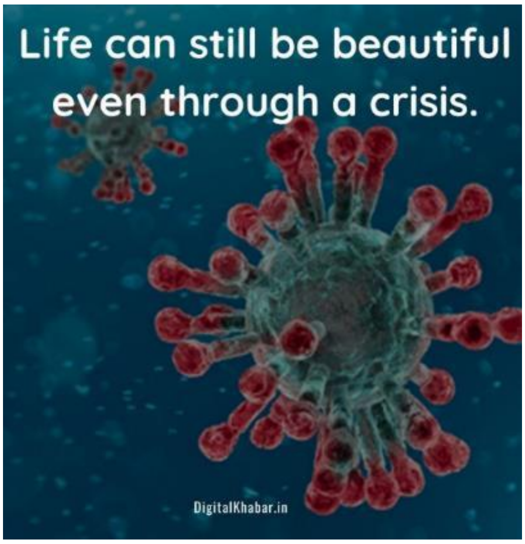
Leading Research and Innovation in Time of COVID-19 Pandemic

SAMRC RCD GRANT HOLDERS' ANNUAL MEETING

Virtual | 2 March 2021

samrc advancinglife



1 Image source (www.DigitalKhabar.in)

SAMRC RCD GRANT HOLDERS

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MESSAGE FROM DIVISION MANAGER

Dear Colleagues

2019/2020 financial year was our first meeting of SAMRC-RCD Grant holders as a group. We realise now just how important and correct it was to distinguish the Grants Portfolio from the Scholarships Portfolio. Both Portfolios are growing differently and a dedicated focus by Portfolio has become essential.

While 2020 was an extremely challenging year, the three programmes in the Grants portfolio of the RCDI ("HDI's"), the Mid-Career Scientist Programme and the Post-doctoral Fellowships managed to grow nevertheless...!

In 2020/2021 financial year we have a strong new cohort of PIs in the RCDI (HDI) programme and interesting new nodes of research represented within the Mid-Career Programme. SAMRC's Intramural Post-doctoral Fellowship is gaining momentum with more Intramural Research or Business Units participating by hosting the young scientists.

All our programmes remain strong in the transformation agenda. Through the Grants programmes we are demonstrating that with proper financial support, transformation is also strongly associated with high performance as show by the accelerated numbers of publications that we are able to report from the Grants.

We are noticing with much appreciation that PIs are now correctly acknowledging their funding programmes in their publications. This is very important for the SAMRC to demonstrate generation of scientific knowledge for justification of continued funding received from Government. Our Division wishes you success in the next 12 months with your research, and we remain privileged to serve you.

ACKNOWLEDGMENTS

We would like to thank the organizing committee for their effort and contribution in making the meeting, a success.

THE ORGANIZING COMMITTEE

Dr Frederic Nduhirabandi (Program Manager: RCD Grants Portfolio)

Ms Asanele Ngcauzele (Project leader: RCD Grants Portfolio)

Mrs Philistia Joshua (Program administrator: RCD Grants Portfolio)

Mrs Mandy Salomo (SAMRC Events Management)

KEYNOTE SPEAKERS

Professor Keolebogile Shirley Motaung

Prof. Keolebogile Shirley Motaung is a Full Professor, Biomedical Scientist and Director: Technology Transfer & Innovation at the Durban University of Technology.

She is the founder and Chief Executive Officer of Global Health Biotech (Pty) Ltd, and President of the African Tissue Engineering and Regenerative Medicine International Society. Her research and innovation focused on the role of medicinal plants in tissue engineering of bone and cartilage. Based on her own scientific exploration into the use of medicinal plants in tissue engineering of bone and cartilage, she founded a company called Global Health Biotech (PTY) Ltd in 2016. She is an award winner and has received a number of accolades from far and wide because she has thrown the gauntlet in bridging the gap between science and entrepreneurship. As a Professor, research scientist and entrepreneur, she trains her postgraduate students not just on how to do research, and become a scientist, but also on how to become entrepreneurs. By becoming entrepreneurs, they can create jobs for themselves after completing their studies at a time, when jobs are scarce, and unemployment is high.

Global Health Biotech has developed a natural anti-inflammatory ointment named La-Africa Soother (LAS) from medicinal plants which helps relieve muscle and joint aches, thus offering athletes and sportsmen and women an alternative natural anti-inflammatory ointment. This is the first product of its kind aimed at preventative care, meaning it is applied ahead before and after physical activity to prevent anticipated muscle aches, as well as after the fact. This product, packaged in a green and white tube, is already available on the market. Motaung has also licensed a technology from Stellenbosch University to develop a second product named pump protein shake (vegan friendly plant-based). The product simultaneously leads to decreased muscle inflammation which leads to accelerated regeneration and may be more effective as an anti-inflammatory agent than known non-steroidal anti-inflammatory drugs (NSAID) and with less side-effect.

Professor Kelly Chibale

Professor Kelly Chibale is a full Professor of Organic Chemistry at the University of Cape Town (UCT) where he holds the Neville Isdell Chair in African-centric Drug Discovery & Development. He is also a Full Member of the UCT Institute of Infectious Disease & Molecular Medicine, a Tier 1 South Africa Research Chair in Drug Discovery, founding Director of the South African Medical Research Council (SAMRC) Drug Discovery & Development Research Unit at UCT and the Founder and Director of the UCT Drug Discovery and Development Centre (H3D).

Kelly obtained his PhD in Synthetic Organic Chemistry from the University of Cambridge in the UK (1989-1992). This was followed by postdoctoral stints at the University of Liverpool in the UK (1992-94) and at the Scripps Research Institute in the USA (1994-96). He was a Sandler Sabbatical Fellow at the University of California San Francisco (2002), a US Fulbright Senior Research Scholar at the University of Pennsylvania School of Medicine (2008) and a Visiting Professor at Pfizer in the UK (2008).

In 2018 Kelly was recognized by Fortune magazine as one of the World's 50 Greatest Leaders and in 2019 he was named as one of the 100 Most Influential Africans by New African magazine. In 2020 he was named as one of the world’s top 60 most inspirational leaders in the pharmaceutical industry (one of the world’s top 20 inspirational medicine makers in the field of small molecules) on The Medicine Maker's 2020 Power List.

OVERVIEW OF RESEARCH CAPACITY DEVELOPMENT GRANTS/FUNDED PROJECTS

RESEARCH CAPACITY DEVELOPMENT INITIATIVE PRINCIPAL INVESTIGATORS			
No.	**Institution**	**Project title**	**Beneficiaries**
1	**WSU**	The Management and building of bridges for selected Non-Communicable Diseases and HIV Risk Factors, Morbidity and Mortality in the Eastern Cape Province: A Population, Hospital, Laboratory, and Community Study. **(abstract 1)**	**Apalata Teke**
2	**SMU**	The stop rheumatic heart disease (RHD) through awareness raising, surveillance, advocacy, and prevention (A.S.A.P.) research programme: longitudinal studies of primary and secondary prevention of rheumatic heart disease (RHD) **(abstract 2)**	**Maposhane Nchabeleng**
3	**MUT**	Molecular modelling design, synthesis and bio-analytical tests of new small molecules to target enzymes and receptors for cancer treatment **(abstract 3)**	**Njabulo Gumede**
4	**UWC**	Precision Medicine: Pharmacogenomics and Development of Individualized drug therapy for sub-Saharan African Population **(abstract 4)**	**Mongi Benjeddou**
5	**UWC**	Improving Health Systems for Traumatic Spinal Cord Injury in South Africa and Sweden: A novel investigation of processes and outcomes **(abstract 5)**	**Anthea Rhoda**
6	**UFH**	The development of an intervention to combat the physical and psychological risk factors associated with non-communicable diseases among adolescents in the Eastern Cape, South Africa and its potential impact **(abstract 6)**	**Maya van Gent**
7	**UFH**	Supportive Triad Interpersonal Relationships Intervention Programme (STIRIP) during the perinatal period for maternal and child health positive outcomes **(abstract 7)**	**Nonceba Vellem**
8	**UL**	Anti-cancer, Anti-diabetic, Anti-Obesity and Anti-inflammatory potential of plant extracts/plant-derived compounds. **(abstract 8)**	**Vusi Gordon Mbazima**

RESEARCH CAPACITY DEVELOPMENT INITIATIVE PRINCIPAL INVESTIGATORS			
9	**UNIVEN**	ADME polymorphism in tuberculosis: Pharmacogenetic analysis of samples from patients in Hospitals in the Vhembe District of Limpopo, South Africa**(abstract 9)**	**Afsatou Ndama Traore-Hoffman**
10	**UNIVEN**	Determinants of high neonatal and child mortality rates in the rural areas of Limpopo province, South Africa **(abstract 10)**	**Thivhulawi Malwela**
11	**UNIZULU**	Elucidating the mechanisms of action and clinical implications of herb-drugs interactions: focusing on anti-diabetic and lipid lowering drugs and ethinylestradiol based oral contraceptive **(abstract 11)**	**Nokulunga Hlengwa**
12	**UNIVEN**	Transmitted and Acquired HIV drug resistance in Limpopo Province **(abstract 13)**	**Pascal Bessong**
13	**UNIZULU**	Anti-diabetic activity of a lactic acid bacteria enriched Kombucha tea concentrate fermented from Cyclopia sp. (L.) and Sutherlandia sp. (L.) **(abstract 12)**	**Mathews Simon Mthembu**

RESEARCH CAPACITY DEVELOPMENT INITIATIVE POST-DOCTORAL			
No.	**Institution**	**Project title**	**Beneficiaries**
14	**UL**	Detection of aberrant methylation of *RARβ2* (retinoic acid receptors-β2) and *APC* (adenomatous polyposis coli) in black South African women diagnosed with breast cancer. **(abstract 14)**	**Kgomotso Poopedi**
15	**UNIVEN**	Phenotypic characterization of putative resistance mutations in HIV-1 subtype C viruses **(abstract 15)**	**Daphney Matume**

MID-CAREER SCIENTIST			
No.	**Institution**	**Project title**	**Beneficiaries**
16	**UCT**	Proteomics approaches for hair testing and scarring Alopecias **(abstract 16)**	**Nonhlanhla Khumalo**

MID-CAREER SCIENTIST			
17	**SMU**	Substance Abuse and Adolescent mental health **(abstract 17)**	**Kebogile Mokwena**
18	**UWC**	Identification of prognostic and target therapy markers in cancer using multi-omics data **(abstract 18)**	**Alan Christoffels**
19	**SUN**	Tumour Microenvironment in Cancer of the Cervix **(abstract 19)**	**Sengeziwe Sibeko**
20	**UKZN**	A pilot study on helminthiasis and microbes interactions: macrobiotic control of microbiota and the effects on Human Immunodeficiency Virus and Mycobacterium tuberculosis diseases, immune responses and nutritional status: Human and in vitro studies **(abstract 20)**	**Zilungile Kwitshana**
21	**SUN**	Online group CBT for symptoms of anxiety and depression among university students: A pragmatic open trial. **(abstract 21)**	**Jason Bantjes**
22	**UCT**	Improving stillbirth data recording, collection and reporting in Africa **(abstract 22)**	**Salome Maswime**

SAMRC INTRAMURAL POST-DOCTORAL PROGRAMME			
No.	**Institution**	**Project title**	**Beneficiaries**
23	**BRIP**	Effects of rooibos phenolic compounds on microbiota regulation and prevention of the metabolic syndrome **(abstract 24)**	**Ntevhegi Thovogi**
24	**BODRU**	Does a verbal autopsy narrative provide accurate information about treatment default for people who have died from HIV? **(abstract 26)**	**Monique Maqungo**
25	**Centre for TB Platform**	Role of the microbiome in tuberculosis disease and treatment outcomes **(abstract 24)**	**Charissa Naidoo**
26	**GHRU**	Community-led cross-sectional study of social and employment circumstances, HIV and associated factors amongst female sex workers in South Africa: Study protocol and baseline characteristics **(abstract 28)**	**Jenny Coetzee**

