WITS HEALTH CONSORTIUM

ANNUAL REVIEW

2021

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Great things in business are never done by one person. **They're done by a team of people.**

Annual Review 2021

INTRODUCTION

EXECUTIVE SUMMARY

The Wits Health Consortium (Pty) Ltd (WHC) is a private, wholly owned company of the University of the Witwatersrand (Wits), Johannesburg.

WHC was established as a result of an initiative proposed by the Faculty of Health Sciences, to unlock commercial opportunities that would provide additional sources of revenue for the Faculty and its Departments. Council approved the Faculty's proposal in October 1997 and the Company was registered in 1998.

All academic endeavors are directed, managed and controlled through the University structures with WHC research active staff jointly appointed with the University, conducting research, managing donor-funded activities, clinical trials and pursuing entrepreneurial innovation in health related activities.

OUR Shared Services Centre (SSC)

WHC operates a Shared Services Centre (SSC) to support our various research entities or divisions that operate within WHC. Academically, these divisions fall under their relevant university department but they are viewed as independent divisions of the WHC and managed according to structures, project plans and budgets set out by the division directors

Academic and other Divisions
24

Major Institutes and Units,
11

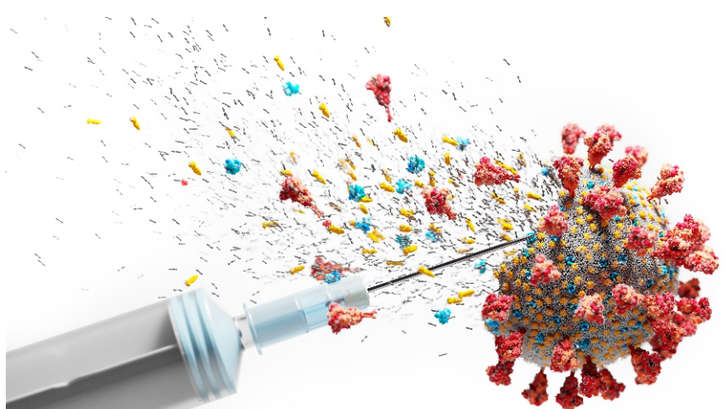
ABOUT OUR

COMPANY

WHC has proven experience in managing complex sponsorships, commercially-funded contracts and grants. We manage over 300 new contracts and grants each year, worth more than $72 million annually, with all our operations transparently audited:

WHC, as part of the University of the Witwatersrand, is a tax-exempt private company

- WHC is audited annually by PricewaterhouseCoopers.Inc
- WHC has an internal audit function that is outsourced
- WHC employs Deloitte & Touche Inc to conduct audits required for Federal and other grants
- Over 110 audits are conducted annually on Grant awards to ensure transparency and optimal management of donor funding, grants and corporate sponsorships



Launched
1998

WHC manages around
22%
of the University's total group income

Our SSC supports over
100
research syndicates from the Faculty of Health Sciences

Our SSC assists over
4000
people each year

List of branches

THE MAIN BRANCH

- 272 Bronkhorst Street South Block, Brookfield Office Park, Nieuw Muckleneuk, Pretoria, 0075
- New Nurses Home, Chris Hani Baragwanath Hospital, 26 Chris Hani Road, Diepkloof, Soweto, 1860
- Wakefield Court, 145 Prince Street, Durban, 4001

HEAD OFFICE

31 Princess of Wales Terrace, Parktown, Johannesburg, 2193

GPS : -26.1779738, 28.0464528

www.witshealth.co.za

COMPANY PROFILE

WHERE WE WORK

South Africa

Africa

United States

Europe

The research entities we support work in South Africa, across Africa, in the US and in Europe. WHC Head office is based in Johannesburg, South Africa.

DEAN'S

STATEMENT

The University of the Witwatersrand has placed at the forefront of its strategic agenda, the enhancement of academics and the strengthening of institutional capacity and postgraduate research.

This ensures our ability to remain globally competitive and locally relevant by creating an enabling environment that nurtures lifelong learning and innovative thinking.

Our vision is and continues to be driven by our desire to be a research-intensive Faculty, leading the way in developing innovative solutions that above all, meet the needs of our immediate communities. Our reach extends beyond the shores of the African continent, with collaborative partnerships that are addressing some of the world's most challenging health issues. We therefore remain proud of our postgraduate training programmes that are helping to develop a robust research pipeline that will contribute to our knowledge economy.

PROFESSOR SHABIR MADHI

Non Executive Director and Chairman

Dean of the Faculty of Health Sciences at the University of the Witwatersrand

MBBCh (Wits), MMed (Wits), FCPaeds(SA), Ph.D

The Faculty of Health Sciences, in its endeavour to continue to be a centre of excellence for service, teaching, research and innovation, continues to build on its reputation for training and developing competent healthcare professionals at an undergraduate and postgraduate level. In doing so, graduates enter the local and global arena armed with the requisite knowledge to serve the most vulnerable members of society. At its core, the Faculty is dedicated to the most basic of human rights: equitable access to healthcare for all.

CEO'S

STATEMENT

WE ALWAYS TRY TO GIVE MORE VALUE & INNOVATION TO THE BUSINESS...

"At WHC we continue to thrive despite the challenging times brought by the pandemic. While Covid tested our resilience, we continue to emerge stronger. We signed several new divisions and contracts in 2021 and delivered world class administrative support that we promise our syndicates. The portfolio of development and research programmes managed through our Shared Service Centre has grown. The total income has grown from R2 601 813 097 in 2020 to R2 890 345 259 in 2021."

professional, excellent, and efficient, administrative, and financial management for our syndicates. The great performance we continue to show is indeed a result of our concerted efforts and the commitment we have in ensuring that our syndicates and stakeholders get the support and service they deserve. It is our ambition to always drive a high-performance environment by remaining true to our purpose and values.

MR ALFRED FARRELL

Executive Director

Chief Executive Officer of Wits Health Consortium (WHC)

B Comm, B Compt (Honours), CA (SA)

I am grateful for the support of our Board. Their support has been a big benefit for the Consortium and for its various shareholders. I would also like to express my admiration for our syndicates that continue to grow in various fronts. I am Incredibly proud of the support and resolve shown by our skilled WHC teams in making sure we continue to deliver

BOARD OF DIRECTORS

PROFESSOR SHABIR MADHI

MBA, PhD (Genetics)

Professor Madhi is Dean of the Faculty of Health Sciences at the University of the Witwatersrand. A National Research Foundation A-rated scientist. Professor of Vaccinology in the School of Pathology at the University of the Witwatersrand and Director of the world-renowned Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit (Wits VIDA). National Research Foundation/ Department of Science and Innovation SARChI Chair in Vaccine Preventable Diseases. Co-Director of African Leadership in Vaccinology Expertise (ALIVE).

As a trained paediatrician, Prof Madhi's research has focused on the epidemiology and clinical development of vaccines against pneumonia and diarrhoeal disease. These studies have informed World Health Organization Recommendations on the use of the lifesaving pneumococcal conjugate vaccine and rotavirus vaccine in children, and influenza vaccination of pregnant women.

MR ALFRED FARRELL

B Comm, B Compt (Honours), CA (SA)

Mr Farrell is a skilled financial and accounting manager with many years of experience in senior financial management positions at companies such as the Automobile Association of South Africa, Interleisure and the Premier Group. Prior to joining WHC in 2002, Alf held the position of Chief Financial Officer for BDFM Publishers (Pty) Ltd.

Mr Farrell has steered Wits Health Consortium (WHC) with invaluable insights gained through his successful career. Since joining Wits Health Consortium Mr Farrell has directed its portfolio of development and research programmes, managed through the Shared Service Centre, and has ensured the growth of WHC has been combined with high standards of delivery.

MR DESMOND ARNOLD

CA (SA), FCMA, AMP (Wharton)

A highly-skilled accountant and has held numerous financial positions in some of South Africa's leading corporates. He is a past President of the South African Institute of Chartered Accountants (SAICA) and was awarded honorary life membership in recognition of his services to the accounting profession. Mr Arnold is Chairman of the WHC Audit Committee and is also a member of the WHC Risk Committee. He is also a Trustee of the Absa Pension Fund.

PROFESSOR DAYNIA BALLOT

MB BCh, FCPaeds SA, PhD

Professor Ballot is a renowned pediatrician with a subspecialty in neonatology and an NRF C2 rated researcher and Head of the School of Clinical Medicine at the University of Witwatersrand.

DR RACHEL CHIKWAMBA

MBA, PhD (Genetics)

Dr Chikwamba is responsible for strategic alliances and communication and is an expert in scientific and industrial research. Her research has focused on metabolic engineering for nutrition and pharmaceutical applications. She has studied in the US and Australia and was an Honorary Research Fellow at St George's Hospital at the University of London. She has also taught post-graduate classes at the University of Pretoria.

MR PRAKASH DESAI

B Comm, B Compt (Honours), CA (SA)

Mr Desai supports WHC in areas such as risk, audit, strategy and investment. He is currently Chief Executive Officer at Afrifocus Securities and worked as a former Group Chief Executive and Group Finance Director at Avusa. Prior to this, he was a non-executive director at M-Net Supersport Ltd and at Caxton Publishers and Printers Ltd.

PROFESSOR JOHNNY MAHLANGU

MB BCh, M Med (Haem), FCPath (SA) (Haem) (Clin Haem)

Head of the University of the Witwatersrand's School of Pathology and Head of the Haematology Diagnostic Section in the Department of Molecular Medicine and Haematology. Peer reviewed many journal publications and international congress presentations. He sits on the editorial boards of various haemophilia treatment guideline committees and participates in multi-national clinical trials.

MS PHAKAMA MBIKWANA

B Comm., BCTA , IEDP (Duke Corporate)

Phakama graduated at Rhodes University in 2002 with a Bachelor in Commerce in Accounting and Economics. She then further completed a Bridging Certificate in Theory of Accounting at RAU in 2005. She also holds an International Executive Development Program certificate from Duke Corporate (Duke University affiliate). She is an independent non-executive director on the Storage Property REIT Limited board of directors, a JSE Listed REIT.

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PROFESSOR LYNN MORRIS

Deputy Vice-Chancellor: Research and Innovation

Professor Lynn Morris is the Deputy Vice-Chancellor of Research and Innovation at the University of the Witwatersrand in Johannesburg, South Africa. She obtained her PhD from the University of Oxford in 1988. She is the founding Director of the Antibody Immunity Research Unit based at the National Institute for Communicable Diseases (NICD) where she also served as the interim Executive Director. Over the last 30 years she has made significant contributions to the understanding of the antibody response to HIV infection and vaccination. Lynn is an NRF A-rated scientist, has published over 270 papers holding an H-Index of 66 and has featured in the Web of Science list of highly cited researchers. She is a member of Academy of Science of South Africa (ASSAf), member of the Council for the National Advisory Council on Innovation (NACi), the African Academy of Sciences (AAS), the Royal Society of South Africa (FRSSA) and The World Academy of Sciences (TWAS).

DR TSHEPO MOTSEPE

MB BCh; MA (Public Health)

Dr Motsepe is a KwaZulu-Natal and Harvard University graduate. She has worked in private medical practice locally and abroad and has developed specialist knowledge in several fields, including family health, refugee health and HIV. She was Deputy Director of the Chris Hani Baragwanath Hospital in Johannesburg and Chairperson of the Health Accreditation Committee for the Gauteng Provincial Government.

PROFESSOR MARIA PAPATHANASOPOULOS

Bsc (Hons), Msc, PhD

Professor Papathanasopoulos is an established scientist who has built an exceptional reputation in the infectious diseases, bioinformatics, and virology fields. She has established world class laboratories that conduct innovative research on HIV-1 drug discovery, and vaccine designs that are recognised at a national, regional and international level.

PROFESSOR HELEN REES

OBE, MB BChir, MA, MRCGP, DCH, DRCOG, MBA (Harvard)

Professor Rees is Executive Director of the Wits Reproductive Health and HIV Institute. Her specialist area focuses on HIV and Reproductive Health and she has published extensively in these fields. She has been internationally recognised for her expertise and for her contribution both nationally and internationally to research and medical advances in these areas. She is an Honorary Professor in the Department of Clinical Research at the London School of Hygiene and Tropical Medicine (LSHTM).

PROFESSOR MARTIN VELLER

MB BCh, FCS (SA), M Med (Surg)

Professor Veller is Dean of the Faculty of Health Sciences at the University of the Witwatersrand and a Professor in the University's Deparment of Surgery. He is an expert in Vascular Surgery with extensive academic, research and teaching experience. Professor Veller also serves on the Board of Directors of the Wits Donald Gordon Medical Centre. He has trained at the University of Witwatersrand and at St. Mary's hospital at London's Imperial College

PROFESSOR ZABULON VILAKAZI

PHD (Physics)

Professor Vilakazi is Deputy Vice-Chancellor of Research and Post-Graduate Affairs at the University of the Witwatersrand. His research interests include computational physics and heavy-ion collisions at high energies and his work saw him nominated as a Young Global Leader by the World Economic Forum in 2010. He is globally recognised for his expert knowledge in physics and nuclear research.

MS TASNEEM WADVALLA

Legal advisor at University of the Witwatersrand

Ms Tasneem Wadvalla currently serves as the Head of Legal Services and the Chief Staff to Professor Zeblon Vilakazi, the current Vice-Chancellor and Principal of the University of the Witwatersrand. She previously served as the Chief of Staff to Professor Adam Habib and prior to that as a Senior Legal Advisor in the University's Legal Office, bringing her unbroken service to the institution to 14 years.

Ms Wadvalla is responsible for managing and overseeing the functions of staff and the activities in the Office of the Vice-Chancellor, including the coordination and management of certain strategic projects. One such project was the 4IRSA collaboration that involved several public, private and higher education sector partners. She represents the Vice-Chancellor's Office and the University in her administrative, legal and other capacities across multiple platforms and engages with the University's governance structures in this capacity, including the University's Council and its sub-committees, the Senate and the Wits Foundation Board of Governors.

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A SKILLED EXECUTIVE TEAM OVERSEES DAY-TO-DAY OPERATIONS OF WHC

MEET OUR
EXECUTIVE

MR ALFRED FARRELL
Chief Executive Officer

DR ITUMELENG FUNANI
Chief Academic Officer

MR SAGIE PILLAY
Chief Operating Officer

MRS CHRISTINE GROBLER
Deputy Chief Operating Officer

MR JEAN DU RANDT
Chief Financial Officer

MR DANIEL MOSIA
Chief Commercial Officer

MR KARL BASSON
Chief Technology Officer

OUR VISION

Vision provides DIRECTION.

To be a valued strategic partner of Faculty, recognised for the additional resources, commercial/business expertise and supplementary income we are able to make available to it.

OUR MISSION

Mission creates FOCUS.

To support the teaching, research and public health service mission of Faculty; either through the provision of commercial and administrative support for income-generating activities ancillary to the main objectives of Faculty.

OUR VALUES

Values define BEHAVIOUR.

Stewardship (S)
We recognize our role as stewards of the Faculty's assets by managing our resources responsibly, effectively, and efficiently.

Employees (E)
We are committed to the success of our employees, as they are our most valuable resource, and so provide them opportunities for development, growth and personal success.

Respect (R)
We are courteous, conscientious and respectful in our dealings with our customers, employees, Faculty and the communities where we work.

Variety (V)
We embrace different viewpoints and support mutually beneficial partnerships among a diverse mix of individuals, departments, institutions, and community groups.

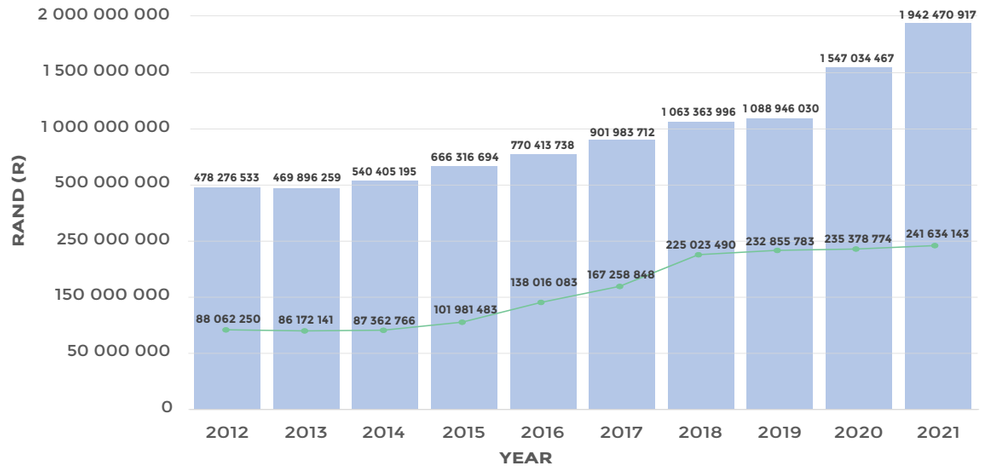
Integrity (I)
We conduct ourselves in a fair, ethical and honest manner. We strive to make all decisions in the best interests of our customers, employees, Faculty and the communities where we work. We are accountable and answerable for our actions.

Customer Service (C)
We value innovative, timely, efficient, solution-oriented, and cost-effective services and systems. We are committed to achieving the highest levels of customer satisfaction achievable, given the resources at our disposal.

Entrepreneurship (E)
We foster a culture where entrepreneurship and prudent risk taking are encouraged, where the entrepreneur is able to benefit as a partner in their venture.

THE FINANCIALS

CASH BALANCE AND PROPERTY PLANT & EQUIPMENT

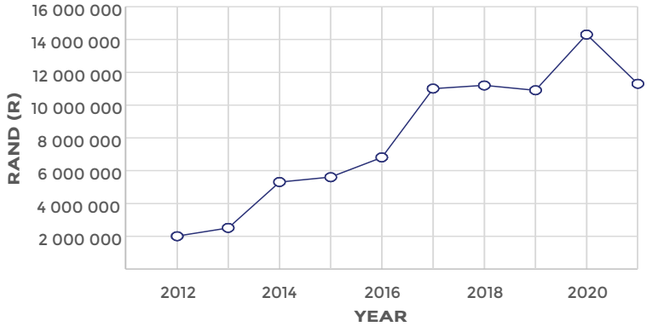


Cash Balances **R 1 942 470 917 for Year 2021**

Property Plant & Equipment **R 241 634 143 for Year 2021**

DIVIDEND DECLARATIONS BALANCE - GROUP

Dividends paid
Dividends paid during the year to the University of the Witwatersrand, Johannesburg.



Dividends paid **R 11 300 000 for Year 2021**

STATEMENT OF PROFIT OR LOSS AND OTHER COMPREHENSIVE INCOME

INCOME	2021	2020
Sponsored funds received	2 591 369 118	2 464 392 514
Pharmaceutical income	247 649 424	88 879 949
Sale of goods and rendering of services	43 429 286	43 213 992
Other	8 111 579	5 809 064
Gross income	**2 890 559 407**	2 602 295 519
Cost of sales	(10 965 231)	(10 289 607)
Surplus before operating expenses	**2 879 594 176**	2 592 005 912
Operating expenses	**(2 762 658 496)**	(2 547 039 986)
Foreign exchange gains/(losses)	30 156 897	(27 446 617)
Operating surplus before net finance income	147 092 577	17 519 309
Net finance income	38 626 947	42 461 378
Finance income	43 241 299	47 109 368
Finance costs	(4 614 352)	(4 647 990)
Surplus before income tax	**185 719 524**	59 980 687
Income tax expense	(571 903)	(453 108)
Surplus for the year	185 147 621	59 527 579
Total comprehensive income for the year	**185 147 621**	**59 527 579**

STATEMENT OF FINANCIAL POSITION

ASSETS	2021	2020
Non-current assets	R	R
Property, plant and equipment	241 634 143	235 378 774
Goodwill	485 608	485 608
Shareholder's loan	2 200 000	
Deferred tax	449 589	139 811
	244 769 340	236 004 193
Current assets		
Inventory	435 952	
Trade and other receivables	453 749 225	357 524 775
Tax receivable		52 943
Cash and cash equivalents	1 942 470 917	1 547 034 467
	2 396 656 094	1 904 612 185
Total assets	**2 641 425 434**	**2 140 616 378**

EQUITY AND LIABILITIES	2021	2020
Equity	R	R
Share capital	100	100
Accumulated reserves	713 886 004	540 038 383
	713 886 104	540 038 483
Liabilities		
Non-current liabilities		
Borrowings	15 795 249	18 910 452
Lease liability	17 421 496	11 505 147
	33 216 745	30 415 599
Current liabilities		
Borrowings	3 137 242	2 896 149
Bank overdraft	14 923 100	5 249 901
Lease liability	11 726 174	8 803 684
Current tax payable	40 318	
Trade and other payables	342 142 778	333 761 252
Income received in advance	1 508 276 044	1 206 868 398
Unallocated receipts	14 076 929	12 582 912
	1 894 322 585	1 570 162 296
Total liabilities	1 927 539 330	1 600 577 895
Total equity and liabilities	**2 641 425 434**	**2 140 616 378**

Annual Review 2021

HUMAN RESOURCE

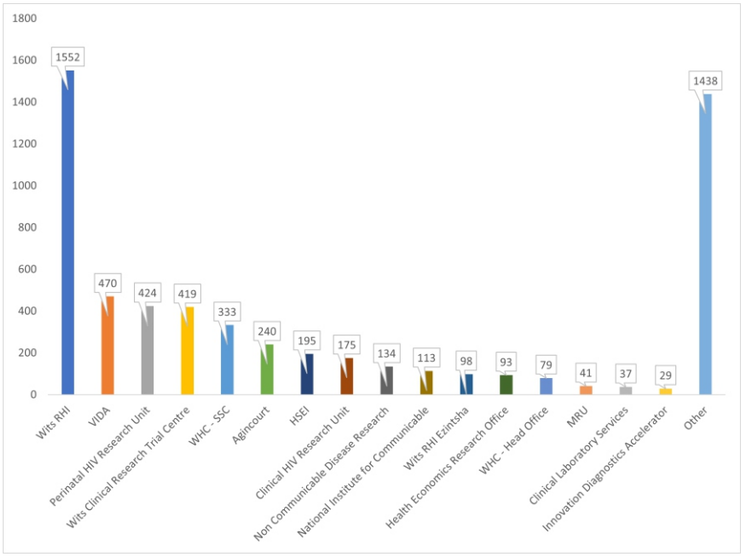
OVERVIEW

Effective and comprehensive Human Resource management services are a core element of our support. Our role is both functional and strategic.

The team consists of a group of passionate, experienced and skilled individuals who offer organisational support in the following key areas: Careers Portal; Employee Relations; Performance Management; Advice and HR Consulting; Remuneration Benchmarking; Skills Training and Development.

HEADCOUNT

FOR THE YEAR ENDED 31 DECEMBER 2021



Our company is growing rapidly.

JOINT APPOINTMENTS

FOR THE YEAR ENDED 31 DECEMBER 2021

141

JOINT APPOINTMENTS

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Financial Administration

Our Financial team treats each project or syndicate as a stand-alone unit that can be ring-fenced and operated using a dedicated bank account, overseeing commercially-funded projects.

Contract and Legal Services

The Contracts team works very closely with the Legal Services specialists who review all documentation and check-lists to ensure full compliance prior to projects being submitted for sign-off and approval.

Grant Management

A strong element of our work lies in comprehensive grant management. A team of experts assist in specialist areas, including the following: Grant Application, Budget Support, Donor Reports and Audits.

Internal Audits

Robust internal checks and balances are in place to ensure that our business dealings are ethical and well managed from a financial and compliance perspective.

Human Resource Management

Effective and comprehensive HR management services are a core element of our support. Our role is both functional and strategic. The team offer organisational support.

Payroll Services

Our payroll solutions can be tailored to suit unique needs and to ensure compliance with plans and budgets. A centralised efficient team works closely with syndicates to take care of all their payroll related requirements.

Research Ethics

Provides valuable support to the University of the Witwatersrand's Wits HREC. In addition to maintaining up-to-date documents, policies, check-lists guidelines, processes clinical trial submissions and more.

Clinical Trials Service

Established expertise in clinical trials, assisting with regulatory research support, protocol review applications, staffing and trial management. Assists with Clinical Research Support, Clinical Trial Management and Clinical Research Courses.

Continuing Professional Development

Professionals working in the healthcare environment are required to comply with requirements in terms of earning points for Continuing Professional Development (CPD points).

Training and Development

Provides a wide range of training and development initiatives, delivered through our training subsidiary, Academic Advance. Training provided at selected venues in Johannesburg, Durban or Cape Town and can be made available offsite on request.

OUR

SERVICES

WHC provides world-class administrative support to its divisions through a wide range of Shared Services Centre functions. Our skilled teams have acquired extensive knowledge and experience, enabling WHC to manage complex projects professionally and efficiently.

OUR

SUBSIDIARIES

ACADEMIC ADVANCE TRAINING AND DEVELOPMENT

Specialise in delivering training in the field of clinical research, HR management courses along with soft-skills development and critical skills.

