NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

2022/23

Annual Overview

CONTENTS

LIST OF ABBREVIATIONS

AFP	Acute flaccid paralysis
Africa PGI	Africa Pathogen Genomics Initiative
AFRO	African Region Offices
AMR	Antimicrobial Resistance
ANC	Antenatal care
ARL	Arbovirus Reference Laboratory
ART	Antiretroviral Therapy
BSc	Bachelor of Science
BSL	Biosafety Level
BMGF	Bill and Melinda Gates Foundation
CCHF	Crimean-Congo Haemorrhagic Fever
CDC	Centres for Disease Control and Prevention
CDW	Corporate Data Warehouse
CED	Centre for Enteric Diseases
CEZPD	Centre for Emerging Zoonotic and Parasitic Diseases
CHARM	Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses
CHIVSTI	Centre for HIV and STIs
CoVICIS	Combating SARS-CoV-2 Pandemic
CRDM	Centre for Respiratory Diseases and Meningitis
CSIR	Council for Scientific and Industrial Research
CTB	Centre for Tuberculosis
CVI	Centre for Vaccines and Immunology
DATCOV	Daily Hospital Surveillance for COVID-19 Report
DBB	The Division of Biosafety and Biosecurity
DHIS	District Health Information System
DoH	Department of Health
DPHSR	Division of Public Health Surveillance and Response
DRC	Democratic Republic of the Congo
DTRA	Defence Threat Reduction Agency
DUT	Durban University of Technology
EIA	Enzyme Immunoassay
EOC	Emergency Operations Centre

EPBCR	Ekurhuleni Population-Based Cancer Registry
ESKAPE	*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species
FETP	Field Epidemiology Training Programme
GERMS	Group for Enteric, Respiratory and Meningitis Surveillance – South Africa
GIISER	Global Immunology and Immune Sequencing for Epidemic Response
GLASS	Global AMR Surveillance System
IAEA	International Atomic Energy Agency
IANPHI	International Association of National Public Health Institutes
IARC	International Agency for Research in Cancer
IgG	Immunoglobin G
IgM	Immunoglobulin M
INH	Isoniazid/ Isonicotinic Acid Hydrazid
IT	Information Technology
LSHTM	School of Hygiene and Tropical Medicine
MRC	Medical Research Council
MSM	Men-who-have-sex-with-men
NCR	National Cancer Registry
NDoH	National Department of Health
NGS	Network for Genomic Surveillance in South
NHLS	National Health Laboratory Service
NICD	National Institute for Communicable Diseases
NIHR	National Institute for Health and Care Research
NIOH	National Institute for Occupational Health
NMC	Notifiable Medical Conditions
ORU	Outbreak Response Unit
PCR	Polymerase Chain Reaction
PET	Provincial Epidemiology Team
PGI	Pathogen Genomics Initiative
POPIA	Protection of Personal Information Act
RCoEBB	Regional Centre of Excellence for Biosafety and Biosecurity
RfA	Results for Action

LIST OF ABBREVIATIONS

RNA	Ribonucleic Acid
RVF	Rift Valley Fever
SACCESS	South African Collaborative COVID-19 Environmental Surveillance System
SADC	Southern African Development Community
SAFETP	South African Field Epidemiology Training Programme
SAHPRA	South African Health Products Regulatory Authority
SAMVAC	South African mRNA Vaccine Consortium
SANAS	South African National Accreditation Systems
SARS	Severe Acute Respiratory Syndrome
SBI	Surveillance and Business Intelligence
SBPRL	Special Bacterial Pathogens Laboratory
SCF	Sequencing Core Facility
STI	Sexually Transmitted Infection
SVPL	Special Viral Pathogens Laboratory
TB	Tuberculosis
TPT TB	Preventative Therapy
UNAIDS	Joint United Nations Programme on HIV/AIDS
UP	University of Pretoria
US	United States of America
WRC	Water Research Commission
VCLR	Vector Control Laboratory Research
VHF	Viral Haemorrhagic Fevers
WGS	Whole Genome Sequencing
WHO	World Health Organization


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EXECUTIVE DIRECTOR'S OVERVIEW

PROF ADRIAN PUREN
Executive Director

It gives me great pleasure to deliver the National Institute for Communicable Diseases (NICD) Annual Overview for 2022/23. This report accounts for the organisation's usage of its resources and the several building pieces that contribute to attaining its purpose of being a knowledge resource for South Africa and the Southern African Development Community (SADC) region regarding infectious diseases and cancer.

COMMUNICABLE DISEASES

The NICD plays a vital role in the early detection, containment, and response to infectious disease threats across South Africa, the SADC, and Africa. It provides technical support to the National Department of Health (NDoH), as well as the World Health Organization (WHO), Africa Centre for Disease Control and Prevention (CDC), and other relevant bodies through the surveillance of communicable diseases, outbreak response, specialised diagnostic services, research and training, capacity building, and the various scientific outputs in terms of guidelines or publications.

The year under review was the declaration of enteric fever, measles, and cholera outbreaks while continuing to monitor the COVID-19 pandemic. These outbreaks have highlighted the fundamental role of the Emergency Operations Centre (EOC) in tackling a public health crisis and the power of molecular epidemiology through next-generation sequencing to investigate the source of specific outbreaks.

The Centre for Enteric Diseases (CED) integrated genomic and epidemiologic surveillance for enteric fever, detected multiple localised but expanding clusters in several provinces, and demonstrated the spread and establishment of the Klerksdorp typhoid fever cluster strain into other provinces.

The Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD), which houses the only negative pressure BSL-4 laboratory on the continent, supported outbreak responses to mpox (previously monkeypox) and provided specialist reference diagnostic services. The centre supports the malaria elimination programme in South Africa and the region by providing antimalarial drug resistance surveillance and malaria vector surveillance. CEZPD also provided reference laboratory diagnostics research and training relating to zoonoses and vector-borne infections of public health importance in South Africa and the region. The centre shares its knowledge, skills, and capacities to promote prevention, rapid and accurate detection, and support for effective outbreak responses to the provincial and national Departments of Health in South Africa and other national, regional, and international stakeholders. The centre provides laboratory-based surveillance for several formidable pathogens that are notifiable such as, medical conditions in South Africa, including anthrax, arboviral infections, malaria, rabies, and viral haemorrhagic fevers.

The Centre for Healthcare-Associated Infections, Antimicrobial Resistance, and Mycoses (CHARM) has been working on several initiatives to combat antimicrobial resistance (AMR) in South Africa. Regarding neonatal infections, Baby GERMS-SA surveillance data were published and led to collaborations for developing age stratification of Global Burden of Disease AMR data, a weighted incidence syndromic combination antibiogram analysis, and work on a Klebsiella vaccine. CHARM's One Health AMR efforts included contributing to a joint public and private report on AMR and antimicrobial use in animals and humans in South Africa, leveraging wastewater SARS-CoV-2 surveillance to monitor multi-drug-resistant bacterial and fungal pathogens in the environment, and establishing a regional partnership with four Southern African countries for fungal disease surveillance.

In the area of HIV-related infections, the centre facilitated the inclusion of flucytosine in the South African standard treatment guideline for cryptococcal meningitis for HIV-related conditions and initiated isolate-based surveillance for *Cryptococcus* at sentinel hospitals to screen recurrent episode isolates for 5-FC resistance. The Centre co-led a National Institute for Health and Care Research (NIHR)-funded Global Health Research Group on HIV-associated Fungal Infections alongside the London School of Hygiene and Tropical Medicine (LSHTM) and NICD/Wits to improve the diagnosis and treatment of five HIV-associated fungal infections of public health importance.

The Centre for HIV and STIs (CHIVSTI) focused its efforts on a diverse array of surveillance and research. The analysis of the key outcomes of the biennial antenatal HIV survey revealed a decline in HIV prevalence for women under the age of 25 years and an overall decline in prevalence for the first time. There was a good agreement between the negative and positive HIV point-of-care results when compared to reference laboratory testing. A major achievement of the antenatal programme is that 96% of HIV-positive were on antiretroviral treatment. In addition, 64% of women were on the dolutegravir treatment regimen. There are areas for improvement, in that only 74.1% of those women on ART were virally suppressed, and the proportion of women with viral loads greater than 1000 copies/ml was 10%.

RECOMMENDATIONS INCLUDED STRENGTHENING RETENTION IN CARE AND ADHERENCE TO TREATMENT

The survey also noted the missed opportunities for on-site syphilis testing, with 18% of women having pending results. This included secure online distribution, via the NICD's Self Service Portal, of Results for Action (RfA), reports as per the 2019 National HIV guidelines, monthly reports on Early Infant Diagnosis, Paediatric and Adolescent HIV Viral Load monitoring, Maternal prevention of mother-to-child transmission (PMTCT), HIV VL monitoring, and validation of UNAIDS 95-95-95 target achievement at the district-level.

The Centre for Respiratory Diseases and Meningitis (CRDM) in South Africa reported an outbreak of pertussis in the Western Cape during the second half of 2022, which exceeded the numbers reported during the peak in 2018. In response to the outbreak, the CRDM updated pertussis preparedness guidelines and submitted an advisory on pertussis vaccination, including the vaccination of pregnant women, to the National Advisory Group on Immunisation (NAGI).

The National Influenza Centre (NIC) for South Africa continued to support the WHO by characterising influenza viruses through serologic and genetic testing to guide the composition of the annual seasonal influenza vaccines. Additionally, the NIC provided technical assistance in diagnosing and characterising respiratory viruses in the region.

CRDM also continued to support the COVID-19 response and conducted ongoing COVID-19-related research activities, including studying the burden of disease, transmission, seroepidemiology, and viral sequencing.

Tuberculosis (TB) continues to be a national priority in terms of the disease burden in South Africa. However, the COVID-19 pandemic has impacted TB control progress and reversed years of gains. Consequently, in June 2022, the NDoH implemented the National TB Recovery Plan. The Centre for TB (CTB) played a pivotal role in directing the plan's strategies by using its national and provincial surveillance and forecast models to assess and monitor the impact of the COVID-19 pandemic on laboratory investigations and diagnosis.

The centre further strengthened control efforts of the national implementation of SMS notifications of TB laboratory results to patients endeavouring to enhance linkage to care and a novel rapid diagnostic for drug-resistant tuberculosis investigations to direct clinical management at an earlier stage. The centre enhanced surveillance activities by linking the laboratory test data to the EDRweb (drug-resistant TB register) and geospatial analysis of TB burden and incidence using facility-level laboratory data to identify facility-level TB hotspots in 12 high-burden districts in South Africa. As the National TB Reference Laboratory, the centre coordinated the USAID South African TB Diagnostic Network Assessment. The aim was to assess current practices and algorithms and identify challenges that prevent the overall diagnostic network from performing efficiently and effectively. The centre proposed evidence-based interventions to improve the overall ability of the TB diagnostic network to meet the goals and targets of the national strategic plans for tuberculosis. Research efforts included completing several novel diagnostic evaluations to inform global policy decisions and the application of whole genome sequencing to enhance microbiological and epidemiological surveillance of drug-resistant tuberculosis in South Africa.

During the review period, the NICD declared measles outbreaks across all provinces in South Africa. The Centre for Vaccines and Immunology (CVI) conducted testing on 6 664 serum samples, of which 995 (15%) were confirmed positive for measles. The most affected age groups were 5-9-year-olds (43%), and the national immunisation campaign targeted children aged six months to 15 years. The NICD partnered with the South African Centre for Epidemiological Modelling and Analysis (SACEMA) to provide transmission trend estimates, and the reproduction number declined below one in March 2023.

The NICD also supported sub-Saharan African countries in surveillance for acute flaccid paralysis (AFP) and poliovirus detection. The laboratory processed 5 536 samples for poliovirus isolation, with the detection of wild poliovirus type 1 in seven cases, imported from

Mozambique and vaccine-derived poliovirus in multiple cases. Environmental surveillance identified Sabin/Sabin-like viruses and vaccine-derived polioviruses in various locations.

Additionally, the NICD led the SACCESS network for COVID-19 environmental surveillance, analysing 413 wastewater samples. SARS-CoV-2 was identified in 392 samples (95%), and viral variants, including Delta and Omicron lineages, were successfully detected using next-generation sequencing. Virus levels varied across different regions.

The NICD's Division of Public Health Surveillance and Response (DPHSR) provided epidemiological support for eight of the nine provinces through provincial epidemiologists. The division expanded event-based surveillance, and EOC staff conducted training on emergency management locally and in several other African countries. The 24-hour hotline assisted clinicians with diagnosing and investigating suspected mpox, cholera, and rabies cases. The inclusion of mpox, rubella and congenital rubella syndrome as category 1 Notifiable Medical Conditions (NMC) and the end of the DATCOV COVID-19 hospitalisation system led to additions and improvements in the NMC Surveillance System. In the past year, the NMC system received 59 757 notifications, of which 12% (n=6, 940) were Category 1 NMC, and by March 2023, there were 18 367 active users. The Group for Enteric, Respiratory and Meningeal Disease Surveillance (GERMS) collected data on key pathogens, which were used to monitor trends in disease burden.

