound healing and Boyden chamber invasion assays. The acetone extract exhibited moderate to low levels of FRAP and DPPH activities. The acetone extract reduced cell viability of metastatic MBA-MB-231 cells between 150 and 250 µg/ml and between 100 and 250 µg/ml for Vero normal kidney cells. Moreover, exposure to the acetone extract significantly inhibited cell attachment, cell migration, and invasion of metastatic MDA-MB-231 cells. This study suggests that the acetone extract of *Tarchonanthus camphoratus leaves* may be a potential source of antioxidant compounds and may exhibit inhibitory effects against metastatic MDA-MB-231 cells.

3. Development Of Antiviral Screening Assays for The Identification Of SARS-COV-2 Inhibitors

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The COVID-19 pandemic pathogen, SARS-CoV-2, is the 3rd highly pathogenic coronavirus (CoV) to emerge in the human population in the last 20 years - with devastating global implications. Currently there are 2 approved anti-SARS-CoV-2 drugs available, although the efficacy of these is unclear. As pathogenic human CoV species are likely to emerge again, there is a need for novel therapeutics. In this study, *in-silico* modelling was used to identify compounds in a zinc database that are predicted to interact with SARS-CoV-2 non-structural proteins - RNA-dependent RNA polymerase (nsp12) and guanine N7-methyl transferase (nsp14). Selected compounds were purchased, and their antiviral activity was examined in SARS-CoV-2 infected cells. To quantify SARS-CoV-2 inhibition in our VeroE6 cell model, an immunodetection assay was developed to establish infectious virus titres. Based on antibody-binding to a specific viral protein and the formation of infection foci, this method is less time-consuming than the traditional plaque assay and has been adapted here to be performed in a 96-well microplate format; allowing more compounds to be processed per batch. Additionally, a CPE-based $TCID_{50}$ assay was optimised to titre virus. The concentration of viral genomic RNA copies present in samples was determined using qPCR. A hit compound was defined as one that exhibits over 90% SARS-CoV-2 inhibition. Characterised antivirals remdesivir and

nirmatrelvir were used to validate our assays and the level of viral inhibition was reproducible for both compounds. To date, 14 novel compounds have been tested in our system. Single-point screening revealed cytotoxicity from 2 compounds, with >50% cell death at a concentration of 10μM. Against live SARS-CoV-2 infection, no viral inhibition was observed at the same concentration - virus titres in treated samples were similar to that of the untreated control. Compound identification is ongoing, and our optimised protocol enables more efficient screening going forward.

4. Knowledge Translation Platforms for Bridging Public Health and Health Systems Research Into Universal Health Coverage Related Policy And Practice In South Africa (KTP-UHC)

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Background: Knowledge Translation Platforms (KTPs) can support evidence-informed decision-making by providing relevant and timely research evidence and they can bridge the gap between research, policy and practice. There are several KTPs in South Africa (that self-identify as such or not), however, there is a need to explore their full potential as interventions that can support NHI related decisions. The aim of this study is to understand and strengthen KTPs in supporting NHI related decisions in South Africa.

Methods: A multi-method study, including a scoping review and formative qualitative research.

Preliminary findings: Our findings are from the (1) scoping review and (2) formative qualitative research.

(1) The scoping review revealed a clear challenge in defining and conceptualising a KTP, which raised methodological issues around screening and extracting data from the literature. Additionally, most of the KPTs identified were located in a high-income setting, which speaks to the limited research on KTPs in low- and middle-income settings, similar to South Africa.

(2) Our formative qualitative research comprised of a mapping exercise and interviews with research cluster heads at a KTP in South Africa of the knowledge translation (KT) activities and processes being planned and implemented. We organised the mapping and interview results according to the six KT themes described in the Cochrane KT Framework (prioritization and co-production; sustainable infrastructure; engaging with audiences; packaging, communication, and dissemination; building audience capacity; and advocacy). Packaging, communication, and dissemination was identified as the weakest KT theme by researchers at the KTP.

Discussion and conclusion: The ongoing scoping review and formative qualitative research are contributing to an understanding of KTPs, in terms of their conceptualisation and characteristics. The next step in the project will involve enhancing an existing framework for KTPs or developing a new one for identifying and evaluating KTPs if necessary and relevant.

5. Discovery of SARS-CoV-2 Human Angiotensin-Converting Enzyme 2 (hACE2) And Targeting Transmembrane Serine Protease 2 (TMPRSS2) Inhibitors from South African Plant-Based Product.

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Introduction: The study focuses on the discovery of South African plant-derived target drugs as SARS-CoV-2 angiotensin-converting enzyme 2 (hACE2) and targeting transmembrane serine protease 2 (TMPRSS2) Inhibitors, which serves as an entry receptor for SARS-CoV-2 to infect people. However, viral entry requires not only binding to the hACE2 receptor but also priming of the virus's spike (S) protein by TMPRSS2 by cleavage of the S proteins at the S1/S2 sites. This cleavage step is necessary for the virus-host cell membrane fusion and cell entry. Thus, the study aimed to discover SARS-CoV-2 hACE2 and TMPRSS2 inhibitors from South African plant-based products.

Materials and methods: Secondary metabolites present in the leaf extracts of Sweet annie and Artemisia afra were determined using UPLC-MS/MS. Ions from both ESI- and ESI+ were imported for multivariate analysis. A Principal Component Analysis (PCA) was used as an unsupervised method for data visualization and outlier identification. Partial Least Squares Discriminant Analysis (PLS-DA) and Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) were used to identify the potential metabolites. xCELLigence Real-Time Cell Analysis System was used to determine the cytotoxicity of plants.

Preliminary results: The UPLC-MS base peak chromatograms of the leaves of Sweet annie and Artemisia afra showed the presence of a total of 121 and 81 peaks for negative and positive ionization modes, respectively. The identified compounds belong to different classes of secondary metabolites including flavonoids, phenolic acids, iridoid glycosides, phenylethanoid glycosides, lignan glycosides, and triterpenes. The highest metabolites from (-) ionization mode were Dolichotheline, LysoPC and Quercetin 3-(6''-malonyl-glucoside). However, the highest biomarkers from the (+) ionization mode were 1,3,4-Oxadiazepine and 2'-Hydroxynicotine. All plant extracts exhibited 30% cytotoxicity (CC50) at concentrations of more than 30 μg/mL signifying their safety on these cells.

Expected results: To discover new South African-based phytotherapeutic agents that can inhibit SARS-CoV-2 TMPRSS2 and hACE2 receptors.