THIRD STREAM IT SERVICES AND SOLUTIONS

Best practice in IT systems, software, network connectivity, cloud storage and IT management solutions.

INTEGRATED HEALTH DELIVERY NETWORK

Self-funding clinical health centres and medical teaching platforms that offer affordable and quality healthcare.

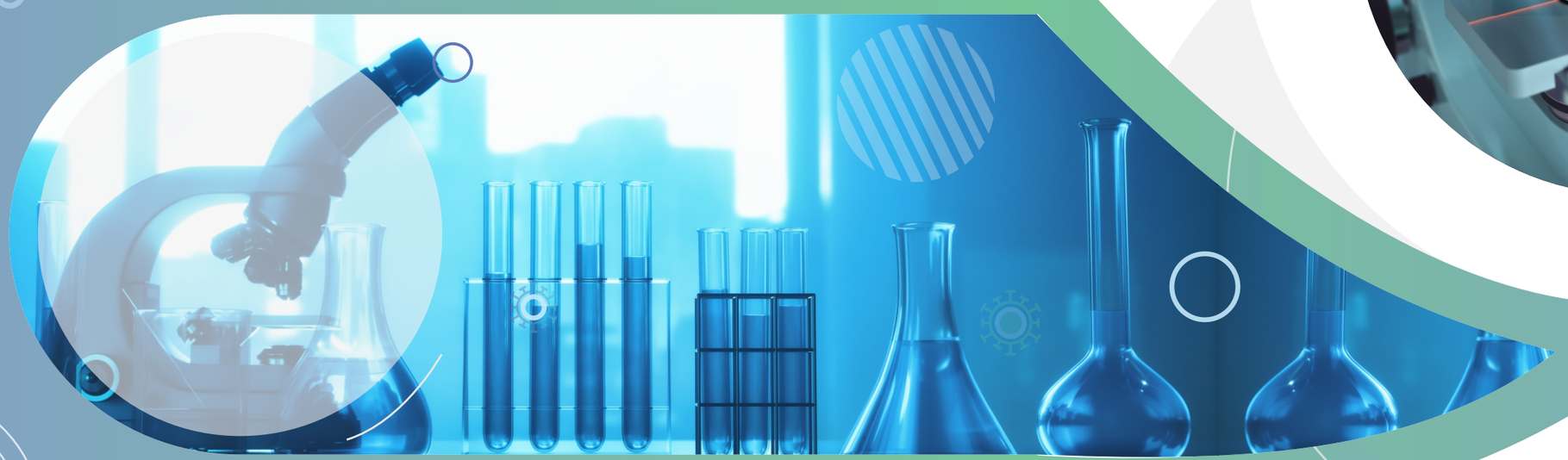
UKWENZA STUDIOS

Print media services, graphic design, multi-media productions, presentations, branding and conference packages.

OUR DIVISIONS

INSTITUTES AND UNITS
OTHER RESEARCH UNITS

WHC operates a Shared Services Centre (SSC) to support our various research entities or divisions that operate within WHC. Academically these divisions fall under their relevant university department but they are viewed as independent divisions of the WHC and managed according to structures, project plans and budgets set out by the division directors.



Annual Review 2021

University of the Witwatersrand
WITS RHI

WHO WE ARE

The Wits Reproductive Health and HIV Institute (Wits RHI) is the largest Research Institute affiliated to the Faculty of Health Sciences at the University of the Witwatersrand. The Institute was established by Prof Helen Rees in 1994 to assist the new South African government to formulate and implement new national policies around sexual and reproductive health. We are an African institute leading multi-disciplinary research and focusing largely on HIV, sexual reproductive health and vaccine-preventable infectious diseases, COVID-19, and other emerging issues.

With a highly skilled and motivated staff complement led by predominantly female directors with expertise in various fields we lead and deliver successful research and implementation projects within our focus areas that address global and local health issues and have an impact on the communities we serve. Our research studies are carried out in collaboration with multiple partners within and outside the African region. We are also a joint United Nations Programme on HIV/AIDS (UNAIDS), World Health Organization (WHO) and South African Medical Research Council (SAMRC) collaborating centre, as well as a strategic partner of the United Nations Population Fund (UNFPA).

PROFESSOR HELEN REES

EXECUTIVE DIRECTOR

Hillbrow Health Precinct
22 Esselen Street
Hillbrow
2001

Tel: +27 11 358 5300

rhicomms@wrhi.ac.za
www.wrhi.ac.za

As a non-profit organisation, Wits RHI's income is generated through donor funding. Its successful grant-writing track record, undeterred by the COVID-19 pandemic, has been pivotal in attracting funding. This has recently included funding for COVID-19 and Climate and Health studies. This funding has enabled the institute's researchers to generate world-class, groundbreaking evidence in its focus areas.

The work of Wits RHI culminates in local and global policy development and implementation support. This is largely shaped by the body of evidence generated from its work. This is done through participation in key policy advisory platforms, including recently the Ministerial Advisory Committee (MAC) on COVID-19 vaccines, led by Professor Rees. The institute participates in local and global academic platforms, in which evidence generated from its work is disseminated. Its directors and senior staff also provide technical support to the Department of Health for policy implementation.

OUR KEY FOUNDER

The Reproductive Health Research Unit (RHRU) was founded in 1994 by Professor Helen Rees as a joint initiative between the University of the Witwatersrand (Wits), Faculty of Health Sciences and the Greater Johannesburg Metropolitan Council. RHRU is now named Wits RHI.

WITS RHI'S YEAR IN REVIEW

The Wits RHI 2021 research agenda was shaped by ongoing scientific contribution towards COVID-19 prevention, transmission and treatment, expanding our scope to include maternal, child and adolescent cohorts. We also expanded our portfolio to include climate change to better understand the impact of excessive heat on maternal and child health outcomes. We led world class HIV prevention studies with breakthrough findings in HIV prevention technologies and conducted sexual reproductive health (SRH) focused clinical trials on biomedical innovations and technologies that mitigate HIV infection and ongoing transmission. Our sexually transmitted infections (STI) portfolio aimed to introduce new drugs to mitigate growing AMR.

As a hybrid Institute, we continued to deliver high-quality implementation programmes in 2021. These programmes have enabled us to deliver HIV prevention, care and treatment services to general and key populations and provide technical assistance to the South African Department of Health. A highlight in 2021 was the successful application of one of the largest United States President's Emergency Plan for AIDS Relief (PEPFAR)-funded HIV care and treatment grants ever awarded to the University of the Witwatersrand. Through

University of the Witwatersrand
WITS RHI

this grant, we were able to significantly grow the institute, expand our geographic footprint for a wider reach into the communities we serve and create employment opportunities targeting women and young people. Implementation science projects within Wits RHI have provided a unique platform to introduce and evaluate new HIV and SRH technologies.

We also continued to play a key role in contributing to, and influencing, local and global health policy, with a significant focus on COVID-19. Our input was mainly shaped by scientific evidence and expertise in our focus areas.

Within the institute, 2021 saw the appointment of two directors as Associate Professor. This is a significant academic milestone. We had staff members who commenced with PhD and master's studies and most of the topics covered by the students will contribute to our body of evidence as an institute. Despite a challenging COVID-19 working environment, 119 academic manuscripts were published, 13 as first authors. Our staff complement has grown rapidly over the past five years, from 874 in 2017 to 1 548 in 2021. Our staff turnover rate remains below the industry norm. All 41 grant applications submitted in 2021 were successful, of which 31 were research related. The institute's income for 2021 exceeded R800 million and is projected to reach R1 billion in 2022. Our income enabled us to invest in state-of-the-art renovations to the Research Centre building, previously owned by the University of the Witwatersrand. This is where most of our cutting-edge research and clinical trials are conducted. All in all, despite a challenging pandemic year, we exceeded expectations, continued to deliver excellent results in our focus areas and plan to continue along this trajectory in 2022.

STAFF IN 2021

The Wits RHI has positioned itself as an indispensable organisation for aspiring young professionals, who are keen to build a career in scientific research and policy implementation support. Its staff complement has grown rapidly over the past five years, from 874 in 2017 to 1 548 staff members in 2021. However, the past year witnessed a drop in staff numbers due to the planned conclusion of the PEPFAR surge funding. This brought about inevitable staff retrenchments. Despite the reduction by 17.8% (or 334 staff members) in its staff component in 2021. Its staff turnover rate remains below the industry norms. Its staff packages are competitive, resulting in its ability to retain key and talented staff members. Its overall growth throughout the years has provided Wits RHI an opportunity to be socio-economically responsive through the creation of local job opportunities, targeting women and young people.

INCOME AND SUSTAINABILITY

The total income for 2021 is R878 873 723.49. There were in total 92 active Wits RHI grants, this excluding 9 additional Wits RHI CTU grants. 16 grants ended in 2021.

AWARDS

Wits RHI made significant contributions to the development of national, regional, and global health policies and guidelines (predominantly COVID-19) in 2021. Under the Leadership of Executive Director Professor Helen Rees, the Institute continued to provide support, technical assistance, and capacity building to ensure evidence-based policy change for the improvement of health outcomes. Subsequently many Wits RHI senior researchers belong to different national, regional, and international committees and boards.

Prof Rees is widely recognised for her work as a global health practitioner and has been appointed as chair and member of many international scientific committees and Boards. She is a member of the South African Ministerial Advisory Committee on COVID-19 and a member of the South African Ministerial Advisory Committee on COVID-19 vaccines. Helen is involved with the oversight of the COVAX facility that GAVI, CEPI and WHO are jointly driving. She is a member of the COVAX committee on COVID-19 maternal immunization and a member of the WHO IHR Emergency Committee on COVID-19, member of the WHO Expert Committee on COVID-19 vaccines, and a member of WHO's Scientific and Technical Advisory Group on Infectious Hazards.

Helen has chaired the WHO's International Health Regulation Polio Emergency Committee since 2014 and co-chairs the WHO SAGE Working Group on Ebola Vaccines. Helen is a member of the Global Alliance for Vaccines and Immunization Board and chairs the Gavi Programme and Policy Committee.

Prof Sinead Delany-Moretlwe is a principal investigator of a population-effectiveness study of one and two doses of HPV vaccination in South Africa. In the past two years she has leveraged her HIV prevention experience and worked on several COVID-19 prevention trials. Sinead is the national principal investigator for the CROWN Coronation phase III trial of MMR vaccine for prevention of symptomatic COVID19. She has served on several Data Monitoring Committees for large randomised controlled trials and is a reviewer for the South African Medical Research Council, the National Research Foundation and the National

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Institutes of Health in the US.

Professor Sinead Delany-Moretlwe is a member of the WHO PDVAC committee, WHO Working Group for therapeutic HPV vaccines, WHO HIV, Hepatitis and STIs Scientific, the South African National PrEP Technical Working Group, HPTN executive committee and serves as a technical advisor to WHO on issues related to STIs, HIV prevention and vaccine development.

Prof Thesla Palanee-Phillips is a Member of the SA DOH PrEP Technical Working Group, a member of the Dual Prevention Pill Advisory Board, IMPT Advisory Council, Initiative on Multipurpose Technology (IMPT) focusing on combination technologies for HIV and the STI prevention and contraception and International Partnership for Microbicides.

Prof Lee Fairlie is a member of the IMPAACT Treatment Scientific Committee, and several IMPAACT protocol teams, as well as the co-chair of MTN 042/DELIVER, and she co-leads the Ubomi Buhle Pregnancy Register with Dr Ushma Mehta.

Prof Saiqa Mullick serves on a number of national and international technical expert committees including the Strategic Leadership Group of the Maximizing Options to Advance Informed Choice for HIV Prevention (MOSAIC) project which is a multi-country, multi-product global project accelerating introduction and scale-up of new and emerging biomedical prevention products. She serves on a number of national and international technical expert committees including the National PrEP technical working group, the IAPAC Fast Track Cities Implementation Science Fund Expert Advisory Committee and the WHO STI Guidelines Development Group. She serves as an advisor to the Lancet HIV-IAPAC Commission on the future of urban HIV Responses and co-chair of the WHO technical working group on strategic information for HIV prevention.

Dr Gloria Maimela is currently a member of the Dira Sengwe Board and is the chairperson of the SA AIDS 2023 conference, she is also a member of the Africa Telehealth Collaboration steering committee that seeks to address barriers to the expansion of telehealth in South Africa and the rest of the African region.

2021 PROJECT HIGHLIGHTS

In 2021, Wits RHI led and delivered high quality **Research and Implementation** projects that have placed us at the cutting edge of science and have resulted in the growth of the Institute, expanding our footprint for further reach into communities we serve. We also continued to play a key role in contributing to and influencing local and global health policy, with our input mainly shaped by scientific evidence and expertise in our focus areas.

Highlights in our recently expanded COVID-19 portfolio include the extension of vaccine efficacy studies: **ChAdOx1nCoV, NOVAVAX, Ensemble and COVPN** to pregnant women: **Pfizer C4591015**. We also extended COVID-19 surveillance and sero-survey studies from the general population: **SAPRIN, EDCTP-COREP Household Transmission** to include pregnant women: **Pregnancy Surveillance study**. COVID-19 therapeutic studies: **CROWN CORONATION, UNITY, WHO Solidarity and the Recovery Trial** also ensued and contributed to the body of evidence on COVID-19 treatment.

In our HIV prevention portfolio, our significant breakthrough was the approval of the long-acting injectable cabotegravir (CAB-LA) by the U.S. Food and Drug Administration (FDA). CAB-LA is the first long-acting injection for use as pre-exposure prophylaxis (PrEP) for the prevention of HIV. The FDA approval was based on data from two multicenter studies: **HPTN 083 and 084**, which we led. Furthermore, we were the recipient of a large PEPFAR-USAID grant: **MATRIX** for the research and development of new HIV prevention technologies to address the unmet needs of AGYWs, pregnant and breastfeeding women - and key populations in South Africa (SA). This grant has linkages with **HPTN** for future HIV prevention research opportunities and **MOSAIC** – also a Wits RHI USAID award, to expedite access to a range of biomedical products that are safe, acceptable and affordable. These studies place us in a unique position to significantly contribute to local and global evidence of current and future HIV prevention technologies along with collaborators across Sub-Saharan Africa and globally.

Another milestone was the significant expansion of our HIV care and treatment portfolio through the successful re-competition of the PEPFAR-CDC funded **GOPHELEGA** grant. This grant is one of the largest implementation awards ever received by Wits RHI and the Faculty of Health Sciences at Wits University. This grant provides Wits RHI with a great and unique platform to introduce new HIV technologies, implement HIV care and treatment services and technical support to the Department of Health and a platform to evaluate the impact of our services, science and technologies within the communities we serve.

In Climate and Health, we successfully applied for National Institutes of Health (NIH) and European Union (EU)

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funding for the **HE²AT Centre, ENBEL, CHAMNHA** and soon to be implemented **HIGH HORIZONS** studies to develop innovative systems to monitor and mitigate the impact of climate change on the health of vulnerable populations including pregnant women, infants and healthcare workers in Africa. Through this funding, we will be leaders in building capacity on data science and climate change as well as be a resource for climate change and health initiatives across the African continent and globally.

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WHO WE ARE

The Clinical HIV Research Unit (CHRU) facilitates scientific based evidence to expedite novel treatment and offer improved treatment through the use of variant combinations of existing regimens for people living with HIV, TB and its comorbidities.

The unit's research impact has improved the standard of care of treatment and increased access and equity to healthcare.

Over the past year global collaboration included the US National Institute of Health's (NIH) AIDS Clinical Trial Group Network (ACTG); IMPAACT; CoVPN; Aids Malignancy Consortium, Medicines Sans Frontier (MSF), Bill and Melinda Gates Foundation, World Health Organization, European DCTP, BMBF, The Union, TB Alliance, Vital Strategies, USAID, and Merck International amongst others.

The CHRU takes pride of its inclusive community engagement program with workshops which empowers members of the community to contribute to the relevant and scientific requirements specific to their community.

ACADEMIC AFFILIATION

The CHRU is affiliated to the Department of Internal Medicine at the School of Clinical Medicine of the Faculty of Health Sciences of the University of the Witwatersrand. All Principal Investigators are joint appointed staff members. Over 34 peer reviewed articles were published in 2021.

2021 PROJECT HIGHLIGHTS

CHRU Helen Joseph Hospital clinical research site (HJH CRS) director, Dr Sharlaa Faesen, served at the forefront of additional site capacitation for the South African Medical Research Council's Sisonke clinical trial. The trial was the first access to Covid-19 vaccines afforded to the country's healthcare workers since the outbreak of the pandemic in 2020. CHRU in collaboration with Right To Care, were able to grant vaccine access to healthcare workers in remote facilities in the Northern Cape.

CHRU HJH Director, Dr Mohammed Rassool, Served as the PI on Practecal, a TB drug-resistant clinical trial in collaboration with MSF. The results proved that the new all-oral six-month treatment regimen is safer (reduced toxicity), shorter, and more effective at treating rifampicin-resistant tuberculosis (RR-TB) than the currently accepted standard of care.

Dr Francesca Conradie, Executive Director of CHRU's Isango Lethemba TB Research Unit was the principal investigator of the Nix-TB and ZeNix clinical trials, sponsored by the Global TB Alliance. These clinical trials have contributed significantly to the body of knowledge which has informed global policy on the treatment of drug-resistant TB. This was announced in a recent press release, after the World Health Organization (WHO) released the rapid communication in May 2022 on key changes to the treatment of drug-resistant TB. This is a significant development which will benefit patients with DR-TB in SA and globally.

Through an innovative public private partnership with the SA National TB Programme (SANTP), under the leadership of **Dr Norbert Ndjeka**, recently Chief Director for TB, the WHO proposed shortened, fewer drug regimen is already being delivered to some DR-TB patients through the BPaL clinical access programme (BPaL CAP) since March 2021. This early access programme is funded by USAID, of which Dr Conradie is also the principal investigator, and is being offered in four provinces of South Africa with expansion to further sites underway.

At the CHRU Sizwe CRS, **Dr Pauline Howell** is proud to significantly contribute towards data of the IMPAACT 1108 clinical trial, which informed the World Health organization (WHO) recommendation for use of bedaquiline (BDQ) in children aged below six years.

In addition, Dr Howell presented the final results for the Nix trial at the 2021 Annual Conference on Retrovirus Opportunist Infections which informs the rapidly changing guidelines around BPaL (regimen comprised of bedaquiline, pretomanid and linezolid). The BPaL regimen was first clinically studied in the Nix trial.

2021 NEW PROJECTS

NEW COVID-19 TRIALS

The CHRU HJH CRS conducted four new Covid-19 vaccine clinical trials, a trial which sought to assess the safety and immunogenicity of AZD2816 for the prevention of Covid-19. A clinical trial which provided a single-dose Ad26.COV2.S to the South African healthcare workers in the Sisonketrial and the Sisonke Boost, which evaluated the effectiveness of a homologous Covid-19 vaccine boost among Sisonke participants. The CoVPN 3008 study evaluates the clinical efficacy of different dosing regimens of the COVID-19 mRNA vaccine (100 mcg) in preventing COVID-19 disease in people who are living with HIV or have comorbidities associated with elevated risk of severe COVID-19, with the different vaccine regimens assessed determined by whether the participant had evidence of prior SARS-CoV-2 infection at enrollment.

The A5401 clinical trial evaluated the safety and efficacy of investigational agents for the treatment of symptomatic non-hospitalized adults with COVID-19.

NEW HIV TRIALS

New HIV clinical trials conducted in 2021 included the prevention of HIV-1 infection in women at high risk (IMPOWER).

Another HIV clinical trial evaluates the safety and tolerability of an ART regimen for heavily treatment-experienced participants

HIV Co-infectious Disease:
Evaluation of HEPISLAV-B-Enhancement of HBV Vaccination in Persons Living With HIV (BEe-HIVe).

NEW DR TB TRIALS

The TB research activities at the Isango Lethemba TB Research unit continue to be integrated with the goals of the South African National TB Programme, as is evident in the USAID funded cooperative agreement, and flagship project-BEAT Tuberculosis. This is being conducted in Port Elizabeth, Eastern Cape and expanded in 2021 to include a second research site in Durban.

It is a pragmatic randomized open-label clinical trial to establish the efficacy and safety of a Study Strategy consisting of 6 months of Bedaquiline, Delamanid and Linezolid with Levofloxacin and/or Clofazimine compared to the current South African standard of care for 9 months for the treatment of Rifampicin resistant TB.

Due to the pragmatic nature of this study and fast enrollment, the unit has become responsible for treating a large proportion of patients within the Nelson Mandela Bay Metropolitan, with very few patients being found ineligible.

This trial represents an ongoing collaboration between WHC and the South African National TB Programme, and particularly the Eastern Cape and KwaZulu Natal DoH. There is also ongoing active collaboration with key international players such as USAID, WHO, the pharmaceutical companies Janssen and Otsuka and the Global TB CAB.

CHRU Sizwe CRS started the BPaMZ-SEM trial, which will inform multi-dose paediatric pretomanid trials in the near future.
Another new TB clinical trial is the PanACEA DElpazolid Dose-finding and Combination Development (DECODE) To Evaluate the Safety, Tolerability, Pharmacokinetics and E x p o s u r e - ResponseRelationship of different doses of Delpazolid in combination with Bedaquiline, Delamanid and Moxifloxacin in Adult Subjects

2021 ONGOING PROJECTS

ONGOING COVID-19 TRIALS

Vac31518cov3001 / Ensemble Vaccine Study (ongoing)

The study aimed to enrol more than 40,000 participants in order to evaluate the efficacy of Ad26.COV2.S in the prevention of molecularly confirmed moderate to severe/critical COVID-19, as compared to placebo, in adult participants. received a booster shot in 3rd quarter 2021

Cassper Hcw/Ezcov004 (ended May 2021)

Optimizing COVID-19 testing in South Africa for Health Care Workers through self-sampling.

Crown Coronation (ended Mar 2022)

The objective of Crown Coronation is the prevention of symptomatic COVID-19 by using combinations of approved and safe repurposed interventions, with complementary mechanisms of action.

UNSW-COHIVE

COVID-19 in people living with HIV: Evaluation of risk factors and outcomes in resource-limited settings. A pooled sub-study of ADVANCE, D2EFT, DolPHIN2, and NAMSAL

ONGOING HIV CLINICAL TRIALS

A5375

Pharmacokinetic Study to evaluate double-dose Levonorgestrel Emergency Contraception in combination with Efavirenz-Based Antiretroviral Therapy or Rifampicin - containing Anti-Tuberculosis.

Therapy (A5375)

The purpose of this pharmacokinetic (PK) study is to evaluate if a double dose (3 mg) of Levonorgestrel (LNG) emergency contraception (EC) overcomes known drug- drug interactions (DDIs) with Efavirenz (EFV)-based antiretroviral therapy (ART) or Rifampicin (RIF)-containing Tuberculosis (TB) therapy. The safety of double-dose (3.0 mg) LNG EC versus standard-dose (1.5 mg) will also be compared.

ONGOING HIV CLINICAL TRIALS

A5381

This is a study for people who have HIV and qualify to switch to or receive Dolutegravir containing antiretroviral therapy (ART, group of medicine used to treat HIV). Taking TLD (combination pill of three medicines for HIV, Tenofovir-Lamivudine-Dolutegravir) has shown to be better tolerated, work better against the virus known as virologic efficacy, have fewer drug-drug interactions, and have less frequent onset of HIV drug resistance than Efavirenz containing ART. In August 2017, a decision was made to start using TLD for first and second-line ART in many places in the world. This study is designed to help us understand the risks and benefits of TLD roll-out in low and middle-income countries that may not use viral load testing and HIV resistance testing (a way to measure if a drug will work against your HIV) to guide ART management.

D2EFT

A phase IIIB/IV randomised open-label trial to compare Dolutegravir and Pharmaco-enhanced Darunavir versus recommended standard of care antiretroviral regimens in patients with HIV infection who have failed recommended first line therapy.

MK 8591-016

This study will evaluate the safety, tolerability and Pharmacokinetics (PK) of 6 once-monthly doses of oral Islatravir (60 mg and 120 mg) compared with placebo for the prevention of HIV infection in adults that are at low risk of HIV-1.

200204 - GLAXO

A Phase 3b, randomised, open-label study of the antiviral activity and safety of Dolutegravir compared to Lopinavir/Ritonovir both administered with duel nucleo-

side reverse transcriptase inhibitor therapy in HIV-1 infected adult subjects with treatment failure on first line therapy.

A5332
Randomized trial to Prevent Vascular Events in HIV–REPRIEVE.

A5360
A single arm study to Evaluate the Feasibility and Efficacy of a Minimal Monitoring Strategy to Deliver Pan-genotypic Ribavirin-free HCV Therapy to Chronically Infected HCV Treatment Naïve Populations Globally: The MINMON Study.

ONGOING TB, MDR AND XDR TB TRIALS
A5300B - The purpose of this study is to compare the efficacy and safety of 26 weeks of Delamanid (DLM) versus 26 weeks of Isoniazid (INH) for preventing confirmed or probable active Tuberculosis (TB) during 96 weeks of follow-up among high-risk household contacts (HHCs) of adults with Multidrug-Resistant Tuberculosis (MDR-TB) (index cases). High-risk HHCs are those with HIV or non-HIV immuno suppression, latent TB infection, and young children below the age of 5 years.