The National Cancer Registry (NCR) continued to serve as South Africa's primary source of cancer incidence data, through pathology-based cancer surveillance, the Ekurhuleni population-based cancer registry, and key epidemiological and genetics cancer research. The NCR, in collaboration with the University of KwaZulu-Natal, launched the KwaZulu-Natal population-based registry to enhance cancer data in the province.

"Move like a chameleon, look in front, and watch behind."

South Africa faces several challenges in recovering from the impact of COVID-19, including infection control programmes. The world has been navigating the COVID-19 epidemic for over three years, and the NICD has made a significant contribution to South Africa's response. The need for building a metanarrative around health and science's essential role has been more evident than ever. The multiple self-reflection activities will guide the NICD in preparing for the next pandemic.

The organisation has had to adapt during the year under review; it has given life to the statement that "there is nothing permanent except change" when viewed through the lens of infectious diseases. Through our collective adaptability, we have survived the COVID-19 storm and recognise that adaptability is essential to success in a rapidly changing world.

As work on the NAPHISA collaboration with stakeholders continues, we plan to move to an integrated disease surveillance system for South Africa.

"If You Want to Go Fast, Go Alone. If You Want to Go Long, Go with Others"

Our successes and victories accord with our service to the populace because of the collective efforts of our staff's combined service to the institution and the community. I am pleased to report an overall performance improvement during the period under review compared to the previous financial year.

The Institute surpassed its key performance indicator goals with supreme quality, among other achievements. NICD obtained several noteworthy accomplishments, including the following:

- Exceeding the percentage of identified prioritised diseases under surveillance by 9% of the target;
- Achieving a prodigious 100% of national HIV and TB surveillance reporting;
- Surpassing the number of articles published in peer-reviewed journals; and
- An impressive number of field epidemiologists qualified.

The NICD is committed to enhancing quality management systems, customer satisfaction, reputation, risk management, and employee engagement and productivity. ISO 9001 accreditation is important to our success, and this year, we successfully added several transversal departments to our accredited list, including HR, IT, Finance, The Division of Biosafety and Biosecurity (DBB), Surveillance and Business Intelligence (SBI), and the Communications Unit, without any non-conformances.

The late Dr Elvira Singh posthumously received the AG Oettlé Memorial Award as a fitting recognition of her extraordinary cancer registration and epidemiology efforts as a distinguished scientist who contributed to advancing cancer research and understanding a devastating disease, underscoring CANSA's recognition of the National Cancer Registry's efforts.

The CEZPD Team, led by Dr Givemore Munhenga, received recognition from the International Atomic Energy Agency (IAEA). This leading intergovernmental organisation seeks to promote the peaceful use of nuclear energy. The IAEA recognised the team's work on the Sterile Insect Technique (SIT) project. As a result, the Vector Control Lab Research (VCLR) was nominated to host an insect control fellowship under Dr Munhenga through the agency's fellowship programme.

At the 11th TEPHINET Global Scientific Conference held in Panama City, Dr Thendo Ndou, a graduate of the FETP Frontline programme, made a significant impact with his research on "Epidemiology of ESKAPE Pathogens at a Tertiary Care Hospital in South Africa, January 2019-August 2021." Flying the SAFETP-DPHSR flag, Dr Ndou was recognised for the "Best Oral Presentation by a Frontline FETP Fellow or Recent Graduate" for his presentation.

In addition to our international awards, the Benedyke Polak Award 2022 was awarded to Prof Janusz Paweska. An award is given to a Polish and a foreign scientist who has achieved outstanding achievements in exploration and research. The activities of these organisations strengthen the ties between Poland's science and culture and the international heritage of research, imagination, and thought.

The CTB's Dr Shaheed Vally Omar has received Global Health funding to continue the TB Surveillance Programme at the NICD/NHLS. During the Global Health Fund visit in Geneva, Dr Shaheed Vally Omar was seconded to assist the CEO with support from the NDoH.

Dr Arshad Ismail's appointment as a special category researcher at the University of Venda's Department of Biochemistry and Microbiology is a testament to his expertise in the sequencing field. Dr Ismail, the head of the Sequencing Core, has been recognised for his contributions to the area and appointed an Adjunct Professor at the university.

Mr Zibusiso Masuku was instrumental in the designation of the NICD's Regional Diagnostic Demonstration Centre (RDDC) as the first Regional Centre of Excellence for Biosafety and Biosecurity (RCoEBB) in Africa, which was conferred by the Africa CDC.

The International Association of National Public Health Institutes (IANPHI) recognised Dr Harry Moultrie for outstanding success in building a collaborative modelling consortium for COVID-19 as the winning project of the African Network for the Recognition of Success in 2022.

During the year, we celebrated three ribbon-cutting ceremonies. The first was the ribbon-cutting by Dr Imtiaz Sooliman and Dr Kamy Chetty for the opening of the donated Modular unit for accommodating Field Epidemiology Training, and the second was the inauguration of the NCR as the IARC GICR (Global Initiative for Cancer Registry) Collaborating Centre for Sub-Saharan Africa, recognising the NCR's contributions to cancer research in the region. The third ceremony celebrated the opening and RDDC's designation as an RCoEBB.

Representatives of the Institute attended several high-level meetings with governmental officials and diplomats. These meetings included the USG PEPFAR, SA-RCC Workshop on Strengthening NPHI, Illumina Global Health, the IAEA Technical Cooperation Programme, and the technical workshop between China CDC and the Embassy of the People's Republic of China in South Africa.

As we look forward to a new financial year filled with significant achievements, we will need to carefully explore how to surpass our accomplishments from the previous year within an operating environment laden with increasingly limited financial resources.

OUR SUPPORT FUNCTIONS' TENACITY PULLS US FORWARD

The IT Department has worked diligently to complete 53 software development and business intelligence projects and continued to provide infrastructure and support amid major power disruptions.

Notably, the IT department has advanced the development of the Notifiable Medical Condition Surveillance system to be more agile and to incorporate a hospital surveillance system for notifiable medical conditions based on the lessons learned from the DATCOV system designed during the pandemic.

The Communications Unit has remained a reliable and fact-based source of information for various stakeholders, including healthcare providers and media professionals. The Unit has been committed to enhancing the reputation of the NICD and protecting its brand. During the review period, the Unit achieved significant growth in media coverage across broadcast, online, and print media. In addition, the Unit published 252 peer-reviewed articles through the quarterly Science Focus publication, exceeding the annual target of 140 peer-reviewed articles, and maintained a strong online presence with over 1.4 million followers on various social media channels. The NICD website achieved a significant 31% increase in website users for the year 2022/23. The Communications Unit achieved ISO 9001 certification and was recognised by the WHO as part of the Vaccine Safety Net initiative.

RESEARCH, DEVELOP, AND INNOVATE FOR AND WITH THE REST OF AFRICA

Public health collaborations are crucial to advancing research and innovation that will address pressing health challenges. The

RDDC's recent designation as the first Regional Centre of Excellence for Biosafety and Biosecurity underscores the importance of such collaborations. The RDDC's new designation was made possible through partnerships with various organisations, including the Africa CDC and the NICD's RDDC, highlighting the importance of shared expertise and resources in advancing public health outcomes.

The NCR was inaugurated as the collaborating centre for childhood cancers and monitoring of cervical cancer elimination in sub-Saharan Africa by IARC's Global Initiative for Cancer Registry (GICR) development. The NCR trained 65 participants from Ministries of Health and Cancer registries from 12 sub-Saharan African countries on cervical cancer record linkage and 17 cancer registrars on childhood cancer registration from population-based registries in Tanzania.

PEOPLE WITH A MISSION

Any institution's success largely depends on its employees' passion and commitment, and the NICD is no exception. With a team of 513 skilled and dedicated employees, the NICD has been able to carry out a wide range of activities to advance public health outcomes. A recent report indicates that 73% of NICD employees held permanent employment, while 27% were grant-funded or fixed-term personnel. Despite this mix, the institution has maintained a staff turnover rate of 1.5%. In addition, the NICD has invested in capacity building through workplace skills plan interventions, internal seminars, and post-COVID debriefing sessions, among other initiatives. These efforts demonstrate the institution's commitment to nurturing and retaining its talented workforce to continue delivering impactful work in the public health sector.

The NICD values diversity and recognises the importance of having leaders from different backgrounds, expertise, and experiences. We congratulate the following staff for their respective new appointments as Centre Heads: Dr Jacqueline Weyer (CEZPD), Dr Nishi Prabdial-Sing (CVI) and Dr Mazvita Muchengeti (NCR).

CONCLUSION

Staff at the NICD continue to strive for excellence and improvements in public health, and I would like to thank them all for their hard work over the last year. The donors, partners and collaborators are acknowledged for contributing to the success of the NICD.

DEPUTY DIRECTOR'S OVERVIEW

DR NATALIE MAYET
Deputy Director

The past year provided the opportunity for an intense reflection on the preparedness and response to the COVID-19 pandemic of the transversal functions of Biosafety and Biosecurity, Communication, Information Technology, Field Epidemiology, and Occupational Health Services. The team engaged extensively with multiple partners in design thinking, scoping new strategies, and rapidly implementing scalable capacity-building initiatives.

The NICD reaffirmed its interdependence with multiple stakeholders at local, national, regional, and international levels and continues to consolidate partnerships and strengthen networks with the common goal of improving global health security.

DIVISION OF BIOSAFETY AND BIOSECURITY

The Division of Biosafety and Biosecurity (DBB) provides the specialised service of Biorisk Management which includes Biosafety, Biosecurity and Biocontainment Engineering, to ensure the safe and secure operation of high and maximum containment laboratory infrastructure. The division has built the capacity of a team of biocontainment engineering and biorisk specialists who provide subject matter expertise for national institutions, the African region, and internationally.

DBB manages and reports on the use of legislative National Department of Health (NDoH) Diagnostic and Research Import/Export Blanket Permits, with a total of 894 copies of the Blanket permit issued for the transfer of 26 218 biological materials, 223 copies for the export of 10 190 units, and 671 copies for the import of 16 028 units.

A significant milestone was the official opening of the NHLS/NICD Regional Diagnostic Demonstration Centre (RDDC) on the 9th of December 2022. The event was officiated by Dr Joseph Phaahla (Minister of Health), Dr Ruben Brigety II (U.S. Ambassador to RSA), Dr Talkmore Maruta (Senior Biosafety and Technical Officer, Africa CDC), Dr Robert Pope (DTRA Director), the NHLS Board Chairperson, and the NHLS CEO. At the event, the RDDC received its formal accreditation as the first Regional Centre of Excellence for Biosafety and Biosecurity for the Southern Africa Region.

As the first centre of excellence on the continent, the facility serves as a benchmark, with the RDDC providing mentorship for the establishment of other centres of excellence elsewhere in Africa. To date, more than 440 participants from at least 33 countries have been trained at the RDDC.

Key milestones of the DBB include:

National

- Membership of the Biological Weapons Working Committee (BWWC) of the South African Council for The Non-Proliferation of Weapons of Mass Destruction (NPC).
- Membership of the national WHO Joint External Evaluation (JEE), the National Action Plan for the Implementation of the International Health Regulations (IHR), and Biosafety and Biosecurity Technical Working Group.
- Voting membership on the South Africa Bureau of Standards (SABS) technical working committees and sub-committees in the development of Bachelor of Science (BSc) national standards.

Regional

Regional Training and Certification Programme for Biosafety and Biosecurity Professionals

- Co-hosted the Africa CDC's inaugural meeting of the Examination and Certification Council.
- Hosted the first offering of the Level 1 Biorisk Management and Biological Waste Management Certification training and examinations.

Participants were drawn from all ten (10) Member States of the Southern Africa Regional Collaborating Centre.