6. Prevalence Of Putative Drug Resistance Mutations In HIV-1 Subtype C In Africa: A Systematic Review and Individual Sequence Level Meta-Analysis

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Over the years, research has determined mutations that give rise to drug resistant viruses. However, other amino acid changes at the sites of known drug resistant mutations - putative resistance mutations - have not received adequate attention. The goal of this systematic review and individual sequence level meta-analysis was to

determine the scope and types of putative drug resistance mutations for HIV-1 subtype C in drug naïve individuals in Africa, and to understand their potential implications. African HIV-1 subtype C protease (PR), reverse transcriptase (RT) and Integrase (IN) Sanger and Next Generation Sequences obtained from drug naïve individuals were retrieved from Los Alamos HIV Sequence Database, and from clinical specimens from a South African cohort. Sequences were aligned and translated to amino acids using Geneious® software version 8.1.5. Changes at positions known to confer classical drug resistance according to the Stanford HIV Drug Resistance Database were examined to identify amino acid substitutions of unknown implications for PR, RT and IN inhibitors. A total of 9528 sanger sequences comprising complete PR (n=6464), RT (n=1858), and IN (n=1206) sequences from HIV-1 subtype C drug naïve individuals were available (1989-2014) for analysis. A total of 241 NGS genereted sequences from clinical specimens from South Africa were also analysed for RT and PR putative mutations. Sanger based RT, PR and IN sequences had a prevalence of 4.4%, 0.4% and 1.2% respectively of putative mutations. The prevelence increased to 11.6% and 7.9% for RT and PR respectively when minor variant were accounted for with the NGS data. A systematic review was conducted to document drug resistance profiles of some of the putative mutations, and a total of 10 articles were included for the analysis, with putative mutation from the PR gene as the most investigated mutations using both in silico and in-vitro subtype C-based phenotypic approaches. It will be important to assess the phenotypic impact of these putative mutations, with the view of enhancing the effectiveness of PR, RT and IN inhibitors used in first line treatment in HIV-1 subtype C infections.

Key words: HIV subtype C, Putative drug resistance mutations, Africa

7. Phytoconstituents Analysis of Cyclopia Genistoides (Red Honeybush Tea Kombucha) And Its In Vitro Antidiabetic and Antioxidant Activities.

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Kombucha tea is a sweetened tea beverage fermented by a symbiotic consortium of bacteria and yeast (SCOBY). Due to its claimed health benefits, such as its anti-atherosclerotic, anticarcinogenic, anti-diabetic, anti-microbial, anti-mutagenic, and chemoprotective properties, Kombucha tea has attracted considerable attention in the modern era of medicine. The purpose of this study was to investigate the antidiabetic and antioxidant properties of *Cyclopia genistoides* kombucha (*Cg*-kombucha) on days seven and fourteen of fermentation. To the best of our knowledge, *Cg*-kombucha has not yet been studied to date. The Phytochemical screening of the red honeybush tea Kombucha was done via the Fourier transform infrared spectroscopic (FTIR) and Gas chromatography–mass spectrometry (GC-MS). The Enzyme inhibitory capacity including α-Amylase and α-Glucosidase inhibitory capacity was also performed. IR spectra revealed several peaks including 3308, 2911, 1660, 1266, and 1037 corresponding to the OH, CSP^3H, C=O, C=C, CSP^2O, and CSP^3O functional groups, respectively. The compounds commonly identified between day 7 and day 14 in order of predominance via GC-MS include 5-Hydroxymethylfurfural (32.2% and 42.9%, respectively) and 4H-pyran-4-one (8.7% and 10.9%, respectively). Moreover, the day14 sample had the highest α,α-diphenyl-β-picrylhydrazyl (DPPH) radical scavenging activity of IC_{50} value of 3,836 ± 0,709 mg.mL^{-1}, which was significantly lower than that recorded on the day 7 sample (4,172 ± 0,709 mg.mL^{-1}). However, the opposite was true in the 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS$^{•+}$) cation activity of the samples. Furthermore, the IC_{50} values of the *Cg*-kombucha crude extracts (day 7 and day 14) were 3.75±0.115 and 4.13±0.095 mg.mL^{-1}, respectively. However, significant inhibitory capacity towards α-glucosidase was recorded. In conclusion, our data revealed that red honeybush tea kombucha had antidiabetic and antioxidant activities. However, the efficiency of the 7-day ferment compared to the 14-day ferment demonstrates that biological improvement of activity increases with fermentation time until a particular threshold.

8. Liposomal Naringenin Exerts Radio-Sensitizing Effects In Vitro

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Introduction: Incidence, morbidity, and mortality from cancer are on the rise globally. Radiotherapy is a frequently utilized treatment modality, however, it is associated with numerous adverse effects occurring as a factor of dose, causing widespread damage to healthy tissue surrounding the tumour and ultimately lowering patient quality of life. Radio-sensitizers may be used to lower radiation doses, thereby mitigating damage to healthy tissues and subsequent side effects. The flavonoid naringenin exhibits multiple favorable in vitro effects toward cancer treatment, including the sensitization toward radiation therapy. However, the low solubility, poor bioavailability, and poor absorption of naringenin hinders the clinical use of the flavonoid—an issue which may be overcome by liposomal encapsulation of naringenin as a method of drug delivery. Thus, the aim was to investigate the potential radio-sensitizing effects of free and liposomal-encapsulated naringenin with the ultimate goal optimizing radiotherapy.

Methods: Liposomal naringenin was synthesized using the thin-film hydration method and compared to free naringenin. MDA-MB-231 breast cancer cells were pre-treated with the calculated IC50 and a non-toxic dose of both free and liposomal naringenin, respectively, and exposed to increasing doses of radiation (2-, 4-, and 8 Gy). The combined effects of radiation with naringenin, or liposomal naringenin, significantly ($P<0.0001$) lowered cell viability, demonstrated morphological effects indicative of cell death, decreased colony formation, negatively impacted growth curve and surviving fraction.

Results: In this study we demonstrated that the flavonoid naringenin, in both its free and liposomal form, has substantial radio-sensitizing capabilities toward triple-negative breast cancer cells. Furthermore, liposomal delivery of the flavonoid significantly enhanced the reported effects.

9. Contraceptive Failure: Herbal Supplements and Their Effect on The Metabolism Of An Ethinylestradiol Based Contraceptive.

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For many years prior to the advent of modern medicine, herbal plants were the principal agents for primary health care. In both developed and developing countries, such as South Africa, the United States of America, India, and Brazil, there is a growing interest in herbal medicine as a precursor for pharmacological actives. The biggest concern, however, is the concurrent use of herbal medicine and conventional drugs. Many physicians are uninformed of the potential risks of herb–drug interactions, as approximately only 40% of patients reveal herbal medicine use. Of particular interest in this study are the two commercially available herbal immune boosters Immunity plusTM and Air ImmuneTM. Given their ability to positively affect the immune system, immunocompromised individuals such as TB and HIV/AIDS patients, as well as those suffering from colds and other respiratory diseases, commonly take herbal immune boosters. The effects of natural immune boosters such as Immunity plusTM and Air ImmuneTM on ethinylestradiol (EE) based contraceptives commonly used by immunocompromised female patients are unknown, and since the commercial availability of herbal medicines continues to rise, herb-drug interactions are a concern. To prevent conception, EE contraceptives inhibit the release of eggs from the ovaries, alter the mucus surrounding the opening of the cervix, and alter the lining of the uterus. The principal sites of EE metabolism are the intestines and liver. Phase II metabolism of EE produces pharmacologically active metabolites 17-ethinylestradiol-3-O-sulfate (EES) and 17-ethinylestradiol-3-O-glucorinide (EEG). The concomitant use of Immunity plusTM and Air ImmuneTM with EE may alter the metabolism of EE and result in the loss or diminution of EE's efficacy. This study aims to investigate whether the co-use of Immunity plus™ and Air Immune™ influences the rate of metabolism and efficacy of EE.