BEAT Tuberculosis (2nd site July 2021)
USAID cooperative agreement awarded in 2018. This is a 5-year project providing funding to the sum of $9 million. It is a pragmatic randomized open-label clinical trial to establish the efficacy and safety of a study strategy consisting of 6-months of Bedaquiline, Delamanid and Linezolid with Levofloxacin And/or Clofazimine compared to the current South African standard of care (Control Strategy) for 9-months for the treatment of Rifampicin resistant TB. The recruitment target is 400 participants and to date 342 participants have been enrolled in total across this site and the PE site.

This trial represents an ongoing collaboration between WHC and the South African National TB Programme, and particularly the Eastern Cape DoH. There is also ongoing active collaboration with key international players such as USAID, WHO, the pharmaceutical companies Janssen and Otsuka and the Global TB CAB.

Patient-reported Experiences and Quality of Life Outcomes in the TB-PRACTECAL Clinical Trial (PRACTECAL PRO)
Tolerability of drugs for TB is a complex and dynamic course for patients with drug resistance and can be affected by many different factors. A deeper understanding of the perspectives and experience of men and women participating in novel TB treatment trials will add to the understanding of the safety and efficacy of treatment.

TB-PRACTECAL is a multicentre, open label, phase 2-3 randomised controlled trial evaluating exclusively oral 6-months regimens containing Bedaquiline, Pretomanid, Linezolid +/- Moxifloxacin or clofazimine for the treatment of microbiologically confirmed pulmonary M/XDR-TB. It is registered with the ClinicalTrials.gov with identifier number NCT02589782. The trial aims to recruit 630 adults from two sites in Uzbekistan (Nukus and Tashkent) and one site each from Belarus and South Africa.

The TB-PRACTECAL trial assumes that even if the investigational arms would have non-inferior efficacy and safety compared to the standard of care outcomes, patients would prefer a shorter, exclusively oral regimen with a lower pill count. This study therefore aims to describe patient experiences (i.e. the quality of the treatment experience as opposed to the quantity of treatment or the amount of time spent on it).

BPaL CAP –
Sub-study under BEAT Tuberculosis
The BPaL CAP is a single arm intervention study to evaluate the effectiveness and safety of the BPaL Regimen for 400 patients with Extensively Drug-Resistant Tuberculosis (XDR-TB), fluoroquinolone resistant TB and selected Rifampicin Resistant TB (RR-TB) via pre-approval access. The program will be conducted at Department of Health DR TB treatment sites through an innovative public private partnership.

ZeNiX (Nc007)
The TB Alliance sponsored the NiX-TB study a study with a 6-month treatment duration with the BPaL (Pretomanid, Bedaquiline, and Linezolid) regimen in participants with XDR-TB or MDR TB not responsive to or intolerant to therapy. The Isango Lethemba TB Research Unit is conducting the follow-on trial-ZeNiX, which will provide important information on the toxicity and efficacy of the regimen under alternate doses and durations of Linezolid to optimize the dosing scheme for the best benefit to risk balance. This is a phase 3 partially-blinded, randomized trial looking to enrol a total of 180 participants across multiple sites.

SimpliciTB (Nc008)
Sponsored by the Global Alliance for TB Drug Development, the overall purpose of SimpliciTB is to assess the efficacy, safety and tolerability of the BPaMZ (Bedaquiline plus Pretomanid plus Moxifloxacin plus Pyrazinamide) regime after 4-months of treatment in adult participants with drug sensitive TB and after 6-months of treatment in participants with multi-drug resistant TB. The trial will also generate data

of the potential for a shorted treatment duration with the BPaMZ regime after 4-month compared to a 6-month HRZE/HR (control) treatment regime in adult participants with drug-sensitive TB.

STREAM II

STREAM Stage 2 is sponsored by The International Union Against Tuberculosis and Lung Disease and assesses two new short course regimens for MDR-TB in comparison with the 9-month regimen developed in Bangladesh. In the 9-month oral regimen, the new drug Bedaquiline is given throughout treatment in place of the injectable Kanamycin, which frequently gives rise to side effects such as loss of hearing. High dose Moxifloxacin is replaced by Levofloxacin to minimise potential cardiac side effects such as QT prolongation. The 6-month regimen has a shorter intensive phase, and as in the 9-month oral regimen Bedaquiline is given throughout treatment and Levofloxacin replaces Moxifloxacin. Prothionamide and Ethambutol have both been dropped. The primary objective of the study is to assess whether either the full oral or the 6-month regimen are non-inferior to the 9-month regimen under study in STREAM.

TMC207-C211

A Phase 2, open-label, multicenter, single-arm study to Evaluate the Pharmacokinetics, Safety, Tolerability and Anti-mycobacterial activity of TMC207 in combination with a background Regimen (BR) of Multidrug Resistant Tuberculosis (MDR-TB) Medications for the Treatment of Children and Adolescents 0-Months to <18 Years of Age who have confirmed or Probable Pulmonary MDR-TB.

BPaMZ/SEM: sponsored by TB Alliance

An open-label Phase 2 Trial to Evaluate the Male Reproductive Safety of a 6-month combination Treatment for Pulmonary Tuberculosis of Bedaquiline plus Pretomanid plus Moxifloxacin plus Pyrazinamide (BPaMZ) in Adult Male Participants with Drug Resistant (DR-TB) Pulmonary Tuberculosis

Nix-TB

The TB Alliance-sponsored trial completed follow-up in 2020, and the final results showed a durable curein 90% of participants, with only one additional relapse at month 15 of follow-up and one participant who was last to follow up after a monthtwelve follow-ups (but was culture negative at the time. Side effects from Linezolid were common but manageable, with most resolving by the end of the study follow-up, two years after completion of treatment.

International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT) Network

P1108: This Phase II trial is looking at Safety, Tolerability and Dose Finding of Bedaquiline in Infants, Children and Adolescents with Drug Resistant Tuberculosis, in both HIV Infected and Uninfected Participants. This trial has already informed updated dosing recommendations for Bedaquiline and is still recruiting.

I2005: This Phase II trial is looking at the Safety, Tolerability and Dose Finding of Delamanid in both HIV Infected and Uninfected Infants, Children and Adolescents with Drug Resistant Tuberculosis.

I2026: This trial has several parts, but the Sizwe CRS will be focussing on arm 4, looking at the pharmacokinetics of newer tuberculosis drugs in second and third trimester pregnancy. This trial is being done in partnership with the Shandukani CRS.

OTHER ONGOING

Chlamydia Study

Sample collection for the Development and Evaluation of a Rapid Chlamydia Tracho-matis/Neisseria Gonorrhoeae Test.

A5243

Plan for obtaining Human Bio0logical Samples at non-US Clinical Research Sites

Paternity Questionnaire

A Survey Assessing Male Reproduction during or after Treatment containing Pretomanid – all sites (Questionnaire for all male participants of NC-006, NC-007, NC-008 and Nix).

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WHO WE ARE

The Health Economics Research Office (HE²RO) is part of the University of the Witwatersrand's Faculty of Health Sciences.

An internationally recognized research and technical assistance unit, HE²RO delivers clinical, epidemiologic and health economic research services.

The unit also ensures that research information is invested at an operational level for the prevention, treatment and management of HIV and associated diseases.

The Health Economics and Epidemiology Research Office (HE²RO) aims to conduct applied, policy and program relevant research and evaluation on issues of public health importance in South Africa. It focuses on understanding the economic and epidemiological consequences of the HIV, TB, and NCD epidemics and other public health problems and the effectiveness, benefits, and costs of interventions.

HE²RO's headquarters are in Parktown, Johannesburg with sites based in Giyani and Tzaneen.

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2021 PROJECT HIGHLIGHTS

Despite ongoing challenges as the COVID-19 pandemic continued, 2021 saw achievements in progress and productivity across several projects with new collaborations and exciting opportunities for studies in key public health areas. The Health Economics and Epidemiology Research Office (HE²RO) continued to expand its research and evaluation projects in South Africa and its neighbouring countries. The Sentinel protocol for the Bill and Melinda Gates Foundation (BMGF) funded Alternative Models of ART Delivery: Optimising the Benefits (AMBIT) study was approved in all three focus countries (Malawi, South Africa and Zambia) and field work resumed as COVID-19 restrictions were lifted. Along with colleagues at the Department of Global Health, Boston University School of Public Health, HE²RO was successfully awarded the Retain6 grant through BMGF and the National Institutes of Health (NIH) funded CETA study both of which commenced project work in the last quarter of 2021.

A proposal for ongoing funding (AMBIT 2.0) was also submitted.

By the end of the year, HE²RO had over 20 grants for research projects and associated studies underway. The highlights of the year are :

EVIDENCE (Evaluations to Inform Decisions using Economics and Epidemiology is a 5-year cooperative agreement with United States Agency for International Development (USAID). As HE²RO moved into year 3 of this activity, 33 different studies and projects were conducted in 2021 resulting in 30 publications. Some of the highlights of the EVIDENCE Project included the following studies:

1. Economic evaluations, costing studies and modelling

South African HIV Investment Case - the 2021 update to the HIV Investment Case was launched, together with SANAC, on 3 December 2021. Updates include a new version of Thembisa (version 4.4), an updated cost model to 2021 prices, the inclusion of HIV self-testing, and the impact of an ART retention intervention. A report has been made available A report has been made available (https://www.heroza.org/ publications/ south-african-hiv-investment-case-2021-full-report). The investment case is used to inform budgets and decision-making on HIV services.

TB National Cost Model - costing service delivery and optimising interventions for different populations and geographic locations. Activities support data required for the TB National Cost Model and TB Investment Case.

Scale-up of TPT preventative therapy among people living with HIV (PLHIV) - costing and budget impact modelling of existing work by DSPs to support scale-up of TPT preventative therapy among PLHIV as well as determining barriers and facilitators to TPT use in outpatient settings and preferences for TPT regimens and service delivery models. This study also includes a Behavioural Insights Test (BIT) that has been designed to "nudge" community healthcare workers during monthly home visits to improve TB preventative therapy uptake and completion among children under 5 years.

TRANSLATE (Applying the TRANSLATE framework to optimise implementation) - the TRANSLATE modelling framework translates the results of qualitative and DCE studies into the expected cost and impact of various proposed interventions. In a recent HE²RO study on the expected impact of modifiable facility-level attributes in increasing HIV/contraceptive service uptake for youth, preferences for providing Wi-Fi and youth-only services cost the least per additional youth accessing services (ICER US$7).

Long-acting injectable PrEP - a cost-effectiveness analysis of long-acting injectable pre-exposure prophylaxis (LA-PrEP with cabotegravir. The study also included a threshold analysis that estimates the price at which LA-PrEP remains as cost-effective as standard-of-care oral PrEP, which would help inform policymakers and other stakeholders.

2. Evaluation and implementation of HRH interventions.

Supporting NDoH with PBI Implementation – technical assistance driven support aimed to build on the first phase implementation of a non-financial performance-based incentive scheme, targeting Operation Phuthuma, the strategic project management arm of the NDoH's HIV cluster. The aim is to foster a sense of teamwork with healthcare workers creating a sustained link between HIV testing, linkage to and retention in care. Quarterly, six-monthly and annual rewards and recognition were planned, including vouchers to the top-performing facilities by province and district as well as the use of peer and community recognition through social and traditional media.

INSPIRE (Improving performance through a non-financial reward and recognition programme for District Support Partners providing HIV services) – an impact evaluation to understand the effect of a non-financial reward and recognition programme on the performance and motivation of staff employed by District Support Partners providing HIV services at PHCs. Indicator selection was based on performance against targets and a communication strategy was developed with a strong focus on recognition of well performing teams and facilities.

PBI DCE (Performance-Based Incentives Discrete Choice Experiment) – a mixed- method study using discrete choice experiment methodology examining the baseline awareness and acceptability for team-based non-financial rewards and recognition among facility and operational managers, as well as lay and professional healthcare workers who deliver HIV services.

Thusa-Thuso (Motivational Interviewing training and support program for lay counsellors) - a Motivational Interviewing (MI) training program for lay HIV counsellors in South Africa showing that the Thusa-Thuso MI intervention can improve counsellor motivation and skills over time. The program can be scaled up using an adapted training of trainer process and is valuable for skills development and ongoing maintenance.

3. Tuberculosis studies.

DR-TB Cohort - a long-term DR-TB cohort dataset enrolling patients since 2013 to support analyses on cost, outcomes and long-term consequences of DR-TB treatment. HE²RO continues to generate evidence on the all-oral short course regimen for RR/MDR-TB, the feasibility of the implementation of the all-oral short-course regimen, adverse events during second-line TB treatment, post-TB wellbeing, and mortality, and the cost and outcomes of DR-TB treatment.

TB MITE study - commissioned by the National TB Think Tank aimed at understanding how TIER.Net, specifically the TB module is being implemented/operationalized at facility level and how the data captured on the TB module is processed and used. The study documented lessons learnt from implementing the TB/HIV integrated system towards improving the TB/HIV integrated data system and fostering long-term sustainability of the system.

4. Health systems and healthcare service preferences.

Ideal Clinic rapid review - As part of the EVIDENCE grant, HE²RO undertook a review of the Ideal Clinic Realisation and Maintenance program, focusing on the experiences of primary healthcare clinic staff and patients' perceptions of the quality of primary health care. This survey collected data from ten percent of facilities across the Gauteng province.

REACH (Reaching and understanding South African women aged 30-49): Exploring HIV service preferences) – a mixed methods study to determine cost-effective interventions for HIV testing, linkage to and retention in care in women aged 30-49 years. This includes translating these

results into a costed strategy, and finally developing policy recommendations and potentially supporting guideline changes, based on these findings.

Men's Choice (A discrete choice experiment to understand South African men's healthcare preferences) – a study to explore preferences among men who are missing from the HIV care continuum.

COVID-19 response – HE²RO continued its involvement with the COVID-19 Modelling Consortium alongside MASHA (University of Cape Town), SACEMA (Stellenbosch University) and NICD. During 2021, we continued consultation with national and provincial Departments of Health and Treasuries and the two Ministerial Advisory Committees on COVID-19. Activities included analytical work towards the preparation of MAC advisories, epidemiological modelling, cost modelling to inform government budgets (National COVID-19 Cost Model), including for the vaccine roll-out, and public and government dashboards to monitor COVID-19 case development to assist with planning during the second, third and fourth COVID-19 wave (https://sacmcepidemicexplorer.co.za/). Other contributions the HE²RO team have made to the COVID-19 response is working on prioritising vaccination populations and conducting economic evaluations of pharmaceutical interventions for COVID-19. This work was partly funded by USAID (EQUIP Health Project), and in 2021 HE²RO secured funding from BMGF to continue this work.

COVID-19 costing - involves costing aspects of the service delivery platforms for the COVID-19 vaccine program in order to propose more efficient models as the vaccine program moves into a different phase of implementation. The costing work also includes an in-patient hospital cost and resource utilisation analysis of patients admitted for COVID-19 treatment at Helen Joseph Hospital and Chris Hani Baragwanath Academic Hospital.

AMBIT - a research and evaluation project to understand the scope and impact of differentiated service delivery (DSD) models for HIV treatment. Data collection continued in the project's three focus countries, South Africa, Malawi, and Zambia, under the GREAT (Gathering Records to Evaluate Antiretroviral Treatment) protocol to access and analyze existing medical record data of patients enrolled in DSD models. Implementation of the multi-country SENTINEL protocol also began at 42 sentinel sites including patient and provider interviews, time and motion observations and resource utilization. The ADAPT (Alternative Delivery of ART oPTimization) model (designed to help guide DSD model mix and expansion) was completed.

Indlela – (Behavioural Insights for Better Health) a behavioural economics unit within HE²RO in collaboration with the Centre for Health Incentives and Behavioural Economics (CHIBE), University of Pennsylvania. Indlela aims to build capacity to design and test nudges and other behavioural solutions to achieve better health outcomes for HIV in South Africa. In 2021 Indlela completed a series of workshops with 32 participants from 21 partner organisations building capacity in behavioural economics and released a request for proposals for behavioural insights tests (BIT projects). Indlela has provided technical and financial support to six projects, co-designing interventions with seven implementing partners. Indlela has also expanded its portfolio with the BRAVO project focussing on COVID-19 vaccine hesitancy.

Indlela - BRAVO (Behavioural Research Advancing Vaccinations) - a research and evaluation project that uses behavioural insights to increase COVID-19 vaccine registrations and uptake in South Africa, providing technical support to the DG Murray Trust and collaborating with the National Department of Health on the national COVID-19 vaccine programme.

PREDICT (Prioritising Retention Efforts using Data Intelligence and Cohort Targeting) – this project applies machine learning to routinely-collected patient visit and laboratory data to build a predictive model of loss from ART care with a primary outcome of clinic attendance within 28 days of a scheduled clinic visit. A collaboration with Pallindrome, the Indlela Behavioural Economics team and Right to Care to develop the algorithm into three application tools: a paper-based adherence scorecard, a digital adherence scorecard and a treatment referral plan.

TB collaborative projects with Sahlgrenska University Hospital, Sweden – post-graduate TB related projects focusing on "Economic, psycho-social, and clinical factors at tuberculosis treatment completion associated with poor long-term retention in the TB Sequel study" and "Use of process indicators to assess the feasibility of the implementation of the all-oral short course regimen for multidrug and rifampicin-resistant tuberculosis in Johannesburg, South Africa"

TB Sequel socio-economic sub-study – a sub-study of TB Sequel, an ongoing multi-country, multi-center observational cohort study that aims to advance the understanding of clinical, microbiologic, and host immune factors affecting the

long-term sequella of pulmonary TB. This includes "TB Sequel ENHANCE" a sub-study to evaluate Post-TB HRQOL and lung function in DR-TB patients and continued to estimate the per-patient cost of TB treatment to the health system in different African settings.

IeDEA TB SRN - a prospective cohort study to identify factors associated with short and long-term outcomes in patients with pulmonary TB through the Tuberculosis Sentinel Research Network (TB-SRN), within the International Epidemiology Databases to Evaluate AIDS (IeDEA) consortium. This is a 5-year project that started in 2021, and patient enrolment is scheduled to start in April 2022

ENCORE – (Evaluating Universal Test-and-Treat (UTT) with a National HIV Cohort to Optimize South Africa's HIV Response) - this study aims to update the NHLS National HIV Cohort through the UTT era and link it with data from South Africa's facility-based ART monitoring and evaluation system. This integrated cohort will be used to quantify losses at each stage of the UTT cascade and to assess system-wide retention and transfer in the UTT era. This is followed by an evaluation of the impact of two UTT policies – eliminating CD4 criteria and implementing same-day ART – on time from clinical presentation to ART uptake, retention, and viral suppression.

INTUIT (Integrating U=U into HIV Counselling in South Africa) - the INTUIT study is a theory-driven, contextually grounded communication intervention to support counselling on HIV TasP through developing and piloting web application-based video communication materials to support HIV counsellors in confidently sharing accurate information on HIV treatment as prevention science with persons living with HIV (PLHIV).

CETA – (A randomized controlled trial of HIV-infected women to evaluate the impact of the Common Elements Treatment Approach) (CETA), an evidence-based intervention comprised of cognitive-behavioural therapy elements, at improving HIV treatment outcomes among women with HIV who have experienced intimate partner violence (IPV) and have an unsuppressed viral load on HIV treatment. A CETA team of counsellors were recruited and trained on the CETA approach and enrolment commenced in November 2021 and will continue during 2022.

PREGNANCY COHORT (The South African National HIV Pregnancy Cohort: evaluating continuity of care among women living with HIV) – a project utilizing routinely-collected laboratory data to develop a cohort of pregnant women living with HIV in South Africa. In 2021, the project team worked closely with colleagues at the NHLS and NICD to finalize the integration of the linkage algorithm into the NICD surveillance data warehouse environment and prepare for the first extract of linked and de-duplicated cohort data. We also worked on expanding our methodology for linking the HIV cohort data to these gold standard validation cohorts through the use of barcodes.

Economic Impact of HIV Policy Briefs - under this project, HE²RO Prof Gesine Meyer-Rath together with Markus Haacker from University College London synthesised the evidence on the economic impact of HIV into a series of 17 policy briefs and seminars that can help decision makers in the Ministries of Finance and Health in low and middle-income countries (LMIC) decide on the future financing of their country's HIV programme (https://hivecon.co.za/).

MIHPSA collaboration – (Modelling to Inform HIV Programmes in Sub-Saharan Africa Collaboration) - HE²RO researchers work with other South African and international HIV modellers across four sub-Saharan African countries through the HIV Modelling Consortium to inform the planning of HIV programs in Sub-Saharan Africa and to understand the epidemiological and economic impact of current and future interventions.

Project II: Gambia sample referral network (Diagnostic Network Optimization analysis in the Gambia: designing data-driven supply chain and sample referral network for TB/HIV diagnostics) a project designing a data-driven supply chain and sample referral network for TB/HIV diagnostics in the Gambia to determine the optimal device mix and placement for TB molecular diagnostic testing, HIV viral load and early infant diagnosis under different demand and capacity scenarios in the Gambia.

Project III: OptiDx (Multicentre study to assess the readiness and usability of the OptiDx open access software and associated processes for TB/HIV diagnostic network optimization in low and middle-income countries) - HE²RO worked closely with FIND on a multi-centre study to assess the readiness and usability of an open access diagnostic network optimization software, OptiDx, in low and middle-income countries (LMIC). OptiDx enables Ministries of Health and donors to identify cost-effective approaches to increase diagnostic reach in LMICs, guide decision-making and the development of data-driven strategic plans. OptiDx has been piloted in Zambia, Vietnam, Bangladesh, India, Kenya and Burkina Faso.

Project IV: ACT-A COVID - HE²RO is part of the team that leads the ACT-Accelerator Rapid Antigen

Diagnostic Modelling Consortium. The first phase of the work involved synthesising use cases on rapid antigen diagnostics (Ag-RDTs) for SARS-CoV-2 and contributed to the report: Expanded use case analysis for Rapid antigen diagnostics for SARS-CoV-2 mitigation. Phase 2 involves the development of an agent-based model, which aims to develop an understanding of the optimal allocation of Ag-RDTs to different testing strategies within a given country under different sets of resource constraints.