- Hosted the inception and orientation workshop of the first to be certified as Africa Regional Subject Matter Experts (Af-RSME) in Biorisk Management and Biological Waste Management.
- On-boarded the first cohort of Level 2 Biorisk Management and Biological Waste Management Certification candidates.
- Facilitated the Assessor and Implementer regional training efforts for the Regulatory and Certification Framework for Institutions Handling High-Risk Pathogens for the Africa Region.
- Membership of the Africa Centres for Disease Control and Prevention's (Africa CDC) Southern Africa Regional Collaborating Centre Regional Biosafety and Biosecurity Regional Technical Working Group (RBB-TWG).
- The Biorisk Specialist serves as the current President of the African Biological Safety Association.
- Contributed to the Creating Safe and Sustainable High Containment Laboratories workshop hosted by Gryphon Scientific.
- Co-hosted a workshop on global catastrophic biological risks (GCBR) with SynBio Africa, with participants from countries in Southern Africa.
- Co-hosted the Protecting Genomic Data Project being run by the U.S. Department of State and CRDF Global with participants from health institutions in Kenya and South Africa.
- Attended the Africa CDC Biobanking Network Workshop in Zambia for the review of the Africa CDC Manual on "Establishment of a Biobanking Network as a Sustainable Mechanism to Accelerate Development and Evaluation of Diagnostic Tests in Africa."

International

- Qualified Experts for the United Nations Secretary-General's Mechanism for the Investigation of the Alleged Use of Chemical, Biological or Toxin Weapons (UNSGM).
- Member of the WHO Technical Advisory Group on Biosafety (TAG-B).
- Co-hosted the first UNSGM Basic Training Course for qualified experts on the UNSGM Roster in Africa.
- Co-hosted a pre-conference workshop on "Strengthening Biosafety and Biosecurity Capabilities Globally" at the Global Health Security Conference.
- Contributed to operationalising the Signature Initiative to "Mitigate Biological Threats in Africa and Strengthening the Africa CDC's Regional Health-Security Capabilities Workshop."
- The Biorisk Specialist served as an International Federation of Biosafety Associations (IFBA) mentor in the IFBA mentorship programme.
- The Biorisk Specialist is a committee member developing the adjunct Biorisk Management (BRM) standard for biosafety professionals' adjunct to ISO35001.

COMMUNICATIONS

The NICD experienced a significant increase of 148% in media coverage during 2021 and 2022. Media coverage experienced a decline after peak COVID-19 activity; the year under review has, however, witnessed a noteworthy positive growth of 28% in media coverage as compared to the pre-COVID period of 2020/2021.

A total of 252 peer-reviewed articles were published, while the previous year saw the publication of 254 peer-reviewed articles. All of these publications were in highly reputable journals.

The Communications Unit maintained an impactful online presence on all its social media channels by monitoring and dispelling misinformation and rumours concerning communicable disease outbreaks. While there was a slight decrease of 0.59% in followers compared to the previous year's count of 1 466 068 when compared to the pre-COVID period, the follower count reflects a significant increase from the pre-COVID baseline.

The website has recorded a strong online presence and audience reach, with more than 50.7 million page views and 12.1 million users over the past 5 years. The number of website users has declined from the previous year, but when compared to the pre-COVID period of 2020/2021 there has been a 31% increase in website users for the year 2022/23.

The Communications Unit achieved a significant milestone: ISO 9001 certification. Furthermore, the WHO recognised the Communications Unit as part of the Vaccine Safety Net initiative.

INFORMATION TECHNOLOGY

The NICD IT Department has three functional pillars: software development, infrastructure support, and business intelligence. Throughout the reporting period, a total of 53 projects were completed, with significant improvements achieved in the Notifiable Medical Conditions (NMC) system.

The team developed case investigation forms for Category 1 NMCs, including Congenital Syphilis, Enteric Fever, Listeria, and Measles, and has developed a hospital-based surveillance system for NMCs.

An IT Steering Committee was established with representation from all NICD Centres and is supporting the collective implementation of IT functions by setting strategic direction, prioritising tasks, and contributing to the objectives of the department. The team has been exploring universal dashboard displays for the institution and has begun the process of the integration of private sector data into the Surveillance Data Warehouse.

With major disruptions in power supply, the team has maintained a 95% service level and has spent a substantial amount of time exploring sustainable solutions to build resilience in systems, hardware, and storage.

THE SOUTH AFRICAN FIELD EPIDEMIOLOGY TRAINING PROGRAMME (SAFETP)

The South African Field Epidemiology Training Programme (SAFETP) uses an established applied epidemiology curriculum, providing an accredited Master of Science (MSc) degree from either the University of Pretoria (UP) or the University of the Witwatersrand (Wits) with mentored practical field experience. In addition to the Advanced tier, SAFETP offers the Frontline and Intermediate tiers. The Frontline tier launched in 2016 as a three-month in-service training programme being the first step in the three-tiered FETP model of training. The Intermediate tier, which launched in November 2021, is a nine-month in-service programme designed for surveillance officers and public health professionals at the district level of the health system. Both Frontline and Intermediate tiers equip participants with the essential skills used in surveillance, disease detection, monitoring, management and analysis of data, investigation, response, and scientific communication.

To date, the programme has more than 110 advanced-level graduates who are employed in various sectors such as the Department of Health (DoH), private sector, public health institutes, Africa CDC, US CDC in-country office, and the WHO. More than 350 abstracts have been presented at major scientific conferences.

The significant impact of SAFETP in this reporting period was the completion of the first FETP-Intermediate cohort in November 2022. Fifteen health workers selected from across all the health districts of the Eastern Cape Province graduated from this first cohort.

The WHO and the Global Health Security Agenda (GHSA) have recommended that every country attain a minimum target of one field-trained epidemiologist per 200 000 population as one of the key workforce development indicators to ensure optimal public health security. In the year under review, four residents from the 2020 cohort graduated with a Master of Public Health (MPH) conferred by the University of Pretoria (UP) and three graduated with a Master of Science in Epidemiology conferred by the University of the Witwatersrand. The 14 residents of the 2022 cohort and the SAFETP staff welcomed 11 residents of the 17, 2023 cohort, representing environmental health practitioners (4), nurses (2), nutritionists (1), health promoters (2), clinical associates (1), and medical scientists (1). Two residents are from Lesotho and Eswatini.

SAFETP residents and staff, in collaboration with NICD centres' staff and provincial or district Communicable Diseases Control coordinators, responded to more than 35 disease outbreaks in this reporting period.

To increase epidemiologic capacity for outbreak response and public health surveillance, SAFETP enrolled a second cohort of FETP-Intermediate in September 2022. Twelve healthcare professionals from across all three districts of the Mpumalanga Provincial Department of Health joined the cohort. Five in-person workshops were conducted in this reporting period, accompanied by five field intervals for the field component of the training.

The first FETP-Intermediate cohort completed the training in November 2022, graduating 15 healthcare professionals for the Eastern Cape Province. The training was delivered through a partnership with the Eastern Cape Department of Health, the US CDC, the NDoH and the WHO. As part of the graduation ceremony, a two-day scientific seminar was held to showcase the scientific work completed by the graduates.

In this reporting period, SAFETP has conducted three Frontline training sessions for healthcare professionals from KwaZulu-Natal, Gauteng, and the Eastern Cape, with a total of 26 healthcare professionals completing the three-month training.

In addition to Frontline training, the SAFETP team facilitated a short course in basic epidemiology for 20 health professionals from Gauteng Province, as part of the Foundations for Research and Evaluations Training Programme.

SAFETP also facilitated a short course in basic epidemiology for the Tshwane University of Technology third- and fourth-year students in the School of Environmental Health.

WORKSHOPS

- The SAFETP collaborated with the CDC Foundation to facilitate an online scientific writing course for FETP residents from 13-17 of June, 2022. The writing course had 15 second-year residents attend and produce 12 draft manuscripts.
- A train-the-trainers scientific communication course was hosted in collaboration with the CDC Foundation in March 2023; ten mentors were trained under the facilitation of Pascale Krumm from the CDC Foundation with support from the Bloomberg Philanthropies Data for Health initiative.
- The SAFETP team facilitated the orientation of 15 new supervisors at a workshop in March 2023.

OCCUPATIONAL HEALTH

Occupational Health Medical Surveillance for all staff exposed to Occupational Health risks is maintained as per protocols, with physical annual medicals conducted for staff working in the laboratories, drivers, and SAFETP students.

Immunity checks on 89 staff were conducted at the clinic. Since January 2022, NICD has partnered with the DoH travel clinic, and 46 vaccines were administered at this clinic, resulting in significant cost savings. Previously staff had to obtain it at their own expense and thereafter claim it back from NHLS. The clinic further assisted in providing yellow fever and malaria prophylaxis to staff that needed to travel for work purposes. 164 tests were done for SARS-CoV2, with 45 testing positive.

There were also significantly fewer injuries on duty this financial year. In the previous two years, the average was 40 injuries per year during the 2021/2022 financial year, and the total injuries (excluding COVID) were 16 for the 2022/2023 financial year.

Ongoing assistance was provided through formal training programmes, as stipulated by the SHE department of the NIOH. A team effort within the SHE department provided various COVID-19 awareness training presentations for the NHLS and updated existing training material when needed. The latest training material for Formaldehyde and Xylene is in the process of approval. Induction training for new staff continues, as does external training for First Aid and Fire Wardens.

DEPUTY DIRECTOR

The Deputy Director serves as the focal point for IANPHI and IANPHI Africa. A notable advancement was the signing of an MOU between the WHO and IANPHI in support of advancing science-based national public health institutions globally. Janine Bezuidenhout, an epidemiologist at CTB, and the Deputy Director participated in the *Conceptualisation of an integrated disease surveillance strategy globally* with IANPHI, with recommendations presented at the World Health Summit, where the Deputy Director was a panellist discussing "*Outsmarting Pandemics: Collaborative Surveillance and the Role of Public Health Institutes*."

We retain our commitment to shaping global strategy by building field epidemiology capacity with representation on the Global Strategic Leadership Group at TEPHINET and also regionally at AFENET. Additionally, the NICD is part of a Technical Advisory Group for framing the African Epidemic Service.

The Deputy Director continues to mentor the Kofi Annan Global Health Leadership Programme and participates in multiple forums at the NDoH in crafting a post-pandemic future and in drafting the IHR Strategic Tools for the Assessment of Risks. The office holds several Board memberships in the Social and Health Sciences, focusing on injury and violence prevention and burn surveillance; the Surveillance Outbreak Response Management and Analysis System Foundation; and the Southern African Centre for Infectious Disease Surveillance (SACIDS) as a One Health consortium.

There is extensive collaboration with the WHO to advance epidemiological capacity in provinces, with the WHO providing financial support to the NICD for surveillance activities. The Office of the Deputy Director hosted a Regional Collaboration Centre delegation to explore the advancement of Public Health Institutes and hosted a delegation from Namibia as a joint partnership.

During the reporting year, Gift of the Givers donated a Modular Office Unit with an estimated value of R2 million to support FETP staff and student training.

We continue to strengthen our partnerships and collaboration with the private sector, the Regional Collaborating Centre, USAID, and Right to Care. The US CDC Foundation and Bloomberg Philanthropies continue to support the establishment of a National Public Health Bulletin and advance Data for Action outputs.

RESEARCH OUTPUT

Journal articles

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3. Sikhosana ML, Sucher M, Kuonza L, Cutland C, Slogrove A, Otwombe K, Motaze NV. Association between preeclampsia and HIV: a case-control study in urban South Africa. AJOG Glob Rep. 2022 Apr 15;2(3):100056. https://doi.org/10.1016/j.xagr.2022.100056.
4. Singh T, Duba T, Muleba L, Matuka, DO, Glaser D, Masuku Z, et al. Effectiveness of low-cost UVGI chamber for decontaminating filtering facepiece respirators to extend reuse. Journal of Occupational and Environmental Hygiene. https://doi.org/10.1080/15459624.2022.2137299.

Conference Presentations

- International conference: 38
- Local conference: 9

Centre for Enteric Diseases (CED)

Centre for Enteric Diseases (CED)

DR JUNO THOMAS
Centre Head

BACKGROUND

The goal of the CED is to provide up-to-date, locally relevant information to facilitate the understanding, management, and prevention of enteric diseases. The centre focuses on six areas of interest, namely

1. Foodborne diseases, which are globally recognised as a threat to food safety and security.
2. Waterborne diseases, which can affect public health in instances where unsafe water is utilised and are often associated with large outbreaks.
3. Priority enteric diseases under routine surveillance, which comprise epidemic-prone conditions such as enteric fever, cholera, and listeriosis.
4. Rotavirus, which is a vaccine-preventable disease in South Africa.
5. Diarrhoeal disease syndromic surveillance.
6. Genomic surveillance of priority enteric bacterial pathogens.

The centre comprises a small team of specialists with extensive experience in enteric diseases. Activities include surveillance, public health-oriented research, outbreak investigation and response, reference laboratory services, regional technical and laboratory testing assistance, as well as international collaborations.

The year under review was marked by a resurgence of enteric fever across several provinces. The routine use of whole-genome sequencing (WGS) as a surveillance tool detected multiple localised but growing clusters and showed the spread and establishment of the Klerksdorp enteric fever cluster strain into other provinces. This enabled a more targeted investigation of cases and possible sources of infection by the DoH and assisted in our understanding of the complex epidemiology of this endemic disease.