10. Investigating And Understanding Factors Associated with Health Outcomes and Quality Of Life In People With Spinal Cord Injury In South Africa

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Purpose: To investigate and understand different factors (e.g., environmental and employment) and outcomes associated with health benefits and quality of life for people with spinal cord injury (SCI) in South Africa.

Method: Various data from the International Spinal Cord Injury (INSCI) Community Survey, which formed part of a previously MRC-funded SCI project, were analysed. Various statistical models were computed to determine 1) factors influencing employment among people with SCI in South Africa. 2) the role of environmental factors on health conditions, general health and quality of life in persons with SCI in South Africa.

Results: *Study 1*: Of the 200 participants included, 61% reported being employed before SCI onset whereas only 25% reported being engaged in paid work. Requiring physical assistance in the home environment, the number of education years before SCI, household income, having worked before SCI onset, and environmental factors were factors associated with employment after SCI.

Study 2: The commonly reported environmental barriers were public access, lack of short and long-distance transport and finances. Environmental factors such as public access, short and long-distance transport, friends and colleagues' attitudes and communication were significantly associated with the presence of secondary health conditions. Finances, family attitudes, and communication had a significant association with worsened mental health.

Conclusion: The results from the studies give insight into modifiable factors policymakers need to consider or adapt to improve the lives of people with SCI in South Africa with respect to employment, health (secondary health conditions), and general and mental health.

11. ADME Polymorphism in Tuberculosis: Pharmacogenetic Analysis Of Samples From Patients In Healthcare Facilities In The Vhembe District

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Background: Tuberculosis is caused by Mycobacterium tuberculosis and is categorised into multidrug-resistant (MDR) and extensively drug-resistant (XDR). Resistance to at least isoniazid and rifampicin is known as MDR TB. XDR TB is resistance to isoniazid and rifampicin and fluoroquinolones, including capreomycin, kanamycin, amikacin. Several studies on drug-resistant tuberculosis have been conducted in South Africa; however, there are limited studies that have reported on the prevalence of DR-TB among patients receiving treatment in the northern region of South Africa.

Materials and methods: In total, 61 patients receiving treatment were enrolled in the study since September 2022 (61 samples each for sputum and blood). After pre-treatment with NALC-NaOH, DNA was isolated from sputum samples and Genomic DNA extraction was done using QIAamp® DNA Mini Kit. Detection of resistance was done using the Allplex™ MTB/MDR/XDRe PCR assay. A questionnaire was administered to identify the risk factors associated with TB. NGS was performed and still in progress.

Results: From the 61 patients enrolled in the study, 48% were male, 28% of patients were still TB positive while 3,3% had resistance TB; 21% of the patients had bacterial co-infection and 56% of them were HIV positive. Several risks factors were identified.

Conclusion: The study found a 3,3% prevalence of resistance in the patients and correlation between risk factor and TB was observed. More studies investigating the prevalence are required in the study region, Limpopo province (SA).

12. In Vitro Antidiabetic, Antioxidant and Cytotoxic Evaluation of Honeybush Tea (Cyclopia Genistoides) Extracts

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This study evaluated *in vitro* antidiabetic and antioxidant properties of different extracts (n-hexane, dichloromethane (DCM), and 70% ethanol) of honeybush tea (*Cyclopia genistoides*). Over a period of 28 days antiprotein glycation was evaluated, some antidiabetic indicators (α-amylase, α-glucosidase, and pancreatic lipase inhibitory effects) and antioxidant activities (DPPH, ABTS, hydroxyl radical, metal ion chelating and reducing power) for each of the crude extracts were also investigated. The results showed that all of the tested *C. genistoides* extracts had strong α-amylase and lipase inhibitory activity in a concentration-dependent manner with IC_{50} values from 0.018 mg/ml (DCM extract) to 9.93 mg/ml (hexane extract), respectively. The extracts also displayed inhibitory effects on protein glycation between the 14th and 28th day. The DCM and ethanolic extracts further exhibited strong antioxidant activities as they effectively scavenged most of the radicals tested, with IC_{50} values ranging from 0.014 – 0.048 mg/ml and 0.019 – 0.043 mg/ml. Two hundred and seventy-four chemical constituents had been identified by GC-MS, with the n-hexane extract having the highest number of peaks (127) followed by DCM extract (107). Six compounds were identified across all the three extracts; Decane (RT: 6.4), Undecane (RT: 7.7), Dodecane (RT: 9.00), Phytol (RT: 21.32), Heptadecanoic acid, 9-methyl, methyl ester (RT: 21.65), and 9-Octadecenamide (RT: 24.30). The cytotoxicity of the extracts against C3A cell lines was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) (MTT) assay, which demonstrated that honeybush tea had a toxicity effect ranging from 66.3 – 88.4 µg/ml on C3A cell lines. The results showed that honeybush has antioxidant and antidiabetic activities, which could be partially attributed to the phytochemical compounds identified within the extracts.

SAMRC CLINICIAN POSTDOCTORAL PROGRAMME

1. The Longitudinal Impact of Air Pollution And Environmental Tobacco Smoke Exposure On Childhood Respiratory Diseases In An African Birth Cohort.

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Air pollution, a global health emergency, impacts health from early-life and may influence lung health trajectories. Sources include indoor (alternate household energy), outdoor (industry, traffic) and tobacco smoke. Key pollutants contributing to air pollution are particulate matter, nitrogen dioxide and volatile organic compounds.

The overarching research aim is to investigate the impact of environmental factors (indoor air pollution (IAP), environmental tobacco smoke (ETS) and outdoor air pollution (OAP)) on respiratory health in children in a South African birth cohort, the Drakenstein Child Health Study (DCHS), up to 10 years of age, in a low- / middle-income country setting in Paarl, South Africa.

The DCHS, investigated the impact of IAP and ETS on lower respiratory tract infections in early childhood. However, as children grow and increasingly spend time outdoors, further study is planned to evaluate the impact of OAP and thereby the longitudinal impact of environmental exposure on respiratory health.

To understand the effect of early-life environmental exposures on health, we conducted a birth outcomes study. We assessed the impact of IAP and ETS on birth outcomes, using IAP exposures (particulate matter, nitrogen dioxide and volatile organic compounds) measured at an antenatal home visit and maternal urine cotinine (for ETS exposure). Multivariable analysis assessed the impact of IAP and ETS on birth outcomes.