SAMRC INTRAMURAL POST-DOCTORAL PROGRAMME			
27	**TB Platform**	Resistance Sniffer: An online tool for prediction of drug resistance patterns of Mycobacterium tuberculosis isolates using next generation sequencing data **(abstract 27)**	**Awelani Mutshembele**
28	**Cochrane**	A global bibliometric analysis of research productivity on vaccine hesitancy from 1974 to 2019 **(abstract 29)**	**Anelisa Jaca**
29	**UWC**	Precision Medicine: Pharmacogenomics and development of individualized drug therapy **(abstract 30)**	**Brendon Pearce**
30	**BRIP**	Developing an advanced cell culture model for pancreatic beta cells **(abstract 31)**	**Ebrahim Samodien**
31	**ATODRU**	Closing the treatment gap: implementation insights for task-shared counselling for depression and harmful alcohol use in South Africa **(abstract 32)**	**Carrie Brooke-Sumner**
32	**SUN**	Understanding the evolution of drug resistant tuberculosis: a molecular epidemiologic and bioinformatics analysis of Mycobacterium tuberculosis strains acquiring drug resistance. **(abstract 33)**	**Marisa Klopper**
33	**SUN**	Elesclomol an anticancer drug with potential therapeutics as antituberculosis drug candidate **(abstract 23)**	**Andile Ngwane**
34	**NCDRU**	Elesclomol an anticancer drug with potential therapeutics as antituberculosis drug candidate **(abstract 34)**	**Kim Nguyen**
35	**NCDRU**	Elesclomol an anticancer drug with potential therapeutics as antituberculosis drug candidate **(abstract 35)**	**Liske Kotzé-Hörstmann**

**Abbreviations : WSU- Walter Sisulu University, SMU- Sefako Kgofatso University, MUT-Mangosuthu University of Technology, UWC- University of the Western Cape, UFH- University of Fort Hare, Ul- University of Limpopo, UNIVEN- University of Venda, UNIZULU- University of Zululand, UCT- University of Cape Town, SUN- University of Stellenbosch, UKZN- University of KwaZulu Natal, BRIP- Biomedical Research and Innovation Platform Research Unit, BODRU- Burden of Disease Research Unit , GHRU- Gender Health Research Unit, ATODRU- Alcohol , Tobacco and other drugs Research Unit, NCDRU-Non-communicable Disease Research Unit.

PROGRAMME

THEME: LEADING RESEARCH AND INNOVATION IN TIME OF COVID-19 PANDEMIC		
Grant Holders' Annual Meeting 2 MARCH 2021 "Turning Adversities into Success"		
08h00– 09h00	**Setting up Virtual Conference**	
Session 1	**GHAM Program Director: Dr Nadine Harker**	
09h30 – 09h45	Opening remarks and Welcome address	Dr Thabi Maitin
09h45 – 10h10	Address by SAMRC Vice-President	Prof Jeffrey Mphahlele
10h10 – 10h40	Keynote speaker: *From the bench side to the market*	Prof Keolebogile Shirley Motaung
10h40 – 10h50	**TEA (10 min)**	
Session 2	**Dr Nadine Harker**	
10h50 – 11h00	Brief overview of RCD Programmes- Building & Strengthening Research Team (Dr T Maitin)	
11h00 – 11h15	RCDI perspective: *Reflection of the Research Strengthening Program at Under Resource Universities*	SAMRC - Prof Johan
11h15 – 11h25	*SAMRC-RCDI: Strengthening Research at the University of Venda*	RCDI - Prof Bessong - UNIVEN
11h25– 11h45	*Navigating between funding programmes*	MCSP – Prof Kwitshana – UKZN
11h45 – 11h55	*Strengthening a research team for a neglected problem: the case of SMU and nyaope research*	MCSP – Prof Mokwena - SMU
11h55 – 12h05	*Enhancing the Emerging Scholar through Research Teams*	RCDI - Prof Rhoda - UWC
12h05 – 12h15	*Competition, collaboration and negotiating power differentials in large research projects*	MCSP – Prof Bantjes – SUN
12h15 – 12h35	Discussion and Conclusion	
12h35 – 12h50	**LUNCH (15-20 min)**	
Session 3	**Dr Nadine Harker**	

THEME: LEADING RESEARCH AND INNOVATION IN TIME OF COVID-19 PANDEMIC		
12h55 – 13h20	Address by SAMRC President/CEO	Prof Glenda Gray
13h20 – 13h50	Keynote speaker: *Research Leadership: personal experiences from a personal journey*	Prof Kelly Chibale
10 min	**Questions**	
14h05– 14h30	Legal matters	Ms Sumaya Behardien
	Finance matters	Ms Noluthando Sikhutswa
10 min	**Questions**	
14h45- 15h15	**Closing remarks** **Vote of thanks (Program Chair: Dr Frederic Nduhirabandi)**	

RESEARCH CAPACITY DEVELOPMENT INITIATIVE (PRINCIPAL INVESTIGATORS)

1. The Management and building of bridges for selected Non-Communicable Diseases and HIV Risk Factors, Morbidity and Mortality in the Eastern Cape Province: A Population, Hospital, Laboratory, and Community Study

Research Area: NCDs and HIV Risk Factors

T Apalata[1], S Nomatshila[1], S Mabunda[1], CR Sewani-Rusike[1], Y Yako[1], P Mda[1], Z Vundle[1], N Katende[1], EJ Ndebia[1]

[1]*Faculty of Health Sciences, Walter Sisulu University, Mthatha, Eastern Cape*

Background

Among patients on antiretroviral therapy (ART), the World Health Organisation (WHO) suggests that non-communicable diseases (NCDs) should be monitored. It is hypothesised that prolonged exposure to ART and/or HIV-associated chronic inflammation poses additional risk in the development of NCDs. Since 2011, task shifting has been advocated as a strategy for addressing the healthcare worker shortages impeding scaling up of ART programmes in South Africa. Limited evidence on the success of this programme in Eastern Cape province exists.

Objectives: To assess the determinants, risk factors and complications of selected NCDs and whether there is a causal link with HIV/AIDS; and to evaluate the efficiency of the health system in managing NCDs and HIV/AIDS.

Methods

A mixed study design was used. Twelve primary care facilities were selected following a four-stage cluster sampling method. Patients were enrolled using a systematic sampling approach, and the WHO STEPwise instrument was used for data collection. Venous blood was collected.

Results

Patients' recruitment is still ongoing but 680 patients were enrolled thus far. Preliminary analysis of 177 patients with HIV/AIDS and type-2 DM compared with 354 non-DM HIV/AIDS showed that the odds of diabetes increased by more than three-folds for those who had been on ART for more than 6 years ($p<0.005$). The risk of developing hypertension over the duration of ART was 2.2-fold and 7.9-fold higher for patients aged ≥35 years ($p= 0.04$) and those with elevated levels of triglyceride ($p=0.046$), respectively. Patients (67.2%) were more likely to report dissatisfaction with services. Absence of regular transport by 40% of patients and long waiting time in clinics were more likely to be associated with lower CD4 counts after ≥ six months of ART ($p<0.0001$).

Conclusion

Preliminary findings established the association between prolonged ART use, type-2 DM and the occurrence of abnormal BP. Patients' dissatisfaction with task-shifting was noted with major concerns.

2. The Stop Rheumatic Heart Disease (RHD) Through Awareness Raising, Surveillance, Advocacy, and Prevention (A.S.A.P.) Research Programme: Longitudinal Studies of Primary and Secondary Prevention of Rheumatic Heart Disease (RHD)

Research Area: Infectious Diseases

Sub-study 1: Prevalence and Characterization of Streptococcus pyogenes in patients presenting with pharyngitis at Dr George Mukhari Academic Hospital and selected surrounding clinics in 2019 to 2020.

ST Mashailane[1], X Khosa[1], O Kgasha[1], **M Nchabeleng**[1]

[1]*Department of Microbiology, Sefako Makgatho Health Sciences University*

Background

Group A streptococcus (GAS), a common cause of pharyngitis has immune-mediated complications like rheumatic fever which may subsequently lead to rheumatic heart disease (RHD). RHD continues to have high morbidity and mortality in developing countries hence the need for effective preventative strategies like vaccines. A 30-valent M protein-based vaccine is currently under clinical trial stage of development. Potential vaccine coverage will depend on the geographical distribution of emm (M protein) types.

Objectives

To determine the prevalence of GAS, characterize the emm types, and determine antimicrobial susceptibility profiles of the isolates in the northern-western part of Pretoria. To correlate the emm types with the 30 valent vaccine types.

Methods

Throat swabs were collected from patients aged 3-20 presenting to a local clinic with pharyngitis. Clinical isolates were also collected from NHLS/DGM tertiary laboratory. Emm typing was performed using conventional PCR amplification of the emm genes and sequences were subjected to homology searches on Basic Local Alignment Search Tool. E-test method was used to determine MICs of penicillin, clindamycin and erythromycin and the results were interpreted according to CSLI guidelines.

Results

Of the 400 throat swabs collected, 33 were positive for GAS (8%). Additional 62 clinical isolates were collected from the laboratory. To date 87 of the 95 GAS isolates were successfully typed and there was a total of 26 emm types. Twelve of these are vaccine types. The most prevalent was emm82(16%), followed by emm22(8%), emm1(7%), emm25(7%) and emm66(7%). Forty isolates (46%) were non-vaccine types. All the isolates were susceptible to the antibiotics tested.

Conclusion

Twenty-six emm types were identified, showing diversity of emm types in the region. The most prevalent was emm82 compared to emm92 shown previously in the same region. Fortyseven (54%) isolates were vaccine types. GAS remains susceptible to the commonly used antibiotics. The study will be expanded.

Sub-study 2: Immunology of GAS in patients with pharyngitis

ST Mashailane[1], X Khosa[1], O Kgasha[1], **M Nchabeleng[1]**

[1]*Department of Microbiology, Sefako Makgatho Health Sciences University*

Background

Pharyngitis due to GAS may cause immune mediated complications such as acute rheumatic fever (ARF) leading to rheumatic heart disease (RHD). Persistence of protective immunity in different patients presenting with pharyngitis is not completely understood. There is scarcity of data on the immunological aspects of pharyngitis and ARF amongst the local population.

Aim

To study the immune response in sera of patients with positive GAS pharyngitis, to determine the presence of protective immune response against recurrent GAS pharyngitis. The study will also determine the role played by M-type specific immune response in pharyngitis and ARF caused by homologous M-serotype.

Methods

Paired blood samples will be collected from pharyngitis patients who had positive GAS cultures from the throat swabs. Samples will be stored at -20ºC freezers for immunological analysis at a later stage. Detailed immunological studies will be conducted and correlated with clinical outcomes such a recurrence of ARF.

Results and discussion

To date sera has been stored for 20 patients. The PhD protocol is currently under development.

3. Molecular modelling design, synthesis and bio-analytical

tests of new small molecules to target enzymes and receptors for cancer treatment

Research Area: Molecular modeling and medicinal chemistry

NJ Gumede[1]

[1]*Mangosuthu University of Technology*

Background

The re-emergence of prostate cancer to patients after undergoing therapies has proved deadly. Mutations are the major cause of metastases castration resistant prostate cancer (mCRPC).

Objectives

To perform hit-to-lead identification by designing molecular hybrids and screening by docking. Lead optimization using reaction-based enumeration and cloud-based Free Energy perturbation (FEP+).

Methods

A more modern drug discovery and medicinal chemistry approach was undertaken. Hits identified were selected based on their docking scores, and their binding modes. Filtered compounds were tested using a Cell Titer-Glo Luminescent Assay. The hits sought from in vitro experiments were optimized by adding fragments that are common in approved prostate cancer drugs, generating molecular hybrids. The optimized hybrids were filtered using docking. PathFinder reaction-based enumeration was also employed to traverse the chemical space. Cloud-based Free Energy perturbation predicted the relative binding affinities of the enumerated compounds.

Results

The hit identification using high throughput virtual screening yielded 33 drug-like molecules. The hits were tested for bioactivity using a cell-viability assay. The most active compound 8 exhibited an IC50 20-37 uM against 8 PCa cell-lines. The structure of compound 8 was optimized by adding new fragments and docking was performed to predict the binding affinity. There was a slight improvement in affinity. Since the affinity was not significant, a PathFinder reaction-based enumeration was performed. This approach afforded the traversing of the chemical space following the active learning approach. Cloud-based FEP+ was performed to predict the binding affinities of the hits. The leads sought revealed an improved binding affinity with $\Delta G°$ ranging from -7.09 to -10,09 kcal/mol.