Another notable event was the re-emergence of indigenous pandemic cholera following importation. The centre played a key role in supporting the DoH through collaborative epidemiologic and laboratory work with multiple stakeholders and provided technical guidance for outbreak investigation and response activities.

SURVEILLANCE

ACUTE DIARRHOEAL DISEASE SURVEILLANCE

Diarrhoeal disease sentinel surveillance is active at nine sites in five provinces. During the reporting period, 622 cases were enrolled (209 from Mpumalanga, 167 from the North West, 132 from Gauteng, 84 from the Western Cape, and 30 from the Free State). Children ≤5 years constituted 75% of cases (466/622) with an average age of 14 months. Patients >5 years comprised 23% (144/622) of enrollments, with an average age of 31 years. Most cases (403/622, 75%) were inpatients. Where results were available, among children up to 15 years of age, 2.9% (14/478) were HIV-infected, while 46% (52/114) of adults 16 years or older were HIV-infected. Outcome data were available for 95% (582/622) of the enrollments, with 95% (552/582) of the cases discharged and 5 deaths reported.

Rotavirus was detected in 20% of the samples tested by ELISA (112/555), with detection rates and case numbers at their highest during September 2022. Multiplex PCR testing for other enteric viruses, bacteria, and parasites was performed. Excluding rotavirus, the most common enteric viruses detected were norovirus (34/347, 10%), adenovirus (72/347, 20%), and astrovirus (23/347, 6%). *Shigella* spp. was the most common enteric bacterial pathogen identified (53/358, 15%), followed by *Campylobacter* spp. (14/358, 4%), nontyphoidal *Salmonella* (6/358, 2%), and *Yersinia enterocolitica* (5/258, 1%). The most common parasites detected were *Cryptosporidium* spp. (46/352, 13%) and *Giardia lamblia* (14/352, 4%).

Rotavirus and shigellosis remain the two most common causes of diarrhoea in hospitalised children under 5 years, a finding consistent with that reported in many other low- and middle-income countries. Unlike children and adolescents, a large proportion (almost half) of adults hospitalised for diarrhoea are HIV-infected.

NATIONAL CHOLERA SURVEILLANCE

All presumptive cholera cases notified through the NMC, or other sources are followed up immediately upon receipt of the alert or notification. This includes liaison with microbiologists, technologists, and clinicians and expediting the referral of samples/isolates to the CED for emergency testing.

In the reporting period, a total of 82 clinical specimens and isolates were tested. Of these, 16 were confirmed as cases of *Vibrio cholerae*, and further characterised as toxigenic serogroup O1 *V. cholerae* (11 cases) and non-toxigenic, non-O1 *V. cholerae* (5 cases). Isolates from water and food samples were also tested but they were all non-toxigenic non-O1 *V. cholerae*.

NATIONAL LISTERIOSIS SURVEILLANCE

All cases of listeriosis alerted through the NMC system and NHLS corporate data warehouse (CDW) were followed up by the centre's staff to ensure the collection of additional data, a comprehensive food history, and an isolate referral for WGS.

Seven provinces reported 83 laboratory-confirmed cases of listeriosis. Most cases were from the Western Cape (39%, 32/83), followed by Gauteng (25%, 21/83) and KwaZulu-Natal (17%, 14/83). No cases were reported from Limpopo and Mpumalanga. Persons aged 15-49 years accounted for 42% (35/83) of cases, while 25% (21/83) of cases were neonates, and 14% (12/83) of cases were 65 years and older.

NATIONAL ENTERIC FEVER SURVEILLANCE

A total of 194 laboratory-confirmed cases of enteric fever were reported from eight different provinces. The majority of cases were from Gauteng (53%, 103/194) followed by the Western Cape (19%, 36/194) and North West (10%, 20/194) provinces. No cases were reported from the Northern Cape. Outbreaks were identified in several provinces through genomic surveillance, as described in the following section.

OUTBREAKS

The centre continues to play a leading role in the investigation and response to outbreaks of epidemic-prone enteric pathogens and food- and water-borne diseases. The centre's staff routinely follow up on alerts of suspected enteric disease outbreaks reported through the NMC system and other sources, investigate clusters identified through routine and genomic surveillance activities and provide epidemiological and laboratory support for investigations as needed.

ENTERIC FEVER (TYPHOID FEVER)

Through core-genome multilocus sequence typing (cgMLST) analysis of WGS data, clusters (small, localised outbreaks) were previously identified in the Western Cape, the North West, and Gauteng: three clusters in different districts in the Western Cape, one cluster in the North West, and two clusters in Gauteng. The first identified case in all clusters occurred in 2020. As of March 31, 2023, the City of Cape Town cluster comprised 23 cases, with four new cases identified in the last quarter of 2022; the Winelands and Garden Route clusters in the Western Cape comprised 11 and 15 cases, respectively, but no new cases belonging to these clusters were identified in the current reporting period.

An additional 41 cases belonging to the Klerksdorp cluster were identified in the period under review. As of March 31, 2023, there are 76 confirmed cases across 6 provinces (NW=36; GP=27; MP=6, KZN=3; FS=2; WC=2).

The first Gauteng cluster consists of 32 cases identified from January 2020 through October 2022. Most of the cases were reported from the City of Tshwane Metro (78%, 25/32), with most (53%, 17/32) of the cases aged ≤15 years. The second Gauteng cluster consists of 12 cases identified from June 2020 through April 2022.

Outbreak investigations are ongoing for all clusters. Previous in-depth interviews of 26/35 Klerksdorp cluster cases showed an association with consumption of contaminated water in illegal gold mines located in the district, but more recent cases linked with this cluster have originated from other provinces, and infection was acquired through other transmission pathways. No definite source(s) of infection have been identified for the Western Cape or Gauteng clusters. Contamination of municipal water is very unlikely to be the source of infection in any of the clusters described, and the ongoing challenge of identifying the source(s) of infection attests to the complex epidemiology and range of transmission pathways for this pathogen. The CED continued to provide technical advice and support to the provincial and district departments of health with outbreak investigations. Updates and alerts were placed on the NICD website, and centre staff members (Drs Juno Thomas, Linda Erasmus, and Mr Phuti Sekwadi) responded to media queries and gave radio and TV interviews on the topic.

CHOLERA

Following reports of cholera outbreaks in several African countries (including Malawi and Mozambique), the NICD issued an alert in December 2022 for healthcare workers, highlighting the risk of imported cases. From January 1 through March 31, 2023, 11 confirmed cholera cases were identified (toxigenic *Vibrio cholerae* O1 serotype Ogawa) and one death was reported. All cases occurred in Gauteng, and ages ranged from 3 to 50 years. All isolates tested were susceptible to ciprofloxacin and azithromycin. The first three cases were imported or import-related cases following travel to Malawi. All subsequent cases acquired the infection locally and are classified as indigenous cases. Exposure to the Jukskei and Klip rivers during cleansing or baptism ceremonies was reported as a possible source of infection in several cases.

The CED has supported the DoH in cholera case investigation, field investigation, and contact tracing activities, including in-depth face-to-face interviews with confirmed cases and contacts, the collection of stool specimens from symptomatic contacts, and testing the stool specimens at the CED laboratory. The CED produced several technical guidance documents, which were placed on the NICD website and circulated by the DoH to healthcare facilities. These included a clinical management summary guide, a specimen collection guide, a treatment flow chart, and an advisory for all NHLS labs on the processing of samples for cholera investigation. Updates and alerts were placed on the NICD website, and updates were presented at the weekly MNORT meetings. Centre staff members (Drs Juno Thomas and Linda Erasmus and Mr Phuti Sekwadi) responded to media queries and gave radio and TV interviews on the topic.

OUTBREAKS OF NONTYPHOIDAL SALMONELLOSIS IN HEALTHCARE FACILITIES

MULTI-FACILITY HEALTHCARE-ASSOCIATED OUTBREAK OF *SALMONELLA ENTERICA* SEROVAR ISANGI, EASTERN CAPE PROVINCE

From April through July 2022, the NHLS laboratory in Port Elizabeth noted an increase in cases of extended β-lactamase producing (ESBL) nontyphoidal *Salmonella*; by September 2022, 43 cases had been identified. The cases included children and adults, and most were patients at the three largest public hospitals in the Nelson Mandela Bay Metropolitan Municipality. Isolates submitted to the centre from all patients diagnosed with nontyphoidal salmonellosis in the Eastern Cape from 2020 through 2022 underwent phenotypic serotyping and WGS. Phenotypic serotyping identified the isolates as *Salmonella* serovar Isangi, and antimicrobial resistance testing confirmed their antimicrobial susceptibility profile as multi-drug resistant, resistant to ciprofloxacin, and ESBL-producing. On cg-MLST analysis of WGS, a cluster of highly related *Salmonella* serovar Isangi isolates was detected and showed that the first two cases due to this unique 'strain' occurred in late 2021. Records showed that the majority of patients with the outbreak strain were tested for and diagnosed with NTS infections at least 48 hours after admission. The few patients who tested positive on admission had recent exposure to one of the three hospitals. The transfer of patients between these facilities is common practice, and likely facilitated the transmission of strain from patients in one hospital to the next. Following the implementation of targeted and enhanced infection prevention and control measures in these hospitals, the number of cases decreased dramatically. Sporadic cases of colonisation and symptomatic infection have since been identified, mostly in patients with prior admissions to these hospitals during the outbreak.

THE OUTBREAK OF FOODBORNE *SALMONELLA* SEROVAR ENTERITIDIS IN A HOSPITAL, FREE STATE (SEPTEMBER 2022)

Twenty-four cases of febrile gastroenteritis (10 healthcare workers and 14 patients) were reported from September 7 through September 9. All cases reported the consumption of chicken pasta served for lunch on September 7, by an outsourced food supplier. Food samples were collected and submitted for testing, but due to a five-day delay in transit, the results were invalid. Stool samples were collected from 15 cases, and nontyphoidal *Salmonella* was isolated from all samples. All isolates were confirmed to be *Salmonella* serovar Enteritidis and shown on analysis of WGS to be highly related, confirming the presence of an outbreak. In addition, it was reported that 25 food handlers working for the food supplier also reported gastroenteritis following consumption of the chicken pasta meal on September 7, but no clinical samples were collected and limited epidemiological information was available for this group.

OTHER FOOD- AND WATER-BORNE DISEASE OUTBREAKS

The centre continues to play a leading role in the investigation and response to outbreaks of food- and water-borne disease and clusters or suspected outbreaks of epidemic-prone enteric pathogens. The centre's staff routinely follow up on alerts of suspected enteric disease outbreaks reported through the NMC system and other sources and provide epidemiological and laboratory support. During the 2022/2023 reporting period, the centre responded to 13 reported outbreaks with epidemiologic and laboratory testing support as needed. Another 97 suspected foodborne disease outbreaks were reported to NICD/CED through NMC or other sources and followed up, but because of insufficient epidemiological data and the absence of clinical/food/environmental sample collection and testing, they were not investigated further.

Shigella and norovirus featured prominently among outbreaks where causative pathogens were identified. Unlike previous years, very few outbreaks of nontyphoidal salmonellosis were reported. Outbreaks of foodborne disease continue to be underreported and suboptimally investigated, and improper storage and temperature abuse of food are commonly identified as likely contributing factors in reported outbreaks.

POLICY CONTRIBUTIONS

A document detailing the recommendations for diagnosis, management, and public health response to enteric fever was updated and uploaded on the NICD website.

DIAGNOSTIC SERVICES

The virology and bacteriology reference laboratories provide a range of specialised tests to support diagnostic laboratories in the public and private health sectors, and also to provide rapid diagnostic and confirmatory testing for epidemic-prone pathogens. Testing is performed on isolates (from clinical specimens and environmental or food specimens) and directly on faecal specimens as indicated. The range of tests performed includes:

1. Specialised rotavirus testing and rotavirus typing.
2. Specialised testing for other enteric viruses, including astrovirus, adenovirus, norovirus, and bocavirus.
3. Specialised adenovirus typing was provided for acute hepatitis of unknown cause cases during 2022/2023.
4. Specialised molecular screening for enteric pathogens (including multiplex PCR).
5. Specialised testing for *Vibrio cholerae*, including phenotypic and molecular testing.
6. Specialised phenotypic characterisation and molecular testing for diarrhoeagenic *E. coli*, including Shiga toxin-producing *E. coli.*
7. Specialised testing for *Salmonella* species, including serotyping and molecular testing.
8. Specialised testing for *Listeria* species.
9. WGS for enteric bacterial pathogens were indicated.