Of 1143 live births, the median weight-for-age (WfA) z-score was -0.25 [interquartile range: -0.93, 0.43], and 78 (7%) had respiratory distress at birth. Maternal smoking was associated with a decreased WfA z-score (β: -0.43; 95% confidence interval (CI): -0.62, -0.24). Of the air pollutants, only particulate matter exposure doubled the odds of respiratory distress at birth (adjusted odds ratio (aOR): 2.00; 95% CI: 1.05,3.80).

This study showed that environmental exposures impact health from birth. Low birth weight has been shown to be associated with adverse health outcomes and there is increasing evidence that lung health trajectories are set in early-life and insults at this susceptible time may impact this. Understanding the longitudinal impact is key in developing appropriate interventions, especially in vulnerable populations, with potentially far-reaching societal impacts. The overall study will include investigating the longitudinal impact of environmental exposures on health and lung function from birth through adolescence, using already measured IAP and ETS and measuring OAP as an additional exposure

2. Matching Study Using Health and Police Datasets For Characterising Interpersonal Violence In The Community Of Khayelitsha, South Africa 2013–2015

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Objectives: The Cardiff Model of data sharing for violence prevention is premised on the idea that the majority of injury cases presenting at health facilities as a result of interpersonal violence will not be reported to the police. The aim of this study was to determine the concordance between violent crimes reported to the police with violence-related injuries presenting at health facilities in Cape Town, South Africa.

Methods: We conducted a retrospective analysis of secondary cross-sectional health and police data, from three health facilities and three police stations in the community of Khayelitsha, Cape Town. 781 cases of injuries arising from interpersonal violence seen at health facilities were compared with 739 violence-related crimes reported at police stations over five separate week-long sampling periods from 2013 to 2015. Personal identifiers, name and surname, were used to match cases.

Results: Of the 708 cases presenting at health facilities, 104 (14.7%) were matched with police records. The addition of non-reported cases of violence-related injuries from the health dataset to the police reported crime statistics resulted in an 81.7% increase in potential total violent crimes over the reporting period. Compared with incidents reported to the police, those not reported were more likely to involve male patients (difference: +47.0%; p<0.001) and sharp object injuries (difference: +24.7%; p<0.001). Push/kick/punch injuries were more frequent among reporting than non-reporting patients (difference: +17.5%; p<0.001).

Conclusion: These findings suggest that the majority of injuries arising from interpersonal violence presenting at health facilities in Khayelitsha are not reported to the police. A data-sharing model between health services and the police should be implemented to inform violence surveillance and reduction.

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3. National And Regional Burden of Chronic Kidney Disease and Its Risk Factors In South Africa: A Systematic Analysis Of The Global Burden Of Disease Study 2021

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Introduction: Chronic kidney disease (CKD) is an increasing global public health problem, associated with major economic implications to healthcare systems worldwide. In 2017, CKD was the cause of death in 1.2 million people worldwide, while the global prevalence of CKD was 9.1%. The burden and risk factors of CKD

varies worldwide, with differences existing not only between different countries, but also within regions in countries. This burden remains understudied in many parts of the world, including South Africa. In this analysis, Global Burden of Disease (GBD) study data and methodologies will be used to 1) describe the variation in CKD burden in South Africa by province/region, sex, and cause of CKD from 1990 to 2021, 2) analyze factors associated with changes in CKD burden, and 3) describe the influence of socioeconomic factors on CKD burden.

Methods: This systematic analysis will utilize secondary data analysis and methodologies from GBD 2021. CKD will be defined as an abnormality of kidney function (eGFR <60 ml/min/1.73m2 or albumin to creatinine (ACR) ratio >30mg/g). Data for cause-of-death will be obtained from data retrieved from vital records and verbal registries. International Classification of Diseases 10 codes will be used to assign cause of death attributed to CKD. Registries for end-stage kidney disease will be used to analyze the contribution of each cause to ESKD and CKD mortality. Crude and age-standardized overall CKD prevalence rates, incidence, mortality, number, and age-standardized rate for years of life lost, years living with disability, disability -adjusted life years, and deaths will be used as measures of CKD burden. Counts and age-standardized rates (per 100 000 population) will be computed to quantify CKD burden.

Conclusion: We anticipate that this will be the most up-to-date and comprehensive information available, empowering policy makers to make informed decisions regarding kidney care in South Africa.

SAMRC INTRAMURAL POSTDOCTORAL PROGRAMME

1. Developing A Long-Read Sequencing Method for Identifying and Quantifying SARS-Cov-2 Variants Of Concern In Wastewater

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Genome sequencing of severe acute respiratory syndrome coronavirus (SARS-CoV-2) has culminated the evolutionary monitoring of variants of concern (VOCs) linked to the covid-19 pandemic. Significant advancements in the field of genomics have since been established to facilitate SARS-CoV-2 surveillance in communities through wastewater-based epidemiology (WBE), which has emerged as an effective public health tool. Sequencing short fragments of viral genomes from wastewater permits robust tracking of known SARS-CoV-2 VOCs and information pertaining to dominant strains in circulation. It is therefore imperative to identify these VOCs rapidly to keep up with evolutionary changes and to further assist the public in limiting their emergence and, their impact when they do arise. However, the major obstacle with short read sequencing is that amplicons are from a mixed pool of individuals and quantifying VOCs has proven to be challenging, partly due to difficulty of assembling small reads from multiple viral particles. We therefore aim to develop and implement a sequencing data analysis pipeline using both long-read and short read sequencing of wastewater samples collected from different wastewater treatment plants across South Africa to identify and quantify SARS-CoV-2 VOCs. To this end, we are currently optimising sequencing methods capable of long-read sequencing using Oxford Nanopore Technologies' MinION and GridION sequencers. The read accuracy of these instruments is inferior to short-read sequencers, and we therefore hypothesize that combining data from long-and-short-read sequencers will allow for more accurate VOCs quantification and lineage deconvolution. Samples will be collected as part of the ongoing SAMRC Wastewater Surveillance Research Program. All samples will be sequenced using long-and-short-read platforms. Following this, new data analysis pipelines will be developed to combine reads for more accurate VOCs detection in wastewater samples. Results emanating from this study will be invaluable to scientists at the forefront of SARS-CoV-2 genomic surveillance and WBE.

2. The Effect of Childhood Trauma Type and Timing on Acute Posttraumatic Response Following Adult Rape Exposure

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Background: Childhood trauma (CT) is prevalent across all socio-economic settings, although exceptionally high levels of CT is often reported in low- and middle-income countries (LMICs). CT is also associated with an increased risk for adult revictimization and an increased risk for the development of posttraumatic stress disorder (PTSD) in adulthood. Factors that may mediate the risk between CT and adult revictimization and PTSD risk include the type of CT exposure, CT polyvictimisation and the developmental stage in which exposure occurred.

Objectives: To investigate CT types (neglect, emotional abuse, physical abuse and sexual abuse), polyvictimisation, and exposure to trauma in childhood (0-11 years) vs adolescence (12-18 years) as predictors of acute posttraumatic response in adult women who have been raped and assessed within 20 days of the rape.