Conclusion

Hit-to-lead has enabled the identification of drug-like molecules that can be further optimized to yield lead compounds. Cloud-based FEP+ was able to correctly predict the binding affinity of the lead compounds, with a mean unsigned error of <0,1 kcal/mol. FEP+ results were used to prioritize leads for further synthesis, followed by bioanalysis.

4. Precision Medicine: Pharmacogenomics and Development of Individualized drug therapy for sub-Saharan African Population

Research Area: Precision Medicine

L Xhakaza [1], Z Abrahams-October [1], B Pearce [1], CM Masilela [1], OV Adeniyi [2], R Johnson [3, 4,] JJ Ongole [5], **M Benjeddou** [1]

[1]Precision Medicine Unit, Department of Biotechnology, Faculty of Natural Sciences, University of the Western Cape, Robert Sobukwe Road, Bellville, South Africa, [2]Department of Family Medicine, Walter Sisulu University, East London, South Africa, [3]South African Medical Research Council, Parow, Cape Town, South Africa, [4]Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa, [5]Department of Family Medicine, Piet Retief hospital, Mkhondo, Mpumalanga, South Africa

Background

Type 2 Diabetes mellitus is a progressive metabolic disease characterized by relative insulin insufficiency and insulin resistance resulting in hyperglycemia. Despite the widespread use of metformin, there is considerable variation in treatment response; with approximately one third of patients failing to achieve adequate glycemic control. Studies have reported the involvement of single nucleotide polymorphisms and their interactions in genetic pathways i.e., pharmacodynamics and pharmacokinetics.

Objectives

This study aims to investigate the association between 19 pharmacogenetics biomarkers and response to metformin treatment.

Methods

MassARRAY panels were designed and optimized by Inqaba Biotechnical Industries, to genotype 19 biomarkers for 140 type 2 diabetic outpatients.

Results

The CT genotype of the rs12752688 polymorphism was significantly associated with increased response to metformin therapy after correction (OR=0.33, 95% CI [0.16–0.68], p-value=0.006). An association was also found between the GA genotype of SLC47A2 rs12943590 and a decreased response to metformin therapy after correction (OR=2.29, 95% CI [1.01–5.21], p-value=0.01).

Conclusion

This is the first study investigating the association between genetic variants and responsiveness to medication for diabetic patients from the indigenous Nguni population in South Africa. It is suggested that rs12752688 and rs12943590 be included in pharmacogenomics profiling systems to individualize metformin therapy for diabetic patients from African populations.

5. Improving Health Systems for Traumatic Spinal Cord Injury in South Africa and Sweden: A novel investigation of processes and outcomes

Research Area: Health Systems for individuals with neurological conditions

A Rhoda[1], C Joseph[2], E Nizeyimana[1], B Boggenpoel[1]

[1]*University of the Western Cape* [2]*University of Stellenbosch*

Background

Spinal cord injuries result in mortality and morbidity. To combat this impact, specialised care in a time-sensitive manner has shown to be effective. However, little is known about the provision of spinal cord injury care in different contexts, information which is required for strengthening policy and practice.

Objectives

The objectives of the study were: understanding the nature of health care processes in the management of TSCI - acute and chronic cohorts; assessment of short-term (e.g. health status and mortality) and long-term (e.g. mortality and functioning) outcomes and the development of a health care decision-making model for the prediction of mortality and functioning.

Methods

A prospective (regional), population-based cohort study was conducted where individuals with acute spinal cord injuries were consecutively recruited. Data collected included processes of acute care, survival status, secondary complications, and functional status. The International Spinal Cord Injury Dataset, ASIA impairment scale and the Spinal Cord Injury Secondary Conditions Scale guided data collection. Data was analysed using SPSS version 26. Ethics was obtained from the University of the Western Cape (BM/18/1/17).

Results

The mortality rate was 10.3%. With regards to process outcomes the following were found; the mean number of days to surgery was 35.2, duration of acute care 19.7 days (mean), duration of rehabilitation 29.5 days (median). Predictors related to survival: include Age; neurological level of injury, ASIA classification, presence of secondary medical complications and mechanism of injury.

Conclusion

The identified predictors could guide decision making with regard to the candidate factors which should be included in a preliminary risk stratification model.

6. The physical and psychological risk factors associated with Noncommunicable diseases among adolescents in the Eastern Cape, South Africa.

M van Gent[1]

[1]*University of the Free State*

Background

The physical and psychological health concerns and risk factors associated with Non-communicable diseases (NCDs) among adolescents has been prioritized on the agenda of international health institutions globally. Living healthy lives and maintaining healthy lifestyles is often neglected in many countries and specifically low-income countries. Therefor this study aims to explore the physical and psychological risk factors associated with NCDs among adolescents in the Eastern Cape, South Africa.

Methodology

A three-phase research project is proposed to achieve the aims and objectives of this study. In phase one, a mixed methods approach will be followed to determine the physical and psychological risk factors of adolescents. While the qualitative approach will explore the lived experiences of adolescents' physical and psychological risk factors, the quantitative approach will require them to complete a biographical questionnaire and various validated tests to determine their body composition, physical activity, nutritional status, mental health and wellness, stress, body self-image and dependency behavior. Phase two proposes a pre-pest post-test with control group experimental design, to test an intervention program developed from the results of phase 1. In phase three, a one-year follow-up study is proposed. In all phases, a stratified random sample of adolescents in eight schools in four districts of the Eastern Cape will be selected to participate in the study.

Data analysis

Analysis of texts in the qualitative phase of the research will be done through thematic coding, while analysis of the quantitative phases will be done with SPSS. Frequencies, proportions, means and standard deviations will be calculated to represent biographical and inferential results. Relationships between variables will be calculated with correlations, while group comparisons will be done through Independent samples t-tests and one-way Anova. Main and interaction effects in the experimental design and one-year follow-up study will be calculated with Repeated Measures Manova.

The pilot test will include the completion of the validated tests to yield data to confirm their suitability for the study and the intervention will be implemented in phase three. The participants will participate in focus group discussions during this phase, to determine whether any changes or amendments should be made to the intervention.

7. Supportive Triad Interpersonal Relationships Intervention Programme (STIRIP) during the perinatal period for maternal and child health positive outcomes

Research Area: Mother and child

N Vellem[1], N Rala[1], Z Dasheka[1]

[1]*University of Fort Hare*

Background

Increased litigations are exacerbated by poor interpersonal relationships between midwives, pregnant women and the community. Interpersonal relationships are crucial in building trust in the health system and respectful care despite the challenges such as shortage of staff. There is an increase in prediabetes and gestational diabetes; and a decrease in exclusive breastfeeding in the first six months of life, increasing perinatal morbidity and mortality. Interventions to reduce these challenges are necessary.

Objectives

The objectives are to reduce incidences of pre-diabetes and gestational diabetes using Modified Diabetic Risk Score and lifestyle modification; identify and intervene in incidents of litigations and Disrespect, Abuse, Abandonment and Neglect (DAAN); and contributing factors to non-maintenance of exclusive breastfeeding in the first 6 months for children in the Eastern Cape Province South Africa.

Methods

A multi-method approach will be used. A comparative before-and-after evaluation design to test the combined interventions. Surveys will be conducted at baseline and focus groups after the intervention.

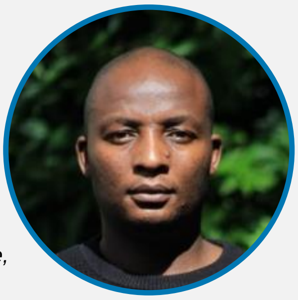
Results

The research results will be disseminated throughout the research project at different stages of the project. Research papers, reports, meetings, workshops, and conferences will be used throughout the research project to disseminate results. The community will receive results through radio talk and non-scholarly papers published also in local languages. A final report will be written to close the project.

Conclusion

The project will encourage supportive relationships between the nurses, pregnant women, companions and the community thereby improving communication, incidents of litigation and DAAN, and building trust in the health system and provision of respectful care despite the challenges such as shortage of staff.

8. Anti-cancer, Anti-diabetic, Anti-Obesity and Anti-inflammatory potential of plant extracts/plant-derived compounds



Research Area: Anti-diabetes, Anti-obesity, Cancer cell apoptosis, Epigenetics and Antimetastatic cancer.

VG Mbazima[1]

[1]*Department of Biochemistry, Microbiology and Biotechnology, Faculty of Science and Agriculture, University of Limpopo*

Background

Cancer, obesity and diabetes are huge health problems and are amongst the leading cause of death worldwide (Bray et al., 2018; Martin et al., 2015). Preliminary work in our research group has identified three medicinal plants, *Dicerocaryum senecioides*, *Ozoroa paniculosa* and *Momordica balsamina* as promising lead extracts in combating the indicated therapeutic indications.

Objectives

The purpose of the project is to identify and develop plant extracts or plant-derived compounds that could selectively induce cancer cell apoptosis, modulate DNA methyltransferases and inhibit cancer metastasis as well as have therapeutic indications of antidiabetes and anti-inflammation that can be marketed as herbal supplements, nutraceuticals, or topical creams.

Methods

Cell viability and proliferation assays will be conducted to determine the toxicity of the extracts on experimental cell lines. Optimal working extract concentrations will then be used to determine the effects of the extract on cancer cell apoptosis, DNA methylation, cancer cell metastasis, metaflammation, diabetes and obesity using various in vitro and in vivo assays. Western blot and qRT-PCR analyses will be used to assess the effect of the extracts on the apoptosis, metastasis, inflammatory and diabetes regulatory genes.

Results and Conclusion

The findings of the study could lead to the identification of plant extracts or plant-derived compound(s) with the ability to impede metastasis, selectively induce cancer cell apoptosis and modulate DNA methylation through the regulation of DNA methyltransferases and alleviate metaflammation, diabetes and obesity. Moreover, it is anticipated that the project will lead to knowledge generation as to how the extracts under investigation modulate various genes involved in the regulation of cancer, diabetes, obesity and inflammation as well as some of the extracts being marketed as an inflammatory ointment(s) and neutraceuticals

9. ADME polymorphism in tuberculosis: Pharmacogenetic analysis of samples from patients in Hospitals in the Vhembe District of Limpopo, South Africa

Research Area: Vhembe District (Limpopo Province, South Africa)

AN Traore-Hoffman[1]

[1]*University of Venda*

Background

Tuberculosis (TB) is of great concern for public health in South Africa. Indeed, South Africa is among the countries with the highest incidence of TB and multidrug-resistant (MDR) TB in the world. The emergence of drug resistant strains adds to the challenges already encountered in treating TB in South Africa and worldwide. The importance of developing anti-TB drugs is not only to cure the infection but also to reduce the possible transmission of the microorganism and increase adherence. There is a lack of efficient and effective strategies for the identification of TB cases in rural sub-Saharan Africa. It has been reported that pharmacokinetic/pharmacodynamic do impact on TB patients in Africa and the pharmacokinetic variability may contribute to different TB treatment outcome.

Objectives

To (1) determine the extent of TB resistance; (2) determine ADME polymorphisms expressed by TB patients and (3) evaluate the relationship between ADME polymorphism and drug levels from the TB patients.

Methods

A cross-sectional study will be conducted among TB patients admitted in 3 referral hospitals in the Vhembe District (rural) of Limpopo (South Africa). The study will include 275 participants (225 TB patients and 50 healthy controls) aged 7 years and above. Interviews will be conducted to collect socio-demographic information and other factors related to TB and samples (Blood, Saliva and Urine) of the participants will be collected. DNA isolated from Saliva and Blood samples will be analysed using the AnyplexTM MTB/MTN RT-PCR and AllplexTM MDR/XDRe RT-PCR. Afterwards, all MDR/XDRe isolates will be sequenced using the NGS. To understand the risk associated with treatment failures. The levels of drugs (INH, RIF and PZA) in urine will be measured using HPLC.

Results

The incidence of MDR-TB is projected to be around 7% and most drug resistance in isolates strains will be attributed to chromosomal mutations.

Conclusion

Overall, understanding the mechanisms related to resistance will provide an important insight into TB pathogenesis and predict the future trend of MDR-TB global pandemic.

10. “Determinants of high neonatal and child mortality rates in the rural areas of Limpopo province, South Africa”

Research Area: Maternal Child and Women Health (MCWH)

T Malwela, LN Netshikweta, L Mabasa

University of Venda, University of Cape Town and SAMRC

Background

Neonatal mortality accounts for almost 47 per cent 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 of information in Limpopo about the improvements of neonatal and child mortality.