RESEARCH ACTIVITIES

African network for improved diagnostics, epidemiology, and management of common infectious agents (ANDEMIA)

NICD investigators: NA Page, J Thomas, S Nadan, S Johnstone
Collaborators: F Leendertz, C A.-Koffi (CHU Bouake), S Ouangraoua (Centre Muraz), JJ Muyembe Tamfum (INRB), M Venter (UP)

Sub-Saharan Africa bears a disproportionately high burden of infectious diseases and associated morbidity and mortality. While European countries tend to focus research on tropical or neglected diseases, due to the impact on travellers from those countries, they rarely investigate common infectious diseases like acute respiratory tract infections (RTI), gastrointestinal tract infections (GTI), and acute febrile disease of unknown cause (AFDUC). Sentinel surveillance was established in Democratic Republic of the Congo (DRC), Ivory Coast, Burkina Faso, and South Africa (Kalafong, Matikwana, and Mapulaneng hospitals), enrolling patients presenting with RTI, GTI, and AFDUC syndromes. Control participants were also enrolled between 2019 and 2022. The project provided information on the utility of diagnostic results for clinical management, including antimicrobial susceptibility patterns and diagnostic gaps, and generated data on SARS-CoV-2 genomes in areas without any previous surveillance.

TEACHING AND TRAINING

CED staff provided and contributed to the following teaching and training activities during the period under review:

- Undergraduate and postgraduate teaching: Field Epidemiology Training Programme (FETP); MSc Epidemiology and Biostatistics, MSc Vaccinology, and Diploma in Tropical Medicine and Hygiene (DTM&H) courses at the University of the Witwatersrand; registrar

training courses hosted by the NICD; NICD intern medical scientist rotational training.
- Postgraduate supervision: staff from the centre supervised 5 PhD students, 3 MSc students, 1 MMed student, and 1 MPH student.
- Five intern medical scientists were trained in the centre, with 2 obtaining registration with the HPCSA for independent practice.

Training for healthcare workers and DOH officials on enteric fever and cholera was performed on request for national, provincial, and district audiences.

PROFESSIONAL DEVELOPMENT

Two postgraduate candidates were enrolled, comprising the following:

- MSc: 1
- MPH: 1

One centre staff member graduated and was awarded a National Diploma in Biomedical Technology.

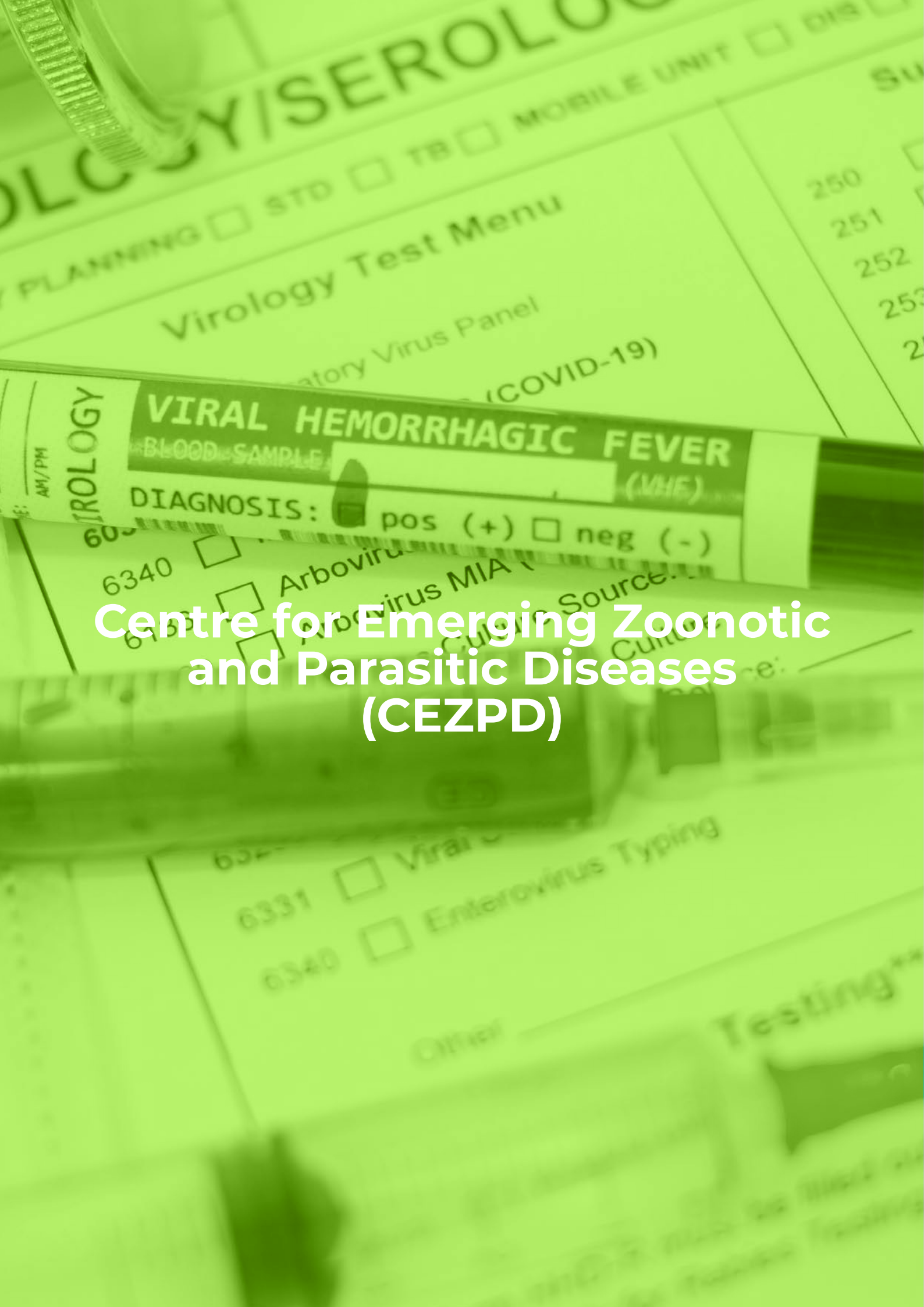
RESEARCH OUTPUT

JOURNAL ARTICLES

1. Badr HS, Colston JM, Nguyen NH, Chen YT, Burnett E, Ali SA *et al*. Spatiotemporal variation in risk of Shigella infection in childhood: a global risk mapping and prediction model using individual participant data. Lancet Glob Health. 2023 Mar;11(3): e373-e384.
2. Davedow T, Carleton H, Kubota K, Palm D, Schroeder M, Gerner-Smidt P *et al*. 2022. PulseNet International survey on the implementation of whole genome sequencing in low and middle-income countries for foodborne disease surveillance. *Foodborne Pathogens and Disease* 19:332-340 (DOI: 10.1089/fpd.2021.0110).
3. Gallichan S, Perez-Sepulveda BM, Feasey NA, Hinton JCD, Thomas J, Smith AM. 2022. Multiplex PCR assay for clade typing of *Salmonella enterica* serovar *Enteritidis*. *Microbiology Spectrum*. 10(6): e0318222 (doi:10.1128/spectrum.03182-22).
4. Gallichan S, Perez-Sepulveda BM, Feasey NA, Hinton JCD, Smith AM. 2022. Multiplex PCR assay for clade-typing Salmonella Enteritidis. https://www.protocols.io/(https://dx.doi.org/10.17504/protocols.io.4r3l2ok1jv1y/v1).
5. Guga G, Elwood S, Kimathi C, Kang G, Kosek MN, Lima AAM et al. Burden, Clinical Characteristics, Risk Factors, and Seasonality of Adenovirus 40/41 Diarrhoea in Children in Eight Low-Resource Settings. Open Forum Infect Dis. 2022.
6. Johnstone SL, Page NA, Groome MJ, du Plessis NM, Thomas J. Diagnostic testing practices for diarrhoeal cases in South African public hospitals. BMC Infect Dis. 2022 Nov 9;22(1):827May 13;9(7): ofac241.
7. Mattock J, Smith AM, Keddy KH, Manners EJ, Duze ST, Smouse SL, Tau NP *et al*. 2022. Genetic characterization of *Salmonella* Infantis from South Africa, 2004-2016. *Access Microbiology* 4:000371 (https://doi.org/10.1099/acmi.0.000371).
8. Mwangi PN, Page NA, Seheri ML, Mphahlele MJ, Nadan S, Esona MD *et al*. Evolutionary changes between pre- and post-vaccine South African group A G2P [4] rotavirus strains, 2003-2017. Microb Genom. 2022 Apr;8(4).
9. Onyeka LO, Adesiyun AA, Keddy KH, Hassim A, Smith AM, Thompson PN. 2022. Characterization and epidemiological subtyping of Shiga toxin-producing *Escherichia coli* isolated from the beef production chain in Gauteng, South Africa. *Preventive Veterinary Medicine* 205:105681 (doi: 10.1016/j.prevetmed.2022.105681).
10. Yamba K, Kapesa C, Mpabalwani E, Hachaambwa L, Smith AM, Young AL *et al*. 2022. Antimicrobial susceptibility and genomic profiling of *Salmonella enterica* from bloodstream infections at a tertiary referral hospital in Lusaka, Zambia, 2018-2019. *International Journal of Infectious Diseases Regions* 3:248-255 (https://doi.org/10.1016/j.ijregi.2022.04.003).

CONFERENCES

- International: 5
- National: 6



Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD)

Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD)

DR JACQUELINE WEYER
Centre Head

BACKGROUND

The Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD) is a national and regional hub of expertise in laboratory-based diagnosis and surveillance, research, and teaching and training related to viral, bacterial, and parasitic zoonoses. The infectious diseases under the purview of the Centre include high-consequence infections (such as anthrax and Ebola virus disease) but also malaria and neglected tropical infections, such as schistosomiasis and helminthic infections. These diseases are of public health importance in South Africa:

1. Diseases listed as Category 1 notifiable medical conditions (NMCs) including viral haemorrhagic fevers (VHFs) (such as Ebola virus disease, Crimean Congo haemorrhagic fever, Lassa fever, and Marburg virus disease), anthrax, botulism, yellow fever, plague, Rift Valley fever (RVF), rabies, and malaria;
2. Diseases listed as Category 2 NMCs: brucellosis, schistosomiasis (or bilharzia), and soil-transmitted helminthic infections;
3. Category 3 NMCs: endemic and non-endemic arboviral infections;
4. Other neglected tropical diseases including leptospirosis and opportunistic parasitic infections; and
5. Other emerging zoonoses, such as mpox (previously monkeypox) and Lujo haemorrhagic fever (these are also Category 1 NMCs).

As a centre of expertise, the CEZPD supports public health responses, including policy advice and technical support to the NDoH and many other national and international stakeholders, including the WHO and the Africa CDC. The CEZPD shares its knowledge and skills in emerging and re-emerging zoonotic and parasitic diseases, in the training of scientists, laboratorians, epidemiologists, health care workers, and medical doctors.

SURVEILLANCE

HUMAN RABIES SURVEILLANCE

The CEZPD's Special Viral Pathogens Laboratory (SVPL) is the national reference laboratory for human rabies in South Africa. The laboratory offers testing for ante-mortem and post-mortem diagnosis through a range of ISO15189:2012 accredited tests. The SVPL holds a database of epidemiological and clinical information for all confirmed, probable, and suspected rabies cases, and contributes to the accurate reporting of rabies as a Category 1 NMC through a passive surveillance approach.

SURVEILLANCE SUPPORTING MALARIA ELIMINATION IN SOUTH AFRICA ANTIMALARIAL RESISTANCE MONITORING

The Laboratory for Antimalarial Resistance Monitoring and Malaria Operational Research (ARMMOR) strengthened antimalarial drug and diagnostic surveillance efforts following the confirmation of African malaria parasites resistant to the artemisinin component of the recommended treatment for uncomplicated malaria in 2021. Although none of the 1 971 specimens analysed carried any of the validated molecular markers of artemisinin resistance, a number of isolates from districts targeting malaria elimination had non-validated molecular markers. This highlights the need for routine drug efficacy surveillance in South Africa. In addition, the surveillance data suggests that there was no need to change the recommended point-care-diagnostic, histidine-rich protein 2 (HRP2)-based falciparum-specific rapid diagnostic tests, as all parasite isolates analysed carried wild-type HRP2 genes.

PESTICIDE RESISTANCE MONITORING

The Vector Control Reference Laboratory (VCRL) continued to monitor the occurrence and phenotypic intensity of insecticide resistance in malaria vector populations in the KwaZulu-Natal and Mpumalanga provinces. Several resistance phenotypes have been detected in the major malaria vector *Anopheles arabiensis*, especially in northern KwaZulu-Natal, but they are currently of low intensity and are not considered to pose a significant threat to the efficacy of vector control at present. Surveillance data across all three of South Africa's malaria-endemic provinces (KwaZulu-Natal, Mpumalanga, and Limpopo) shows the perennial presence of several malaria vector species, illustrating continued high risk and receptivity for malaria.