NEW GRANTS IN 2021

Retain6 (Models of care for the first six months of HIV treatment) – this 3,25-year award from Bill and Melinda Gates Foundation aims to apply the principles of patient-centred design to inform recommendations for differentiated models of care for the first six months on ART for the WHO's global ART guidelines, PEPFAR's programmatic guidance, and national guidelines in sub-Saharan Africa. Over the duration of the award, we will pursue this research agenda through a combination of 1) analysis of existing data; 2) enrolment of a prospective cohort of ART initiators to evaluate preferences, needs, and triaging potential; 3) consultation with patients and providers to develop one or more new models of care; and 4) a pragmatic evaluation of the effectiveness and cost-effectiveness of the new model(s) in improving early retention rates. Total award amount (including indirect costs): $1,689,288

BRAVO (Behavioural Research Advancing VaccinatiOns) - the objective of this project is to rapidly determine whether removing hassle factors, re-framing available choices, leveraging social norms and incentives have the potential to increase COVID-19 vaccine registrations and uptake. Duration: 12 months. Funder: Bill and Melinda Gates Foundation (INV- 036204) Total award amount: $244 686

RADx-sim (Cost-effectiveness and optimal resource allocation of Rapid Antigen Diagnostics using simulation modelling) - the overarching aim of the continuation of the modelling consortium work is to conduct a comprehensive evaluation of the cost-effectiveness and impact of different Ag-RDT implementation strategies in different country archetypes. Duration: January 2022- December 2022. Funder: FIND. Total award amount: $100,680

Sustaining advanced analytics for Diagnostic Network Optimization - the objective of this project is to establish and sustain routine and systematic use of advanced analytical modelling tools for optimizing diagnostic networks for control of TB, HIV and other priority diseases in LMICs. Duration: January 2022- December 2024
Funder: FIND/BMGF. Total award amount: $418,800

FIND (Foundation for Innovative New Diagnostics - the goal of this project is to evaluate the yield and cost of adding a rapid diagnostic algorithm for complex chronic conditions, in particular hypertension and diabetes mellitus, as well as COVID-19 rapid testing in urban COVID-19 vaccination clinics in Johannesburg, South Africa. Duration: 2021-2022
Funder: FIND. Total award amount: $125,814 (Prime: HE²RO)

MIHPSA collaboration (Modelling to Inform HIV Programmes in Sub-Saharan Africa Collaboration) the goal of this project is to support a consortium of modellers across four sub-Saharan African countries to inform the planning of HIV programs in Sub-Saharan Africa and to understand the epidemiological and economic impact of current and future interventions. Duration: 2021-2022. Funder: Bill and Melinda Gates Foundation. Total award amount $32,739 (Prime: University College London)

Taxi rank project (Rapid Screening for Complex Chronic Conditions) - the goal of this project is to evaluate a rapid diagnostic algorithm for complex chronic conditions, in particular hypertension and diabetes mellitus, as part of COVID-19 rapid testing in urban transport hubs in South Africa. Duration: 2021-2022. Funder: Foundation for Innovative New Diagnostics (FIND). Total award amount: $77,300 (Prime: Boston University, School of Public Health (BUSPH))

OPTI-VAX (COVID-19 priority vaccine modelling for South Africa and beyond) - HE²RO secured funding from the Bill and Melinda Gates Foundation (BMGF) for continuing HE²RO's work on COVID-19 vaccination as part of the South African COVID-19 Modelling Consortium. The project aims at updating the National COVID-19 Epi Model (NCEM) to include priority populations, new SARS-CoV-2 variants and their specific characteristics, as well as the impact of the vaccine roll-out, continuing engagement with national government departments on planning and resource allocation for COVID-19 vaccination, and also supporting governments of Southern African Development Community member states in developing their own capacity for modelling of COVID-19. Duration: 2021-2022. Funder: Bill and Melinda Gates Foundation (INV-035464). Total award amount: $492,367 (Prime: HE²RO)

EXPAND (Evaluating the Cost of Scaling PrEP Access through Novel Delivery) – this is a planning grant awarded by the Bill and Melinda Gates Foundation (BMGF) to prepare a full proposal for an economic evaluation of 3 large PrEP implementation studies carried out in Cape Town, KwaZulu-Natal and

Gauteng. Duration: 2021-2022. Funder: Bill and Melinda Gates Foundation (INV-036772). Total award amount: $218,805 (Prime: HE²RO)

TMED (Translation of Modelled Evidence to Policy) - the main objective of this research project is to explore how modelled evidence is produced, translated and used by public health stakeholders in South Africa for policy and decision making, thereby facilitating research-to-policy collaboration and exchange in public health. Duration: Six months. Funder: Results for Development. Total award amount: $51,663

OTHER HIGHLIGHTS:

Researchers from HE²RO continue to play active roles in national think tanks and working groups including the National TB Patient Cost Survey Technical Advisory Group (Denise Evans), National TB Think Tank - Optimizing TB Treatment Outcomes and TB Epidemiology Modelling and Health Economics Task Team (Denise Evans), Member of the National TB Patient Cost Survey Technical Advisory Group (Denise Evans), Global DSD Research Collaborative (Sophie Pascoe), National Essential Medicines List Committee (Jacqui Miot), Ministerial Advisory Committee on COVID-19 (Jacqui Miot) and others. Further details on other highlights are :

HE²RO has also been leading in advising the South African government on aspects of the COVID-19 response, including as part of the Ministerial Advisory Committee on COVID-19 (Jacqui Miot and Gesine Meyer-Rath), several work streams of the Ministerial Advisory Committee on COVID-19 Vaccines (Gesine Meyer-Rath), and the COVID-19 Costing Committee (Jacqui Miot, Gesine Meyer-Rath and Kerensa Govender). Gesine Meyer-Rath, Lise Jamieson and Brooke Nichols are additionally part of the South African COVID-19 Modelling Consortium.

Dr Denise Evans was appointed as Executive Committee and Secretary for the Child Health Priorities Association.

Dr Mhairi Maskew, participated in the Systematic Review workshop in collaboration with Molly Beestrum, Librarian at Galter Health Sciences Library, Northwestern University Feinberg School of Medicine (October 2021), NHLS technical working group workshop (Cape Town, February 2022) and was an invited speaker: NHLS Development and Innovation Programme session on 11th June 2021 “Secondary Data Analysis: Using routinely collected data in public health research”

Sarah Girdwood has been collaborating closely with FIND on diagnostic network optimization work in the Gambia and Zambia, as well as contributing towards FIND's ACT-Accelerator Rapid Antigen Diagnostic Modelling Consortium. Whilst these projects and grants were completed in the 2021 review year, aspects of the projects are going to be continued in new grants during 2022.

Dr Sophie Pascoe has continued as one of the members of the Global DSD Research Collaborative which is facilitated by the IAS and meets twice a year to review current DSD research that is ongoing around the globe. She is also a faculty member of what was the SA AIDS 2021 Conference Committee and Co-Chair of the Epidemiology track and was asked to continue as part of the conference organising committee and co-chair for SA AIDS 2023.

In addition, Dr Sophie Pascoe was invited to be part of the HIV Continuum of Care panel and to present at the International Association of Providers of AIDS Care (IAPAC) Adherence Conference, held in Orlando, Florida, in November 2021. The presentation was entitled “Models of Care: Enhancing multi-disciplinary patient-centred collaboration” (presented virtually).

The success of the Indlela project continues. The team has completed a series of workshops and webinars and convened a meeting of expert behavioural scientists to explore new ideas and research priorities. Indlela has expanded the team to include 5 behavioural scientists, all trained in behavioural economics, who are based at the HE²RO offices.

SOCIAL IMPACT

MENTORSHIPS; Principal Researchers from HE²RO supervised 11 PhD students, 4 Master's and 4 MBBCh students from local and international universities. In addition, we hosted 3 Fogarty fellows as an international research site of the HBNU Fogarty Global Health Training program.

STAFFING IN 2021:

By December 2021, HE²RO had a total head count of 96 staff members and the total grant income for HE²RO in 2021 exceeded R73 million

HE²RO published 42 peer-reviewed journal articles in 2021.

HE²RO KEY FUNDERS:

USAID remains HE²RO 's key funder both through the EVIDENCE award as well as under the EQUIP Health Project. In addition, the Bill and Melinda Gates Foundation (BMGF) has provided funding for 2 studies, including the launch of a behavioural economics unit in collaboration with the University of Pennsylvania for 2020 and we received funding from the NIH for three R01 and one R34 studies.

Health Economics and Epidemiology Research Office
HE²RO
Wits Health Consortium
University of the Witwatersrand

WITS VIDA
UNIVERSITY OF THE WITWATERSRAND
VACCINES & INFECTIOUS DISEASES ANALYTICS

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WHO WE ARE

Wits VIDA (Vaccines & Infectious Diseases Analytics Research Unit), rebranded in 2019, was originally founded in 1997 as the Pneumococcal Diseases Research Unit and subsequently Respiratory and Meningeal Pathogens Research Unit (RMPRU).

VIDA's research is focused on clinical and molecular epidemiology of vaccine preventable diseases, clinical development and evaluation of vaccines, immunology of vaccines including in people living with HIV and basic science research aimed at discovery of potential vaccine candidates. In the last five years, the Unit has expanded its research portfolio to include population level surveillance and epidemiology studies including establishment of a health and demographic surveillance (HDSS) platform to understand the context in which infections occur and how population dynamics are affected by disease trends, both in children and in pregnant women. This HDSS platform has been an integral component to understand COVID-19 epidemiology, SARS-CoV-2 transmission dynamics and the direct and indirect effects of COVID-19 across all age groups.

The Unit has established itself as a premier clinical trial facility for vaccine research and has undertaken pivotal studies on pneumococcal conjugate vaccine, rotavirus vaccine, as well as being an international leader in vaccine studies in pregnant women aimed at the protection of mother-newborn dyads. Over the past two years, VIDA has been at the forefront of COVID-19 vaccine research in Africa, having spearheaded the first two COVID-19 vaccine studies undertaken on the continent. Additionally, the Unit led provincial wide population based Covid-19 seroprevalence studies in Gauteng and the North West provinces and a national one in Eswatini.

The studies done by VIDA on pneumococcal conjugate vaccine and rotavirus vaccine in children contributed to South Africa, being the first African country to include both vaccines in its public immunization program, and underpinned the WHO recommendation for the inclusion of these vaccines in public immunization programs of other low and middle income countries. VIDA also performed the first placebo-controlled randomized trial of the influenza vaccine in pregnant women, that contributed to WHO recommending for the prioritization of pregnant women to be vaccinated with seasonal influenza vaccines. It has also undertaken the first studies of an investigational multi-component Group B Streptococcus (GBS) conjugate vaccine in pregnant women, a portfolio of research that is ongoing, including discovery research on other potential GBS vaccine epitopes. This is pertinent to Africa and South Africa which has reported the highest incidence of invasive GBS disease globally. Most recently, VIDA has pioneered COVID-19 vaccine trials, providing critical evidence on vaccine efficacy in African populations.

A further important respiratory pathogen being investigated by VIDA over the past 25 years is Respiratory Syncytial Virus (RSV). VIDA has been intricately involved in the evaluation of a long-lasting monoclonal antibody that is more affordable than the currently available palivizumab, and is also participating in RSV vaccine trials in pregnant women, including having led the first of such studies of a nano particle F protein vaccine in pregnant women.

In 2019, Wits VIDA set up a sequencing facility that has provided new opportunities for research including a specific focus on drug-resistant bacteria, and particularly Klebsiella pneumoniae as a new research-focus area. Also, the Unit is currently involved in surveillance of ESKAPE organisms, with a specific focus on Klebsiella pneumoniae and Acientobacter baumannii. The research includes whole genome sequencing of ESKAPE isolates. Furthermore, the Unit is involved in BMGF funded activities aimed at the development of vaccines against Klebsiella pneumoniae.

RESEARCH IN 2021

Oxford Covid-19 Vaccine Trial

Officially called the Ox1CoV-19 vaccine VIDA-trial, the 'Oxford trial' was announced on 23 June 2020. Researchers began vaccinating human volunteers with a new vaccine called ChAdOx1 nCoV-19 on 24 June 2020. Results from the study were published on 20 May 2021.

NOVAVAX COVID-19 VACCINE TRIAL

The published data provided additional detail of an initial analysis conducted in January, while more robust data from a complete study analysis was subsequently shared in March 2021. Results were published on 20 May 2021. This is the first published study to show protection against mild Covid-19 caused by the B.1.351 variant circulating in South Africa.

Wits VIDA has secured funding and conducted numerous COVID-19 studies during the reporting period, including the following studies that started during this time:

VACSAFE - Vaccine Information Network project Wits VIDA, in partnership with WITS US at Columbia University, is taking part in this social behavioral sciences initiative around the national vaccine implementation and COVID-19. This project aims to evaluate the motivations for, and barriers to vaccination, and use this information to develop a communication strategy that can support enhanced uptake of vaccines and completion of vaccination series at a local population level. This study is being conducted in South Africa and Zimbabwe with financial support from the Bill & Melinda Gates Foundation, Schmidt Futures and a donation by Aspen Pharmacare.

INTERFERON: IFN-BETA FOR EARLY COVID-19

A multi-centre, placebo-controlled study of interferon (IFN) beta-1a in high risk COVID-19 outpatients. The primary objective of this study is to see whether short-term intramuscular interferon beta-1a, administered early in the disease course, reduces the composite risk of the need for hospitalization or death in high-risk unvaccinated individuals with COVID-19. Secondary objectives include seeing whether interferon beta leads to a quicker viral clearance, or faster symptom resolution.

Impact of COVID-19 on maternal and neonatal health in South Africa

This study investigated the effects of COVID-19 on mother and newborn outcomes in an established pregnancy cohort in South Africa.

Transmission dynamics of SARS-CoV-2 at household level

Nested within the HDSS, this project aims to establish the extent of COVID-19 transmission within households by estimating infection rate for household contacts at an individual level, and factors associated with any variation in the infection risk.

Surveillance of COVID19 in healthcare workers

Surveillance among healthcare workers for SARS-CoV-2 infection - to investigate the epidemiology of SARS-CoV-2 infection among healthcare workers who triage patients and provide care to COVID-19 patients.

Wits VIDA pioneered two COVID-19 studies in the Kingdom of eSwatini:

Effectiveness of COVID-19 vaccination in eSwatini against SARS-COV-2 associated hospitalization and death. This countrywide project has two components: i) vaccine implementation and ii) assessment of vaccine effectiveness. Wits VIDA supported the vaccine roll-out and passive monitoring of serious adverse events following immunization in eSwatini in collaboration with the eSwatini ministry of health and the Luke Commission. VIDA further supported vaccination education through an awareness campaign in collaboration with an experienced marketing team, whilst consulting with government, local traditional leaders, influential voices and other stakeholders in the kingdom of eSwatini. For the vaccine effectiveness component, VIDA further collaborated with the eSwatini ministry of Health and the Luke Commission to determine the vaccine effectiveness of AZ1222 against severe disease due to the various SARS-CoV-2 variants.

Population-based sero-epidemiological investigation of SARS-CoV-2 virus infection in the Kingdom of Eswatini. The aim for this study was to get an accurate estimate of the extent of COVID-19 infections in the Kingdom of eSwatini's population. Wits VIDA, in collaboration with the eSwatini Ministry of Health, conducted this SARS-CoV-2 Seroprevalence survey in all sub-regions of the country.

COVID RSV Dynamics in the context of COVID-South Africa

This study aims to generate epidemiological data on RSV infections during the time of SARS-CoV-2 circulation. The prevalence, severity, timing of infection, and age-groups infected by RSV will be compared with historical data previously collected by VIDA.

CHAMPS

The CHAMPS (Child Health and Mortality Prevention) Project and its various sub-studies continue to generate valuable data

in the COVID-19 era. Sub-studies evaluating the direct and indirect effects of Covid19 at household and community level are underway.

COVID 19: Sero-epidemiological investigation of SARS-CoV-2 in Gauteng and Northwest Province. Results from this study have been published in the New England Journal of Medicine and showed that South Africa had immunity against severe Covid disease & death before Omicron due to prior infection and vaccination. An additional Serosurvey is underway ahead of the next wave of infections in Gauteng in 2022.

Numerous additional COVID-19 clinical trials have also taken place during the reporting period. This includes PRO-CL-002 under the sponsorship of Providence Therapeutics that evaluates a new mRNA vaccine, evaluation of the Pfizer vaccine in pregnant women, evaluation of different dosing schedules of the Astra Zeneca vaccine in older adults and a recent initiation of the vaccine trial from the sponsor called Gritstone which evaluates a novel self-replicating mRNA vaccine in COVID naïve and convalescent subjects.

PUBLICATIONS

Wits VIDA published 64 articles during the reporting period across various high-impact journals, including 3 publications in the New England Journal of Medicine.

LEADERSHIP AND IMPACT

VIDA is internationally recognized for the role it has played in the clinical development of life-saving vaccines such as the rotavirus vaccine and pneumococcal conjugate vaccine. Furthermore, it has been at the forefront of vaccine studies aimed at pregnant women, including reporting on the first placebo-controlled randomized trial of the influenza vaccine in pregnant women. It has also undertaken the first studies of an investigational multi-component GBS conjugate vaccine in pregnant women, a portfolio of research that is ongoing, including discovery research on other potential GBS vaccine epitopes. This is pertinent to Africa and South Africa, which has reported the highest incidence of invasive GBS disease globally. The unit also does important work on vaccines and their impact on Vaccine Preventable Diseases (VPDs). To date, the research undertaken by VIDA was instrumental in informing WHO recommendations for the introduction of pneumococcal conjugate vaccine and rotavirus vaccine into public immunization programs of low and middle-income countries. Also, the studies done by VIDA contributed to South Africa being the first country to include both vaccines in its public immunization program, which was followed by massive reduction in hospitalization for pneumonia and diarrheal disease. VIDA research on influenza vaccination in pregnant women also contributed to WHO recommending for the prioritization of pregnant women to be vaccinated with seasonal influenza vaccine. Data that is generated through the Child Health and Mortality Surveillance Study (CHAMPS) is timeously shared with the Provincial and District Department of Health and with the local hospital (Chris Hani Baragwanath Academic Hospital) to inform on policy and planning as well as clinical practice respectively.

AIMS AND OBJECTIVES

In 2021, Wits VIDA focussed on the following research focus areas

- Epidemiology & vaccines against Group B streptococcus disease
- Epidemiology & prevention of Pneumococcal disease
- Prevention of Diarrheal Disease
- Influenza epidemiology & influenza vaccines
- Child health and mortality prevention surveillance
- Epidemiology & prevention of pneumonia morbidity & sequeale in children
- Immunity in HIV-Expoised and HIV-uninfected children
- Covid epidemiology in South Africa

GRANT AWARDS

The unit received grants in 2021 from the following institutions:

Bill and Melinda Gates Foundation
South African Medical Research Council
EDCTP
The Foundation for Global Health
University College London
Liverpool School of Tropical Medicine
National Institute of Health
Fondazione PENTA
Wellcome Trust
PATH
Biovac
Sanger Institute
Oppenheimer Institute
Aspen
Yale University
Fondation De France
CDC

INDUSTRY FUNDED RESEARCH

GSK
Pfizer
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Sanofi
Providence Therapeutics
Janssen

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WHO WE ARE

The Clinical Laboratory Services (CLS) is a division of Wits Health Consortium of the University of the Witwatersrand, Johannesburg South Africa. It was established in the year 2000 by the Head of Research at CLS, Prof Wendy Stevens to offer diagnostic laboratory services for clinical trials, research studies and hospitals linked to the academic complex. As CLS is committed to supporting research and ensuring a strong academic link CLS continued to support the Wits Clinical Trials Units in terms of laboratory diagnostic services. In 2021 the laboratory served multiple donor funded clinical trials projects through established infrastructure, systems and procedures with an experienced team. CLS has unique strengths with a strong link to the National Health Laboratory Services under the leadership of Professor Wendy Stevens.

Prof Stevens's team is responsible for national implementation of laboratory diagnostics within the public sector (>80% of the state-sector population in South Africa) through an established National Priority Program (NPP) of the NHLS for CD4-counts, reflexed crypto-coccal antigen, early infant diagnosis, HIV viral load, HIV drug resistance and molecular TB diagnostics. In addition, the team has a strong academic base (joint academic affiliations with commitments to teaching, mentoring and laboratory service provision) within the University of the Witwatersrand. This has allowed research driven innovations to be implemented through the NPP with application of their expertise with translation and support of relevant research outputs to the DAIDS network.

RECENT ACHIEVEMENTS (2021)

For the period under review, the following achievements are noted:

1. CLS' diagnostic service, to support tuberculosis (TB) disease management, improved with co-validation of the re-purposed (clofazamine) and novel (linezolid, bedaquiline, and delamanid) anti-TB drugs together with the NHLS' national TB programme. Phenotypic drug-susceptibility testing for the listed drugs is now available to support WHO and Department of Health recommendations on the rollout of the revised short-treatment regimens for drug-resistant TB.

2. Through research collaborations between CLS, suppliers and Foundation for Innovative New Diagnostics (FIND), multi-platform technology evaluations were conducted to inform WHO-endorsement of alternate TB diagnostic platforms, opening up the market to contain test costs. Newer platforms will also increase case detection due to increased sensitivity, offer higher testing throughputs and combined Rif/INH identification. Similarly, the team assessed the performance of the Xpert® MTB/XDR assay as part of a multi-country study evaluation. Findings were included in the WHO recommendation for the use of the assay.

3. CLS demonstrated excellent External Quality Assessment (EQA) performance across all laboratory disciplines, including SARS-CoV-2 tests in the molecular department. The laboratory underwent several audits and maintained the Division of AIDS (DAIDS), Good Clinical Laboratory Practice (GCLP) certification by Qualogy and that of the South African National Accreditation System (SANAS). CLS has successfully provided Elispot EQA panels to various African sites for more than a decade. Panels are prepared under strict sterile conditions with adherence to high quality standards to ensure accurate and reproducible results. CLS handles all shipments meticulously ensuring that all relevant participating laboratories receive EQA panels timely and in satisfactory condition.

4. The SARS-CoV-2 PCR test was introduced together with the upgrading of the molecular laboratory, which was successfully accredited by SANAS according to the requirements of the ISO 15189 standard, and also certified with the Ministry of Health as part of the national pandemic testing programme. CLS successfully completed the role of national testing laboratory for several COVID-19 vaccine trials, resulting in the

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approval of a vaccine to be used both locally and abroad.

5. PROVISION OF LABORATORY SUPPORT AND CAPACITY BUILDING:

- CLS provided these services in approximately 40 different African sites in up to 10 countries through grant-funded research.

a. Through its collaboration with International AIDS Vaccine Initiative (IAVI) and Glaxo SmithKline (GSK), CLS supported several laboratories in both Eastern/Southern African countries.

b. Through GSK-funding, 23 laboratories across Ghana, Malawi, and Kenya were supported in respect of EQA enrolment and support to improve laboratory performance. Laboratories were enrolled on the haematology, chemistry, microbiology, serology and parasitology EQA programs.

c. CLS assisted further by conducting laboratory assessments to improve quality management systems. Laboratory assessments are based on GCLP and ISO 15189 guidelines.

d. CLS continued to offer GCLP training to external clients. This included two sites in Ghana to address the gaps identified during laboratory assessments.

e. The IAVI project to support EQA programs in Zambia, Uganda, Kenya, South Africa and Rwanda and provide quality management system support continued to be a resounding success, leading to sustained process improvements for these Clinical Research Centres.

6. PARASITOLOGY LABORATORY:

- This was setup with GSK funding and support provided by the Parasitology Reference Laboratory at the National Institute of Communicable Diseases (NICD).
- Staff were trained by the Reference Laboratory experts to prepare and supply malaria EQA proficiency testing slides to supported laboratories.
- Proficiency in parasite counting and species identification was also evaluated.
- CLS has supplied these EQA slides independently from 2020.

7. PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) ISOLATION:

- Cryopreservation of and testing PBMCs via an Elispot assay has been performed at CLS since 2001.
- As per preceding years, the PBMC laboratory continued to prepare and ship PBMCs to seven African sites, one site in the United Kingdom and one local site, as part of the EQA programme. The programme aims to standardise testing of immune responses for vaccine studies thereby addressing operator deficiencies in performing vaccine assays.
- CLS offered training and support for PBMC laboratories in South Africa and other African sites.
- The laboratory scope expanded to include immunology assays, DNA/RNA extraction, and quantification assays, with automated DNA/RNA extraction available, using Hamilton robotics, as the method of choice.

8. REPOSITORY AND SHIPPING:

- The organisation has a fully fletched Human Hereditary Health for Africa (H3 Africa) sponsored biorepository for storage and shipping of human specimen aliquots.
- CLS continues to support several clinical research sites within the WHC syndicate by providing much needed repository functionalities plus training for better specimen storage.

9. DAIDS NETWORK TRIALS:

- CLS has been the 'Central laboratory 'for over 1500 clinical trials of varying sizes since 2000.
- COVID-19 vaccine studies in collaboration with clinical research sites in the networks.
- CLS staff on the ACTG and IMPAACT Laboratory Technologist Groups – assisting with creating laboratory testing documents in protocol development.
- CLS was part of the following studies:
  a. IMPAACT 2014 study: received United States (US) FDA's approval for use of Doravirine in Pifeltro and Delstrigo among children.
  b. IMPAACT 2017 (MOCHA): data informed US FDA Approval of Cabenuva for HIV Treatment in virologically suppressed adolescents.
  c. IMPAACT 2007 informed FDA approval of its supplements.
  d. IMPAACT P1093 Informed FDA decision to approve first ever Dolutegravir Dispersible for treatment of children living with HIV.
  e. HPTN studies informed FDA's approval of CAB-LA injections for HIV prevention completed in studies HPTN 083 and HPTN 084.

Under Prof Steven's leadership, CLS continued to strengthen its diagnostic capacity to include the following pathology disciplines: molecular pathology (precision medicine) and virology (including HIV VL, HIV DR, HIV qualitative and quantitative testing); mycobacteriology; microbiology (including urine analysis); haematology (including CD4 and flow cytometric assays), cytopathology, serology, immunology (including transplantation medicine and cytokines), and clinical chemistry.

CLINICAL LABORATORY SERVICES

PRICELESS SA
Priority Cost Effective Lessons for System Strengthening

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WHO WE ARE

PRICELESS SA is the South African MRC Centre for Health Economics and Decision Science based at the Wits School of Public Health. We undertake policy relevant research and capacity building in the field of priority setting. We produce evidence to demonstrate how to improve health and maximize life expectancy in South Africa and across sub-Saharan Africa. We focus on Health Services and the broader social, economic and commercial determinants of health. Our priority areas are maternal and child health, non-communicable disease, nutrition in the first 1,000 days, preventing road traffic injuries, health-promoting polices, and health systems reform.

PRICELESS SA is a leading Southern African institution for formal, Postgraduate teaching in health economics and decision science. We also offer a short course on priority setting and HTA for public health professionals and academics.

PRICELESS SA publishes extensively in peer-reviewed academic journals.

Our Unit engages with senior policymakers, the public and the media to strengthen expertise for setting health priorities for South Africa.

RESEARCH IN 2021:

In 2021 PRICELESS published 28 peer reviewed articles on a range of topics. We performed innovative research in health economic evaluation and developed new methodologies. We performed an extensive evaluation of the Health Promotion Levy and used a novel tool to determine community perspectives relating to priorities for mother and child health and similar research on nutrition. In addition, we developed a model framework that is SA specific, and that can be used during HTA analysis that accounts for moral and ethical principles espoused in the NHI white paper. We performed numerous studies related to Covid that encompassed costing and legal, ethical, and economic issues.