Objectives

The proposed study will aim to explore and assess 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.

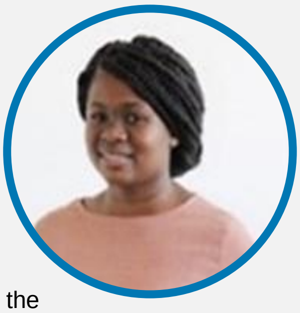
Methods

Mixed method will be used; qualitative participatory action research and quantitative non-experimental and experimental design will be used. Population will include midwives and operational managers from selected hospitals, child age bearing women (pregnant and non-pregnant) and their neonates as well as community members above 18 years. Non-probability purposive and probability sampling will be used. Focus group discussions, field notes reflection and questionnaire will be used to collect data, and laboratory test 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 professional Statistician. Aspect of the trustworthiness will be ensured through credibility, authenticity, dependability, transferability and confirmability, validity and reliability of the instrument in quantitative strand will be ensured. Ethical principles will be applied.

Results

Dissemination of the results will be done through perinatal mortality meetings, community forums (IMBIZOs), workshops presentations. Articles will be published in peer reviewed/accredited journals.

11. Elucidating the mechanisms of action and clinical implications of herb-drugs interactions: focusing on anti-diabetic and lipid lowering drugs and ethinylestradiol based oral contraceptive



Sub-project 1: Evaluation of the effect of P. longifolia extract and its bioactive lanosteryl triterpene compounds on the metabolism of anti-diabetic and lip lowering drugs.

Sub-project 2: Contraceptive failure: Herbal supplements and their effect on the metabolism of an ethinylestradiol based contraceptive.

Research Area: Herb-drug interactions

N Hlengwa, N Chellan, CJF Muller[2]

[1]Department of Biochemistry and Microbiology, University of Zululand, Kwa-Dlangezwa, South Africa, [2]Biomedical Research and Innovation Platform, South African Medical Research Council, Cape Town, South Africa.

Background

Approximately, 80% of people globally use herbal medicines, in addition to, rather than in place of, conventional pharmaceutical drugs. Resultantly, this has raised serious safety concerns regarding the possible herb-drug interactions that could lead to adverse effects. Adverse herb-drug interactions interfere with normal drug pharmacokinetics and pharmacodynamics, either reducing their efficacy or inducing drug toxicity. Therefore, studies aiming to elucidate the pharmacokinetic and pharmacodynamics effects of herbal medicines are essential to ensure their safe and effective use. At a higher risk of herb-drug interactions are orally administrated such antidiabetic drugs and oral contraceptive because of their narrow therapeutic index. Therefore, this study will investigate the potential for herb-drug interaction P longifolia extract and compounds with commonly prescribed oral anti-diabetic medications and a lipid lowering statin. The second part of this study aims to investigate whether the co-use of Immunity plus™ and Air Immune™ influences the rate of metabolism and contraceptive efficacy of ethinylestradiol oral contraceptive.

Objectives

To investigate the effects of P longifolia extract and compounds, Immunity plus™ and Air Immune™ on the intestinal bioavailability of selected anti-diabetic medications, a lipid lowering statin and an ethinylestradiol contraceptive using a Caco-2 cell model respectively.

Methods

Transport experiments across Caco-2 cell monolayers, using selected anti-diabetic medications, a lipid lowering statin and oral contraceptive will be conducted in the presence and absence of herbal products respectively, and the effect on uptake/efflux rates will be monitored using LCMS.

Results

The changes in the intestinal bioavailability of the selected drugs due to the co-administration with the herbal products may reduce therapeutic plasma concentrations ultimately resulting in reduced efficacy.

Conclusion

Assessing the effect of P longifolia extract and compounds, Immunity plus™ and Air Immune™ will establish the potential risk of co-administrated with the respective drugs which potentially could lead loss of efficacy.

12. Anti-diabetic activity of a lactic acid bacteria enriched Kombucha tea concentrate fermented from *Cyclopia* sp. (L.) and *Sutherlandia* sp. (L.)

Research Area: Pharmacognosy

ND Cele[1], AR Opoku[1], **MS Mthembu[1]**

[1]*Department of Biochemistry and Microbiology, University of Zululand, South Africa.*

Background

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and hyperlipidaemia, as well as increased oxidative stress and protein glycation. The inhibition of glycoside and lipid hydrolases, as well as non-enzymatic glycation may curb postprandial hyperglycemia, fat absorption and the formation of AGEs, which might be imperative approach for alleviating diabetes and associated complications.

Objectives

This study evaluated an antidiabetic, anti-glycation and antioxidant properties of the crude extracts from the Kombucha tea concentrates.

Methods

The hexane, ethanolic and dichloromethane crude extracts of Kohumba tea will be screened for their antioxidant properties, and the antiprotein glycation activity of the extracts will be determined over a period of 28 days at 7-days' intervals. The hexane, ethanolic and dichloromethane crude extracts of the Kombucha tea will also screened for their inhibitory effect on α-amylase, α-glucosidase and pancreatic lipase activities in vitro. The fructose streptozotocin (STZ) model will be used to induce diabetes mellitus in rats. The rats will be divided into two major groups: normal group and fructose-STZ induced group. The diabetic rats will be orally administered with the extract daily for 28 days. The serum liver and, brain tissues will be removed for biochemical analysis and protein expression

Results

On completion of the research, it is expected that the crude extracts will display a concentration dependent antioxidant properties, α-amylase, α-glucosidase and pancreatic lipase inhibitory properties. Moreover, crude extracts will be expected to inhibit glycation of haemoglobin as well as fructose-induced protein glycation, the formation of AGEs in a concentration-dependent manner and as well as a markedly reduction of the levels of fructosamine in-vitro. Reduced blood glucose level and serum fructosamine content will be observed after 28 days of treatment in diabetic rats. Ethanolic extract are also expected to exhibit some inhibitory effects on α-amylase, α-glucosidase and pancreatic lipase activities in vivo.

Conclusion

If the results are obtained as expected, these will be indicative of the presence of the antioxidant and antidiabetic properties of the crude extract of Kombucha tea. Further tests will be conducted for their possible applications in human models as potential therapeutic agents against diabetes.

13. Transmitted and Acquired HIV drug resistance in Limpopo Province

Research Area: HIV drug resistance

N Matume[1], B Ogola[1], L Tambe[1], L Mavhandu[1], D Tebit[3], **P Bessong**[1,2]

[1]AIDS Virus Research Laboratory, University of Venda, Thohoyandou, South Africa; [2]Center for Global Health Equity, University of Virginia, USA; [3]Global Biomed Scientific, Virginia, USA.

Background

The 'test and treat' approach to manage HIV infection assumes that the untreated population is not exposed to antiretrovirals and that the level of drug resistance in the untreated population will not significantly reduce the efficacy of the first line standard treatment regimen.

Objectives

To determine drug resistant mutations and exposure to antiretrovirals in pre-treated individuals in selected treatment sites in Limpopo Province.

Methods

Three ml of venous blood and hair from the occipital region were collected from consented participants prior initiation of ART at three clinical sites in Limpopo Province. Plasma was prepared from whole blood, and HIV viral DNA was generated, sequenced by next-generation sequencing. Viral sequences were assessed for quality with Geneious software and interpreted for transmitted drug resistance according to the Calibrated Population Resistance tool. Plasma and hair were analysed for the presence of Tenofovir (TDF), Emtricitabine (FTC) and Efavirenz (EFV)) by a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method. Samples were collected before the introduction of dolutegravir in the standard first line treatment regimen in South Africa. All participants answered 'no' to a question on whether they have received antiretrovirals prior.

Results

Of the 241 successfully sequenced HIV polymerase region (protease/reverse transcriptase), 23 (9.5%) had at least one surveillance drug resistance mutation (SDRM) detected at >20% threshold, with a prevalence of 7.5% (n=18), 3% (n=7) and 0.4% (n=1) for NNRTI, NRTI and PI respectively. The number of participants with SDRMs increased to 31 (12.9%) when minority variants were accounted for at >5% threshold. Most subjects with SDRMs were females; (23/31; 74.2%) and (15/23, 65.2%) at >5% and >20% thresholds respectively. The most frequent SDRMs based on drug class were; K103N/E (7.9%-NNRTI), K65R (2.5%-NRTI) and D30N (0.8%-PI). Four cases of dual NRTI/NNRTI mutations were identified. All consensus sequences were HIV-1 subtype C, except three which were confirmed as C/A1, C/F1 and C/G recombinants. Paired plasma and hair samples were collected from 77 individuals newly initiating ART. At least one of the test drug was detected in the plasma or hair of 41/77 (53.2%) patients who responded 'no' to a question on whether they have received antiretroviral, prior to their initiation into treatment. We observed that 31/77 (40.3%) of the participants had TDF in either plasma or hair. FTC and EFV was observed in the plasma or hair of 12/77 (15.6%), and 25/77 (32.4%) of participants respectively, while 6/77 (0.08%) had all three drugs in plasma or hair.

Conclusion

Next-generation sequence analyses confirms that individuals entering HIV treatment programmes at the study sites haboured moderate levels of SDRMs, including cases of dual-class drug resistance. SDRM studies may be required to better understand resistance in the drug naïve population in the era of “diagnose and treat”. TDF concentrations in plasma or hair imply a common undisclosed pre-exposure to treatment in individuals initiating treatment. The consequences of SDRM in the pre-treated population and non-disclosure of exposure to antiretrovirals among those entering the ‘test and treat’ programme in attaining viral suppression, in at least 90% of patients on treatment, are unknown.

RESEARCH CAPACITY DEVELOPMENT INITIATIVE-LINKED POST-DOCTORAL FELLOWSHIP PROGRAMME

14. Detection of aberrant methylation of RARβ2 (retinoic acid receptors-β2) and APC (adenomatous polyposis coli) in black South African women diagnosed with breast cancer.

Research Area: Epigenetics and breast cancer

KW Poopedi[1], MP Mokgotho, FO Ooko[2], T Pheeh[1,3], LJ Mampuru[1]

[1]Department of Biochemistry, Microbiology & Biotechnology, University of Limpopo, Private Bagx1106, SOVENGA. [2]Department of Oncology and Radiology, Polokwane Hospital, Private Bag X9315, Pietersburg, 0700, South Africa. [3]National Health Laboratory Health Services, Polokwane Hospital, Private Bag X9315, Pietersburg, 0700, South Africa

Background

Global cancer statistics state that breast cancer accounts for 2,088,849 (11.6%) of new cancer cases and 626,679 (6.6%) of deaths globally. Traditionally, mammography has been the best option in breast cancer diagnosis. However, it is subject to false-positive results with the sensitivity being inversely proportional to the density of the breast. Therefore, the current study aims to increase the sensitivity and specificity of breast cancer screening tests by using blood-based biomarkers instead of traditional tumour markers.

Objectives

i. To determine whether the detection of methylation changes of epigenetic origin in retrospectively collected serum samples have clinical utility.

ii. To compare the diagnostic efficacy of methylation changes in epigenetic genes among the traditional tumour marker CA15.3 that is currently used.

Methods

This is a retrospective study and ethical approval for the study has been acquired. The selection of stored serum samples from the National Health Laboratory Services in Limpopo Province was completed between January-July 2020. DNA will be extracted from cell-free serum samples using QIAamp MinElute ccfDNA Mini Kit (Qiagen). Bisulfite modification of DNA will be performed using the EpiTecht bisulfite kit (Qiagen), which includes successive steps of conversion, desalting, and desulfonation. PCR amplification will be performed to detect the presence of hypermethylation within the promoter CpG islands of RARβ2 and APC, using primers purchased from Inqaba Biotech (RSA), specific for methylated and unmethylated DNA. PCR products will be detected using 2% agarose gel.

Results

Methylated RARβ2 and APC would result in higher specificity and sensitivity compared to the classical tumour marker CA 15.3. Both epigenetic markers would significantly be higher in breast cancer patients but not detected in healthy subjects.

Conclusion

The findings of the study will suggest that epigenetic markers (RARβ2 and APC) in serum have clinical applicability in breast cancer screening.