PLAGUE SURVEILLANCE

The Special Bacterial Pathogens Reference Laboratory (SBPRL) conducts surveillance for plague in susceptible rodent populations in the Nelson Mandela Bay (Coega area) and eThekwini municipalities in order to alert public health authorities to the possibility of increased human plague risk. No rodents tested positive for plague anti-F1 antibodies.

SURVEILLANCE FOR VIRAL HAEMORRHAGIC FEVERS

The SVPL provides referral diagnostics for Ebola virus disease, Marburg virus disease, Crimean-Congo haemorrhagic fever, Lassa and other mammarenavirus infections, and yellow fever through a passive surveillance approach. The SVPL operates high and maximum containment facilities that allow for the safe and secure handling, testing, and storage of specimens for suspected and confirmed cases of VHF.

OUTBREAKS

The CEZPD supported responses through the laboratory analysis of suspected cases and assistance in case investigations in various zoonotic disease outbreaks. During the reporting period, ongoing outbreaks of rabies in domestic dogs were reported from districts in KwaZulu Natal and the Eastern Cape. The CEZPD reported a total of 16 confirmed human rabies cases during the reporting period. These reports are shared with the Provincial and National DoH, the Department of Agriculture, Land Reform, and Rural Development, and the multisectoral Rabies Advisory Group in order to prioritise actions for the control of rabies in domestic dogs in affected areas and also to inform targeted public health actions to prevent human rabies.

Since May 2022, a multi-country outbreak of mpox has evolved, with more than 85 000 confirmed cases from 110 countries. This became the largest outbreak of mpox recorded to date and involved cases reported from countries where mpox is not considered endemic. The CEZPD provided reference laboratory testing for mpox cases in South Africa but also received submissions from a number of African countries for laboratory support. Genomic sequencing using next-generation sequencing platforms of the initial mpox cases reported in South Africa assisted in indicating that these local cases were linked to the multi-country outbreak. The CEZPD contributed to training in the laboratory diagnosis of mpox for representatives from laboratories from 17 African Union Member States in order to support the improved diagnosis of mpox on the continent. In addition, the CEZPD provided control material to private laboratories in South Africa to assist in the verification and quality control of commercial assays in support of the decentralisation of mpox testing in South Africa.

Odyssean malaria is acquired when infected *Anopheles* mosquitoes are accidentally transported to non-endemic areas and transmit the parasites. In October and November 2022, two cases were investigated in the Ekurhuleni and Johannesburg Metros. These were unusual in being caused by *Plasmodium malariae*, rather than the usual *P. falciparum*, but they were apparently unlinked. Most Odyssean malaria cases occur in the Gauteng province. Nevertheless, in January 2023, a case was investigated in Langa, Cape Town, by local health authorities. A national database of known cases is maintained by CEZPD.

POLICY CONTRIBUTIONS

The Centre contributed to reviewing and developing policies, guidelines, operating procedures, and strategies for the following:

1. The latest WHO technical guidelines and recommendations for malaria vector control methods and technologies;
2. The national and provincial malaria control policies and programmes in the southern African region as part of the Elimination 8 (E8) Initiative;
3. The National Malaria Treatment and Diagnosis Guidelines;
4. The WHO Global Outbreak Alert and Response Network (GOARN) strategy for 2022-2026;
5. The WHO Manual for the Laboratory-based Surveillance of Yellow Fever;
6. The updates to the National Guidelines for the Recognition and Diagnosis of Viral Haemorrhagic Fever in South Africa;
7. The Master Plan for Elimination of Neglected Tropical Diseases in South Africa; and
8. The standard operating procedures for handling specimens for suspected and confirmed cases of VHF and mpox at NHLS laboratories.

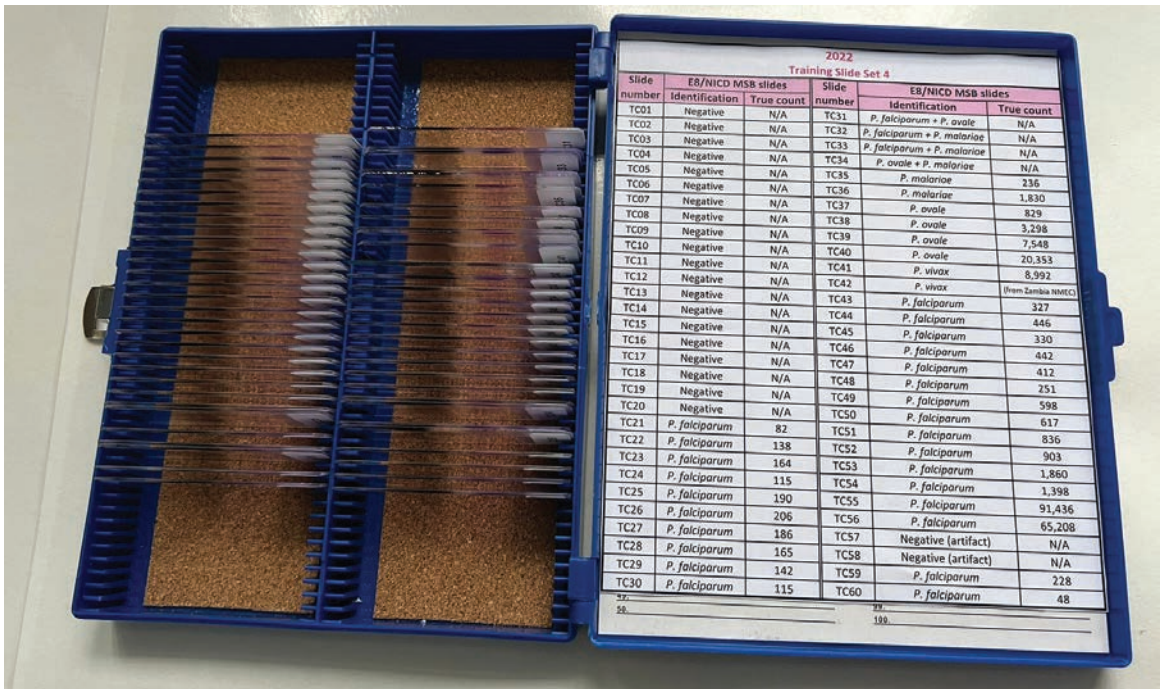
DIAGNOSTIC SERVICES

The CEZPD provides specialist referral diagnostic services for the diseases mentioned in the introduction of this report. A summary of diagnostic services during the reporting period is provided per the CEZPD section.

The SBPRL provided specialised diagnostic services for zoonotic bacterial pathogens causing diseases including anthrax, plague, leptospirosis, botulism, and brucellosis. There were 28 probable cases of leptospirosis and one case of brucellosis detected. No cases of anthrax, botulism, or plague from South Africa were detected during the reporting period.

The SVPL investigated 23 suspected viral haemorrhagic cases during the period under review. Two cases of CCHF were confirmed from the Free State (but may have been acquired in the Eastern Cape or Free State provinces) and the Western Cape provinces, from 1st April 2022, to 31st March 2023. An imported case of Lassa fever involving a traveller returning from Nigeria to South Africa was confirmed. The SVPL tested in excess of 220 suspected mpox specimens and diagnosed the first 3 South African cases of the multi-country mpox outbreak. The Electron Microscopy Laboratory (EML) and SVPL confirmed the first human case of tanapox to be acquired south of equatorial Africa (in the Kruger National Park), which was also the first case to be reported globally in 19 years. The SVPL confirmed 12 human rabies cases from April 1, 2022, to March 31, 2023 (according to time of death), reported from the Eastern Cape (n=6); Limpopo (n=4) and KwaZulu-Natal (n= 2). In addition, there were six probable rabies cases identified during the same time period in the Eastern Cape (n=5) and KwaZulu-Natal (n=1).

The PRL provided specialised diagnostic services for parasites of medical importance both by conventional methods and, increasingly, polymerase chain reaction (PCR) assays. There was a high rate of positives among the *P. jirovecii* PCR tests (43%, 25/58). The majority of referred tests for malaria PCR were positive (76%, 62/82), including 11 non-falciparum and 4 mixed infections. Interesting and unusual parasites identified included *Balamuthia mandrillaris and Cephalobus cubaensis*. The CEZPD PRL, with financial support from the Global Fund and the Eliminating Eight (E8) countries, maintained and managed the Regional Malaria Slide Bank and Proficiency Testing (PT) scheme for supporting malaria laboratory diagnosis in southern African countries. In the last 12 months, 12 997 slides in 52 batches were manufactured for microscopist training and external quality assessment by participating regional laboratories. Three PT surveys were conducted, and a comprehensive training slide set was also prepared (Figure 1) and supplied to each country.



2022
Training Slide Set 4

Slide number	E8/NICD MSB slides		Slide number	E8/NICD MSB slides	
	Identification	True count		Identification	True count
TC01	Negative	N/A	TC31	*P. falciparum + P. ovale*	N/A
TC02	Negative	N/A	TC32	*P. falciparum + P. malariae*	N/A
TC03	Negative	N/A	TC33	*P. falciparum + P. malariae*	N/A
TC04	Negative	N/A	TC34	*P. ovale + P. malariae*	N/A
TC05	Negative	N/A	TC35	*P. malariae*	236
TC06	Negative	N/A	TC36	*P. malariae*	1,830
TC07	Negative	N/A	TC37	*P. ovale*	829
TC08	Negative	N/A	TC38	*P. ovale*	3,298
TC09	Negative	N/A	TC39	*P. ovale*	7,548
TC10	Negative	N/A	TC40	*P. ovale*	20,353
TC11	Negative	N/A	TC41	*P. vivax*	8,992
TC12	Negative	N/A	TC42	*P. vivax*	(from Zambia NMEC)
TC13	Negative	N/A	TC43	*P. falciparum*	327
TC14	Negative	N/A	TC44	*P. falciparum*	446
TC15	Negative	N/A	TC45	*P. falciparum*	330
TC16	Negative	N/A	TC46	*P. falciparum*	442
TC17	Negative	N/A	TC47	*P. falciparum*	412
TC18	Negative	N/A	TC48	*P. falciparum*	251
TC19	Negative	N/A	TC49	*P. falciparum*	598
TC20	Negative	N/A	TC50	*P. falciparum*	617
TC21	*P. falciparum*	82	TC51	*P. falciparum*	836
TC22	*P. falciparum*	138	TC52	*P. falciparum*	903
TC23	*P. falciparum*	164	TC53	*P. falciparum*	1,860
TC24	*P. falciparum*	115	TC54	*P. falciparum*	1,398
TC25	*P. falciparum*	190	TC55	*P. falciparum*	91,436
TC26	*P. falciparum*	206	TC56	*P. falciparum*	65,208
TC27	*P. falciparum*	186	TC57	Negative (artifact)	N/A
TC28	*P. falciparum*	165	TC58	Negative (artifact)	N/A
TC29	*P. falciparum*	142	TC59	*P. falciparum*	228
TC30	*P. falciparum*	115	TC60	*P. falciparum*	48

Figure 1: Comprehensive malaria and other blood parasites training slide set.

A total of 4103 *Anopheles* mosquitoes was referred to the VCRL from sentinel sites in the KwaZulu-Natal, Mpumalanga, and Limpopo provinces. The presence of five malaria vector species that contribute to ongoing residual malaria transmission in South Africa, were identified among these collections: *Anopheles arabiensis, An. merus, An. vaneedeni, An. funestus* **and** *An. parensis*.

RESEARCH ACTIVITIES

The CEZPD engages in research on zoonoses of public health importance to South Africa and the region.

Establishing a targeted malaria amplicon sequencing platform to strengthen malaria surveillance in the Elimination 8 countries

NICD Investigators: J Raman
Collaborators: B Greenhouse, A Aranda-Diaz, J Smith (University of California-San Francisco), A Wesolowski (Johns Hopkins University), I Kleinschmidt (London School of Hygiene and Tropical Medicine), and M Chisenga and C Sikaala (E8)

Building on the success of genomic surveillance in informing COVID-19-related interventions, the feasibility of incorporating a genomic surveillance platform into routine malaria surveillance activities to inform malaria elimination interventions will be evaluated. Malaria specimens collected from six southern African countries will be analysed on a targeted amplicon next-generation sequencing platform at the NICD. Data on antimalarial drug and diagnostic resistance, parasite relatedness, and parasite flow within and between the participating countries will be generated and used to guide intervention selection and targeting. The optimisation of the platform has been completed, with sample analysis underway at the time of this report.