OUR KEY FOUNDERS

The PRICELESS research unit was founded in 2009 by Prof Hofman and was nested in the MRC/WITS Agincourt unit 2013. For the past decade it has been independent and was honored by the SA MRC in 2019 as an extramural Unit of the SA MRC – The Centre for Health Economics and Decision Science. Prof Hofman has been recognized as a leader in research leading to best buys for health, and was instrumental in introducing the Health Promotion Levy and the Salt regulations. She is as member of the WHO working group on Commercial Determinants of Health; the Norwegian Institute of Public Health research advisory panel; the NRF Centre of Excellence on Food Security Science Advisory panel and the ASSAf standing committee on Health

COVID 19 WORK

PRICELESS has contributed in an ongoing way to the COVID-19 Pandemic effort. This is includes a major grant from a UK funder to perform research on the impact of covid on routine health systems. We have responded to calls to translating the science for the popular press, engaging with international and local audiences. Presentations at prestigious conferences on topics such as “The Impact of COVID on Food Systems in sub-Saharan Africa – what have we learnt?” and “The Impact of COVID on women and gender relations” and “Promoting Healthy Behaviour that Reduces the Spread of COVID-19 in mass gathering events” at the QATAR Health Virtual Conference. PRICELESS continues to work on nutrition related non-communicable diseases and the financial impacts of these NCDs, in addition to the impact obesity and NCD's have had on COVID-19.

SOCIAL IMPACT:

PRICELESS also donated funds to the Gift of the Givers following the July unrest in KZN.

Health Systems Enablement & Innovation

WHO WE ARE

Health Systems Enablement and Innovation Unit is a division of the Wits Health Consortium, which works with government in various provinces in enabling the health systems to perform better and service their clients with dignity. HSEi supports national health systems in South Africa and across the African continent through research, professional advice, clinical service, and healthcare delivery systems redesign.

We harness ideas and initiatives and test innovative alternatives as the health systems prepare for universal health coverage. Our unique Public-Private-University-Partnership model and patient-centric solutions look to create access to appropriate, affordable, efficient, quality, and equitable healthcare.

HSEI PROGRAMMES

1. CLINICAL SERVICE DELIVERY

HSEi implements clinical service delivery initiatives in partnership with national and provincial departments of Health in South Africa, with the focus of narrowing the inequity in accessing quality clinical services for rural populations. Clinical service delivery initiatives are currently being implemented in the Eastern Cape and Mpumalanga Provinces through the development of centres of excellence that provide oncology services to the provincial populations, the decentralisation of cancer services to lower levels of care and the provision of radiology services to tertiary and regional health facilities of the Mpumalanga province.

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1.1.Mpumalanga Oncology Initiative

In August 2019, the Mpumalanga Provincial Department of Health entered into a service level agreement with the HSEI to provide cancer care oncology services. At the time of the award, no oncology services were available at state-run health care facilities in the province. Patients were instead referred to the Steve Biko Academic Hospital located in the Gauteng province, about 320 km away. The distance, time, and finances required to access care were a barrier to timely access, diagnosis, and treatment of cancer, which manifested in high morbidity and mortality amongst patients. To address this gap, HSEI was requested to provide oncology services at the Rob Ferreira tertiary hospital with the intention of decentralizing the services to regional and district hospitals in the province.

As an initial start to this service, oncology units were established at Rob Ferreira Hospital and later in 2021 at Witbank Hospital to provide the following medical interventions:

- Diagnosis
- Chemotherapy
- Palliative care

To date, diagnosis, chemotherapy, and Palliative care services are offered in the Oncology units, with radiotherapy services being planned for implementation by the Mpumalanga Department of Health.

ACHIEVEMENTS

In a bid to decentralize and increase access to oncology services in the province, Oncology services have been rolled out in four distinct areas. These were

- Set up of Witbank Chemotherapy Services - commenced operations in April 2021
- Outreach services to communities to raise awareness and increase demand - an ongoing activity
- Training staff in referring hospitals. This is an ongoing activity aimed at all levels of health workers who support Oncology services
- Palliative care in lower levels of care
- Provide Specialist clinicians (oncologists) on daily basis to the RFH & Witbank oncology units

In June 2021, a twelve-bed cancer ward (5 female, 4 male, 3 paediatric) was opened at Rob Ferreira hospital which now allows for around-the-clock care and admission of patients. Hospital medical officers provide after-hour care in the ward. The inpatient ward admits patients requiring long-term observation, further investigation for disease staging, and those that need advanced treatment and in-patient care that cannot be concluded during the normal daily operating hours.

MPDoH identified space that could be utilized as an in-patient ward and refurbished it to suit the needs of an Oncology ward. All equipment in the expanded Oncology unit was procured by the MPDoH. The new Oncology unit is now a site of both the day clinic for outpatient treatment and the inpatient ward providing around-the-clock oncology care as needed.

What have we Learned?

The quality of care in public facilities is variable in Mpumalanga. There are pockets of good practices worth commending. However, the growing challenges of long waiting times, drug shortages, and lack of adequate infrastructure and resources in public facilities worsen the inherent effects of inequality amongst the poorest quintiles.

Oncology services have experienced drug stock-outs which have at times compromised patient care. Oncologists have in the past decided to delay starting treatment for patients on certain regimens due to limited or no availability of drugs. Where there has been limited availability, clinicians have determined that available medication will be reserved for patients already on treatment so that there is no treatment interruption. This situation undoubtedly compromises patient care and treatment outcomes. Persistent drug stockouts can add to the financial burden on hospitals as doctors substitute with second-line drugs which are at times more costly than the recommended first-line treatment.

What's Next?

Set up of Radiation Therapy services by MPUDoH is currently underway. Currently, patients requiring this treatment are referred to Steve Biko Academic Hospital in Pretoria. Patient transport is provided for travel to SBAH. Set up of radiation therapy equipment at Rob Ferreira will eliminate the need to travel and improve the oncology service offered in the province.

1.1.Decentralized Cancer Care Programme

Cancer care services exist primarily in tertiary centres, which are generally located in urban areas. However, centres of excellence where patients have access to safe, effective, quality, and affordable medicines have not been developed outside of these centres. Consequently, cancer services in non-tertiary care centres and primary health care facilities are generally underdeveloped. They lack the necessary infrastructure, resources, and expertise to provide quality, safe and accessible oncology services.

The Mpumalanga and Eastern Cape Provinces of South Africa are confronted with similar challenges. Patients from rural communities, who generally cannot afford private health care and are dependent on state health services for cancer care, are compelled to travel long distances to the urban-based tertiary cancer care centres in order to access cancer care.

In response to the increasing burden of cancer and centralization of currently available cancer services, HSEI is currently responding by implementing a decentralized cancer care delivery model in the Eastern Cape and Mpumalanga provinces.

The main objective of the Decentralized Cancer Care Programme was to establish a centre of excellence for cancer care based at Nelson Mandela Academic Hospital in the Eastern Cape and Rob Ferreira Tertiary Hospital in Mpumalanga Province that would enable earlier detection of cancer, through accurate diagnostic procedures, provide palliative care, and improve morbidity and mortality rates.

ACHIEVEMENTS

The project has made a significant contribution to advocacy work for cancer in the eastern part of the Eastern Cape, sensitizing the communities about cancer prevention and lifestyle modifications. The milestones achieved

In include but are not limited to:

- Establishing a fully operational centre of excellence in Mthatha with a mobile trailer that is used to conduct awareness and outreach campaigns monthly.
- The Oncology Unit is the only unit at NMAH that offers psychosocial (in the form of counselling and other psychosocial initiatives) support to its patients
- Supporting 5 satellite sites that were previously not offering cancer services to cancer patients in their regions. The support included purchasing diagnostic equipment, training health professionals and hosting outreach campaigns at each of the sites.
- Establishing a decentralized oncology unit in Lusikisiki which is set to offer chemotherapy and responds to the decanting of cancer care services to tertiary

facilities. Patients in that region have significantly reduced travel times and costs as they receive care closer to their homes.
- Training of health care professionals and community health care workers of referring hospitals in Palliative Care, Breast and Cervical Cancer Screening, and basic signs and symptoms of cancer.
- Hosting of outreach and awareness campaigns using equipment purchased through the programme. These campaigns are the project's greatest achievement as a majority of new cases (which would otherwise not have been diagnosed) are identified during these campaigns and people are more informed about cancer resulting in early diagnosis.
- The project funded four Medical Doctors from NMAH to graduate with Palliative Care Diplomas from UCT.

What's Next?

An attempt to further reduce travel times and waiting periods for patients, The Eastern Cape Department of Health will be purchasing radiotherapy machines which will ensure that we offer these services at the hub. Decentralized Oncology Clinics in two other referring hospitals are planned to be established as part of furthering the decentralization of cancer services.

1.3. RADIOLOGY ACCESS PROGRAMME

It was further identified that the Mpumalanga province had no reliable Radiology support for its tertiary and regional hospitals. The service was outsourced making it difficult for the department of health to provide it in an efficient and cost effective manner to its population. Thus, tapping into the support WITS University and HSEi is currently providing in the province, and the proven success of the private-public partnership for the provision of oncology services, the department entered into an SLA in March 2020 for the provision of Radiology Services and teleradiology support to two tertiary and two regional hospitals in the province.

Through this partnership, HSEi has employed software and IT solutions to systematically enhance radiology services in the hospitals.

The Radiology Information System allows for improved patient care by optimizing workflow for Radiographers and Radiologists and by ensuring single-point desktop access to radiology information. This together with the integrated PACS system allows Radiologists to view medical images anywhere, anytime, and on any device. The PACS system reliably archives medical images and can dispense them on the web or via digital media for Radiologists to view medical images at diagnostic quality or print them on film or media paper.

ACHIEVEMENTS

Since the inception of the Radiology Access Programme in March 2020, the service has:
- Significantly reduced waiting time for radiology reporting,
- Accelerated diagnostic processes thus improving patient management,
- Ensured the accessibility of and to radiologists' clinical consultations, including weekends and public holidays, allowing clinicians to interact with radiologists during working hours and after hours and,
- Improved accessibility to radiology information enabling literature review for research purposes

What's Next?

The Radiology Access Programme will move into a new phase in the coming year which will include putting systems in place to strengthen sustainability as well as scaling up all services and offerings

The planned activities include:
- Bring Mapulaneng Hospital to par with the other peer Hospitals
- Expand LogiPacs to allow for access to all Hospitals, from single login per hospital
- Strengthen Level 1 IT support, particularly Ermelo and Witbank Hospitals (hospital-based IT technicians)
- Expand RIS/PACS training (TOT) in each district
- Expand teleradiology to referral sites (cost-effectiveness)
- Mobile Radiology services (outreach)

1.4. TRAINING AND DEVELOPMENT

Beyond the core mandate of providing oncology and radiology services, HSEI is also responsible for skills transfer to Department of Health staff to support service continuity, even after project closure. This has been achieved through on-site supervision by Oncologists, structured training, and facilitation of continuous professional development talks. Through these efforts, medical staff in the province are being equipped to continue the provision of oncology and radiology services even after the HSEi assignment has been concluded.

ACHIEVEMENTS

In addition to this structured training, in-service training has been provided by Oncologists placed at the units. These sessions covered various topics such as:
- Basics on Cancer
- What is Chemotherapy
- Roles and responsibilities of the team
- Standard operating procedures for chemotherapy
- Standard operating procedures for administrators
- Approach to Lymphoma

Continuous professional development (CPD) talks are another way in which capacity is being built. Depending on the availability of the facilitators, CPD talks are scheduled weekly. CPD sessions focus on the below-listed areas

- ENT and Maxillofacial meetings
- Combined surgical meetings
- Combined urology meetings

Oncologists also provide ongoing mentorship to medical officers and nurses in the units. The goal of all these pieces of training is to ensure that skills transfer takes place so that high-quality service delivery can continue long after the HSEi assignment has been concluded.

1.5. Community Healthcare Worker Upskilling Project

In the 2021 period, the Health Systems Enablement & Innovation (HSEI), forged a partnership with the Gauteng Department of Health (GDoH) to assist in a programme to train 3079 Community Health Workers (CHWs) as Health Promotion Officers. This qualification is accredited by the Quality Council for Trades and Occupations (QCTO) and registered with the South African Qualifications Authority (SAQA). Five hundred (500) CHWs were enrolled in the last quarter of 2021 with the hope of them sitting for the External Integrated Summative Assessment (EISA) for Health Promotion Officer (ID 94597, NQF Level 03) occupational qualification in October 2022.

Next Steps

HSEi has planned to increase the skilled workforce in the Department of Health to enable health system strengthening. This will be achieved through the upskilling of CHWs and increasing their employability to improve economic participation.

2. RESEARCH PROGRAMS

As a learning institution, HSEI strives to ensure the service delivery is informed by sound evidence. To this end, several research studies are conducted at the hospitals where HSEI is supporting service delivery. Results of these research studies will inform further recommendations for improved health care service delivery in the provinces.

2.1. Redesign Cancer Research Programme

- The aim of this programme is to explore alterative eg. impact of decentralizing cancer care on
  - Health outcomes
  - Patient experiences of care and,
  - Economic burden of cancer care.

2.2. Cancer Health Economics And Evaluation Research Programme (Cheer)

The aim of the CHEER programme is on building capacity, producing local & continental knowledge on Cancer financing & Economic evaluations of cancer care and delivery systems.

CHEER seeks to contribute to equitable distribution of quality cancer care services by:

- Developing skills, systems and tools for cancer health economics research,
- Conducting economic analysis and evaluations of cancer care,
- Conducting cancer delivery systems research and,
- Assessing the scope, quality, delivery and distribution of cancer care services.

2.3 Public Hospitals Performance Evaluation Research Programme (HOPE)

The Aim of the HOPE programme is on exploring strategies to improve performance of public hospitals, focusing on:

- Describing key clinical governance areas & factors to consider when strengthening the hospital's capacity to perform,
- Describing the pre-intervention implementation of selected clinical governance protocols in selected hospitals and,
- Implementing a co-designed intervention package focusing on selected clinical governance protocols in 2 intervention hospitals.

2.4 Information Behaviour

The Aim of this programme is to investigate the information behaviour of doctors and nurses in the Provinces of Mpumalanga, Limpopo, Eastern Cape, and Northern Cape.

The focus includes :

- Information needs of Tertiary and Central hospitals in South Africa hospitals,
- Information sources and channels used by health professionals in the four Provinces,
- The intervening variables that hinder access to information and knowledge by health professionals.

2.5. Hospitals As Learning Organisations

The aim of this programme is to examine learning practices or strategies used by hospitals in various Eastern Cape hospitals to achieve the principle of a Learning Organisation (LO).

The focus areas include:

- Access to knowledge by Healthcare Professionals,
- Quality improvement Challenges facing health care professionals,
- System for Collaborations and team learning among health professionals,
- In South Africa, the LO framework could assist public hospitals to improve healthcare quality.

3. Grant Awards in 2021

HSEi received grants towards the improvement of research in the field of Clinical Governance, Health Economics and Health Systems, as well the provision of Nephrology services in the Mpumalanga Department of

Health. Grant funding in the 2021 period was received from the South African Medical Research Council (SAMRC), The Bristol Myers Squib Foundation (BMSF), the Mpumalanga Department of Health, Gauteng Department of Health, and the Health and Welfare SETA.

4. HSEI PARTNERS

In 2021 period HSEi has partnered with
(1) The Bristol Myers Squib Foundation,
(2) The Gauteng Department of Health,
(3) The South African Medical Research Council,
(4) The Gorge Institute for Global Health,
(5) The University of the New South Wales,
(6) The Health and Welfare Sector Education and Training Authority (HWSETA).

5. FUTURE FORWARD

5.1. ECDOH Vaccination Scale Up Project

Covid-19 has sent shockwaves around the world and has sharpened global inequalities, with countries in the global South at the end of the queue for treatments and vaccines. Covid has also taken full advantage of people living with existing diseases, and it has supercharged poverty, unemployment, and inequality.

HSEi supports the Eastern Cape Department of Health through a donation provided by the Solidarity Fund to nursing staff (Professional and Enrolled Nurses) in the Eastern Cape Province.

The need for additional human resource capacity has been identified as a contributor to the vaccination outcomes identified in the province, particularly in the rural areas. The Eastern Cape province is characterised by very rural and hard to reach areas. HSEI will be supporting three districts in the province, namely, OR Tambo, Joe Gqabi, and Alfred Nzo Districts. HSEI will be supporting the province with their current challenges in an attempt to boost its demand creation activities and assist the province in reaching its Covid-19 vaccination targets.

5.2. Nephrology Services

HSEI intends to provide assistance to the Mpumalanga Department of Health with the nephrology services as an attempt to centralise the delivery of nephrology services to the tertiary hospitals of the Mpumalanga Province. These services will be provided daily to the patients of Rob Ferreira and Witbank Hospitals.

The implementation of the Mpumalanga Renal Dialysis Services will take into account the current number of public sector dependent patients who are being dialysed in the current outsourced service, ensure that the two hospitals have the necessary capacity to meet current and future demand for Renal Dialysis, and guarantee safe transition and transfer of patients.

This means that patients must not fall through the cracks, and that no disruption of clinical services and no mortality should be encountered because of the change in service delivery mechanism.

The implementation will in the main, follow the broad principles of setting-up of infrastructure with medical equipment and operating the clinical units with a qualified team of specialist Nephrologists and nephrology-trained nurses.

HSEi
Dignity through healthcare
Health Systems Enablement & Innovation

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

WHO WE ARE

The South African partners of the ANDEMIA project, funded by the German Federal Ministry of Education and Research (BMBF), are the Centre for Enteric Diseases at the National Institute for Communicable Diseases (NICD) and the Centre of Viral Zoonosis, Department of Medical Virology, University of Pretoria.

The Centre for Enteric Diseases focusses on diarrhoeal disease surveillance, public health orientated research, outbreak investigation and response, reference laboratory services, regional technical and laboratory testing assistance, delivered by a small team of specialists with extensive experience in enteric diseases.

The Centre of Viral Zoonosis conducts research on emerging neurological arboviruses and respiratory diseases affecting humans and animals. The main research themes include defining the epidemiology, pathogenesis and control mechanisms to emerging and zoonotic viruses, virus discovery, development of diagnostic tools and molecular epidemiological studies in clinical cases in humans and animals.

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INTRODUCTION

Africa has a disproportionally high morbidity and mortality related to infectious diseases. While traditional vertical programmes funded by international organizations tend to focus on HIV, TB and malaria, they rarely support programmes on common infectious diseases. These common infectious diseases include acute respiratory tract (RTI) and gastrointestinal (GI) infections and acute febrile disease of unknown cause (AFDUC), including antimicrobial resistant (AMR) pathogens. The ANDEMIA project aims to address some of these gaps and has hospital-based sentinel sites in Cote d'Ivoire, Burkina Faso, Democratic Republic of Congo and South Africa with German collaborators.

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

WHO WE ARE

The Wits Health Hubb (WHH) aims to provide community health care through developing youth skills in the health sector and positioning the same trainees in the local community to conduct basic health checks, refer patients to their local clinics and bring awareness about important health and wellness issues. The WHH works with local public healthcare facilities in Soweto to extend their reach into their local communities. In the last year, we have also built significant relationships with non-governmental organisations working in health in Soweto.

WHH aims to equip the youth with the crucial skills and resources they need to improve their lives and become agents for change. Improved health is central to development and WHH believes that young people play a key role as role models for their peers and communities, for health awareness and positive health behaviours. However, we are not oblivious to the many structural and socioeconomic challenges, such as unemployment and lack of education, experienced by many young South Africans. With the help and support of our funding and coordinating partners, we have been able to operationalise our vision and take steps towards addressing the challenges experienced by young adults in Soweto.

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The WHH team includes the initial founders (Dr Lisa Ware – health researcher; Dr Delan Naidoo – psychologist; and Mr Lethu Kapueja – business strategist and our operations manager, Ms Mimi Mhlaba.) Mimi was previously the coordinator of the Great Leap Forward Programme, in which the Health Hubb was born and comes with great experience.

Most excitingly, during 2021 we moved into our new home at the Jabulani Dlab (Development Lab) and Sports Complex in Soweto – a secure sports, wellness and development facility designed especially for youth.

STAFF IN 2021

After their training, WHH employed 4 of the 2020 youth cohort as research assistants and facilitated job placements for many others, also hiring a part-time professional nurse (Sister Keletso Mmoledi) to oversee activities.

RESEARCH IN 2021

We continue to evaluate the impact of the programme on the health advocates and community. With University of Glasgow (UK) Global Health Team, we measured how well community members can screen themselves for chronic disease if given online instructions and equipment. This approach reduces human resource where this is not available or cannot be mobilised (such as in a pandemic). Working with the Wits Centre for Exercise Science and Sports Medicine (CESSM) and Temple University, USA, we added physical activity assessments and feedback surveys to our community health checks. Our feedback from the community has been excellent. We also interviewed health advocates as youth at the intersection of the community and the health system on their perspectives of vaccine hesitancy working with the Wits Health Communications Research Unit. Our findings give some interesting insights into communication policies and approaches used by the state as South Africa debated implementing mandatory vaccination policies.

Calvert C, Kolkenbeck-Ruh A, Crouch SH, Soepnel LM, Ware LJ. Reliability, usability and identified need for home-based cardiometabolic health self-assessment during the COVID-19 pandemic in Soweto, South Africa. Sci Rep. 2022 May 3;12(1):7158.

Watermeyer J, Scott M, Kapueja L, Ware LJ. To trust or not to trust: An exploratory qualitative study of personal and community perceptions of vaccines amongst a group of young community healthcare workers in Soweto, South Africa. Health Pol Plan. 2022 under review.

LEARNERSHIPS AND INTERNS IN 2021

During last year, our first 20 young people re-

Annual Review 2021

cruited to the programme all completed the training with a 100% pass rate for the NQF3 Health Promotion Officer exam. Of this group, 85% are now employed or self-employed and the overwhelming majority within the health sector.

2021 also marked a new stage for WHH, creating a new learnership programme with the support of WHC and recruiting 30 new NEET youth living in Soweto to the programme (from over 1,500 applicants). So far, the new group are doing well in their theoretical and practical training, and their communication and research skills training.
In addition to our core learners, the Health Hubb hosts interns for work experience – typically trainee Community Health Workers from other organisations. During 2021, we hosted 27 interns.

Both Mimi and Lethu are completing their Masters research on various aspects of the Health Hubb, and Mimi hopes to begin her PhD journey this year.

SOCIETAL IMPACT IN 2021

Between April 2021 and March 2020, our learners provided health checks and health promotion for 30,130 Soweto community members. This was achieved by home visits and through supporting nine local Soweto primary care clinics during the pandemic. We also contributed blood pressure data to May Measurement Month, a global campaign to benchmark how well countries are achieving hypertension management, and gave health promotion talks in local schools covering issues such as sexual health and drug abuse.

OUR SUPPORTERS

The Health Hubb would not achieve this impact without the generous support and funding from Wits Health Consortium, the Great Leap Forward programme, DSI-NRF CoE Human Development and the Development Bank of Southern Africa (DBSA) social development investment team, alongside our research partners.

Wits Health HUBB

Wits Clinical Research

WHO WE ARE

Wits Clinical Research (WCR) is a leading clinical research facility that forms part of the Wits Health Consortium (WHC) group. We offer turn key clinical trials to all major pharmaceutical companies in most major medical disciplines. Whilst our focus in the past has been Oncology, our strategy is to diversify and offer our services in varied disciplines. Currently we operate from two major sites, namely Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Hospital (CHBH). Unfortunately due to a major fire at CMJAH we had to relocate operations to 31 Princess of Wales.

Due to the fire we also have a temporary site at Wits University Donald Gordon Medical Centre (WDGMC). These are temporary measures until we are able to find our new forever home.

Despite the various challenges during the Covid lockdown and the fire, we did well at retaining patients partaking in our long term trials. Staff worked long hours and overtime to successfully complete a Covid vaccine trial and 2 Covid treatment trials.

A highlight was the fact that we began Pediatric Oncology trials at CHBH.

DOCTOR AYSHA BADAT

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Annual Review 2021

We are privileged to work with many Principle Investigators that have served us well over many years. Unfortunately we had to bid farewell to one, Prof Moosa Patel as the Head of Hematology at CHBH, with whom we had numerous Haematology trials over the years.

We will continue to grow our clinical trial portfolio over the next years and strengthen our professional and quality reputation with our many sponsors. we also look expanding into more provinces in the near future.

Wits Clinical Research

Ezintsha
INVESTIGATE INNOVATE ADVANCE

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WHO WE ARE

Ezintsha works to improve aspects of health care in the public sector, with a particular focus on treatment optimisation, drug access and medical technologies in the areas of HIV and non-communicable diseases (NCDs). Based on our experience, and expertise, we aim to find ways to move the needle on global health. As a result, what we learn informs public health policy and practice in South Africa, the Southern African region, and in other parts of the world.

RESEARCH HIGHLIGHTS IN 2021

Ezintsha continues to lead the ADVANCE study, which has informed international and local HIV treatment guidelines. The study, conducted in inner-city Johannesburg, enrolled 1053 participants into three treatment arms in order to investigate better options for first-line treatment for people living with HIV, and specifically analysed the (at the time) standard treatment regimen of tenofovir disoproxil fumarate (TDF), emtricitabine (FTC) and efavirenz (EFV), also known as TEE, to two newer antiretrovirals, namely dolutegravir (DTG), which replaces EFV, and tenofovir alafenamide (TAF), which replaces TDF.