15. Phenotypic characterization of putative resistance mutations in HIV-1 subtype C viruses

Research Area: HIV molecular genetics

B Ogola[1], **ND Matume[1]**, LG Mavhandu[1], DM Tebit[1,2,] PO. Bessong[1,3]

[1]HIV/AIDS & Global Health Research Programme, University of Venda, Thohoyandou 0950, South Africa. [2]Global Biomed Scientific LLC, P.O. Box 2368, Forest, VA 24551, USA. [3]Center for Global Health Equity, School of Medicine, University of Virginia, Charlottesville, USA

Background

South Africa introduced the "diagnose and treat" universal HIV treatment programme in September 2016. This program enables all identified HIV positive patients to immediately start first line antiretroviral treatment (ART). However, transmission of drug resistant (DR) viruses complicates the choice of ART.

Objectives

Next generation sequencing (NGS) was applied to determine the prevalence and diversity of HIV DR mutations in patients entering HIV treatment programmes in northern South Africa.

Methods

RNA was isolated from plasma of supposed drug naive HIV-1 infected patients. Using RT-PCR, the HIV pol gene comprising the complete protease (PR) and the first 900 amino acids of reverse transcriptase (RT) was amplified and then sequenced on an Illumina MiniSeq platform. Consensus sequences were derived for majority and minority variants using Geneious PRIME® software version 2020.1.2. HIV-1 SDRM was inferred using Calibrated Population Resistance (CPR) tool in HIV Drug Resistance Database. Viral subtypes were determined using REGA and RIP genotyping tools.

Results

The HIV PR/RT region was successfully sequenced from 241 patients. From these, 23 (9.5%) had at least one SDRM detected at >20% threshold, with a prevalence of 7.5% (n=18), 3% (n=7) and 0.4% (n=1) for NNRTI, NRTI and PI respectively. The number of participants with SDRMs increased to 31 (12.9%) when minority variants were accounted for at >5% threshold. Most subjects with SDRMs were females; (23/31; 74.2%) and (15/23, 65.2%) at >5% and >20% thresholds respectively. The most frequent SDRMs based on class were; K103N/E (7.9%-NNRTI), K65R (2.5%-NRTI) and D30N (0.8%-PI). Four cases of dual NRTI/NNRTI mutations were identified. All consensus sequences were subtype C except three which were confirmed to be C/A1, C/F1 and C/G recombinants.

Conclusion

NGS analyses confirms that individuals entering HIV treatment programmes in northern South Africa, habour moderate levels of SDRMs including cases of dual-class drug resistance. SDRM studies may be required to better understand resistance in the drug naïve population in the era of "diagnose and treat".

MID-CAREER SCIENTIST PROGRAMME

16. Proteomics approaches for hair testing and scarring Alopecias

Research Area: Dermatology

H Adeola[1], **N Khumalo**[1]

[1]*Division of Dermatology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa*

Background

Hair loss can have a marked effect on the quality of life and may generate concerns about serious underlying diseases. Understanding the biochemistry of scalp hair and its supporting structure can provide opportunities for the valid use hair as a non-invasive testing substrate in Medicine, as well as the molecular understanding of primary scarring Alopecias. These Alopecias are classified according to predominant inflammatory cells but the treatment is identical for all groups and ineffective. Even though human hair and skin are mostly constituted by proteins, proteomics tools have rarely been used to elucidate hair and scalp biology.

Objectives

To investigate whether there are differences in the hair proteome of people of different racial origin, for valid scientific classification of hair curvature as well as for discovery of alopecia biomarkers.

Methods

We carried out label-free, shotgun, mass spectrometry-based proteomics on geometrically classified hair samples (N=18) collected from African, Mixed Ancestry, Asian and Caucasian volunteers in Cape Town. We also performed shotgun proteomics and MALDI mass spectrometry (MALDI-MSI) on formalin-fixed paraffin-embedded section of scalp biopsies (N=25) from scarring Alopecias. Both qualitative and quantitative bioinformatics pipelines were used to analyze the data generated.

Results

Based on quantitative proteomic analysis, 450 protein groups (FDR=0.01) were identified from this cohort. Proteins classes such as keratin- associated proteins, keratins, desmosomal cadherins and histone proteins were among the hair proteins identified. Both qualitative and quantitative proteomic pipelines did not yield any significantly differentially expressed proteins that differentiate within geometric or racial hair groups.

We identified differentially expressed proteins for lymphocytic variants of scarring alopecia both by shotgun proteomics and MALDI-MSI.

Conclusion

There is no difference in the proteome of racially and geometrically classified scalp hair in our cohort. Further work is needed to explore preliminary data suggesting differences in hair curvature with hair lipids, i.e. that curly contains higher concentrations of structural lipids. This is plausible, as lipids are involved in protein folding which is thought to be the basis of hair curvature. Validation studies are required to confirm differentially expressed proteins in lymphocyitic Alopecias. Proteomics maybe a promising tool both for objective classification of scarring Alopecias and (for the first time) the elucidation of targeted therapies.

17. Strengthening a research team for a neglected problem: the case of SMU and nyaope research

Research Area: Substance Abuse and Adolescent mental health

Kebogile Mokwena[1]

[1]*Department of Public Health, Sefako Makgatho Health Sciences University*

Background

Not only is SMU one of the HDIs, but it is not known to be a research-intensive university, and the research environment is not friendly. On the other hand, nyaope is a very addictive novel psychoactive substance (NPS) whose use spread from Pretoria. Nationally, the interest and efforts on nyaope research does not parallel the social and health challenges associated with the drug. A small university research grant enabled the author to conduct an exploratory qualitative study on nyaope, which resulted in an increase in questions on this area. which was followed by a significant grant from SAMRC, which provided the needed finances to expand the research

Objectives

1. To describe the process of creating an interest in nyaope research at SMU
2. To describe the process of building and strengthening a team for nyaope research at SMU

Methods

The activities included presenting the nyaope research findings on Faculty research days, publishing articles in the University newsletter, organizing a special issue of a SAPSE accredited journal, recruitment of individuals across departments, with a specific role in the bigger project and recruiting postgrad students.

Results

The research team strides across several departments in the School of Health Care Sciences, Medicine and Pharmacy. Postgrad students included some who invited themselves into the project. The awarding of the SARCHi Chair in Substance Abuse and Population Mental Health further strengthened the research and journal publications increased.

Conclusion

The vast field of nyaope and population mental health research continues to expand at SMU. The research team is stronger and nyaope research exists in all 5 schools at SMU.

18. Identification of prognostic and target therapy markers in cancer using multi-omics data

Research Area: Precision Oncology

H Bendou[1], **A Christoffels[1]**

[1]SAMRC Bioinformatics Unit, South African National Bioinformatics Institute, University of the Western Cape

The heterogeneity observed in cancer has been shown to cause resistance to cancer therapies and lead to shortened patient's survival. Precise stratification of tumor heterogeneity is essential to administer and develop more effective therapies. Artificial Intelligence by Machine Learning (ML) can be used to demonstrate the existence of heterogeneity within tumors of the same cancer. And can also be used in combination with other methods to find prognostic signatures of a cancer condition.

Our study applied ML algorithms to (i) Elucidate the molecular mechanisms of neuroblastoma in high-risk patients, and (ii) Identify novel genomic biomarkers for Pediatric Acute Myeloid Leukemia.

Using multi-omics datasets, analyses including differential gene expression, DNA methylation and gene regulatory network were used to create features for creation and validation of ML models. Results include subtyping neuroblastoma tumors into ultra-high risk and high risk based on gene expression and survival. We identified a list of genes with expression abnormalities that explain the short survival in ultra-high risk patients. We further identified, via gene regulatory networks, the SMIM28 gene as having a role in aggressiveness of neuroblastoma tumors. We identified a 5-gene signature using Cox regression analysis that explains the poor survival rate in FLT3-ITD Pediatric AML patients.

The results obtained from this project will help clinicians and scientists better understand cancer heterogeneity and provide useful prognostic signatures for cancer therapies.

19. Tumour Microenvironment in Cancer of the Cervix

Research Area: HIV and HPV Infection in Women

S Sibeko[1]

[1]*Stellenbosch University*

Background

Worldwide, Human Papilloma Virus (HPV) is the most common sexually transmitted virus. HPV has been linked to 90% of cervical intraepithelial neoplasia (CIN) cases, a precursor lesion for cervical carcinoma, and more than 99% of cervical cancer cases. Surrounding non cancer cell components of the cancer are referred to as the tumor microenvironment (TME). TME is comprised of all the nonmalignant host cellular and noncellular components of the tumor niche.

Objectives

(i) Investigation of the association between histological subtypes of cancer of the cervix, age and HIV (ii) investigation of early molecular and cellular events involved in the modification of the normal stroma to peritumor stroma in the progression of CIN2, -3 to cancer of the cervix with a special focus on proangiogenic factors, fibroblast activating factors, proinvasive genes and matrix-metallo proteinases.

Methods

This study is designed as a laboratory based retrospective study that will utilise stored formalin-fixed paraffin embedded (FFPE) tissue specimens representative of CIN and invasive squamous cell carcinoma of the cervix (ISCC) of patients diagnosed at Tygerberg Hospital. Histomorphological studies will be conducted on FFPE samples using immunohistochemistry and molecular studies with gene and protein expression of the various factors above. HPV genotyping will also be conducted.

Results

Focus of this study will be on comparing CIN and ISCC in FFPE tissue samples. We will test associations between age, HIV and cancer subtypes. For all the objectives we will convert exposure and outcome variables into categorical variables and analyse using Chi-square tests. We will do descriptive analyses for objectives two to four before testing various associations.

Conclusion

As this study will analyse samples from women with HPV infection sequalae, CIN and ISCC, it will shed some light on the biomarkers that are relevant in the transition from CIN to cancer of the cervix focusing on TME.

20. A pilot study on helminthiasis and microbes interactions: macrobiotic control of microbiota and the effects on Human Immunodeficiency Virus and Mycobacterium tuberculosis diseases, immune responses and nutritional status: Human and in vitro studies"

Research Area: Immunology of co-infections with neglected tropical diseases (helminth parasites) and their interactions with HIV, TB and microbial flora.

ZL Mkhize-Kwitshana[1]

[1]*University of KwaZulu-Natal*

Background

The project originally funded through the MRC's HDI programme, while the PI was based at Mangosuthu University of Technology (MUT- an HDI with the lowest output within the national research ranking scale). The PI then migrated with the project to the University of KwaZulu-Natal under the Mid-Career Scientist grant. The project has transitioned between two funding programmes and two institutions.

In sub-Saharan Africa, there is extensive epidemiological overlap between helminthic infections (part of the neglected tropical diseases [NTDs]) and TB, HIV/AIDS and malnutrition. In South Africa, the burden of co-infections with these pathogens is highly under-appreciated. Helminth infections have been known to exhibit both immunosuppression and modulation of the immune responses against both HIV and TB infections. Malnutrition is also common in the region. This results in a vicious cycle of malnutrition, infection and immune suppression. On the other hand, intestinal helminth parasites share a niche with intestinal microbial flora. The latter has been reported to promote the development, priming and maturation of the immune system. The effects of intestinal helminth infection and their products on gut bacteria may have beneficial or detrimental effects on the host's overall health and immune competence. It is therefore important to understand the full impact of helminthiasis on other bacterial and viral pathogens and the host's ability to mount an effective immune response in the presence of helminth infections. Located in KwaZulu-Natal, where all these infections are highly endemic, this project explores the immunology of coinfections and other interactions between the pathogens.

Main Objectives

1. To contribute towards capacity building within historically disadvantaged individuals and institutions

2. To build and expand research within the niche of immunology of coinfections with neglected tropical diseases and other bacterial/viral infections by profiling HIV/helminths TB/helminths and microbiota/helminths interactions with nutritional status

Methods

Talented individuals from HDI institutions were identified to carry out the different project sub-objectives.

In vitro helminth-bacterial interactions and the antimicrobial activity of excretory-secretory products and somatic extracts from the adult worm *Nippostrongylus brasiliensis* were analysed against selected strains of Gram-positive and Gram-negative bacteria by growth assays, viable colony-forming units, minimum inhibitory concentration and minimum bactericidal concentration assays.

For human studies, individuals attending Primary Health Care Clinics in eThekwini District are screened for TB, HIV and helminths. The nutritional status is assessed through food recall, BMI and biochemical analysis of macro and micronutrients. Immune response to HIV or TB and will be assessed by Th1 Th2 Th17 and Th3 cytokine gene expression, CD4 counts and HIV viral loads.