Methods: Data from 852 rape-exposed women (between 18 and 40 years old) based in and around the city of Durban, South Africa, were collected in the Rape Impact Cohort Evaluation (RICE) study. Data were analysed using multiple linear regression models.

Results: Exposure to a higher number of different CT types (β=1.6, p<.001), a higher number of lifetime trauma types (β=1.5, p <.001) and increased depression scores (β=0.8, p<.001) were significant predictors of increased PTSD scores. Neglect (β=2.5, p=.035) was a significant predictor of PTSD symptoms in the group as a whole, while emotional abuse exposure in adolescence (β=3.6, p=.013), but not in childhood, was a significant predictor of PTSD symptoms.

Conclusion: Adolescent brain development, which is characterised by higher order cognitive development and synthesis of neuronal signalling across the brain, may be disrupted by exposure to emotional abuse which manifests in an increased risk for PTSD following revictimization in adulthood. Preventing CT and exposure to multiple CT types remains a priority across age groups.

3. Changing Policy Through Creating an Evidence Base: HIV, Violence And Mental Illness Amongst Sex Workers

Coetzee J

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Background: South Africa is currently tabling a bill that will decriminalise sex work. Doing so is one of the most important legislative move to affect the HIV epidemic and in preventing violence against women. Extensive evidence has been collected from across South Africa in support of this move. The aim of the study is to describe the first National Study of Female Sex Workers (FSWs), which has been an important contributing factor towards arguing for legislative change.

Method: Using a community-centric cross-sectional methodology, data was collected in 2018 across 12 sites, with at least one per province. Three thousand and five female sex workers were enrolled, undertook a details psychosocial survey followed by testing for HIV, HIV incidence and drug resistance, and CD4 count. Data was appropriately weighted and multiple sensitivity analyses were conducted. Multiple analyses have been conducted with 10 publications to date.

Evidence shows a 62% and 6%pa National HIV prevalence and incidence, respectively, while 64% of sex workers virally unsuppressed had HIV drug resistance. 60% of women enter into sex work before the age of 24, with younger sex workers being less likely to know their HIV status. 54.8% had experienced non-partner rape in the previous year, and 70.4% of FSWs had experienced physical violence in the past year from a client or the police, with 53.6% having depression.

Conclusion: Our findings highlight the immense vulnerability of this population, and the urgent need for interventions geared to addressing both vulnerability and shortcomings in service delivery. Findings from this study were widely publicised in local media and were used as evidence to justify legislative change in South Africa.

4. An Exploration of The Associations Between Total Phospholipid Fatty Acid Profiles and Cardiovascular Diseases in The SA-DPP Cohort

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Introduction: The prevalence of cardiovascular diseases (CVDs) such as type 2 diabetes mellitus (T2DM), hypertension and dyslipidaemia is rapidly growing in South Africa. Fatty Acids (FA) have been shown to play both a protective and causative role in the development of CVDs, particularly T2DM. The exploration of the FA profiles of participants may give further insight into their lifestyle (physical activity and diet), protein activity and genes, all of which contribute to the development of CVDs. Therefor we set out to explore the differences in FA profiles of urban South Africans from the Western Cape in correlation to their hypertension, dyslipidaemia, and glycaemic status.

Methods: Urban residents in the Western Cape who were at high risk for diabetes were recruited in the South African Diabetes Prevention Programme (SA-DPP). Data collection was done by administered questionnaires, clinical measurements (anthropometry and blood pressure) and biochemical analyses (lipids, oral glucose tolerance test, red blood cell total phospholipids profile for FAs). Multivariate logistics regressions will be performed to examine associations between glycaemic status, dyslipidaemia, and FAs levels in separate models.

Expected results: Among the 915 participants, differences in FAs profiles will be examined including the distribution by age, gender, ethnicity, glycaemic status, hypertension status, and dyslipidaemia status.

Conclusion: This exploration will provide insight into FA metabolism and synthesis and its associations with the development of cardiometabolic diseases in our South African cohort. This may allow for better intervention and treatment for at risk groups and those already diagnosed.

5. Exposures To Abuse in Childhood and Adulthood Are Associated With Prevalent Hypertension In Women-The RICE Study.

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Background: The relationship between abuse/trauma exposure and hypertension suggest that abuse exposures may increase the risk of hypertension by contributing to psychological stress, but this association has not been clearly described. We investigated the associations of various types of 1) childhood abuse (CA) and 2) abuse in adulthood (intimate partner violence (IPV), non-partner sexual violence (NPSV) and sexual harassment (SH) exposures) with adult hypertension; and potential mediators of those associations in South African women aged 18 to 40 years in the Kwazulu-Natal, using the baseline data of the Rape Impact Cohort Evaluation (RICE) study.

Method: History of exposures to 1) sexual, physical, emotional and parental neglect in childhood; and 2) sexual, physical, emotional and economic IPV, NPSV and SH were examined. Hypertension was based on measured blood pressure ≥140/90 mmHg or a previous diagnosis. Logistic regression models were adjusted for traditional hypertension risk factors, previous trauma including a recent rape incident. Potential mediators were explored using multiple mediation analyses.

Results: We studied the data of 1797 women, median age 24 years. 1) Exposures to any CA (adjusted odds ratio: 1.04; 95%CI: 1.01-1.07; p=0.014), sexual (1.05; 1.01-1.10; p=0.026) and emotional CA (1.05; 1.01-1.08; p=0.009) were associated with hypertension. Associations of physical CA (p=0.074) and parental neglect (p=0.132) were borderline to non-significant. Increasing frequency of CA and multiple types of CA were associated with higher odds of hypertension. 2) Frequent physical (1.44; 95%CI: 1.06-1.95) and emotional IPV (1.45; 95%CI: 1.06-1.98) and greater severity of emotional IPV, frequent NPSV (1.63; 95%CI: 1.27-2.67), and any SH (2.56; 95%CI:

1.60-4.03) were associated with hypertension. The observed associations were partially mediated by alcohol consumption, other trauma experienced, depression and PTSD.

Conclusions: Exposures to gender-based violence were associated with hypertension in young women. While gender-based violence must be prevented, there need to be effective mental health interventions to prevent hypertension and ensure regular blood pressure monitoring for early diagnosis and treatment of hypertension in abused women.

6. Screening Potential Repurposed Drugs for Antimycobacterial Activity.

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), is a life-threatening infectious disease, reported to have killed 1.6 million people in 2021. *Mtb* has developed strategies to evade immune responses by inhibiting downstream mechanisms of action within macrophages, and other immune cells responsible for clearing infection. Current treatment entails a multi-drug regimen that must be taken for at least 6 months. Emergence of multiple forms of drug resistant strains to TB drugs are creating a new challenge to combat the TB disease burden. Consequently, there is an urgent need to identify novel anti-TB drugs. Repurposing drugs presents the opportunity to discover novel drug-target interactions of established drug treatments, with an aim to use them to treat different diseases. This approach has gained interest from both pharmaceutical companies and in academia for several reasons, including, reduced investment costs, lower risk of failure and reducing the time required to market the drugs for its additional use.