The newer regimens have been shown in other studies to have side effect and resistance benefits, but had not been studied in an African population.

In 2019, the 48-week outcome results were published in the New England Journal of Medicine (NEJM). In 2020, the 96-week data was published in The Lancet HIV. The study showed that a dolutegravir-containing antiretroviral treatment (ART) performs as well as the efavirenz-containing regimens, with the dolutegravir arms achieving rapid suppression of the virus.

The study has also established that the newer antiretrovirals, DTG and TAF, especially when used in combination, cause weight gain, particularly among African women.

The weight gain signal has emerged as a major concern in the treatment of HIV-positive people, and may be the major long-term clinical challenge in this population. As a result, the study was extended to 192 weeks in order to gather additional data. In addition, the TRIO project began, which will include data from two other trials, NAMSAL and DolPHIN-2, in an analysis in order to compare results. This exercise will be completed in 2022.

In 2021, we continued our work on HIV treatment optimisation, evaluating several novel antiretroviral agents in clinical trials in local populations, including beginning to assess the feasibility of long-acting injectables. With the emergence of the COVID-19 epidemic, the division urgently undertook evaluations of prevention and treatment options for SARS-CoV-2, as well as using our diagnostics team to evaluate COVID-19 self-testing.

Ezintsha has a long-term portfolio of work relating to non-communicable disease and HIV self-care, and the use of medical technologies and diagnostics. We have continued to lead the South African initiative in HIV self-testing, ensuring that tests on the market in South Africa are well regulated, user-friendly and of appropriate quality. Representation on the technical working groups of the WHO and the South African National Department of Health for HIV Self-testing has meant Ezintsha researchers are at the coal-face of shaping national and global regulation and policy.

Digital Health (or mHealth) tools have been the cornerstone of the innovation within the division and have been central to the access to, and optimisation of, these medical technologies. Ezintsha implemented behavioural studies to understand South Africans' experiences during the COVID-19 pandemic. These comprised using digital health platforms to assess early stage adherence and COVID compliance, and, technology behaviour and health communication. Ezintsha also collaborated with PRICELESS SA on two studies, one pertaining to food security, and the other measuring health opportunity costs of COVID-19 on non-COVID-19 health services.

Ezintsha, in collaboration with University Medical Centre Utrecht, Emory University and Harvard University, was awarded a five-year grant from the NIH's National Heart, Lung, and Blood Institute (NHLBI) and Fogarty International Center (FIC) for the Integrating HIV and hEART health in South Africa (iHEART-SA) project.

This project is highly significant for South Africa. Comparatively, South Africa has a successful HIVprogramme. However, there are shortfalls in healthcare for cardiovascular disease (CVD).People with HIV bear at least twice the risk of CVD compared to HIV-negative adults. Through iHEART-SA, the project team hopes to strengthen clinical care and data capacity and research and training by providing implementation science and epidemiology short courses and multiple doctoral fellowship opportunities. Self-management of hypertension and diabetes will also feature, which is pivotal to adherence, particularly in a pandemic, where access to and provision of care is compromised.

Under the leadership of multiple Principal Investigators Profs Francois Venter (Ezintsha (Wits)), Mohammed Ali (Emory University) and Vincent Marconi (Emory University), and led locally by Dr Samanta Lalla-Edward, the iHEART-SA team will implement and evaluate clinical and data interventions which will be co-designed with relevant local and international stakeholders. These interventions are being initially implemented in the Johannesburg inner city and scaled up to rural KwaZulu-Natal.

ACADEMIC OUTPUT

Ezintsha has a total team of around 90. There were 7 masters, 1 doctoral, and 2 honours students registered in 2021. A joint doctoral programme is being run with Utrecht University as part of the iHEART-SA programme. 12 Ezintsha team members were studying in the period under reivew, and were supported with Ezintsha study assistance grants. Core training and development session topics included research methodology, NiMART, academic writing, systematic review, and big data. Ezintsha produced 45 peer reviewed publications, many of which featured in high impact journals such as The Lancet, and PLoS. 24 members of the Ezintsha team were named authors.

OUR SENIOR TEAM

Ezintsha is led by a group of South African academics and health professionals, headed by Professor WD

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Francois Venter, MD, FCP, PhD., working alongside:

Dr Nomathemba Chandiwana, Principal Scientist; Dr Samanta Lalla-Edward, Head of Research Development; Mary Edwards, Head of Funding; Holly Fee, Head of Strategic Development Mohammed Majam, Head of Medical Technologies; Nkuli Mashabane, Head of Strategic Research Operations; Dr Simiso Sokhela, Head of Clinical Research;

In 2021, our colleague and friend Celicia Serenata, Head of Treament Optimisation & Drug Access, passed away. She is greatly missed.

Ezintsha
INVESTIGATE INNOVATE ADVANCE

WRIM

PROFESSOR LIZETTE KOEKEMOER

EXECUTIVE DIRECTOR

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WHO WE ARE

The Wits Medical Entomology Research Group (MERG) investigates the transmission and control of malaria in African mosquito populations and is affiliated to the Wits Research Institute for Malaria and the National Institute for Communicable Diseases.

The Medical Entomology Research Group consists of researchers specializing in medical entomology and especially those insect species that transmit disease-causing pathogens to humans.

Our team is made up of leading international researchers, professors and up-coming scientists.

RESEARCH RESEARCH IN 2021

During 2021 the MERG published 33 scientific papers in peer reviewed international journals, and one book chapter. Various research projects were successfully initiated or completed under the leadership of senior scientists. MERG supervised 29 post-graduate students during this reporting period.

TRANSMISSION BLOCKING STUDIES TO IDENTIFY NEW TARGET DRUGS FOR MALARIA (PROF LIZETTE KOEKEMOER)

The Drug Discovery and Development Centre (H3D) at the University of Cape Town (UCT), in collaboration with the Medicines for Malaria Venture (MMV), and the

South African Malaria Transmission-Blocking Consortium (SAMTC), has had a successful track record, over the last several years, of delivering lead compounds for potential treatment of malaria. The MERG provided vital support in evaluating the reduction in transmisison to main African malaria vector species through a standard membrane feeding assay. The South African Malaria Drug Discovery (SAMDD) project aims to identify antimalarial compounds that have a sexual blood stage (TCP 1) and transmission-blocking (TCP 5) activity against Plasmodium sexual stages and the mosquito.

CHALLENGES WITH COLONIZATION OF THE MAJOR AFRICAN MALARIA VECTOR SPECIES, AN. FUNESTUS (PROF LIZETTE KOEKEMOER)

Anopheles funestus is a major malaria vector in Africa, yet it tends to be refractory to colonisation, limiting research on this species. MERG collaborated with the Ifikara Health Institute in Tanzania on a Bill & Melinda Gates funded project.

MOLECULAR IDENTIFICATION OF MALARIA VECTORS FROM MALI, MOZAMBIQUE, ANGOLA AND ZAMBIA (PROF LIZETTE KOEKEMOER)

Malaria vector species are often morphologically similar and molecular identification is imperative to distinguish between vector and non-vector species. Most African countries lack the facilities to conduct these assays and the MERG is therefore vital in providing support for vector incrimination to guide country-specific vector control programs.

INSECTICIDE RESISTANCE ANALYSIS IN ZAMBIA (PROF MAUREEN COETZEE)

International Centre of Excellence in Malaria Research (ICEMR): lead by the Johns Hopkins Malaria Research Institute (USA), carrying out surveillance for insecticide resistance in Zambia (2017-2023).

ADVANCE STUDIES OF THE STERILE INSECT TECHNIQUE TO CONTROL OUTDOOR BITING MALARIA VECTORS (DR GIVEMORE MUNHENGA)

This is a multi-instituitional funded long-term project to test the feasibility of using the Sterile Insect Technique (SIT) against mosquito malaria vectors in the local context. Current activities include studies to optimise adult sterile male mosquito rearing in preparation of a small-scale pilot field demonstration. This will address technical and operational applicability of the technology under a South African setting. These optimisations included validation of mass-rearing equipment, sex separation strategies, and bulk irradiation protocols. Further more, the team developed a quality assurance system to be used during mosquito mass production. Conditions suitable for handling, transport and release of sterile males are also under investigation. An extensive community engagement to prepare the community for pending sterile male releases was also carried out during 2021. International Atomic Energy Agency, Department of Science and Innovation, National Research Foundation and University of Glasgow jointly fund these activities.

VECTOR STUDIES IN SOUTH AFRICA AND ZIMBABWE (DR GIVEMORE MUNHENGA)

This project is a multi-county research initiative sponsored by Bill and Melinda Gates Foundation. The research activities include investigating genetic variability in relation to anthropophilic behaviour of An. arabiensis populations from South Africa and Zimbabwe.

MOSQUITO SAMPLING TECHNIQUES EVALUATION (DR GIVEMORE MUNHENGA)

This is an operational research project in Mpumalanga comparing novel mosquito sampling methods against traditional sampling techniques in a field setting.

IDENTIFYING THE ENTOMOLOGICAL DRIVERS OF MALARIA TRANSMISSION IN SOUTH AFRICA (PROF BASIL BROOKE)

NHLS Research Trust sponsored project designed to use surveillance techniques to better understand the dynamics of malaria transmission in South Africa.

WHO MULTI-CENTRE STUDY ON DETERMINATION OF INSECTICIDE DISCRIMINATING CONCENTRATIONS FOR MONITORING OF RESISTANCE IN MOSQUITOES (PROF BASIL BROOKE)

Sponsored by WHO, this project aims to design discriminating dosages for assessing insecticide resistance in pathogen-transmitting mosquitoes investigated, including how this changes the epigenetic landscape of these mosquitoes. The role of gut bacteria and its impact on insecticide resistance is also under investigation.

LIST OF FUNDERS

B&M Gates Foundation International Atomic Energy Agency Department of Science and Technology National Institute of Health National Research Foundation
South African Medical Research Foundation
National Health Laboratory Service Research Trust World Health Organization.

Prof Maureen Coetzee is the founder of the Medical Entomology Research Group and was the first syndicate head.

MENTORSHIPS IN 2021

In 2021 MERG actively supported post graduate emerging researchers. Several PhD and MSc candidates were provided with mentorship during their studies.

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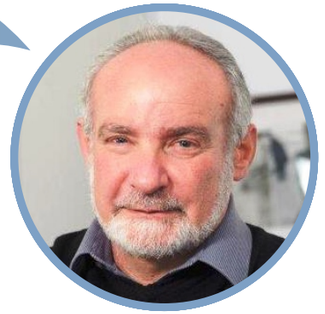
STAFFING IN 2021

MERG consists of three scientists with international standing, four scientists with significant national standing and a number of upcoming junior scientists and research assistants/technicians.

WRIM

30 Years AGINCOURT



WHO WE ARE

Established in 1992 with a focus on underserved rural communities, the MRC/Wits Agincourt Research Unit strives to address the complex 'transitional' nature of health and development challenges confronting South and sub-Saharan Africa. While the intensity of AIDS-related mortality has abated given widespread take-up of antiretroviral therapy, the imperative to understand and respond to interacting chronic infectious and non-communicable disease epidemics – and the ensuing multi-morbidities – provokes vital areas of enquiry:

- An ageing population invites questions about the meaning of 'a long and healthy life for all' in South Africa today.
- The vulnerabilities and potential of adolescent and young adult years speak to the promise of the next generation and the perils if health and social systems fall short.
- New technologies enable genomic, digitally-based and patient-oriented clinical research that until recently were the preserve of high-income societies – yet whether these can meaningfully impact health care in resource-poor settings is an open question.

PROFESSOR STEPHEN TOLLMAN

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INTRODUCTION

Situated in resource-poor rural environments, the MRC/Wits-Agincourt Research Unit undertakes population-based health research to elucidate causal pathways, test interventions at key developmental stages across the life-course, inform health and social systems, and strengthen evidence to guide policy and programmes. This is facilitated by the health and socio-demographic surveillance system (HDSS) platform, that covers a whole population cohort of ~116,000 persons in 31 adjacent villages, and which involves ongoing monitoring of all births, deaths and in and out-migrations. This population data is linked to clinic and hospital records. Together, this provides an exceptional longitudinal platform for observational and intervention research along the life course, with special focus on children (respiratory infections, mortality), adolescents (HIV/AIDS, depression, NCD risk) and older adults (multi-morbidity, cognitive change). Focus on socio-environmental exposures (education, labour migration, socioeconomic status, natural resources, food security) interacts with emphasis on behaviour and physiological risk.

RESEARCH HIGHLIGHTS IN 2021

The Unit's COVID-19 response, rapidly initiated in 2020, was sustained through 2021 making full use of the research platform and infrastructure. By adding a COVID module to the health and socio-demographic surveillance system (HDSS), capitalising on the HDSS-clinic-hospital link and SAPRIN network, and conducting studies with key partners, we have illuminated facets of the pandemic in rural communities:

- COVID screening module (added to HDSS update rounds): spectrum of illness, risks and comorbidities; non-pharmaceutical interventions
- Prospective household study of SARS-CoV-2, transmission dynamics and viral interaction (PHIRST-C): extent and transmission of SARS-CoV-2, including asymptomatic infection.
- Social-behavioural-economic survey: impact of lockdown and post lockdown on rural communities; understanding of barriers to vaccine uptake
- Measuring unanticipated opportunity costs of South Africa's COVID-19 response for children, mothers and people living with non-communicable diseases (MOCCA): burden of COVID-19 on clinic and hospital utilisation
- Extending the ageing (HAALSI) cohort to address long-term cognitive impacts and introducing a COVID-19 serosurvey

The MRC/Wits-Agincourt Research Unit is leading a **multicentre study to determine Excess Mortality in sub-Saharan Africa & South Asia.** Funded by the Bill and Melinda Gates Foundation, USA, this study aims to characterise all-cause and cause-specific (using verbal autopsy data) mortality rates and trends, by age and sex, across a range of rural and urban sub-Saharan African and South Asian settings under continuous health and demographic surveillance. In these settings, verbal autopsy interviews are conducted with people who were present at someone's death to elicit information to assist with determining the cause of death as part of the comprehensive and rigorous mortality surveillance.

To-date, 19 research sites/centres have contributed data. The project data will generate:

- Empirically derived, comparable mortality trends 2015-2019 across all age-sex groups
- Empirically derived mortality rates for 2020 compared with 2015-2019 rates
- Prospective mortality follow-up throughout 2021 monitoring the impact of COVID-19 on mortality trends and rates across age-sex groups.
- Publicly accessible datasets that can provide a clearer picture of pandemic impact on mortality trends / excess mortality across age-sex groups contributing to national, regional and comparative understanding.

RESEARCH COLLABORATORS

- Southern Africa: South African Population Research Infrastructure Network (SAPRIN); Africa Health Research Institute (AHRI), KwaZulu-Natal; DIMAMO Population Health Research Centre, Limpopo; Soweto CHAMPS, Gauteng; Manhica Health Research Centre (Mozambique) .
- East Africa: African Population and Health Research Centre (APHRC) (Kenya); Kaloleni/Rabai (Kenya); Iganga-Mayuge (Uganda); Magu (Tanzania); MEIRU/Karonga (Malawi) Siaya HDSS (Kenya); Manyatta HDSS (Kenya); Kersa (Kenya).
- West Africa: Navronga (Ghana); Nanora (Burkina Faso).
- South Asia: International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) (Bangladesh); Matlab (Bangladesh); Dhaka (Bangladesh); Chakaria (Bangladesh); KEM Hospital (Vadu HDSS) (India); Ballabgargh (India). and introducing a COVID-19 serosurvey

The **COVID-19 lockdown impact on lifestyle behaviours, mental health and sleep patterns in South Africa** study aims to assess the impact of lockdown in response to the COVID-19 pandemic on routine-oriented lifestyle behaviours and symptoms of depression, anxiety, and insomnia in South Africans. Comparisons were made between males and females, and students and non-students. We conducted an online survey on work, exercise, screen, alcohol, caffeine and sleep behaviours; and depression, anxiety, and insomnia before and during lockdown.

Research collaborators: Department of Human

Kinetics and Ergonomics, Rhodes University; Brain Function Research Group, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand; Division of Exercise Science and Sports Medicine, Department of Human Biology, Faculty of Health Sciences, University of Cape Town; Department of Family Medicine, Faculty of Health Sciences, University of the Witwatersrand; UCT Sleep Sciences and Applied Cognitive Science and Experimental Neuropsychology Team (ACSENT), Department of Psychology, University of Cape Town.

In late 2021, national COVID-19 lockdown regulations began to ease such that paused field studies could be resumed.

The **Know your Numbers** study which aims to establish whether screening for hypertension in queues of persons ≥60 years who are receiving SA government Older Persons Grants decreases blood pressure in this population. Prevalence of hypertension in this age group in the queues is high (individuals with elevated blood pressure are referred for care). Qualitative data shows that the intervention is well accepted by pensioners. Final study findings will determine whether the intervention has reduced the mean blood pressure of the intervention queues, and will provide key input on the need for a full trial on the effectiveness of community-based screening for hypertension and referral to primary health care facilities.

Research collaboration with 3 SAMRC intramural Units: Alcohol, Tobacco and other Drugs Research Unit; Non-Communicable Diseases Research Unit; Biostatistics Unit.

The study, **Engaging male partners in antenatal care in rural South Africa** aims to test ways of identifying men who are willing and able to contribute to their partner's antenatal care (ANC) and furthermore, identify the best ways of reaching out to these men. Pilot work has highlighted limited interaction by men with ANC care and our hope is that by supporting male partners, we can improve outcomes for mother and baby.

Research collaborator: Vanderbilt University, Nashville USA.

The project, **Cumulative socioeconomic exposures, cash transfer interventions, and later-life cognitive decline and dementia risk in a low-income region of South Africa** will provide proof-of-concept for socioeconomic interventions as a viable prevention strategy for Alzheimer's disease and related dementias (ADRD) in low-income settings vulnerable to the global ADRD epidemic.
Research collaborators: Indiana University School of Public Health, Indiana, USA; Center for Social Epidemiology and Population Health, Department of Epidemiology, University of Michigan School of Public Health, Michigan, US.

The **Social determinants of Parkinsonism in rural South Africa** pilot study aims to understand the prevalence and determinants of Parkinson's disease and Parkinsonism in a rapidly ageing, rural South African population. In doing so, we hope to develop and refine the tools necessary to identify and refer patients for care within the existing healthcare system.

Research collaborators: Barrow Neurological Institute, Phoenix, USA; Occupational Health, Wits School of Public Health, University of the Witwatersrand.

The research platform was reinvigorated by the launch of **Multimorbidity in Africa: Digital Innovation, Visualisation and Application (MADIVA)** research hub—funded by the National Institute of Health's (NIH) new Harnessing Data Science for Health Discovery and Innovation in Africa (DS-I Africa) program—which addresses the complex interplay, individual and public health challenges, and rising prevalence of multimorbidity in Africa through data science. It draws on the Unit's rich longitudinal health, population and epidemiological data sets, and growing clinical and laboratory records, and genomic data. The purpose is to develop data science techniques and solutions to tackle the problem of multiple co-occurring diseases significantly adding to the health burden in Africa. Data from the rural MRC/Wits-Agincourt Research Centre is complimented by data from the urban African Population & Health Research Center (APHRC), Nairobi, Kenya which has a long track record working in slum communities. Working also with colleagues from Sydney Brenner Institute for Molecular Bioscience and IBM Africa, study investigators develop and apply data science techniques to link the different data sets, build dashboards for different stakeholders and apply new machine learning techniques to automatically stratify populations for risk profiles to different diseases, including the use of polygenic risk scores.

Research collaborators: Sydney Brenner Institute for Molecular Bioscience, University of the Witwatersrand, Johannesburg, South Africa; IBM Research, Johannesburg, South Africa

PUBLICATIONS

In 2021, the MRC/Wits-Agincourt Research Unit produced over **130 peer-reviewed publications**, 18 of which were in journals with an impact factor of 10 or above. These include one in

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the Lancet, one in Lancet Infectious Diseases, five in Lancet Global Health, two in Lancet HIV, two in Nature Communications, three in PLoS Medicine, one in Age and Ageing, one in Sleep Med Reviews, one in Annals of Surgery, and one in JAMA Pediatrics.

MENTORSHIPS

The MRC/Wits-Agincourt Research Unit approaches its activities and work with capacity building and mentorship for academic, administrative, and locally employed staff in mind.

The Unit has a data intern programme, and supervises/mentors doctoral students, postdoctoral fellows, early and mid-career researchers.

Additionally, staff in the Unit are co-leading the following formal mentorship programmes:

- an academic writing mentorship programme which provides peer support and mentorship to, and arranges weekly writing sessions for Project Managers, Data Analysts and early career researchers in the MRC/Wits-Agincourt Research Unit;
- an analytics team aimed at supporting post-docs and analysts to use existing data and newly produced data to expand the number of publications lead by members of the MRC/Wits-Agincourt Research Unit;
- The School of Public Health Career Development Committee which facilitates structured career mentoring and coaching for the career progression of academic and professional and administrative staff within the School of Public Health at Wits University.

STAFFING

New academic, scientific, and committee appointments

Mark Collinson

- Committee member, National Policy Data Observatory
- Committee member, National Migration and Urbanisation Forum

June Fabian

- Member, NICD Safety Committee for the Household transmission of SARS-CoV-2 from HIV-infected and HIV-uninfected adult index cases in South Africa - HTS Study

Professor Cheryl Cohen

- Member, NICD Safety Committee for the SARS-CoV-2 community burden and transmission in two South African communities - PHIRST-C Study (Principal Investigator: Professor Cheryl Cohen)

Carren Ginsburg

- Member, Scientific Committee for the National Forum for Migration and Urbanisation, Department of Social Development and Statistics
- Member, Steering Committee for the National Conference on Migration and Urbanisation

Xavier Gómez-Olivé

- Reviewer, African Research Initiative for Scientific Excellence, Pilot Programme (ARISE-PP)
- Expert reviewer, NIHR Global Health Policy Systems Research Programme

Kathleen Kahn

- Member, Scientific Advisory Group, Special Issue in Memory of Peter Byass. Global Health Action, Volume 14, Issue supp1 (2021)
- Member, World Health Organization Reference Group on Health Statistics (WHO RGHS) Task Force on Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) 2.0
- Member, Technical Committee for National Cause of Death Validation Study, South Africa
- Faculty Member, Harvard Centre for Population and Development Studies, Cambridge, USA

Tshegofatso Seabi

- Member, Scientific Committee 1st African and 2nd Nigerian conference on Adolescence and Youth Health and Development

Stephen Tollman

- Panel member, Concept Review Panel, National institute on Aging, NIH Division of Behavioral and Social Research
- Chair, NIHR-UK Review Panel, new research units
- Deputy Chair, NIHR-UK, new research group selections
- Member, Visiting Committee, London School of Hygiene and Tropical Medicine, UK
- Chair, Global Alliance for Chronic Disease (GACD) Joint Panel Review on Primary and Secondary Cancer Prevention in low-and middle-income countries. UKMRC, London
- Chair, 5-year (quinquennial) reviews of SA MRC intramural research units
- Board member, CDDEP: Centre for Disease Dynamics, Economics and Policy. Delhi and Washington
- Chair, Trial Steering Committee: Insika Yomama (PI A Stein), Oxford University and Africa Health Research Institute, KwaZulu-Natal
- Chair, Fellowships Selection Panel, Africa Research Excellence Fund (AREF), UK MRC
- Faculty Member, Harvard Centre for Population and Development Studies, Cambridge, MA
- Panelist, UK MRC/DfID African Research Leader

Scheme

Alisha Wade

- Academic Editor, Global Health, Epidemiology and Genomics
- Member, Patient Engagement Committee, Endocrine Society, USA
- Board member, Hi Hopes (an early intervention partner for families of deaf and hearing-impaired babies), South Africa

Ryan Wagner

- Member, Paediatric Project Task Force of the Global Advocacy Council, International League Against Epilepsy
- Member, Global Advocacy in Children Task Force, International League Against Epilepsy
- Secretary, Epidemiology Commission, International League Against Epilepsy
- Co-chair, Economic Burden of Epilepsy Task Force, International League Against Epilepsy

AWARDS AND RECOGNITION

In 2021, staff of the MRC/Wits Agincourt Research Unit received accolades from Wits University for their expedient and excellent COVID-19 response efforts.

Ngonidzashe Ngwarai received a 2021 Exceptional Service Award from the Faculty of Health Sciences, University of the Witwatersrand, for dedicated service to the MRC/Wits-Agincourt Research Unit for over 12 years, as well as leading the operational changes needed of the MRC/Wits-Agincourt Research Unit in response to the COVID-19 challenges. Ngoni implemented non-pharmaceutical safety measures and training to protect staff and research participants from contracting or transmitting COVID-19; sourced personal protective equipment (PPE) and sanitiser when this was scarce; expanded the existing call centre for telephonic surveillance; and implemented vaccine education when vaccines became available. Ngoni's actions, with foremost consideration for the safety of staff, fieldworkers, and research participants, ensured that the MRC/Wits-Agincourt Research Unit's high-quality research continued through the COVID-19 pandemic and varying lockdown levels, timeously contributing the rural component to the national COVID-19 response.