The links between insecticide resistance and physiological processes in malaria vector mosquitoes

NICD Investigators: S Oliver, B Brooke
Collaborators: M Allam, A Ismail (United Arab Emirates University), C Lyons (University of Cape Town)

It was shown that blood-feeding increases the longevity of adult female *Anopheles funestus* (major malaria vector) mosquitoes and also enhances their levels of insecticide resistance. These results show that older female mosquitoes may carry high-intensity resistance phenotypes, an important consideration for how insecticide susceptibility is measured in wild vector populations. A link between gut microbiota and insecticide resistance was shown in the major malaria vector *An. arabiensis*. This may have important effects on susceptibility to *Plasmodium* (malaria) infection in insecticide-resistant mosquitoes, which in turn will affect their competence as malaria vectors.

Assessing novel/alternative methods of malaria vector control in South Africa

NICD Investigators: G Munhenga, S Oliver, Y Dahan-Moss, M Kaiser, E Jamesboy, L Koekemoer, B Brooke
Collaborators: H Yamada (International Atomic Energy Agency)

Field releases of sterilised male *Anopheles arabiensis* (malaria vector) mosquitoes in the northern KwaZulu-Natal Province were completed. The results of these experiments in terms of vector population suppression are being analysed and interpreted. This was a major step forward in evaluating the feasibility of the Sterile Insect Technique for malaria control in South Africa.

Genetic characterization of mpox cases, South Africa 2022

NICD Investigators: W Chan, P Mtshali, A Grobbelaar, N Moolla, T Mohale, M Lowe, M Du Plessis, A Ismail, J Weyer

The coding-complete genome sequences of the mpox virus were obtained from skin lesion swabs from the first two human cases detected in South Africa in June 2022. Sequence analyses indicated that the genetic sequences of the viruses associated with these two cases were most closely related to the genetic sequences of other MPXV reported during the 2022 multi-country outbreak and belong to the mpox hMPXV-1 clade (previously West Africa clade) and B.1 lineage.

The first report of tanapox from South Africa

NICD Investigators: M Birkhead, LH Blumberg, V Dermaux-Msimang, AA Grobbelaar, A Mathee, N Moolla, J Weyer
Collaborators: W Grayson (Ampath Laboratories), T Marshall (Ampath Laboratories), A Mathee (South African Medical Research Council), D Morobadi (Ampath Laboratories), M Popara (Mediclinic)

The first case of tanapox was diagnosed in South Africa in 2022. The case involved a visitor to the Kruger National Park. The clinical diagnosis was confirmed through electron microscopy, PCR testing, and genomic sequencing (Figure 2). Tanapox (genus: *Yatapox*; Family: *Poxviridae)* is a rarely diagnosed zoonosis, previously only reported from locations in equatorial Africa. This was also the first human case of tanapox reported in 19 years.

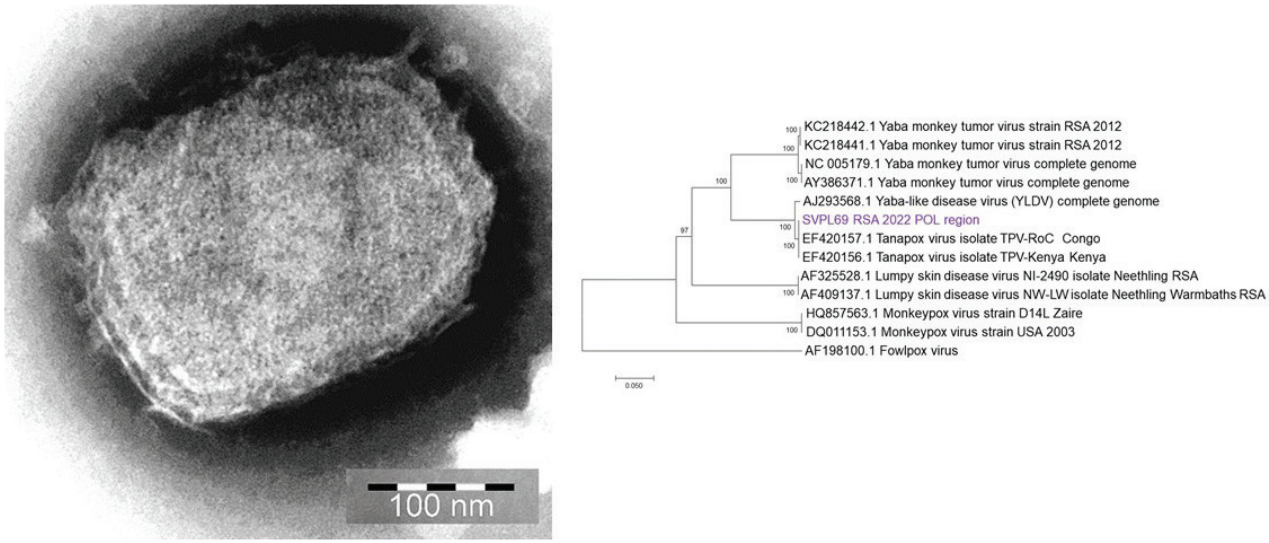


Figure 2: (left) An electron micrograph of the characteristic brick-shaped tanapox virion. (Right) Phylogenetic analysis indicating clustering of the sequence obtained from the sample, with a previously described tanapox partial polymerase gene target.

Host-associated distribution of novel mammarenaviruses in rodents from southern Africa

NICD Investigator: J Weyer
Collaborators: M Geldenhuys (University of Pretoria), T Kearney (Ditsong Museum), W Markotter (University of Pretoria)

Mammarenaviruses comprise diverse zoonotic RNA viruses, including important causative agents of viral haemorrhagic fever in Africa and the Americas. Rodent host surveillance in Southern Africa has revealed a high level of diversity of mammarenaviruses in different rodent species. This collaborative study, led by the University of Pretoria, reported on the PCR screening results of more than 500 rodent specimens from different locations in South Africa. PCR-positive specimens were subjected to next-generation sequencing and indicated the presence of sequences similar to Mariental and Lunk viruses from two rodent species, *Micaelamys namaquensis and Mus minutoides*. This represents the first description of these viruses from South Africa. The genomic sequences reported here partially satisfied the requirements put forward by the International Committee on the Taxonomy of Viruses' criteria for species delineation, suggesting that these may be new strains of existing species.

TEACHING AND TRAINING

The CEZPD supported a number of teaching and training activities, including curriculum development during the reporting period:

TRAINING COURSES AND WORKSHOPS HOSTED

- Malaria microscopy and stool parasitology refresher training conducted for NHLS and for the Malaria Control Programme for Limpopo, Mpumalanga, and KwaZulu-Natal provinces.
- Specialised next generation sequencing training for E8 Genomic Fellows from six southern African countries.
- Laboratory diagnosis and clinical aspects of parasitic infections for Diploma in Tropical Medicine and Hygiene (DTM&H) programmes for local and international students from the University of Glasgow and Sheffield University and from the Médecins Sans Frontières Global Health and Humanitarian Medicine course.
- The EcoHealth Alliance, University of Pretoria and NICD/NHLS Entomology workshop focusing on taxonomy and identification of *Aedes* mosquitoes, March 2022, Regional Diagnostic Training Centre (RDDC).
- The Africa CDC, ASLM and NICD/NHLS training workshop for delegates from 17 African Union Member States on mpox diagnosis using real-time PCR techniques, was hosted in September 2022 at the Regional Diagnostic Training Centre (Figure 3).

Figure 3: Delegates from laboratories across Africa receive training in the safe handling and testing of specimens from suspected cases of mpox, at the Regional Diagnostic Training Centre, September 2022.

OTHER CONTRIBUTIONS TO TRAINING PROGRAMMES AND WORKSHOPS

- Lectures for the NICD Registrar Rotation programme and coordination and lecturing for the virology and parasitology intensive courses for registrars.
- Overseeing and supporting NICD medical scientist intern rotations for virology, microbiology, and parasitology.
- Facilitation of the SADC E8 Workshop for the Training of Trainers for the National Competence Assessment for Malaria Microscopy.
- Lectures on malaria epidemiology, vector & parasite biology, and malaria control to E8 entomology fellowship trainees.
- Lectures on malaria epidemiology, vector & parasite biology, and malaria control to undergraduate students for the University of the Witwatersrand (WITS), the University of the Free State (UFS), and Tshwane University of Technology (TUT).
- Lectures at the WHO International Course on Plague: Laboratory Diagnosis and Surveillance held in Madagascar (July 11-15, 2022).
- Lectures at the United Nations Secretary General's Mechanism (UNSGM): Basic Training Course for Qualified Experts on the UNSGM Roster held in Johannesburg (June 20-July 1, 2022).
- Co-facilitated the Regional Training and Certification Programme for Biosafety and Biosecurity Professionals Workshop on Biorisk Management held in Johannesburg (August 1-5, 2022).
- Co-facilitated training on Shipping on Infectious Substances held in Johannesburg (May 24-25, 2022, and October 25-26, 2022).
- Community outreach through lectures to Grade 9 learners, Deutsche Internationale Schule, Science Expo Week, Johannesburg.

CURRICULUM DEVELOPMENT

- Contributions to curriculum development for the Africa CDC certification of biorisk management in Africa programme in collaboration with the NICD Division of Biosafety and Biosecurity.
- Contributions to curriculum development for the UP-Malaria Leadership and Management Course.

POSTGRADUATE STUDENTS

The CEZPD contributes to the development of the public health workforce for the future by investing in the training of post-graduate students. During the period under review, CEZPD staff supervised or co-supervised 46 post-graduate students (12 BSc Hons; 20 MSc/MTech and 14 PhD students) registered at different national and international universities.

PROFESSIONAL DEVELOPMENT, AWARDS AND HONOURS

The CEZPD invests in the ongoing professional development of staff with the following achievements during the reporting period:

QUALIFICATIONS AND PRESTIGIOUS COURSES

Postgraduate students

Two staff members graduated with PhD degrees during the period under review.

The following staff members received prestigious certifications:

- Y Zungu successfully completed the HPCSA internship hosted at CEZPD.
- Dr C Sriruttan-Nel was invited and successfully completed a Biobanking course, at the Institut Pasteur in Paris, France, with a certificate awarded from the University of Lausanne, Switzerland.
- Dr K Naidoo and H Geyer obtained certification as Biorisk Management Professionals from the International Federation for Biosafety Professionals.

AWARDS

- Dr J Weyer was re-awarded a C2 rating from the National Research Foundation of South Africa in January 2023.

HONOURS (INCLUDING APPOINTMENTS AND SERVING ON BOARDS, COMMITTEES, AND GROUPS)

- Prof B Brooke engaged with the WHO World Malaria Programme as a member of the development group for malaria vector control guidelines, and participated in the United Nations Environment Programme coordinated intercessional process of consultations on the continued use of DDT for public health.
- Dr G Munhenga engaged with WHO on the AFRO-II project: Demonstration of the effectiveness of diversified, environmentally sound and sustainable interventions, and strengthening national capacity for innovative implementation of integrated vector management for disease prevention and control in the WHO AFRO Region.
- Profs B Brooke (Chair) and L Koekemoer participated in the E8 Vector Control Technical Working Group meetings, whilst Dr J Raman participated in E8 Research Subcommittee meetings. Dr Raman also chaired the E8 Diagnosis and Case Management Technical Working Group meetings.
- Prof Basil Brooke chaired the Vector Control Subcommittee of the South African Malaria Elimination Committee (SAMEC), whilst Dr J Raman chaired the SAMEC Case Management Technical Working Group meetings.
- Dr J Raman was appointed to the Steering Committees of the Tanzanian Malaria Molecular Surveillance Initiative and the National Institutes of Health Innovation Equity Forum, and was appointed as Co-chair of the E8 Malaria Molecular Surveillance Coordinating Group.
- Dr J Raman was appointed as a mentor on the Pan-Africa Mosquito Control Association LiftHerUp Initiative.
- Dr J Raman was appointed as guest editor of Frontier's special supplement on Women in Infectious Diseases.
- Dr J Rossouw was selected as an Africa-Regional Subject Matter Expert (Af-SME) for Biorisk Management by the Africa CDC.