In this study, boronic acid derivatives, sulfonamides, antifungal and non-steroidal anti-inflammatory drugs will be screened for antimycobacterial activity against *Mycobacterium smegmatis* mc^{2}155 *(M. smeg)*, *Mtb* H37Rv, clinically drug resistant strains and *Mtb*-infected macrophages as potential repurposed agents. Flow cytometry single cell analysis and Luminex multiplex assay will be employed to evaluate the mode of cell death and immunomodulatory potential of the drugs candidates. Magnetite nanoparticles will be synthesized, characterised and functionalized with potential drug candidates and evaluated for antimycobacterial activity. The minimum inhibitory concentrations for each of the drug candidates are currently being evaluated against *M. smeg.* Preliminary data shows potential antimycobacterial activity of four boronic acid derivatives and two antifungal drug candidates against *M. smeg*

7. Does A Verbal Autopsy Narrative Provide Accurate Information About Treatment Defaulting for People Who Have Died From HIV/AIDS?

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Background: The National Cause of Death Validation (NCoDV) study, using the World Health Organisation (WHO) standard verbal autopsy (VA) questionnaire comprising structured questions and an open narrative in which the next of kin outlines the circumstances leading to the death, identified a relatively high proportion of deaths from HIV/AIDS with a mention of treatment default. The aim of the study is to assess whether the VA narrative can provide valid information about antiretroviral therapy (ART) treatment default by linking the HIV/AIDS related death data with treatment information from the national treatment register.

Methods: This study uses secondary analysis of data from the NCoDV study linked with data about ART treatment from Tier.net maintained by the Department of Health. Variables such as unique study ID, gender, name, other name and surname, date of birth, identity number, place of residence, province of death was used

for linkage. Information of treatment defaulting obtained from VA narratives was compared with that from Tier.net was compared using Cohen's Kappa (k), as well as estimates of the sensitivity and specificity of the narrative.

Results: VA narratives identified 25.7% among 1 174 HIV/AIDS related deaths had defaulted on treatment. Data linkage was successful for 691 (58.9%) deaths but 62 (5.3%) could not be analysed due to inconsistent information. The level of agreement between VA narratives and Tier.net 59.1% with a kappa value of 0.17 (95% CI: 0.10 – 0.24) for the 629 cases. The sensitivity and specificity were 38.2% and 78.8% respectively and positive and negative predictive values of 62.7% and 57.7%, respectively.

Conclusions: Checking for treatment defaulters among HIV/AIDS individuals was not standardized practice during the VA interviews, hence the VA narratives was not sensitive enough to identify treatment defaulters. A high percentage of lost to follow-up (LTFU) was found among the 629 cases in Tier.net.

8. Using Glucocorticoid Hormones in Wastewater as Biomarkers to Assess The Health Status Of A Community

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Wastewater based epidemiology (WBE) has shown to be a promising tool that presents a snapshot to the overall health of a community. WBE has gained significant attention in the COVID-19 pandemic as a complementary approach to track the circulation of the virus in communities. Recent reports show that the global COVID-19 lockdown impact on the stress levels of the general population. Stress causes the body to release the hormone, cortisol and its metabolites. Cortisol is a natural glucocorticoid hormone produced by the adrenal cortex, it regulates blood pressure, metabolism, and immune response. Cortisol is primarily excreted in urine and in lower amounts in faeces. Recent studies reported that a rapid increase in the decay

rate of cortisol in wastewater as the temperature increases above 25 °C. Cortisol and cortisone metabolites, tetrahydrocortisol and tetrahydrocortisone respectively, were shown to be more stable in wastewater in different environmental conditions. Therefore, cortisol, cortisone and tetrahydrocortisol and tetrahydrocortisone will be simultaneously measured in wastewater samples. We aim to develop and validate an analytical method using previously published method with modifications to determine the levels of the cortisol, cortisone and tetrahydrocortisol and tetrahydrocortisone in wastewater samples. The samples will be collected during the wet and dry seasons. Wastewater flow and population data will be provided by the City of Cape Town. Sample clean-up and extraction process will be conducted by the solid phase extraction (SPE) technique using Oasis Hydrophilic-Lipophilic Balance (HLB) cartridges. Symmetry C8 (3.5 µm, 4.6 × 150 mm) column with a gradient mobile phase composed of methanol and acetone solution containing 0.5% formic acid, with a flow rate of 0.4 mL/min will be used to separate cortisol, cortisone, tetrahydrocortisol and tetrahydrocortisone. Liquid chromatography with tandem mass spectrometry (LC-MS/MS) will be used to quantify the glucocorticoid hormones in wastewater. The method will be evaluated for accuracy, linearity, precision, and recovery.

9. Preventing Chemotherapy-Induced Cardiotoxicity

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Background: Recently, 3 genetic variants (RARG, UGT1A6, SLC28A3) have demonstrated strong association with CICD and have been consistently replicated across studies showing evidence of their functional involvement with chemotherapy-induced cardiovascular dysfunction (CICD). *In vitro* evidence from our laboratory demonstrates that the flavonoids pinocembrin (pin) and 2.4DH possess cardioprotective potential that could be useful in mitigating CICD without reducing the efficacy of the chemotherapeutic drug, doxorubicin, in an *in vivo* model. However, very limited evidence exists on the expression of these genes in preclinical intervention studies.

Aim: To study the risk profile of the genetic variants in the development of CICD in pre-clinical models, and the prophylactic benefits of Pin and 2.4DH against CICD.

Methodology: The efficacy of 2.4DH and Pin, to mitigate the risk of CICD, will be studied by means of echocardiography assessment on neoplastic female C57BL/6 mice. In this study echocardiography will be performed at baseline and at the end of the study. RT-PCR will be conducted to quantify the expression of RARG, UGT1A6 and SLC28A3, cardiac biomarkers (troponin T and NT-proBNP), mitochondrial and apoptotic markers to validate the flavonoids cardioprotective potential. Lastly, the efficacy of the chemotherapeutic drug to eradicate the tumors, when used in combination with flavonoids, will be studied by measuring tumor volume and size.

Proposed outcome: Pinocembrin and 2.4DH mitigate CICD by preserving cardiac function and histology in mice treated with doxorubicin. Gene expression analysis reveal a strong association between doxorubicin-induced cardiotoxicity and the expression of RARG and UTG1A6, as well as a correlation between the decreased expression of SLC28A3 and cardioprotective benefits of the flavonoids.

Proposed conclusion: The results suggest that Pin and 2.4DH are suitable prophylactic agents against CICD that can be safely administered with doxorubicin. However, the association of these genetic variants with CICD, within an African population, still require validation.