Preliminary Results

A total of six HDI individuals identified to participate in the research on immunological interactions between NTDs and bacterial and viral pathogens. Completed objective, including a postgraduate qualification and results showing that excretory-secretory products of *Nippostrongylus brasiliensis*, but not its somatic extract, exhibited in vitro antimicrobial activity. Gram-positive (*Staphylococcus aureus*) and Gram-negative bacteria (*Salmonella enterica serovar Typhimurium, Escherichia coli* and *Klebsiella pneumoniae*) were susceptible to excretory-secretory products in a concentration-dependent manner. Antimicrobial activity was heat-stable and resistant to repeated freeze-thaw cycles. Sodium Dodecyl Sulphate-Polyacrylamide Gel Electrophoresis revealed a prominent protein band, 37kDa in size, in excretory-secretory products. Using mass spectrometry, this was identified as a cluster of globin-like proteins.

In the human studies an overall prevalence of intestinal helminth parasites of 28% was found among 240 adult participants. Further recruitments and more laboratory analyses will be undertaken.

Conclusion

A team of postgraduate students from designated groups and institution has been capacitated within a unique research niche area.

Preliminary results suggest that helminth-bacterial interactions do occur and that helminths have the potential to modulate bacteria occupying the same niche. We report broad-spectrum antimicrobial activity of excretory-secretory products of *Nippostrongylus brasiliensis*. Further identification of the active compound and mechanism of antimicrobial activity require elucidation.

21. An investigation of students' mental health care needs and

the development of innovative e-mental health interventions to promote student wellness

Research Area: Mental Health and Suicide prevention

J Bantjes[1], AE Kazdin[2], P Cuijpers[3], E Breet1, M Dunn-Coetzee[4], C Davids[4], DJ Stein[5], RC Kessler[6]

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Background

Both anxiety and depression are common among university students, and university counselling centres are under pressure to develop effective, novel and sustainable interventions that engage and retain students. Group interventions delivered via the internet could be a novel and effective way to promote student mental health.

Objectives

We carried out a pragmatic open trial to investigate uptake, retention, treatment response, and level of satisfaction with a remote group CBT intervention delivered online to university students with symptoms of anxiety or depression during the COVID pandemic.

Methods

Pre- and post-intervention self-report data on anxiety and depression were collected with the GAD-7 and PHQ-9. Satisfaction was assessed post-intervention with the Client Satisfaction with Treatment Questionnaire.

Results

175 students (86.1% female, mean age=22.4 years) were enrolled, 90.3% (n=158) of whom initiated treatment. Mean (SD) number of sessions attended was 6.4 (2.8) out of 10. Among participants with clinically significant symptoms at baseline, mean symptom scores decreased significantly for anxiety, depression, and composite anxiety/depression, with large effect sizes (d=1.0-1.5). Remission rates among participants with clinically significant baseline symptoms were 67.7-78.9% and were not associated with baseline symptom severity. High overall levels of satisfaction with treatment were reported.

Conclusion

These results serve as a proof of concept for the use of online group CBT to promote the mental health of university students.

22. Improving Stillbirth Data Recording, Collection and Reporting in Africa

Research Area: Perinatal health

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Background

Globally, an estimated 2 million third trimester stillbirths occurred in 2019. An estimated 42 per cent of stillbirths occurred in Sub-Saharan Africa where the stillbirth rate was nearly 7 times than found in Europe, Northern America, Australia and New Zealand.3 Progress in reducing the stillbirth rate over the past two decades has been slower than reductions in newborn, child and maternal mortality. Most of these stillbirths could be prevented with universal access to quality care before and during childbirth. Renewed commitment to ending preventable stillbirths is urgently needed. Many countries in Africa, where the most stillbirths occur, do not yet have well-functioning routine data systems; though most have initiated platforms, such as DHIS2 or perinatal death surveillance linked to maternal death surveillance and response. Initiatives, such as the African Health Observatory, were also established to strengthen national health information systems. Despite these initiatives, information on stillbirths particularly is limited in the region. There is an urgent need to improve stillbirth data availability and quality in the Africa continent.

Objectives

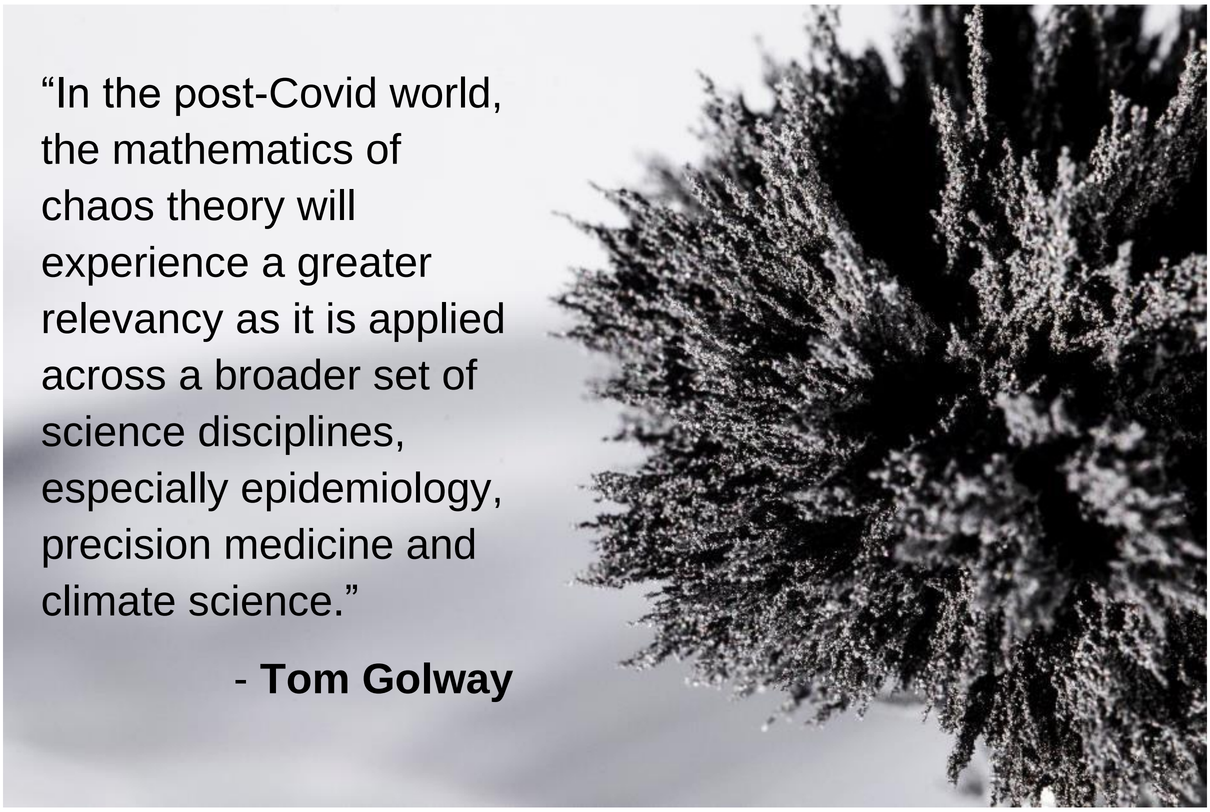
This project aims to gain a better understanding of current data systems and practices in terms of stillbirth recording, data collection, analysis and utilization in Africa and improve the availability and quality of stillbirth data in the continent. It will undertake a cross-sectional study of the data systems currently being used in Africa to record stillbirth data, identifying the gaps in the data systems and the flow of information into the national systems with the view to standardise, enhance and strengthen the recording and reporting of stillbirth data using the existing systems.

Methods

1. Compile and collate information collected using the existing stillbirth data for each country including; definitions of stillbirth currently in use in each African country and compare these to the standard definition recommended in ICD11; and national policies and guidelines on stillbirth surveillance, data collection and reporting.
2. Conduct an online survey to evaluate stillbirth data collection systems, the availability and the quality of stillbirth data per African country.
3. Identify good practices, gaps and challenges in stillbirth data collection, reporting, analysis and utilization and propose recommendations for improvements.

Results and Conclusion

To study will commence in 2021, funded by UNICEF. We hope to understand stillbirth rates in Africa, and the definitions and surveillance systems.


"In the post-Covid world, the mathematics of chaos theory will experience a greater relevancy as it is applied across a broader set of science disciplines, especially epidemiology, precision medicine and climate science."
- **Tom Golway**

SAMRC INTRAMURAL POST-DOCTORAL FELLOWSHIP PROGRAMME

23. Elesclomol an anticancer drug with potential therapeutics as antituberculosis drug candidate

Research Area: Tuberculosis drug discovery

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Background

The finding that the innate immune system employs copper ions to eliminate bacterial infection and the establishment of copper resistance as a virulent factor of *Mycobacterium tuberculosis* (M. tb). In M. tb the activity of heme-copper oxidase is essential for in vitro growth. Furthermore, copper ions are cofactors of periplasmic or surface-anchored superoxide dismutases and multicopper oxidases. Anti-cancer drug elesclomol, which forms an extremely strong complex with copper and exerts its effect by generating oxidative stress in tumor cells, was identified as a compound of choice to explore these findings against M. tb for drug repurposing.

Objectives

To evaluate the antituberculosis activity of elesclomol and whether its effect is enhanced by copper metal ions.

Methods

Initially we employed Mycobacterial Growth Indicator Tube (MGIT) BACTEC 960 system to determine antituberculosis (anti-TB) activity and minimal inhibitory concentration (MIC). Hartmans-de Bont (HdB) minmal medium was later used in order to manipulate copper molecules. Resazurin microtiter assay (REMA), an oxidation-reduction indicator has been used to determine the elesclomol activity in combination with anti-TB front-line drugs.

Results

Our results show that elesclomol is potent against *M. tb* H37Rv (10 µM) and some activity against various MDR/XDR M. tb clinical isolates. Elesclomol synergizes with rifampicin (RIF) and not antagonistic with isoniazid (INH) and ethambutol (EMB). Elesclomol-copper complexes increased *M. tb* hypersensitivity by 5-fold when compared to no copper supplementation.

Conclusion

Elesclomol can be repurposed for anti-TB treatment and the induction of copper hypersensitivity against *M. tb* can be exploited as new target for new TB drugs.

24. Effects of rooibos phenolic compounds on microbiota regulation and prevention of the metabolic syndrome

Research Area: Medical Science

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Background

The development of metabolic diseases is accompanied by changes in gut microbiota composition, including a decrease of beneficial bacterium and increase of pernicious bacteria. Increasing evidence strongly links gut microbiota to the etiology of type 2 diabetes (T2D). Western diets rich in saturated fats and refined carbohydrates changes resident gut microbiota composition and promotes inflammation that increases the risk of developing metabolic diseases. Obesity represents a state of chronic inflammation, characterized by increased levels of proinflammatory cytokines and chemokines resulting in pathological changes in insulin-sensitive tissues. Recent research indicates that gut microbiota plays a crucial role in maintaining health or promoting metabolic disease.

Objectives

The project focuses on the effect of Rooibos polyphenols on the gut microbiota of prediabetic vervet monkeys.

Methods

The vervet monkeys were fed a high fat diet and maintained at the Primate Unit of SAMRC. The monkeys received an aspalathin-rich unfermented rooibos extract (90 mg/kg/day) in a food bolus for 42 days. Baseline and post treatment faecal samples were subjected to 16S rRNA gene sequencing using an Ion Torrent next generation sequencer to profile the gut microbiota composition.

Results

The aspalathin-rich unfermented rooibos extract increased the abundance of several bacterial spp. beneficial to metabolic disease in humans, such as the Eubacterium spp., including Eubacterium halii, Eubacterium rectale and Eubacterium ramulus (beneficial butyrate producing bacteria), Weissella spp. (improves the bioavailability of bioactive phenolic compounds) , Lactobacillus ruminis (enhances intestinal epithelial barrier integrity and modulates of immune responses). Whilst reducing the abundance of harmful bacteria such as Bacteroides vulgatus (causal factors of insulin resistance and obesity).

Conclusion

Our study showed that an aspalathin-rich unfermented rooibos extract has beneficial prebiotic effects on the gut microbiota composition of prediabetic vervet monkeys fed a high fat diet.

25. Role of the microbiome in tuberculosis disease and treatment outcomes

Research Area: Tuberculosis

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Background

The microbiome has a critical role in health and is modified by antibiotics. Yet, our knowledge of the microbiome's relationship with tuberculosis (TB) and the impact of treatment is limited.