Dr Bianca Moffet was recognised as a Wits Hero for her volunteer work with the Hlayisekani Initiative, which she co-established to support the local Bushbuckridge communities through the COVID-19 epidemic. Outcomes of her efforts included:

- setting up a Back-a-Buddy online crowdfunding campaign, which within three months raised over R600,000 to purchase essential personal protective equipment (PPE) for staff of the local clinics and hospitals;
- securing donations of face shields, also for clinic and hospital staff;
- developing a COVID-19 “Clinic Package” to assist the clinics in the Agincourt subdistrict prepare for COVID-19 patient arrivals, screening, testing, initial management, referral as well as to build a stronger link to their referral hospitals;
- producing patient information leaflets in English and Xitsonga, health care worker training guidelines, screening tools and contact tracing tools for the 40 clinics and three district hospitals;
- training clinic staff on the new procedures and systems;
- coordinating volunteers in the building of an isolation ward at Tintswalo Hospital; and
- facilitating training workshops for local school principals and teachers for return to contact teaching.

Dr Jacques du Toit was also recognised as a Wits Hero for his services to Bushbuckridge health care services, delivering clarity of action and contextually-relevant planning and preparation to ready the district for COVID-19 whilst also bolstering the confidence of health workers. Jacques joined the Agincourt Research Unit as COVID-19 Response Advisor for Research and Development Strategy, and with Bianca and others, he co-established the Hlayisekani Initiative, and further participated on the Ehlanzeni District COVID-19 Outbreak Response committee.

With the Hlayisekani Initiative, Jacques was also responsible for the fundraising activities, coordination of COVID-19 training for clinic and hospital staff, and coordinating the building of an isolation ward at Tintswalo Hospital. He also developed the COVID-19 “Hospital Package” for staff training, and training materials. It included a District COVID-19 Handbook which was based on the National Institute for Communicable Diseases "Clinical Management" document but augmented and adapted to the local setting and available resources by

- providing a clear directive on how to manage confirmed/suspected cases - especially given many facilities would have had to keep high risk suspected COVID-19 patients whilst awaiting results (48-72 hour turn around) and prepare for when referral hospitals became saturated;
- addressing other key areas of hospital preparation – such as engaging with essential non-clinical services and preparing a "Surge Plan" to have systems in place to rapidly respond to a demand for increased admissions.
- expanding on infection prevention and control

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(IPC) policies, healthcare worker testing algorithms to limit staff shortages, as well as providing extensive standard operating procedures relating to IPC measures in different departments (e.g. radiographers without mobile machines, an approach to an isolation ward - to include cleaners etc).

On the Ehlanzeni District COVID-19 Outbreak Response committee, Jacques participated in

- district planning and decision making as well as content creation;
- co-creating, with the district Department of Health, locally adapted clinical guidelines, SOPs relating to COVID-19 and organisational systems for COVID-19 preparedness for district hospitals and clinics;
- implementation of systems in the Bushbuckridge subdistrict through building effective relationships with Hospital Management at Tintswalo, Matikwana, and Mapulaneng Hospitals, as well as with the Primary Health Care Coordinator of the Bushbuckridge subdistrict;
- forming a Tintswalo COVID-19 Outbreak Response Committee
- training of hospital and clinic staff in the correct use of PPE, COVID-19 testing techniques, IPC measures, and support of their facilities, and
- establishing data monitoring systems with local hospitals and clinics to quantify patient presentations, monitor PPE usage, and track patient results.

DEGREES AWARDED

Professional development is encouraged of staff at the MRC/Wits-Agincourt Research Unit and many staff are engaged in academic programmes. In 2021, three staff obtained higher degrees:

- June Fabian – PhD in Public Health
- Denny Mabetha – MSc in Epidemiology
- Morelearnings Sibanda – MSc in Epidemiology, in the field of Biostatistics (with distinction).

30 Years AGINCOURT

PHRU
IMPROVING LIFE THROUGH RESEARCH
Perinatal HIV Research Unit of the University of the Witwatersrand

WHO WE ARE

Perinatal HIV Research Institute (PHRU) is a large clinical research unit with capacity to conduct a range of observational and clinical trial studies in multiple research sites across South Africa. Although our primary research site remains Soweto after 23 years we also conduct clinical and community research in Gauteng, Limpopo, North West and Free State, provinces where we are growing capacity.

The Perinatal HIV Research Unit (PHRU) improves life through research.

PHRU's research scope spans HIV and TB prevention and treatment and has an emerging focus on mental and cognitive disorders, cancer and diabetes.

PROFESSOR NEIL MARTINSON

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WHO WE ARE

The Empilweni Services and Research Unit (ESRU), situated at Rahima Moosa Mother and Child Hospital in Johannesburg - South Africa, is comprised of a research clinic as well as a clinic offering routine services.

ESRU is made up of +-30 research staff including academic, administrative and technical staff. ESRU has been functioning as a research entity for the last 13 years, and has produced over 140 publications.

Whilst the unit started out with a focus on HIV it has increasingly acquired the skills and appetite for research in other areas such as Tuberculosis. The unit will actively encourage research into other childhood infectious diseases and infectious diseases in pregnant women.

With the unit seeing itself as being the 'home' of the Paediatric Infectious Disease Sub-specialty Training programme within the Department of Paediatrics and Child Health at Wits, the future looks set to ensure that there is a natural convergence of training, service and research within the site.

RESEARCH IN 2021

UBOMI Buhle

The primary purpose of this project is to establish a national pregnancy exposure registry (NPER) which will incorporate data collected and pooled from individual pregnancy exposure registries (PER) across three provinces in South Africa. The UBOMI BUHLE (Understanding Birth Outcomes from Mothers and Infants, Building Healthcare by Linking Exposures) project will initially focus on safety of antiretrovirals (ARVs) in pregnancy. Using a sentinel site approach, and relying almost exclusively on the robust collection of routine antenatal and perinatal clinical data this project aims to develop a system which is lean and sustainable by adopting a health systems strengthening approach at these sites. Consequently, there will be significant emphasis placed on capacity building activities throughout the course of the project.

The project is led by co-principal Investigators (PI) who are responsible for the coordination and oversight of protocol development, project design, project funding/implementation, and data collection, analysis and dissemination: Ushma C. Mehta, Pharm.D, DrPH - Centre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, University of Cape Town, South Africa and Lee Fairlie, MBChB, DCH (UK), FC Paeds (SA), MMED (Wits) - Wits Reproductive Health and HIV Institute, South Africa.

ESRU's role is to lead the recruitment in one of three Gauteng hubs from clinics feeding to the Rahima Moosa Mother and Child Hospital where ESRU is based.

Enrolment formally commenced in July 2021. The project promises to hold many academic opportunities and avenues to assist Gauteng Department of Health and the City of Johannesburg to improve service delivery since capacity building is an important component of the project.

Anova - APACE project

ESRU is a sub-recipient of USAID funding under Anova Health Institute NPC. As a sub-awardee ESRU's roles includes the following aspects: Provide comprehensive HIV and ART services to support progress towards 909090 including the following: HIV prevention interventions; HIV testing; Linkage to care of all identified in need of ART; On-site ART initiation; Neonatal care (<1m) diagnosed PCR-positive and other complex clinical cases; Paediatric, adolescent and caregiver ART management as per current guidelines for all clients attending Empilweni clinic; Profiling of children identified and/or initiated on ART at RMMCH; Adolescent and Youth Friendly Services provision; Best practice development and dissemination in paediatric and

adolescent are; Children, mental health screening, differentiated care models for children and young adolescents; Staff development.

Essentially the project can be summarised as contributing towards building a paediatric centre of excellence in terms of HIV and TB management at Rahima Moosa Mother and Child Hospital. It is not a research project but rather one of technical support and service provision. The project highlights include the establishment of a robust adolescent mental health service, integration of the high risk antenatal HIV clinic and extensive training provided to doctors and nurses passing through the HIV clinic at Rahima Moosa Hospital.

IeDEA-SA Collaboration
The IeDEA project is also known as the

"COHORT STUDY OF HIV-INFECTED AND EXPOSED CHILDREN RECEIVING CARE AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL SUPPORTED BY THE EMPILWENI SERVICES AND RESEARCH UNIT AND PARTICIPATION IN THE INTERNATIONAL EPIDEMIOLOGICAL DATABASES TO EVALUATE AIDS (IeDEA) COLLABORATION"

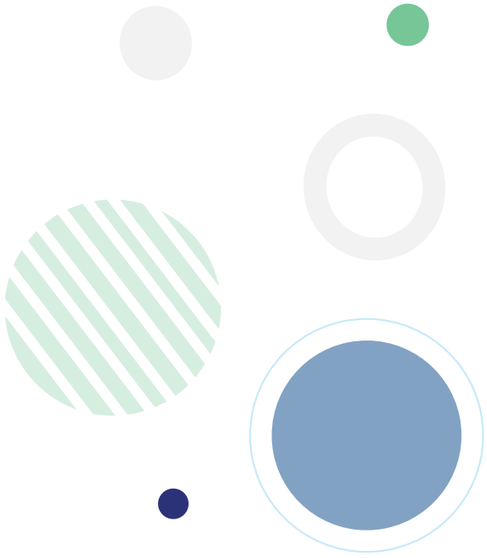
The collaboration has been very successful in terms of contributing to the knowledge around paediatric HIV related care and treatment outcomes. Since its advent, the collaboration has been expanded to provide a platform for data sharing around the issues like TB co-infection and HIV-exposure and prevention of HIV transmission from mother to child. These aspects have been included in the original work following amendments to the original protocol. Multiple publications have emerged over the years and the data platform has enabled the support of many post-graduate students (especially MMeds).

Falling under the IeDEA collaboration is an exciting sub-study known as: **Rahima Moosa Mother and Children's hospital and Adolescent and Young Adult Network of IeDEA (AYANI)**. It aims to investigate how care transitions, key co-morbidities and conditions, mental health challenges, and social environment factors impact the outcomes of ART adherence, viral suppression, care engagement, and mortality among adolescents living with HIV (ALWH). To achieve this we are in the process of enrolling 50 adolescents living with HIV, ages 15-24 years, representing a combination of youth with perinatally and non-perinatally acquired HIV, from Empilweni Clinic, at Rahima Moosa Mother and Children's Hospital, to contribute to the cohort of >300 created by the 6 global regions of IeDEA.

KEY FUNDERS IN 2021
US National Institutes of Health, Bill and Melinda Gates Foundation, Centres for Disease Control and Prevention (USA), USAID/PEPfAR.

MENTORSHIPS IN 2021
The Division supported several post-graduate students in 2021.

STAFFING IN 2021
ESRU supported 19 staff members in various roles including doctors, nurses, data capturers, counselors and project coordinators which work collaboratively in running the projects.



Annual Review 2021

Renal Research Group
The Kidney Fund

WHO WE ARE
An entity to support research on kidney disease.

INFORMATION FOR 2021

NATIONAL/ INTERNATIONAL COM-MITTEES International Society of Nephrology
Executive Committee Member,
Awards Committee Member,
ISN Africa Regional Committee Steering Committee Member,
Emerging Leaders Program Chair Scientific Program Committee, Frontiers in Nephrology Conference

African Association of Nephrology
Board of Trustees/ Council Member

SA Nephrology Society
Council member

Wits University Committees
Faculty Graduate Studies Committee
Executive Committee Member

School of Clinical Medicine
Chair, Graduate Studies & Research Committee
Chair, Plagiarism Committee
Chair, Mentorship Programme

National Kidney Foundation of SA
Member of selection committee for research awards

Journals
Associate Editor
African Journal of Nephrology
Wits Journal of Clinical Medicine

International Advisory Board of Nature Reviews Nephrology

PROFESSOR SARALADEVI NAICKER
HEAD OF DEPARTMENT

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CONFERENCES AND WEBINARS
World Congress of Nephrology, Montreal, April 2021
The Triumphs and Challenges for an African Nephrologist

International Nephrotic Syndrome Research Meeting, Bristol, 11 March 2021
NephroS - the South African Perspective

UK Kidney Week- June 2021
Plenary lecture: HIV & Kidney Disease

Kenya Renal Association, Sept 2021:
Requirements for implementation of a deceased donor program in an African setting

AFRAN Congress, Abidjan December 2021
- Inaugural/plenary lecture: Inaugural lecture: kidney diseases … the following epidemic in Africa
- Kidney involvement in COVID-19
- AFRAN-ISN Advocacy Round Table. Epidemic CKD situation now and in the coming years

African Association of Nephrology YNC webinar, January 2021
Estimation of GFR in Sub-saharan Africa an appraisal of the performance of existing equations

Transplant Association of Nigeria webinar, Nov 2021
Challenges and requirements for implementation of a deceased donor program in Africa.

AFRAN YNC webinar, Oct 2021
Basics of Research Methodology

African Health Network webinar series
- June 2021: A personal Odyssey in nephrology: And the future of patient care, teaching and research in Africa
- Nov 2021: Recognizing the impact of HIV on the Kidney

STUDENT SUPERVISION
Degrees awarded in 2021
- Dr Aliyu Abdu. PhD 2021. Prevalence, histological patterns and genetic variations of chronic kidney disease among HIV infected patients in Kano, Nigeria
- Dr June Fabian. PhD 2021. Prevalence and characterisation of chronic kidney disease in a rural setting in South Africa

On-going
- Prof U Kala. PhD. The Spectrum of Nephrotic Syndrome in Black African Children at Chris Hani Baragwanath Academic Hospital 1982-2017
- Dr Alfred Meremo. PhD. Role of novel biomarkers in prediction of kidney disease progression and death among black chronic kidney disease patients in South Africa.
- Prof Graham Paget. PhD. Pathogenesis of idiopathic nephrotic syndrome – a maladaptive response to Epstein Barr virus infection?

PUBLICATIONS FOR 2021

Naicker S. Nephrology education and training in Africa. Nat Rev Nephrol. 2021 Dec;17(12):784. doi: 10.1038/s41581-021-00486-4. PMID: 34471262.

Bamgboye EL, Omiye JA, Afolaranmi OJ, Davids MR, Tannor EK, Wadee S, Niang A, Were A, Naicker S. COVID-19 Pandemic: Is Africa Different? J Natl Med Assoc. 2021 Jun;113(3):324-335. doi: 10.1016/j.jnma.2020.10.001. Epub 2020 Nov 3. PMID: 33153755; PMCID: PMC7607238.

Reform of research funding processes could pave the way for progress in global health. Ashuntantang G, Luyckx V, Naicker S, Venkatapuram S.
Lancet Glob Health. 2021 Aug;9(8):e1053-e1054. doi: 10.1016/S2214-109X(21)00207-2. PMID: 34297952

Histopathological Pattern of Kidney Diseases Among HIV-Infected Treatment-Naïve Patients in Kano, Nigeria. Abdu A, Atanda A, Bala SM, Ademola B, Nalado A, Obiagwu P, Duarte R, Naicker S. Int J Nephrol Renovasc Dis. 2021 May 18;14:143-148. doi: 10.2147/IJNRD.S304341. eCollection 2021. PMID: 34040416

Profiling Biomarkers in HIV Glomerular Disease - Potential for the Non-Invasive Diagnosis of HIVAN?Naicker S, Dix-Peek T, Klar RM, Kalunga G, Mosiane P, Dickens C, Duarte R. Int J Nephrol Renovasc Dis. 2021 Dec 8;14:427-440. doi: 10.2147/IJNRD.S331484. eCollection 2021. PMID: 34916827

Scope and heterogeneity of outcomes reported in randomized trials in patients receiving peritoneal dialysis. Manera KE, Johnson DW, Cho Y, Sautenet B, Shen J, Kelly A, Yee-Moon Wang A, Brown EA, Brunier G, Perl J, Dong J, Wilkie M, Mehrotra R, Pecoits-Filho R, Naicker S, Dunning T, Craig JC, Tong A. Clin Kidney J. 2020 Dec 31;14(7):1817-1825. doi: 10.1093/ckj/sfaa224. eCollection 2021 Jul. PMID: 34221389

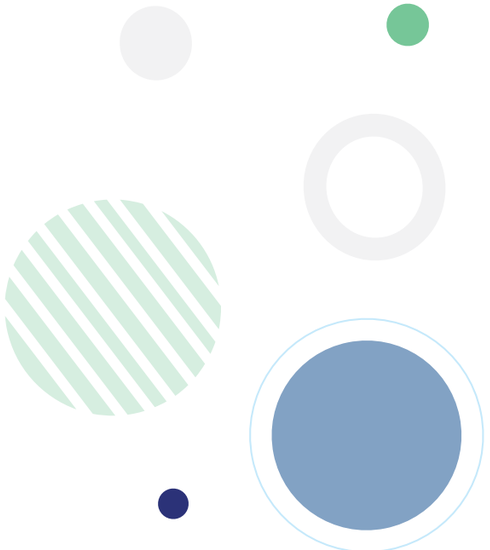
A cohort study of the relationship between anaemia, mean corpuscular volume and mortality among a CKD population in South Africa. Nalado A, Waziri B, Olorunfemi G, Mahlangu J, Paget G, Duarte R, Naicker S. Afr Health Sci. 2021 Dec;21(4):1764-1775. doi: 10.4314/ahs.v21i4.33. PMID: 35283988

Acute Interstitial Nephritis in Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome. Do Vale CL, Naicker S, Lippincott CK.Kidney Int Rep. 2021 Dec 13;7(4):920-923. doi: 10.1016/j.ekir.2021.12.008. eCollection 2022 Apr. PMID: 35497785

Societal Impact

While there is no immediate societal impact of the syndicate, the research projects are based on community needs and attempt to answer relevant questions; the long term impact cannot be quantified at this stage. However, assisting in completion of PhD projects certainly assists in upskilling individuals who would then be able to transfer skills and embark on independent research of their own.

Renal Research Group
The Kidney Fund



NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

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WHO WE ARE

The Mycology Division aims to improve the outcomes of people affected by serious, life-threatening fungal diseases in South Africa and the African region through public health-focused epidemiological, clinical and basic science research and innovation. Our work also stretches to other important infectious diseases.

The Mycology Division was established in 2016 and is affiliated to the School of Pathology in the Faculty of Health Sciences, University of the Witwatersrand and to the Centre for Healthcare-Associated Infections Antimicrobial Resistance and Mycoses at the National Institute for Communicable Diseases.

The Division was initially established to support grant-funded investigator and studentled projects.

RESEARCH IN 2021 CAST-NET

The CAST-NET study is a multi-year observational programmatic study that sought to evaluate the effectiveness of South Africa's national cryptococcal antigen (CRAG) screening and pre-emptive treatment programme, in order to improve HIV care and survival of persons living with advanced HIV disease. This project is supported by an NIH R01 grant (2016-2022); PI: NP Govender.

In Part 1, we conducted a retrospective cohort study of approximately 3000 CRAG-positive participants (who screened positive in 2017-2019 in 27 sub-districts) and used retrospective record review and several other routine data sources to document the clinical care of participants and their 6-month outcomes. The Division partnered with Epicentre Health Research to collect data at facilities. A team of medical officers in the Division completed data abstraction for just over 2000 patient records.

Part 2 of the CAST-NET study, implemented for 6-months during 2021 consisted of a pragmatic cluster-randomized trial, with the aim of assessing whether a health systems intervention at healthcare facility level (mediated through informal appointment of a "Crypto Champion" at each facility could improve follow-up and initiation of pre-emptive fluconazole therapy among newly-diagnosed persons with antigenaemia. We also compared 6-month cryptococcal meningitis-free survival among people with antigenaemia at intervention versus control facilities.

PrE-AIM

The Process Evaluation Assessing Implementation and Mechanisms (PrE-AIM) study was a mixed-methods process evaluation nested within the CAST-NET study and was designed to understand how South Africa's national CRAG screening programme was implemented and incorporated into routine HIV care. The mixed-methods approach used quantitative surveys and qualitative in-depth interviews to collect data on health facility processes, healthcare worker experiences, and other contextual factors with the aim of better understanding how differences in CRAG screening implementation and adoption affected provider action on positive CRAG test results. Healthcare worker surveys were conducted at around 400 health facilities participating in the CAST-NET study, and key findings were explored in greater detail through in-depth interviews and observations in 6 purposively-selected sub-districts. The findings from this sub-study will provide context to the results of the CAST-NET study and will inform possible areas for improvement of the national screening programme in the future.

Baby GERMS

Neonatal deaths account for almost half of deaths in children under 5 years, with infections being the third largest contributor after prematurity and intrapartum complications. Baby GERMS is the first population-based surveillance programme on neonatal infections in Africa and was set up in the latter half of 2019 with funding from the Bill and Melinda Gates Foundation (BMGF). The aim was to provide a baseline description of the aetiology, antimicrobial susceptibility and clinical characteristics of culture-confirmed neonatal bloodstream infections and meningitis in South Africa. Through this surveillance programme, we aimed to identify modi fiable risk factors which could be targeted to reduce neonatal morbidity and mortality. Baby GERMS has been acknowledged as a major new source of strategic data by the National Neonatal Task.

Force was launched in September 2019 to provide technical advice and guidance on surveillance for neonatal sepsis, infection prevention and control, neonatal infection case management, antimicrobial stewardship and containment of neonatal unit outbreaks. In 2021, data from approximately 45 000 laboratory-confirmed cases of neonatal meningitis and blood stream infections were collated and analysed and a publication was submitted to Lancet Global Health. This analysis was shared with stakeholders from the National Department of Health to inform neonatal sepsis prevention guidelines. Isolates collected from 933 episodes of laboratory-confirmed neonatal meningitis and blood stream infections occurring at 6 provincial/regional hospitals between October 2019 and September 2020 underwent further genotypic and phenotypic analysis and results on the numerous Klebsiella pneumoniae infections have been shared with KlebNET, an international group looking at global genomics of Klebsiella K-loci. Aspects of the sentinel surveillance data were shared at the International Symposium on Streptococcus Agalactiae Disease (ISSAD) and the World Symposium on Paediatric Infectious Diseases (WSPID).

DATCOV

In March 2020, DATCOV, a national surveillance system, was established by NICD to monitor COVID-19 hospital admissions in South Africa. While achieving complete coverage of all public and private hospitals in the country, DATCOV had challenges with data completeness and data quality. The Division therefore established an enhanced sentinel surveillance project, funded by the BMGF, in collaboration with the International Severe Acute Respiratory and Emerging Infections Consortium. The first objective of this project was to understand the contribution of NCDs, HIV, and TB to COVID-19 mortality. Seventeen study sites were selected in six provinces, and COVID-19 patients were enrolled during the second (and subsequent waves) of the epidemic in South Africa. An interim analysis has revealed the prevalence of pre-existing, newly diagnosed or undiagnosed co-morbidities, their level of control and their impact on mortality.

FUNGAL GENOMIC SURVEILLANCE

This is a multi-year initiative which seeks to improve fungal disease surveillance in the southern African region by building epidemiology, laboratory and bioinformatics capacity for invasive fungal diseases and outbreaks caused by known, re-emerging and new pathogens. From September through to December 2021, we worked on setting up a regional network by approaching the Africa CDC and Southern African Regional Collaborating Centre (RCC) to support the project, and assist in identifying and/or providing contact details of relevant authorities in the target countries.

EFFECT TRIAL

The EFFECT trial is a multi-centre Phase III study at 11 sites: 3 in Tanzania and 8 in South Africa, sponsored by St George's University of London, and coordinated by WHC. The study will determine if a combination of fluconazole plus flucytosine, is superior to fluconazole alone (current standard of care) for the treatment of HIV-associated cryptococcal antigenaemia. Ethics and SAHPRA approvals were obtained in mid-2021 but due to a number of delays including some related to the ongoing COVID pandemic, as of December 2021, the trial had not opened to recruitment. The trial is set to start recruiting the first participants in Q2 2022.

KEY FUNDERS IN 2021

US National Institutes of Health
US Centers for Disease Control and Prevention
UK Medical Research Council
Bill and Melinda Gates Foundation

MENTORSHIPS IN 2021

The Division supported several post-graduate students in 2021.

STAFFING IN 2021

CAST-NET

In 2021, 9 staff members were supported by the project: Greg Greene (project manager/ epidemiologist), project administrator, research assistant, field project coordinator, epidemiologists x2, medical epidemiologist, medical officer x2. Each of the team members play a significant role in ensuring that the project met its objectives and goals.

Baby GERMS

The programme was nested within the GERMS-SA surveillance programme at the NICD and led by project manager, Dr Susan Meiring. Through the division, we hired an epidemiologist, medical scientist and medical officer to continue the analysis of

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

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the collected data.

DATCOV
Led by Dr Waasila Jassat, the study employed a project manager and an epide miologist and eight qualified nurse as surveillance officers at sentinel hospital sites.