10. A Study to Assess the Association Between Circulating Mirnas And Cardiometabolic Risk In Pregnant Women From Cape Town, South Africa

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Mother and child morbidity and mortality remains a significant burden on health systems, both in South Africa and globally. Access to simple, affordable biomarker testing for screening of pregnant women at risk of metabolic dysregulation could be harnessed to facilitate intervention strategies to improve health outcomes for both mother and child. Studies have shown that microRNAs (miRNAs) are associated with pregnancy complications and adverse pregnancy outcomes. The primary aim of this study is therefore to determine whether miRNAs are associated with pregnancy complications and adverse health outcomes in pregnant women in Cape Town, South Africa. Secondly, we will evaluate the biological function of altered miRNAs in cell culture models. In this cross-sectional study, the participants were 400 women who attended antenatal visits at the Gugulethu community health care facility between November 2019 and June 2022. MiRNAs will be isolated from serum collected between 24–28 weeks gestation, profiled using quantitative real-time PCR and expression profiles correlated with various metabolic parameters such as gestational weight gain, preeclampsia, gestational diabetes and cardiometabolic outcomes such as obesity, hypertriglyceridaemia, high low-density-lipoprotein, low high-density-lipoprotein and hyperglycaemia, assessed during pregnancy. Thus far, miRNAs from the serum samples of 200 pregnant women have been extracted and quantified. It is anticipated that miRNA extraction and profiling will be completed within the next six months. We optimistically expect that our study will identify miRNAs that are associated with pregnancy complications and adverse health outcomes. Furthermore, we predict that results from in vitro cell culture models will demonstrate that these miRNAs have regulatory roles within key metabolic pathways, confirming their role in the pathophysiology of pregnancy complications.

RCD GHAM 2023 Programme

Building research leadership for societal impact

SAMRC Conference Centre, Cape Town, 8-9 March 2023

DAY 1		
Session 1		
10h00-10h10	Opening and House Keeping	Programme Director: Prof Nadine Harker
10h10-10h20	Welcome Address	Line Executive of RCD (Dr Michelle Mulder) SAMRC President/CEO (Prof Glenda Gray)
10h20- 10h50	Research Ethics and Integrity	Prof Leslie London (UCT)
10h50- 11h20	Innovation & Intellectual Property	Dr Michelle Mulder (SAMRC)
11h20-11h40	**TEA BREAK**	
Session 2		
11h40- 11h55	The Longitudinal Impact of Air Pollution and Environmental Tobacco Smoke Exposure on Childhood Respiratory Diseases in An African Birth Cohort	Prof Aneesa Vanker (UCT)
11h55-12h10	ADME Polymorphism in Tuberculosis: Pharmacogenetic Analysis of Samples from Patients in Healthcare Facilities In The Vhembe District	Prof Afsatou Traore (UNIVEN)
12h10-12h25	Evaluation Of Anticancer Potential of Berberine Against Cancer Cells as Monotherapy and Combination Therapy	Prof Blassan George (UJ)
12h25-12h40	Assessing Patients' Experience of Care in Four Referral Hospitals: A Cross-Sectional Survey of Outpatients in Two South African Rural Provinces	Dr Wezile Chitha (Wits)
12h40-13h10	**LUNCH**	

Session 3		
13h10-13h40	Keynote address: Science for Societal Impact	Prof Mosa Moshabela (UKZN)
13h40-14h10	President address: What does it take to reach the top of your game? Establishing a successful research career	Prof Glenda Gray (SAMRC)
14h10-14h25	Changing Policy Through Creating an Evidence Base: HIV, Violence and Mental Illness Amongst Sex Workers	Dr Jenny Coetzee (SAMRC)
14h25-14h40	Process and Outcomes of Spinal Cord Rehabilitation in the Western Cape, South Africa	Prof Anthea Rhoda (UWC)
14h40-14h55	In Vitro Antidiabetic, Antioxidant and Cytotoxic Evaluation of Honeybush Tea (Cyclopia Genitives) Extracts	Dr Nkosinathi Cele (UNIZULU)
14h55-15h10	Women's Surgical Outcomes in Africa	Prof Salome Maswime (UCT)
15h10-15h25	**INTERMISSION**	
Session 4		
15h25-15h40	Clinical Genomics in Southern Africa: Lessons from The Undiagnosed Disease Programme	Prof Shahida Moosa (SUN)
15h40-15h55	Investigating Neutrophil-Associated Proteins in Human TB Granulomas as Targets for Host-Directed Therapy	Prof Mohlopheni Marakala-la(AHRI/UKZN)
15h55-16h10	Harnessing Big Heterogeneous Data to Evaluate the Potential Impact of HIV Responses Among Key Populations in South Africa: The Boloka Project	Prof Refilwe Phaswa-na-Mafuya (UJ)
16h10-16h20	Day 1 Closing remarks	Programme Director: Prof Nadine Harker

RCD GHAM 2023 Programme

Building research leadership for societal impact

SAMRC Conference Centre, Cape Town, 8-9 March 2023

DAY 2		
Session 1		
09h00-09h10	House Keeping	Programme Director: Prof Nadine Harker
09h10-09h40	Keynote address: Research Translation and Dissemination	Prof Charles Shey Wiysonge (SAMRC)
09h40-10h15	Keynote address: African Indigenous Knowledge Systems: A Catalyst for the advancement of Research	Prof Fhumulani Mavis Mulaudzi (UP)
10h15-10h30	**TEA BREAK**	
Session 2	**GROUP 1: MCSP+EIP** Facilitator: Dr Lawrence Mabasa	
10h30-10h45	Prevalence And Correlates Of 30-Day Suicidal Ideation and Intent: Results of The South African National Student Mental Health Survey	Prof Jason Bantjes (SUN/SAMRC) and Prof Charles Shey Wiysonge (SAMRC)
10h45-11h00	Exploring The Antimalarial Potential of Recently Synthesized Novel Pyrimidine Inspired Hybrids.	Dr Ofentse Pooe (UKZN)
11h00-11h15	Mental Health Trajectories in the PURE-SA Cohort	Prof Lusilda Schutte (NWU)
11h15-11h30	Glycosylation Of Protein GBS2106 Using Polysaccharides Derived from Group B Streptococcus Serotype III	Dr Sonwabile Dzanibe (UCT)
11h30-11h45	Establishing Expression Kinetics and Delivery Platforms for Self-Amplifying mRNA Vaccines and Therapies	Dr Kristie Bloom (Wits)
11h45-12h00	Immunology Of Co-Infection: Immunomodulation by Neglected Tropical Diseases	Prof Zilungile Mkhize-Kwitshana (UKZN)
Session 2	**GROUP 2: RCDI** Facilitator: Dr Ebrahim Samodien	
10h30-10h45	Knowledge Translation Platforms for Bridging Public Health and Health Systems Research into Universal Health Coverage Related Policy And Practice In South Africa (KTP-UHC)	Dr Bey Schmidt-Maduneni & Dr Chanelle Mulopo (UWC)
10h45-11h00	The South African COVID-19 Surgical Outcomes Study (SACSOS) - A Prospective Observational Study of Long-Term Patient-Reported Outcomes After Surgery Using a Digital Health Platform	Prof Hyla Kluyts (SMU)
11h00-11h15	Integration Of Metabolomic Fingerprinting and Molecular Docking Analysis of Secondary Metabolites of South African Plants: Focus on Protease (Mpro) And Spike (S) Glycoprotein Of SARS-Cov-2.	Dr Nqobile Mkolo (SMU)