Objectives

We aimed to characterize the oral, sputum, and gut microbiome of TB patients from three cohorts and compare this to individuals without TB.

Methods

Cohort 1: Oral washes, induced sputa, and stool were collected from presumptive TB patients (58 cases, 47 symptomatic controls) at pre-treatment. Whole blood was collected from a patient subset. Cohort 2: Induced sputa and stool were collected from drug-susceptible (DS)-TB patients (n=72) before, during (months 2 and 6), and after treatment (months 12 and 18), and from their close contacts (n=118) at baseline, month 6 and month 18. Cohort 3: Saliva, sputa, and stool were collected from multidrug-resistant (MDR)-TB patients randomized to a conventional (n=4) or bedaquiline-containing (n=5) treatment regimen. 16S DNA sequencing was carried out and analyses done with QIIME and R microbiome packages.

Results

Compared to symptomatic controls, pre-treatment cases were enriched with gut anaerobes (Anaerostipes, Erysipelotrichaceae, Blautia) which correlated with upregulation of pro-inflammatory immunological pathways. In DS-TB patients on treatment, microbial diversity declined within the first two months. These effects persisted in stool until the end of treatment and, in both sputum and stool, did not recover to the baseline state by one-year post-treatment. In MDR-TB patients, diversity, while unchanged in the conventional arm, was reduced in the bedaquiline-containing arm by week 6. This was accompanied by enrichment of Enterobacteriaceae genera in sputum and stool and is likely mediated by linezolid.

Conclusion

This data supports a role for the gut-lung axis in TB and shows treatment induces long-term microbial perturbations in the airways and gut. Future studies will evaluate the association of these changes with treatment outcomes, including post-TB sequelae.

26. Does a verbal autopsy narrative provide accurate information about treatment default for people who have died from HIV?

Research Area: Public Health

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Background

The National Cause of Death Validation (NCODV) study conducted a validation of civil registration and vital statistics (CRVS) cause-of-death information by linking CRVS data to data obtained from verbal autopsy (VA) interviews for a national sample of deaths. The VA is a method used to collect and analyse cause of death data. The underlying cause of death was ascertained by medical doctors based on reviewing the VA questionnaire and the narratives. The questionnaire has a set of structured questions and an unstructured narrative outlining the sequence of medical conditions leading to death. The VA has no questions on treatment defaulting, however the narratives found that a substantial proportion of decedents who died from HIV had defaulted on their treatment.

Objectives

The objectives of this study are to:

Validate the proportion of decedents who defaulted with their antiretroviral treatment (ART) in the VAs with individual level data on the Three Integrated Electronic Registers (TIER.net) database.

Explore how the VA questionnaire can be modified to incorporate questions related to treatment defaulting.

Methods

The narratives identified 1,223 decedents had defaulted on their ART. These deaths will be validated against information regarding treatment defaulting through linkage with TIER.NET data. Identifiers such as the identity number will be utilized to link the two sets of data, however the most appropriate method of linkage is yet to be determined. All the narratives will be assessed to identify more cases and an estimation of 90% sensitivity and 90% specificity of the narratives against information in the TIER.net database will be determined.

Results

The expected results will provide the percentage of agreement between treatment default found in the narratives with the TIER.net data. Not all participants information on TIER.net will necessarily be found.

Conclusion

The information contained in TIER.net provided additional information to the VA findings around treatment defaulting such as the duration of treatment, reasons why patients defaulted, when loss to follow-up occurred and why? The additional information could be of value to improving patient care. Data linkage is useful for enhancing health information.

27. Resistance Sniffer: An online tool for prediction of drug resistance patterns of *Mycobacterium tuberculosis* isolates using next generation sequencing data

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The effective control of multidrug resistant tuberculosis (MDR-TB) relies upon the timely diagnosis and correct treatment of all tuberculosis cases. Whole genome sequencing (WGS) has great potential as a method for the rapid diagnosis of drug resistant *Mycobacterium tuberculosis* (Mtb) isolates. This method overcomes most of the problems that are associated with current phenotypic drug susceptibility testing. However, the application of WGS in the clinical setting has been deterred by data complexities and skill requirements for implementing the technologies as well as clinical interpretation of the next generation sequencing (NGS) data. The proposed diagnostic application was drawn upon recent discoveries of patterns of Mtb clade-specific genetic polymorphisms associated with antibiotic resistance. A catalogue of genetic determinants of resistance to thirteen anti-TB drugs for each phylogenetic clade was created.

A computational algorithm for the identification of states of diagnostic polymorphisms was implemented as an online software tool, Resistance Sniffer (http://resistance-sniffer.bi.up.ac.za/), and as a stand-alone software tool to predict drug resistance in Mtb isolates using complete or partial genome datasets in different file formats including raw Illumina *fastq* read files. The program was validated on sequenced Mtb isolates with data on antibiotic resistance trials available from GMTV database and from the TB Platform of South African Medical Research Council (SAMRC), Pretoria. The program proved to be suitable for probabilistic prediction of drug resistance profiles of individual strains and large sequence data sets.

28. Community-led cross-sectional study of social and employment circumstances, HIV and associated factors amongst female sex workers in South Africa: Study protocol and baseline characteristics

Research Area: HIV, HIV drug resistance and incidence, female sex workers, violence and mental health

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Background

Female sex workers (FSWs) are a very vulnerable group globally. In South Africa, they are perceived to play a pivotal role in the country's HIV epidemic. Understanding their health status, and risk factors for adverse health outcomes is foundational for developing evidence-based health care for this population.

Objectives

This study aimed to use a community-centric approach to researching factors associated with HIV amongst female sex workers in South Africa.

Methods

3,005 FSWs in South Africa were enrolled across 12 SW programmes 12 sites in all nine provinces of South Africa (January-July 2019). Eligible sites had an existing SW network and support programme providing peer education and a range of HIV services. FSWs were actively involved in all stages of the study design, questionnaire development, and data collection. Survey tools were developed in consultation with peer educators and members of different FSW populations.

Results

The median age of FSWs was 32 years, and HIV prevalence was 62%. In consistent ondom use was high (81.6%), as was exposure to childhood trauma (88.4%), and past year intimate partner violence (46.2%). More than half of the women had a mood disorder.

Discussion

This is the first national survey of HIV prevalence and incidence amongst FSWs in programmes in South Africa. Based on the unique methodology and the successful implementation alongside study partners, the outcomes will be utilized to inform further improvements of tailored interventions. Our rapid rate of enrolment, low rate of screening failure and low proportion of missing data showed the feasibility and importance of community-centric research with marginalised, highly vulnerable populations. We also highlight the massive vulnerability this population experience to HIV, violence and mental ill health. It is vital that programmes begin to address the comorbid concerns of this population and leveraging existing programmes is an opportunity to have an impact beyond the HIV wins seen amongst FSWs.

29. A global bibliometric analysis of research productivity on vaccine hesitancy from 1974 to 2019

Research Area: Vaccine Implementation Research

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Background

Vaccine hesitant individuals consist of a diverse group between vaccine acceptors and vaccine rejecters, who have different concerns about vaccines. The vaccine hesitant group may take or accept certain vaccines and deny some while the other may have concerns about the decision to vaccinate. It is therefore imperative to communicate with vaccine hesitant individuals about the benefits of vaccination and address their concerns. Additionally, it is important to understand that vaccine hesitancy is multifaceted and therefore factors that contribute to hesitancy differ across populations, settings and vaccines.

Objectives

The objective of this paper was to conduct a global bibliometric analysis of research productivity and identify country level indicators that could be associated with publications on vaccine hesitancy.

Methods: We searched PubMed and Web of Science for publications from 1974 to 2019, and selected articles focused on behavioral and social aspects of vaccination. Data on country-level indicators were obtained from the World Bank. We used Spearman's correlation and zero-inflated negative-binomial regression models to ascertain the association between country level indicators and the number of publications.

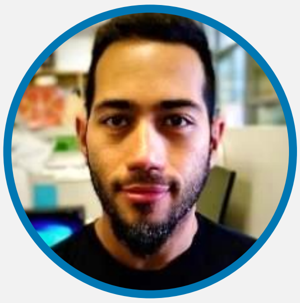
Results

We identified 4314 articles, with 1099 eligible for inclusion. The United States (461 publications, 41.9%), Canada (84 publications, 7.6%), and United Kingdom (68 publications, 6.2%) had the highest number of publications. Although various country indicators had significant correlations with vaccine hesitancy publications, only gross domestic product (GDP) and gross national income (GNI) per capita were independent positive predictors of the number of publications. When the number of publications were standardized by GDP, the Gambia, Somalia and Malawi ranked highest in decreasing order. The United States, Canada, and United Kingdom ranked highest (in that order) when standardized by current health expenditure.

Conclusion

Overall, high-income countries were more productive in vaccine hesitancy research than low-and-middle income countries. There is a need for more investment in research on vaccine hesitancy in low-and-middle income countries.

30. Precision Medicine: Pharmacogenomics and development of individualized drug therapy



Research Area: Biomedical Research

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Background

Advances in pharmacogenomics over the past decade have yielded new tools to evaluate disease susceptibility and prognosis, and an unprecedented opportunity to individualize drug therapy. A plethora of genetic biomarkers for anti-diabetic and anti-hypertensive drug response have been identified, which might be used in treatment selection for these diseases. Research in the field has also enhanced our understanding of diabetes and 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 an anti-hypertensive response. As such, this project is set to make a significant contribution to the development and implementation of personalized medicine in South Africa as well as the Sub-Saharan African region.

Objectives

To investigate genomic associations between genetic variations in pharmacogenomically relevant genes and their influence on the efficacy of antidiabetic and anti-hypertensive drugs.

Methods

Buccal swab samples were obtained from a collective total of 500 Xhosa, Zulu, Swati, Venda and Cape Admixed donors undergoing anti-diabetic/hypertensive therapy. DNA was extracted and quantified using standard protocols. The Agena MassARRAY system was used to genotype 180 clinically relevant single nucleotide polymorphisms (SNPs) and identify haplotypes of responder's and non-responders present within the study sample group. The effect of the identified haplotypes in drug transport was investigated in HEK293 cells using glucose uptake assays. Associations between the presence of an SNP and non-response to an anti-diabetic and/or anti-hypertensive drugs were drawn using statistical analyses.

Results

Several unique haplotypes were identified within the various populations. A marked difference in SNP frequency was observed between responders and non-responders, with numerous SNPs were observed only in the non-responder sub-grouping. Distinct statistical associations were drawn between certain SNPs and non-response to therapy.

Conclusion

The associations obtained in this study may be used to individualise drug therapy and lower the burden of adverse side effects in patients undergoing anti-diabetic/hypertensive therapy.

31. Developing an advanced cell culture model for pancreatic beta cells

Research Area: Biomedical Research (Diabetes)

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Background

The use of rodent beta cell lines is expected to be the benchmark for the foreseeable future in diabetes research and the development of new therapies. Thus, developing cell lines with human pancreatic beta cell dynamics and physiology is required. A crucial feature that is lacking in rodent beta cell lines is that the islet amyloid polypeptide (IAPP) does not polymerize and form toxic amyloid plaques, with this being fundamental to diabetes pathophysiology.

Objectives

The project aims to transfect INS-1 beta cells to express the human islet amyloid polypeptide. Furthermore, the cell line will be characterized with respect to gene expression, nutritional stimulus, metabolite measurements of insulin, glucose and amyloid.

Methods

E. coli BL21 was transformed with DNA plasmids containing IAPP as well as a green fluorescent protein (GFP) tag. Antibiotic kill curves were performed with Hygromycin to ascertain the minimum concentration required to inhibit cell growth. INS-1 cells were transfected with IAPP plasmids using X-tremeGENE™ 360 transfection reagent. Cells were then selected on hygromycin for 14 days. Resulted colonies were visualized using fluorescence microscopy. Quantitative PCR was performed on putatively transfected clones using Taqman probes for several beta cell pancreatic house-keeping genes as well as IAPP.

Results

The selected transfected clones have indeed taken up the respective plasmid as observed by the expression of green florescent protein under the microscope. Quantitative PCR results revealed that several pancreatic beta cell house-keeping genes investigated appear to be regulated and do not show consistent expression levels. These experiments are still ongoing.