PrE-AIM
The sub-study is nested within the CAST-NET study and led by Greg Greene, CAST-NET project manager/epidemiologist as a doctoral research project with assistance from CAST-NET personnel and supervision by CAST-NET Principal Investigator, Nelesh Govender.

Fungal Genomic
The project is led by Dr Sabelle Jallow and Prof Nelesh Govender. The project employed an epidemiologist and medical scientist.

EFFECT TRIAL
Key study staff were identified and appointments were ongoing in 2021.

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

WiSH
WITS SPORT & HEALTH
Healthier, Happier, Higher

WHO WE ARE

Wits Sport and Health (WiSH) is an entity registered as a Division with the Wits Health Consortium; WiSH is also is a research group registered with the University Research Committee (URC); The Division of Sport and Exercise Medicine is housed in the Department of Family Medicine, School of Clinical Medicine.

Key Founding Partners
WiSH is a collaboration between the Faculty of Health Sciences, specifically the Schools of Clinical Medicine and Therapeutic Sciences, Wits Health Consortium and Wits Sport. The WiSH network of collaborators and interest groups stretches across academic and private units in the greater Johannesburg area.

WiSH Research Group members

Director of WiSH:
Prof Jon Patricios, Division of Sport and Exercise Medicine, Department of Family Medicine, School of Clinical Medicine, Faculty of Health Sciences.

Assistant Director:
Dr Siyabonga Kunene, Department of Physiotherapy, School of Therapeutic Sciences, Faculty of Health Sciences.

Chair of the WiSH Management Committee:
Prof Hellen Myezwa, School of Therapeutic Sciences

Other Management Committee members:
Prof Daynia Ballot, School of Clinical Medicine

PROFESSOR JON PATRICIOS

DIVISIONAL HEAD

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- Prof Richard Cooke, Head, Department of Family Medicine, School of Clinical Medicine
- Mr Jean du Randt, Wits Health Consortium
- Dr Brad Gelbart, honorary lecturer, Department of Orthopaedics, School of Clinical Medicine
- Dr Robin Saggers, Lecturer, Department of Paediatrics, School of Clinical Medicine
- Ms Nadine Petersen (administrative support)

Research in 2021

WiSH is currently involved in over 20 research initiatives including systematic reviews, original research studies, national and international collaborations, and undergraduate projects. Currently, there are eight international collaborations (listed later in this report).

Sports-Related Concussion

A key focus area is sport-related concussion (SRC) with the biggest ongoing study being the Children's Head Injury Longitudinal Study in Sport (CHILDS-Sport), a two-year longitudinal study evaluating salivary biomarkers for the detection of concussion in youth sport.

Another important SRC initiative is WiSH's involvement in the 2022 International Concussion in Sport Consensus Guidelines. Jon Patricios is a lead author of one of the systematic reviews (Development of a Sports Concussion Office Assessment Tool), a co-author of the consensus paper and on the scientific committee for the conference.

WiSH and Wits Rugby are collaborating on an International Olympic Committee (IOC)-sponsored study "Prevention, detection and management of concussion in rugby: Evaluation of multisystem involvement." This was disrupted by the COVID-19 epidemic but has resumed and been extended to 2023.

Jon Patricios will co-supervise a World Rugby study starting in August 2022, "Optimizing return to sport following concussion in Rugby Union: a multisystem approach"; this will involve professional teams and clinicians in South Africa, the UK and New Zealand. The project will provide two PhD research opportunities

Other SRC projects include:

- Video analysis of concussion in female varsity rugby players
- A scoping review of the role of chiropractors in SRC
- Baseline assessment of university athletes' saccadic eye movements using the EyeGuide tracking device
- The impact of sport-related concussion on incidence and severity of sleep disturbances
- Optimizing return to sport following concussion in Rugby Union: a multisystem approach

Additional Research

- In collaboration with the University of Pretoria's Sport, Exercise Medicine and Lifestyle Institute (SEMLI), WiSH is partaking in the Athlete with Acute Respiratory InfEction (AWARE) Study (including COVID-19) and has Jon Patricios and Benita Olivier have co-authored the first paper currently under review.
- The use of Fitbits as a replacement for manual sleep diaries in the assessment of sleep and insomnia in a sample South African population and the role of physical activity.
- Mental health and wellbeing in rugby players (MAUL)
- A Whole Genome Sequencing Approach to Anterior Cruciate Ligament Rupture – A Family "Twin" Study

Mentorships 2021

Postgraduate Student Supervision

- Ms Robynne Scheepers, BSC (Hons) (Neuroscience). A systematic review of sleep disturbances following sport-related concussion, Registered January 2021, awarded November 2021 (with distinction); co-supervised by Prof Jon Patricios and Dr Robin Saggers.
- Ms Siwakhile Debby Sikhondze, BSc (Hons) (Neuroscience). Normative data for university athletes using an eye tracking device for baseline screening as part of a sports concussion programme. Registered January 2022; co-supervised by Prof Jon Patricios and Dr Robin Saggers.
- Ms Micaela Rhoda Msc (Med). The use of Fitbits as a replacement for manual sleep diaries in the assessment of sleep and insomnia in a sample South African population. Co-supervised by Dr Alison Bentley and Prof Jon Patricios
- Dr Jozef Breedt MMed (Psych). Co-supervised by Dr Beninda Marais and Prof Jon Patricios
- Ms Carmen Rogans MSc (Biokinetics). Anxiety and Depression as modifying factors in Sport Related Concussion (SRC) in South African Adolescents. Supervised by Prof Jon Patricios
- Dr Clement Plaaitjies, PhD candidate (to be registered May 2022): What is the added value of a comprehensive clinical assessment in the diagnosis of concussion in Rugby Union? Supervised by Prof Jon Patricios, co-supervised by Dr Kathryn Schneider (University of Calgary) and Dr Sharief Hendriks (UCT)
- Dr Janesh Ganda, PhD candidate (to be registered May 2022): Does the comprehensive clinical assessment evaluation detect multisystem issues in sport-related concussion? supervised by Prof Jon Patricios, co-supervised by Dr Kathryn Schneider (University of Calgary) and Dr Sharief Hendriks (UCT)

Undergraduate Student Supervision

- GEMP 3 Group B1 (Alka Rampersad, Kagisho Tibatshi, Nhlonipho Nhlapo, Perusha Gounder, Radina Nenova, Romy Sapire, Sahil Rampurtab, Vhonani Maboho). Myositis ossificans in a child athlete: A case study

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- GEMP 3 Group B2 (Siyabonga Madlala, Matthew Nelson, Nomkhosi Mdluli, Senamile Dlamini, Gift Smith, Yhovaan Mansingh, Katherine Bertrand, Dominique Verhufen, Swetha Maharaj). A cross-sectional study exploring the mental health of South African elite athletes
- GEMP 3 Group D6 Ashwin Luke, Connor Feeney, Mahlatsi Makgamatha, Kealan Dale, Sylvia Ndlovu, Melissa Ward, Tanushri Pillay, Lesego Mahlatse). Ocular manifestations of a sports-related concussion in a professional rugby player: A case study

Fellow
- Prof Jon Patricios has taken on a training fellow, Dr Elené Lourens, to shadow and work with him for 2021

STAFFING 2021
Administrator – Ms Nadine Petersen
Nadine.petersen@wits.ac.za

SOCIAL IMPACT 2021
Webinar Series
WiSH hosted numerous webinars with an international audience during 2021. These are accessible at WiSH webinars https://www.wits.ac.za/wish/wish-webinars

Podcasts
Featuring national and international key opinion leaders in sport and exercise medicine accessible at https://www.wits.ac.za/wish/podcasts/

THE WISH CONGRESS 2022
WiSH hosted its first congress from 11-13 March 2022 at the Hilton Hotel, Sandton. The congress was opened by Prof Hellen Myezwa, Head of the School of Therapeutic Sciences. Three international speakers featured: Prof Jonathan Drezner (University of Washington, Seattle, USA and Editor-in-Chief of the British Journal of Sports Medicine), Dr Jane Thornton (Western University, London, Ontario, Canada) and Dr Joanne Kemp (Latrobe University, Melbourne Australia). Invited national speakers included Dr Phatho Zondi (sports and exercise medicine physician, KZN), Dr Hellen Milson (physio-therapist, Cape Town) and Dr Ross Tucker (World Rugby research director, Cape Town). 160 delegates representing multiple disciplines attended. Keynote plenary presentations included:

Sport and exercise medicine: a vision for the future:
Prof Jon Drezner
"The player's perspective" - Mr Bongani Khumalo (former national football captain)

Prof Ross Tucker
The full programme is accessible here, and consisted of two parallel streams, "Head-to-Toe of sports medicine" and "Issues beyond the sports field". Highlights included:
- Sports Equity
- The female athlete, sport and performance
- Sports concussion update
- Posterior shoulder instability
- Femoroacetabular impingement
- Knee cartilage injuries

Workshops were held discussing rehabilitation of hip and groin injuries (Drs Kemp and Millson), Running gait analysis (Parys Edwards and Lauren Brown) and ECG interpretation in the athlete (Prof Drezner).

A main sponsor, Acino pharmaceuticals was secured for the 2022 event as well as a number of smaller sponsors who exhibited at the event. The response to the congress from speakers, delegates and sponsors was overwhelmingly positive and wish plans to host a similar event biennially.

DISCOVERY VITALITY
WiSH has embarked on a collaboration with Discovery Health to analyse their Vitality data. Projects include:
- The influence of lockdown on physical activity levels in Vitality members (published in the Wits Journal of Clinical Medicine)
- An analysis of the influence of physical activity on adverse outcomes from COVID-19 (published here in the British Journal of Sports Medicine (BJSM))
- The effect of physical activity on vaccine effectiveness against COVID-19 (submitted and under review)

WiSH interest groups also contribute to monthly newsletters for Vitality members.
The "Small steps, strong shield" COVID outcomes paper has received widespread publicity in the medical and social media locally and internationally:
https://www.youtube.com/watch?v=wPoc42V62OQhttps://www.medscape.com/viewarticle/970981https://www.schulich.uwo.ca/about/news/2022/march/feature_physical_activity_reduces_risks_of_severe_covid19_outcomes_study_shows.htmlhttps://www.mynewsdesk.com/za/discovery-holdings-ltd/videos/small-steps-strong-shield-study-reveals-regular-exercise-can-prevent-death-from-covid-19-by-up-to-42-percent-115128https://twitter.com/Vitality_SA/status/1491780827683897347

FUTURE NEEDS
The expanding portfolio of research opportunities in sport and exercise medicine urgently requires a more formalised research support network and discussions are being held with Wits Clinical Research (WCR) in this regard.

WiSH also aspires to a physical presence on campus. Plans for a suitable facility have been drawn and presented to potential donors.

Annual Review 2021

MRU MatCH Research Unit
Department of Obstetrics and Gynaecology
Faculty of Health Sciences
University of the Witwatersrand

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www.matchresearch.co.za

WHO WE ARE

WMRU was previously known as MRU. In 2021 MRU was awarded the privilege of adding Wits as a prefix to its name to make its association with the University of the Witwatersrand clear. WMRU is affiliated to the Faculty of Health Sciences, the School of Clinical Medicine and to the Department of Obstetrics and Gynaecology. WMRU is based in Durban and our research is carried out at our site, in the surrounding communities and in health facilities depending on the project.

Using a range of methodologies, we conduct behavioural, operations and clinical research, actively partnering and involving communities and local structures. We also provide technical assistance, partnering with various stakeholders including the Department of Health and other NGOs to affect policy change and enhance best practice. We work with diverse partners, collaborators and donors, including local and internationally based universities and research centres. In 2021 MRU published 21 articles in peer-reviewed journals and presented our work at a range of virtual international conferences and meetings

INTRODUCTION

Wits MRU (Wits Maternal, Adolescent and Child Health Research Unit) aims to answer priority questions that will translate into improving sexual and reproductive health outcomes through expanding access to appropriate and acceptable contraceptive, HIV prevention and related health technologies and services.

Our core research areas are contraception including barrier methods, HIV prevention, safer conception, menstrual management, postpartum depression and other areas of sexual and reproductive health. MRU engages in pivotal research conducted with vulnerable populations, including youth, sex workers, drug users and residents of informal settlements..

RESEARCH IN 2021

In 2021, we continued to manage our research studies during the COVID-19 pandemic. WMRU continued all its studies during the various lockdowns to ensure staff and participant safety was prioritized. Highlights of our active studies by topic area in 2021 are detailed below:-

HIV Prevention

In 2021 we continued our programme of work in Pre-exposure prophylaxis (PrEP) for HIV Prevention.

We commenced enrollment in the IMPOWER-022 Trial. This double-blinded randomised clinical trial that will test the effectiveness and safety of a new monthly oral pre-exposure prophylaxis pill (PrEP). Daily oral PrEP offer women the ability to protect themselves from HIV-1 infection but taking a tablet every day can be onerous. The new monthly oral PrEP tablet will be compared to the standard daily oral PrEP tablet. Women between the ages of 16 and 45 years will be randomised into one of two groups. Group 1 will take the active monthly oral PrEP tablet and a daily placebo tablet, while Group 2 will take a monthly placebo tablet and the active daily oral PrEP tablet.

We additionally started planning for two further PrEP studies. PURPOSE-1:

A Phase 3, Double-Blinded, Multicenter, Randomized Study to Evaluate Safety and Efficacy of Twice Yearly Long-Acting Subcutaneous Lenacapavir, and Daily Oral emtricitabine/Tenofovir Alafenamide for Pre-Exposure Prophylaxis in Adolescent Girls and Young Women at Risk of HIV Infection. The primary objective of this study is to evaluate the efficacy of lenacapavir (LEN) and emtricitabine/tenofovir alafenamide (F/TAF) in preventing the risk of human immunodeficiency virus (HIV) infection relative to the background HIV incidence rate.

A second study project ENGAGE is a Phase II Acceptability Study of Oral emtricitabine/ tenofovir alafenamide (F/TAF) vs emtricitabine/ tenofovir disoproxil fumarate (F/TDF) for the Prevention of HIV Acquisition in Adolescent Girls

and Young Women (AGYW). This study will be conducted to learn more about young women's experience using a daily oral pre-exposure prophylaxis or PrEP for the prevention of HIV. Both these studies will commence in 2022.

One ground breaking study at WMRU which was completed in 2021 was carried out in collaboration with the University of Alabama. This five-year NIH grant was awarded for the Zivikele ngaphambi kokukhulelwa (ZINK): Protecting yourself before pregnancy study which offered PrEP as part of a safer conception package. Data is currently being analysed.

A successful seed application for a joint collaboration with researchers at Queens University, Belfast was awarded in 2020 to MRU. This study explored women's preferences and attitudes to different vaginal ring product attributes. The focus group discussions (FGDs) were carried out in 2021. The team at Queens developed vaginal rings in different sizes, colours and fragrances which were shown to women and their opinions on the product attributes and preferences were discussed. This seed grant aims to lead to longer term collaboration through joint funding applications between both MRU and Queens.

We conducted a national on-line condom perception survey to assess user knowledge, attitude and perceptions of the public sector male and female condoms - Max and Maxima. Data was presented at the Wits Research day.

MATERNAL HEALTH IN HIV POSITIVE WOMEN

We continued follow-up in our NIH funded study - PEPEHC (Evaluation of Postpartum Engagement in HIV Care) which aims to estimate the rate of attrition from HIV care and to identify factors associated with attrition from and retention in HIV care during the postpartum period. The study enrolled 473 currently pregnant women, living with HIV and currently pregnant. Participants are followed up over a period of two years. An additional COVID component was added to assess the impact of the pandemic on study participants in HIV care.

We are collaborating with the Wits Clinical HIV Research Unit in a study looking at the acceptability of combination treatment for cervical precancer in South African women living with HIV. MRU is involved in supporting the qualitative component of the formative Research for this study.

CONTRACEPTION

We continued to write up the results of the ECHO Trial (The Evidence for Contraceptive options and HIV Outcomes): A Multi-Center, Open-Label, Randomised Clinical Trial Comparing HIV Incidence and Contraceptive Benefits in Women using Depot Medroxyprogesterone Acetate (DMPA), Levonorgestrel (LNG) Implant, and Copper Intrauterine Devices (IUDs). This trial compared the risks of HIV acquisition between women randomised to Depot Medroxyprogesterone Acetate (DMPA), Levonorgestrel (LNG) implant, and copper IUDs. Additionally we followed up a sample of 434 women who completed the ECHO trial in a new study:- CUBE: Contraceptive use dynamics beyond the ECHO trial: This study assessed long-term (24 months) user experiences and method continuation from the two MRU ECHO KZN sites (Durban and Edendale) and the ECHO Zambia site. An additional COVID component was added to assess the impact of the pandemic on uptake and continuation of contraception.

Our condom research programme completed follow-up in the female condom contraceptive efficacy (CoCo) study. Women were randomized to one of three female condom types and are followed up monthly.

We commenced the SHO Study:-
A functional performance and acceptability study of two new male condoms, compared to a standard latex condom. This study was a cross-over randomized trial to determine the functional performance and acceptability of the latex graphene male condom and synthetic nitrile male condom in comparison to the standard latex male condom. The study will be completed in early 2022.

KEY POPULATIONS

The HIDE study:- Hidden Epidemic:
Using respondent-driven sampling to engage people who inject drugs in South Africa into the HIV continuum. This study aims to understand the HIV prevention and treatment needs of this population and how to better engage them into care. It is using qualitative methods to assess access to and acceptability of HIV prevention and treatment services among People Who Inject Drugs (PWID) in KwaZulu-Natal. The study commenced in 2021. WMRU continued to provide support to the Provincial and National Departments of Health (DoH) (SRH) in policy and programme issues in the area of sexual and reproductive health.

OUR KEY FOUNDERS

Prof Jenni Smit, Prof Mags Beksinska and Ms Zonke Mabude.

MRU MatCH Research Unit
Department of Obstetrics and Gynaecology
Faculty of Health Sciences
University of the Witwatersrand

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MENTORSHIPS

WMRU focused on capacity building and training of researchers locally, regionally and internationally during 2021 with three PhD students (one in Uganda completing her PhD), and one Masters study being supervised by WMRU researchers.

STAFFING

Our team consists of highly skilled research, clinical, laboratory, community, data and administrative staff from a wide range of backgrounds including clinical, behavioural and social sciences.

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University of the Witwatersrand

JHB Pulmonology/ ICU

WHO WE ARE

The Unit was established a number of years ago, in the early years of the Wits Health Consortium, and has focused on clinical trials in the field of Pulmonology, mainly in relation to the use of antibiotics in community-acquired pneumonia, but also including asthma and COPD, as well as in various aspects of patient management in the ICU setting.

The Directors of the Research Unit are Professors Charles Feldman and Guy Richards, both highly qualified Respiratory Physician/Critical Care specialists. For many years the Unit was centred around these two individuals, with assistance from many of the training Fellows in Pulmonology and Critical Care. However, more recently, full-time qualified consultants interested in these areas of research have become much more involved in the studies conducted in the Unit, with the aim of these younger individuals ultimately taking over the running of the Unit themselves. The Unit is housed in the Department of Internal Medicine, with the Critical Care component

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being housed, more recently, in the Department of Surgery.

SOCIETAL IMPACT 2021

Two major studies in the field of Pulmonology and Critical Care that were undertaken by Professors Feldman and Richards and their associated collaborators (both local and/or international) between 2019 and 2022, to be published in 2022 in high impact factor journals, but with most of the work having been done in 2021 (due to COVID-19 interruptions), relate to pneumococcal vaccination recommendations for adults in South Africa and communications regarding end-of-life decisions in ICUs worldwide.

AGTRU

saMRC advancinglife

Who we are

The unit currently has approximately 15 members and these comprise molecular biologists and postgraduate students. There are five academic staff appointees in the unit. AGTRU is equipped as a modern molecular biology research laboratory and has expertise in a range of techniques. These are advanced methods of nucleic acid manipulation, gene transfer to mammalian cells, use of lipoplex and recombinant viral vectors. AGTRU is set up to investigate efficacy of antiviral compounds in vivo in murine (e.g. HBV transgenic mice) and cell culture models of viral replication.

Introduction

The Wits/SAMRC Antiviral Gene Therapy Research Unit (AGTRU) works on developing use of nucleic acids (gene therapy) to treat and prevent serious viral infections of public health importance. Gene therapy is based on rational drug design, which in turn is informed by knowledge about DNA sequences.

With impressive advances in sequencing technology, there is now a wealth of information that may be applied to advancing this innovative approach to treating and preventing diseases of global importance, including infection with hepatitis B virus (HBV) and SARS-CoV-2. Following emergence of the COVID-19 pandemic, it became clear that gene therapy technology may be repurposed for vaccination against SARS-CoV-2.

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The approach has been applied by leading international vaccine manufacturers such as AstraZeneca, Moderna, Johnson & Johnson and Pfizer/BioNTech. Formulation of mRNA in lipid nanoparticles and engineering of recombinant adenoviral vectors were previously developed for use in gene therapy in the SAMRC/Wits AGTRU. The methodology has been repurposed for vaccine development and is contributing to the WHO-supported initiative to develop an mRNA vaccination hub in South Africa. The scope of vaccine development now includes non-viral infections such as Mycobacterium tuberculosis (MTB) which are important in sub-Saharan Africa.

Research in 2021:

The research focus is on countering viral infections that are important to South Africa and other parts of sub-Saharan Africa. The approach is to employ nucleic acids (DNA or RNA) as vaccines or therapies. One area of interest is infection with hepatitis B virus (HBV). Chronic infection with HBV is hyperendemic to Africa and this part of Africa and continues to be a significant but underappreciated cause of public health problems. Licensed anti-HBV drugs have at best modest efficacy, and there is a need for improved treatment to prevent mortality resulting from the infection. Research completed to date in our unit shows that gene therapy has the potential to eliminate the virus from infected cells. Three methods have been employed: gene silencing, epigenetic silencing and gene editing. Technology developed in the Wits/SAMRC AGTRU has enabled capacity development in vaccine preparedness. Experience from the COVID-19 pandemic has shown impressively that mRNA-based vaccination is very effective. The unit is involved with assisting in this process through contributions to establishing the WHO-initiated mRNA vaccine hub. During 2021, the Unit published 16 peer-reviewed journal articles.

Our key founders:

SAMRC
SANRF
Afrigen
Medicines Patent Pool (reperesenting WHO and various European and North American governments)
Poliomyelitis Research Foundation
Biovac

Mentorships in 2021:

Training of postgraduate students is an important function of the Wits/SAMRC AGTRU. Also, the postgraduate students' projects are integral to the research programme of the unit described above. During 2021 there were six PhD and three MSc candidates registered in the Unit. Three PhD students graduated during 2021: Shonisani Wendy Limani, Njabulo Mnyandu and Amy Geard.

Staffing in 2021

AGTRU staff members
Prof Patrick Arbuthnot
Ass. Prof. Abdullah Ely
Dr Mohube Betty Mowa (Senior Lecturer)
Dr Kristie Bloom (Researcher)
Dr Kubendran Naidoo (Researcher)
Gladys Gagliardi (Laboratory Manager)

Honorary staff members

Prof Simon Waddington, Professor in Gene Transfer Technology, Institute for Women's Health, Gene Transfer Technology Group, University College London, UK.
Dr Wolfgang Prinz.
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Societal Impact 2021

Much of the work of the Unit during the past year has been devoted to assisting industry partners to apply nucleic acid delivery technology for vaccine development. Particularly, we have engaged with Biovac (Cape Town) to establish facilities and protocols for propagation of adenoviral vectors that may be engineered to express SARS-CoV-2 immunogens. Use of mRNA technology for vaccines has also recently come to the fore. The initial intention has been to tackle COVID-19, but the longer-term goal is to apply the powerful and versatile methodology to prevent infections with other pathogens that are important in sub-Saharan Africa. Our team has been involved with training of scientists from Afrigen, as well as scientists from so-called 'spokes', which are laboratories from other countries that are keen to develop mRNA vaccine technology.

In addition to assisting industry partners, academic collaborations with laboratories in South Africa are being vigorously pursued to establish original new locally-based vaccine technology. This initiative will commence shortly and is again being driven by the WHO with significant financial support from the SAMRC, European Commission, French, Swiss and Italian governments amongst others.

WITS HEALTH CONSORTIUM

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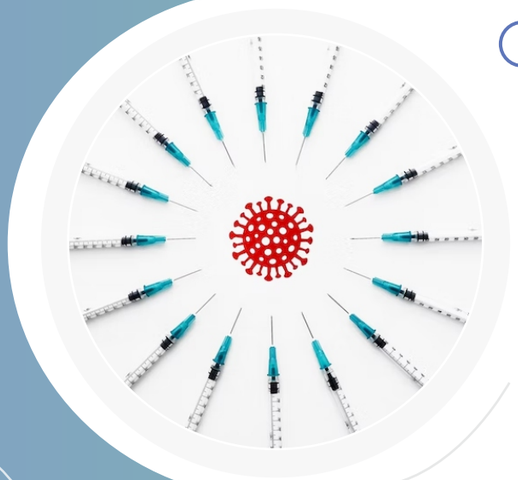

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