11h15-11h30	The Physical, Physiological and Psychological Risk Factors for Non-Communicable Diseases Among Adolescents from The Eastern Cape – A Situational Analysis Report	Prof Maya van Gent (UFH)
11h30-11h45	Designing Neuropharmaceuticals to Permeate the Blood-Brain Barrier and Combat Neurological Disorders	Prof Jacques Joubert (UWC)
11h45-12h00	Anti-Cancer, Anti-Diabetic, Anti-Obesity and Anti-Inflammatory Potential of Plant Extracts/Plant-Derived Compounds	Prof Vusi Mbazima (UL)
Session 2	**GROUP 3: POST-DOCS** Facilitator: Dr Lindokuhle Ndlandla	
10h30-10h45	Exposures To Abuse in Childhood and Adulthood Are Associated with Prevalent Hypertension in Women-The RICE Study.	Dr Kim Nguyen (SAMRC)
10h45-11h00	ADME Polymorphism in Tuberculosis: Pharmacogenetic Analysis of Samples from Patients in Healthcare Facilities in The Vhembe District	Dr Mpumelelo Rikhotso (UNIVEN)
11h00-11h15	Matching Study Using Health and Police Datasets for Characterising Interpersonal Violence in The Community of Khayelitsha, South Africa 2013–2015	Dr Ardil Jabar (UCT/SAMRC)
11h15-11h30	The Antioxidant, Anti-Cancer, And Anti-Metastatic Effect of Tarchonanthus Camphoratus on Metastatic MDA-MB-231 Cells	Dr Bernice Monchusi (UL)
11h30-11h45	The Effect of Childhood Trauma Type and Timing on Acute Post-Traumatic Response Following Adult Rape Exposure	Dr Jani Nöthling (SAMRC)
11h45-12h00	Does A Verbal Autopsy Narrative Provide Accurate Information About Treatment Defaulting for People Who Have Died From HIV/AIDS?	Dr Monique Maqungo (SAMRC)
Session 3		
12h00-12h30	Finance and Legal Matters	Peter Mwewa and Sumaya Behardien
12h30-12h45	Closing remarks and Vote of Thanks	RCD Grants' Manager: Dr Frederic Nduhirabandi Programme Director: Prof Nadine Harker
12H45-14H00	**LUNCH WITH SAMRC BOARD MEMBERS**	

SAMRC RCD Scholarship Programmes

SAMRC Clinician Researcher (MD. PhD) Development
The purpose of this programme is to develop a cadre of highly trained clinician-scientists who are likely to be attracted to and excel in careers in academic medicine. This programme provides support to MBChB and BChD holders who are engaged in health or clinical research. Candidates are awarded full-time PhD scholarships to commence or complete their PhD qualification.

SAMRC Internship Scholarship Programme
This is the SAMRC's inhouse postgraduate training programme that contributes towards the SAMRC's transformation agenda. It seeks to train and develop scientists from under-represented groups, namely African Black, Indian, Coloured and Asian, under research supervision of SAMRC researchers. The programme attracts young scientists of the highest calibre to complement SAMRC senior researchers and influence sustainable long-term collaboration with national and international institutions through joint supervision of South African students.

Bongani Mayosi National Health Scholarship Program (BM-NHSP)
This programme aims to accelerate the development of human health and clinical research capital for South Africa. The programme is administered by the SAMRC on behalf of the National Health Research Committee (NHRC) and is jointly funded by the National Department of Health (NDoH) and the Public Health Enhancement Fund (PHEF). The programme provides full-time scholarships benchmarked according to the salary equivalent of the funded candidate.

SAMRC Biostatistics Capacity Development Initiative
This is a strategic programme that support biostatistics capacity building by funding individuals who are undertaking a Masters in Biostatistics. It attracts students from various disciplines into the field of biostatistics, thereby increasing the pool of well-trained and skilled biostatisticians who can provide statistical support for health research studies and lead statistical studies.

SAMRC Researcher Development Programme
This is a one-year funding awarded to individuals employed in academic institutions or SAMRC research units who are engaged in health/clinical research and are in the last 12 months of their PhD Programme. This once off funding serves to relieve pressure on the candidates in order to speed up the conclusion of their PhDs. The funds can be used for dedicated time to spend on research activities, pay for work relief or any justifiable intervention.

For more on RCD scholarships, visit: https://www.samrc.ac.za/funding/grants-and-scholarships/scholarships

SAMRC RCD Grants Programmes

Mid-Career Scientist Programme (MCSP)
This is a five -year strategic programme for Mid-Career Scientists with the aim to equip scientists in identified research areas to write successful grant proposals in their funded research area, and to mentor and graduate MSc and PhD students as well as Postdocs in order to grow their research teams. An overarching aim is to accelerate the research standing of the funded Mid-Career Scientist.

SAMRC Intramural Postdoctoral Programme
This is a five-year research fellowship programme with the purpose of building research capacity and scientific leadership within the organization by creating positions for early-career Postdoctoral Scientists, particularly Black and female. The applicants must demonstrate potential to become excellent independent researchers.

SAMRC Extra-Mural Postdoctoral Programme
This is an intervention programme to assist in accelerating research capacity development and scientific leadership by creating opportunities to host and retain postdoctoral scientists at selected Extramural Research Units hosted by HDIs and other under-resourced institutions. The intervention seeks to contribute to training and facilitating the retention of talented young scientists with the potential to establish themselves within the Units as independent scientists.

SAMRC Clinician Post-PhD Career Development Programme
This is a two- to three- year intervention programme to address the gap between clinician PhD training, early investigators, and mid-career scientists. The purpose of the programme is to increase opportunities for talented clinicians who recently completed their PhD degrees to learn how to develop and lead their research plans before they establish their own research teams and transition to independent investigators.

SAMRC Research Capacity Development Initiative (RCDI) at Selected Universities
This is a five-year programme known as the "HDI" i.e. Historically Disadvantaged Institutions programme to unearth excellence in researchers at universities previously constrained by inadequate resources. The SAMRC funds researchers in eight (8) such universities which have been identified by the SAMRC Board for capacity building and strengthening.

While the main programme focuses on funding specific Principal Investigators (PI), the programme has two additional intervention programmes (RCDI-Nested Postdoctoral and PHD Scholarships) targeting funding for Postdoctoral fellows and PhD Students working on PI projects

SAMRC Early Investigators Programme
The purpose of this programme is to support the career development of South African scientists at the end of their early postdoctoral stage, facilitating their transition to the next level of established Mid-Career Scientists, and fostering their retention in the public sector in areas of strategic interest to the National Department of Health (NDoH) and the SAMRC for a solid scientific and academic leadership in the country.

For more on RCD grants, visit https://www.samrc.ac.za/funding/grants-and-scholarships/grants

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