Conclusion

Quantitative PCR analysis shows that beta cell house-keeping genes may be regulated and requires further investigation with additional house-keeping genes. Characterization of putatively transfected cell lines with respect to nutritional stimuli and metabolite concentration are yet to be determined.

32. Closing the treatment gap: implementation insights for task-shared counselling for depression and harmful alcohol use in South Africa

Research Area: Implementation Science

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Background

The treatment gap for mental disorders is large in South Africa and task-sharing interventions have gained traction in research and policy. Implementation evidence is needed to support embedding such complex interventions into routine practice in primary healthcare (PHC).

Objectives

This study investigated the experiences of PHC facility managers who implemented task-shared counselling for depression and harmful alcohol use in chronic disease care in the Western Cape.

Methods

Focus group discussions and in-depth individual interviews were conducted with facility managers in Cape Town Metropolitan areas, and rural areas (n=15 total). Data was audio recorded with consent and transcribed verbatim. NVivo 12 was used to store data and enable framework analysis. The four concepts of normalisation process theory (NPT) were used for the initial framework and inductive and deductive coding were conducted.

Results

Participant data mapped onto four themes based on the components of NPT. In Theme 1 - Relational Integration, participants described leadership in changing the mindset of staff to value the new counselling. Under Theme 2 Interactional Workability participants emphasized the importance of referrals within their facilities (to social workers and nursing/clinical staff, including mental health nurses) for improving clinical care. In Theme 3 Skill Set Workability - participants emphasized the need to define responsibilities in relation to screening and counselling for mental health conditions and reorient staff to prioritize mental health. Theme 4 described Contextual Integration of Counselling with organisational climates commonly characterised by resistance to service changes. The need to build resilience among staff, raise morale, and have meaningful engagement with the public around services needs were put forward as key organizational needs.

Conclusion

This study highlights the leadership role of managers as conduits for creating an organisational environment and shaping staff attitudes to introducing this and other innovations. Improving management capacities to support this integration process is indicated.

33. Understanding the evolution of drug resistant tuberculosis: a molecular epidemiologic and bioinformatics analysis of Mycobacterium tuberculosis strains acquiring drug resistance.

Research Area: TB, Biomedical research

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Background

The Eastern Cape Province is an area of concern regarding the prevalence and resistance patterns of TB. Recent studies showed the repeated emergence of beyond-XDR TB, which was essentially untreatable in the pre-Bedaquiline era. Strains of these atypical Beijing genotypes form increasing proportions of drug-susceptible- (4%), MDR- (34%) pre-XDR- and XDR (93%) populations. The prevalence in the isoniazid mono-resistant (IMR) group is unknown. Furthermore, programmatic diagnostic algorithms would frequently miss the presence of IMR, resulting in inadequate treatment and consequent amplification of resistance and sustained transmission.

Objectives

We aimed to describe the population structure of IMR TB in the Kouga district of the Eastern Cape, and to determine the risk factors leading to IMR, and to unfavourable treatment outcomes.

Methods

We enrolled consenting adults with confirmed rifampicin susceptible TB from ten high-burden clinics in the Kouga district. Sputum samples were collected at baseline (pre-treatment), 7 weeks and 23 weeks follow-up. Culture-based isoniazid drug-susceptibility testing was done at Stellenbosch University. Resistant isolates were genotyped to determine the presence of mutations in the katG, and inhA promoter regions. Demographic and outcome data was obtained from the Electronic TB Register (ETR.net) to determine risk factors for IMR, or unfavourable treatment outcomes.

Results

The most prevalent genotype was Beijing (47%). Isoniazid resistance was found in 105/747 (14%) baseline isolates, of which the atypical Beijing genotype comprised 14% (15/105). A large proportion of resistant isolates displayed an intermediate phenotype on repeat MGIT-based susceptibility testing (17/105; 16%), while no katG or inhA promoter mutations were found in a further 52/105 (49.5%). No significant risk factors for IMR or unfavourable outcomes could be found.

Conclusion

An alarmingly large proportion of IMR isolates would be missed by currently used rapid genotypic testing. The prevalence of IMR is higher than previously thought, requiring urgent intervention to prevent acquisition of further resistance, and transmission.

34. Rape Impact Cohort Evaluation (RICE) study

Research Area: Health promotion and Disease prevention

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Background

Together with psychosocial consequences, abuse in childhood or adulthood has adverse physical health outcomes.

Objectives

This study examined the associations of childhood abuse (CA), intimate-partner (IPV) and non-partner abuse with hypertension in South African women aged 18 to 40 years, using the Rape Impact Cohort Evaluation study baseline data.

Methods

History of self-reported childhood sexual, physical, emotional abuse and parental neglect, adult sexual, physical, emotional and economical abuse by an intimate partner (IPV), and sexual abuse and sexual harassment by a non-partner; and measured blood pressure were analysed. Logistic regressions examined the associations of 1) CA (adjusted for traditional hypertension risk factors, rape exposure, HIV-infection, other traumatic exposures, depressive symptom scores and post-traumatic stress disorder scores), 2) IPV and 3) non-partner abuse (additionally adjusted for CA) with hypertension.

Results

The prevalence of overall CA (70.9% vs 57.2%; $p<0.001$) and each type CA was higher in women with hypertension (n=220) than without hypertension (n=1577). The patterns were similar for sexual (25.2% vs. 15.4%), physical (61.9% vs. 47.6%), emotional (62.8% vs. 45%) and economical IPV (29.8% vs. 17.9%), non-partner sexual abuse (27.1% vs.17.6%) and sexual harassment (16.5% vs. 5.8%), $p\leq0.001$ for all. Exposures to sexual CA, emotional CA, an increasing number of CA types and cumulative severity of CA were associated with increased odds of hypertension. More than one episode of sexual abuse by a non-partner, sexual harassment, frequent physical IPV, emotional IPV and greater severity of economic IPV were significantly related to hypertension.

Conclusion

This study highlighted the differential associations of CA, IPV and non-partner abuse with hypertension, with the latter two determined by the types, frequencies, cumulative severity scores and perpetrators of the abuse. While violence against women and girls must be prevented, there is a need for early psychosocial interventions in abused women to curb the development of hypertension.

35. Differential prevalence and sub-optimal care of hypertension and dyslipidaemia by glycaemic status in Cape Town

Research Area: Non-communicable diseases

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Background

Hypertension and dyslipidaemia frequently co-occur with diabetes and increases the risk of cardiometabolic diseases in those with and without diabetes.

Objectives

To describe the prevalence and management of hypertension and dyslipidaemia in adults in Cape Town identified as high-risk for diabetes from a community-based screening programme and subsequently diagnosed with normoglycaemia or newly-diagnosed diabetes on oral glucose tolerance tests, and in adults with established diabetes

Methods

Cross-sectional data collection comprised interviews, clinical measurements and biochemical analyses. Data are presented as median and 25th-75th percentiles for continuous variables and prevalence (percentage) for categorical data.

Results

Among 635 participants with normoglycaemia (n=213), newly-diagnosed diabetes (n=70) and known diabetes (n=352), the median age was 57 (48-63) years and increased by glycaemic category (49 (42-56), 53 (46-58) and 61 (54-68), p<0.001, respectively). The prevalence of body mass index ≥30 kg/m2 by glycaemic status was 73%, 84% and 50% (p<0.001), respectively. Hypertension prevalence was lower in normoglycaemia (57%) and newly diagnosed diabetes (64%) compared to known diabetes (76%) (p<0.001). Among normoglycaemia, newly diagnosed and known diabetes participants with hypertension, awareness was 50%, 61% and 76% (p<0.001), respectively, while hypertension control was 23%, 27% and 53% (p<0.001), respectively. Dyslipidaemia prevalence (low-density lipoprotein cholesterol >3mmol/l or known dyslipidaemia) was lower in normoglycaemia (43%) compared with newly diagnosed diabetes (73%) and known diabetes (70%) (p<0.001). Awareness among those with dyslipidaemia was 13%, 21% and 45% (p<0.001), respectively, and control was 5%, 6% and 26% (p<0.001), respectively. Median HbA1c was lower in newly diagnosed diabetes (7.1% (6.6-8.5)) compared with known diabetes (8.8% (7.1-10.55)), (p<0.001). Diabetes control (HbA1c <7%) in known diabetes was 22%.

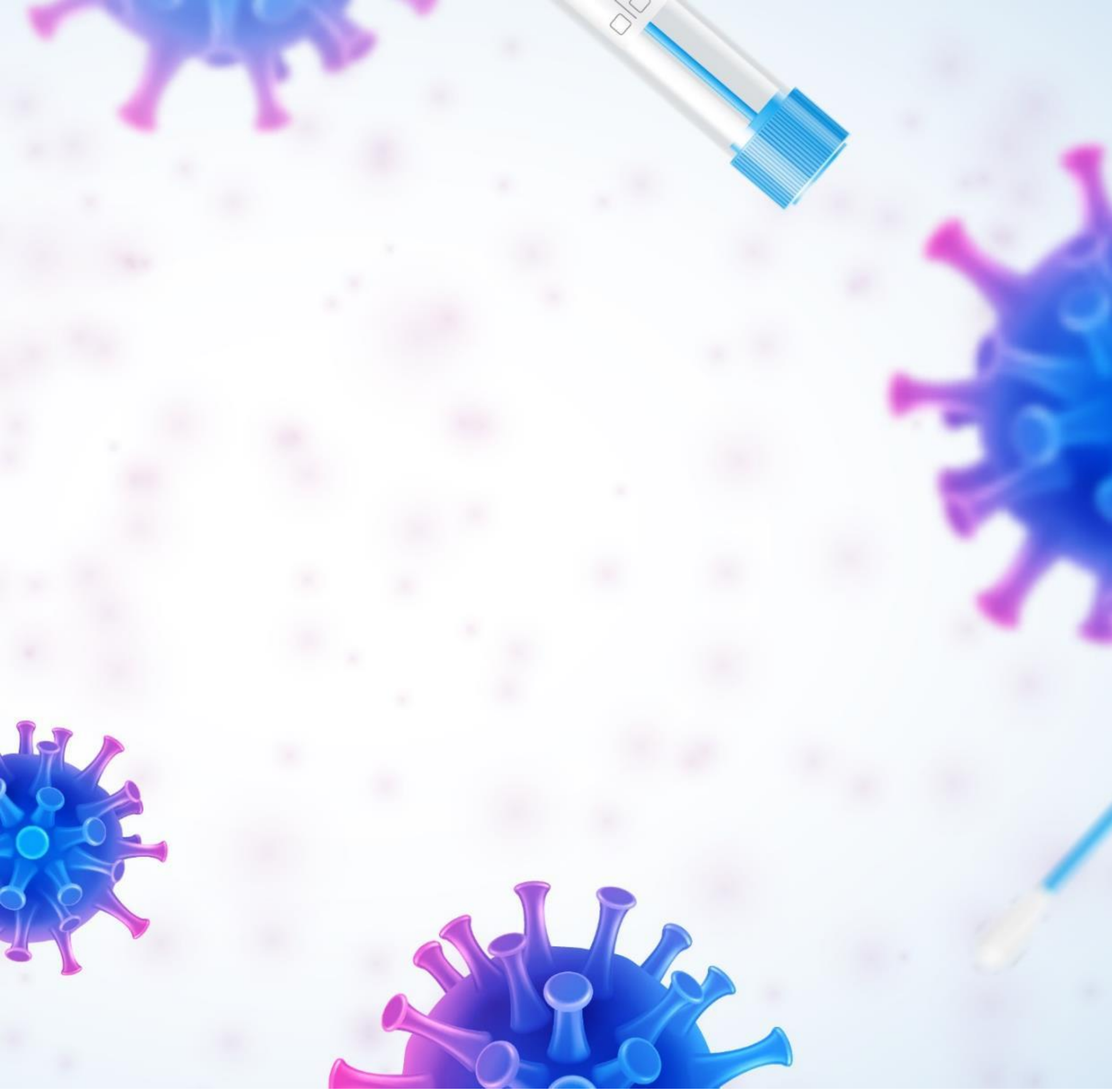
Conclusion

Hypertension and dyslipidaemia are highly prevalent in this population but poorly managed, including in adults with known diabetes. Regular screening and testing of adults at high-risk for, and improved care in those with known, cardiometabolic diseases are required.

2 Photo source: http:www.people.com

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

– Nelson Mandela



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