RESEARCH OUTPUT

Journal Articles

1. Alafo C, Marti-Soler H, Maquina M, Malhela A, Aswart AS and Koekemoer L *et al.* To spray or target mosquitoes another way: focused entomological intelligence guides the implementation of indoor residual spraying in southern Mozambique. Malaria Journal 2022; 21(1): 1-15. DOI:10.1186/s12936-022-04233-3.
2. Bamford C, Blumberg LH, Bosman M, Frean J, Hoek K and Miles J *et al*. Neoehrlichiosis in Symptomatic Immunocompetent Child, South Africa. Emerging Infectious Diseases 2023; 29(2): 407. DOI:10.3201/eid2902.221451.
3. Bradbury RS, Sapp SGH, Potters I, Mathison MA, Frean J and Mewara A *et al.* amarozzi, Where have all the diagnostic morphological parasitologists gone? Journal of Clinical Microbiology 2022; 60(11): e00986-22. DOI:10.1128/jcm.00986-22.
4. Brooke BD. Malaria vector surveillance and control in an elimination setting in South Africa. Tropical Medicine and Infectious Disease 2022; 7(11): 391. DOI:10.3390/tropicalmed7110391.
5. Carrim M, Tempia S, Thindwa D, Martinson DA, Kahn K and Stefan Flasche *et al.* Unmasking pneumococcal carriage in a high HIV prevalence population in two community cohorts with a high prevalence of HIV in South Africa, 2016-2018: the PHIRST study. Clinical Infectious Diseases 2022; 76(3): e710-e717. DOI:10.1093/cid/ciac499/6611495.
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10. Das D, Vongpromek R, Assawariyathipat T, Srinamon K, Kennon K, Stepniewska K *et al.* Field evaluation of the diagnostic performance of EasyScan GO: a digital malaria microscopy device based on machine-learning. Malaria Journal 2022; 21(1): 122. DOI: 10.1186/s12936-022-04146-1.
11. Felamboahangy LNN, Kaiser ML, Zengenene MP, Okumu F, Munhenga G and Koekemoer LL. Optimisation of laboratory-raring parameters for *Anopheles funestus* larvae and adults. Acta Tropica 2022; 238: 106785. DOI:10.1016/j.actatropica.2022.106785.
12. Fernández Montoya L, Máquina M, Martí-Soler H, Sherrard-Smith E, Alafo C and Opiyo M *et al.* The realized efficacy of indoor residual spraying campaigns falls quickly below the recommended WHO threshold when coverage, pace of spraying and residual efficacy on different wall types are considered. Plos One 2022; 17(10): e0272655. DOI:10.1371/journal.pone.0272655
13. Flegg JA, Humphreys GS, Montanez B, Strickland T, Jacome-Meza ZJ and Barnes KI *et al.* Spatiotemporal spread of *Plasmodium falciparum* mutations for resistance to sulfadoxine-pyrimethamine across Africa, 1990 -2020. PLOS Computational Biology 2022; 18(8): e1010317. DOI:10.1371/journal.pcbi.1010317.
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15. Gebhardt ME, Krizek RS, Coetzee M, Koekemoer LL, Dahan-Moss Y and Mbewe D *et al.* Expanded geographic distribution and host preference of *Anopheles gibbinsi (Anopheles* species 6) in northern Zambia. Malaria Journal 2022; 21(1): 1-10. DOI:10.1186/s12936-022-04231-5.
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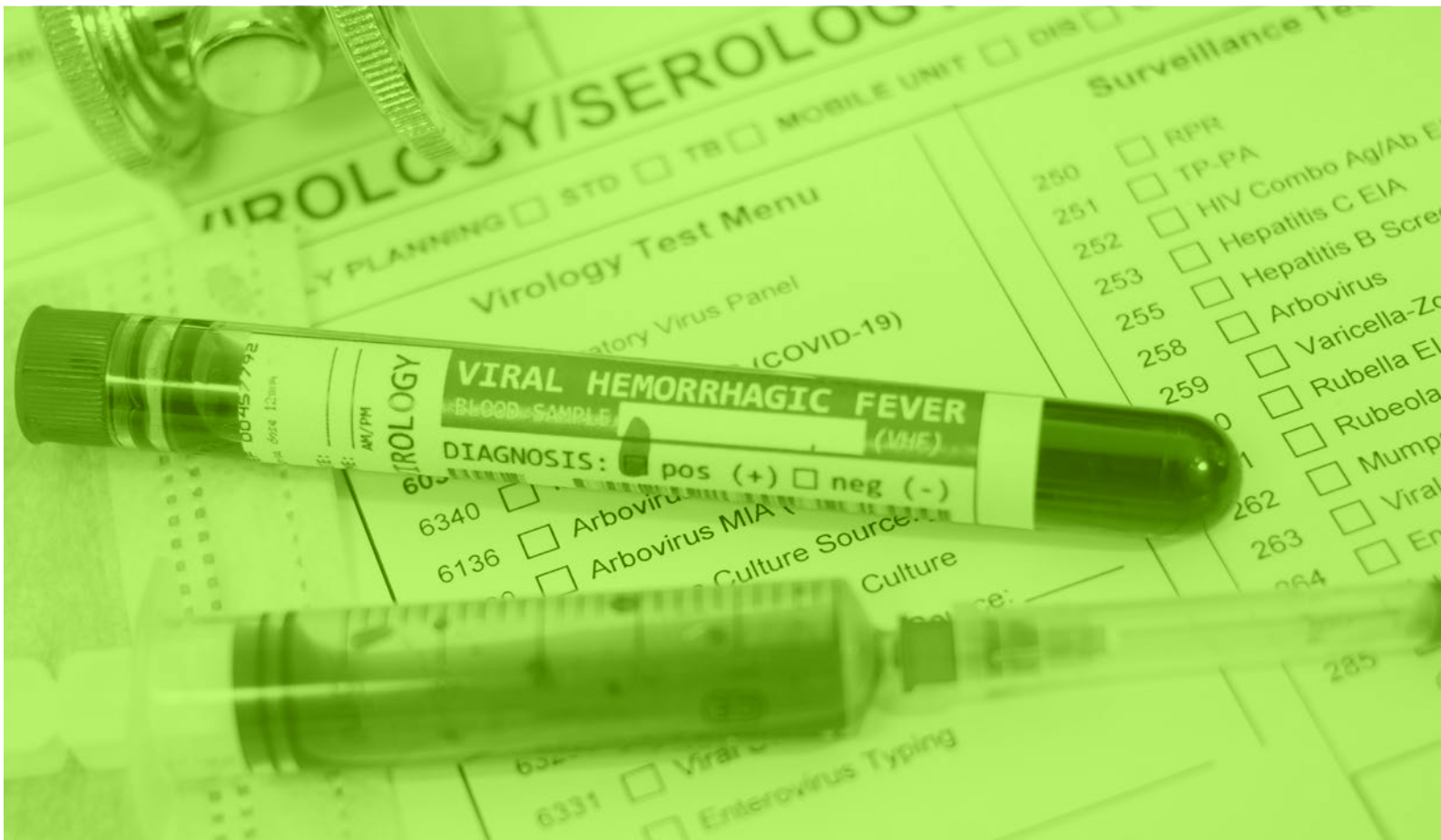
During the year under review, staff from the Centre made 44 contributions to international, national, and local congresses.



CENTRE FOR HEALTHCARE-ASSOCIATED INFECTIONS, ANTIMICROBIAL RESISTANCE & MYCOSES (CHARM)

CENTRE FOR HEALTHCARE-ASSOCIATED INFECTIONS, ANTIMICROBIAL RESISTANCE & MYCOSES (CHARM)

PROF NELESH GOVENDER
Centre Head

BACKGROUND

CHARM incorporates two national reference laboratories for antimicrobial resistance (AMR) and mycoses, both accredited to ISO 15189:2012 requirements and houses the pathogenic bacteria and fungi national stock culture collection. It functions as a WHO AMR Collaborating Centre and is the national focal point for WHO's global AMR surveillance system (GLASS). CHARM's epidemiology team supports priority surveillance projects, conducts outbreak investigations, and is involved in the set-up and evaluation of public health programmes.

SURVEILLANCE

The centre comprises a small team of specialists with extensive experience in antimicrobial resistance and fungal diseases. Activities include surveillance, public health-oriented research, outbreak investigation and response, reference laboratory services, regional technical and laboratory testing assistance, as well as international collaborations.

Baby GERMS-SA: neonatal infection surveillance in South Africa

NICD Investigators: NP Govender, S Meiring, R Mashau, O Perovic, M Smith, R Mpembe, V Quan, A von Gottberg, L de Gouveia, S Walaza, C Cohen
Collaborators: A Dramowski, C Mackay, R Phayane, T Mailula, O Mekgoe, C Kapongo, N Maphosa

Through tier one of this project, the centre conducted national surveillance of culture-confirmed neonatal bloodstream infections and meningitis across South Africa's public-sector hospitals. A manuscript was published summarising data for >37,000 neonatal infection cases from 2014-2019 in the *Lancet Global Health* journal. Updated national data from 2020-2022 were cleaned and analysed, with new results expected to be available in 2023. Tier two focused on a detailed characterisation of neonatal infections at six secondary-level institutions (provincial/regional neonatal units). Clinical data collection on 935 laboratory-confirmed neonatal infection episodes was complete, and sentinel hospital data were analysed for publication. In a new sub-study titled Baby GERMS-SA/Outbreak, epidemiological, laboratory and molecular data were combined to retrospectively identify clusters and outbreaks of healthcare-associated infections caused by major bacterial and fungal pathogens: *Klebsiella, Staphylococcus aureus, Acinetobacter baumannii, Enterococcus,* and *Candida*. Baby GERMS-SA data have been shared with the Institute for Health Metrics and Evaluation for age stratification of Global Burden of Disease AMR data and with the University of Stellenbosch for a weighted incidence syndromic combination antibiogram (WISCA) analysis. Baby GERMS-SA isolates will be shared with the Statens Serum Institut for work on a *Klebsiella* vaccine.

Healthcare-associated infection (HAI) outbreak detection and response

NICD Investigators: NP Govender, L Shuping, H Ismail
Collaborators: S Abrahams, L Mnqokoyi, B Banda, F Khan, A Thomas

The centre implemented a real-time alert system, using a custom-built mobile application, to prospectively detect outbreaks of healthcare-associated bloodstream infections among neonates. A surveillance system evaluation is expected to commence in 2023 at the remaining active site (Dora Nginza Hospital, Eastern Cape) following approvals from an ethics board (protocol under review).

Antimicrobial resistance surveillance

NICD Investigators: O Perovic, NP Govender, L Shuping, H Ismail, M Smith, R Mpembe, S Jallow
Collaborators: GERMS-SA network, SA Society for Clinical Microbiology

CHARM members represented NICD on a newly constituted AMR ministerial advisory committee, WHO AMR surveillance and quality assessment collaborating centres network, WHO AMR strategic and technical advisory group, and the WHO fungal pathogens priority list advisory group. The centre currently uses several approaches for AMR surveillance, including:

- National or sentinel isolate-based surveys: bacterial and fungal isolates, cultured from patients who meet the surveillance case definitions, were submitted to the centre's reference laboratories for identification, antimicrobial susceptibility testing (AST), and genotyping. During the period under review, the centre conducted surveillance for enterococcal bacteraemia.
- Community-based surveillance for urinary tract infections (UTI) was initiated at the Alexandra community health centre in Johannesburg. Limited clinical information was obtained from enrolled non-pregnant women with compatible UTI signs and symptoms, and urine samples were submitted to the centre for identification and susceptibility testing. Enrolment is ongoing and a preliminary report for stakeholders is planned mid-project (once approximately 100 isolates are tested).
- Electronic laboratory surveillance: annual data were compiled on bloodstream infections caused by the ESKAPE bacterial pathogens and, more recently, *Candida*. NICD cleaned and merged line list data from public and private-sector pathology laboratory information systems and made these available through the AMR dashboard on the NICD website. The dashboard displays interactive and exportable AMR maps by geographic location, pathogen, antimicrobial agent, and health sector; AMR data for the public sector are available at the facility level.
- A combined public/private report on AMR and antimicrobial use (AMU) in animals and humans in South Africa over the period from 2016 to 2020 is available from the NDoH: (https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021). AMR data will be displayed alongside AMU data in a new NDoH dashboard in 2023.
- Wastewater-based surveillance for ESKAPE pathogens: a pilot study was initiated for a six-month period to detect *Enterococcus* and *Acinetobacter* species from wastewater at 12 sites.

Surveillance for cryptococcal meningitis

NICD Investigators: NP Govender, R Mashau, R Mpembe, T Maphanga, S Naicker
Collaborators: GERMS-SA network

Since 2018, the WHO has recommended a combination of amphotericin B and flucytosine (5-FC) as first-line induction treatment for patients with cryptococcal meningitis. In December 2021, the South African Health Products Regulatory Authority (SAHPRA) registered 5-FC and the South African standard treatment guideline was updated in 2022; 5-FC is expected to be widely available from 2023 (included in the NDoH antimicrobial tender). The centre initiated isolate-based surveillance for *Cryptococcus* at sentinel hospitals in 2022 in order to screen recurrent episode isolates for 5-FC resistance.

OUTBREAKS

The centre led or participated in investigating several healthcare-associated outbreaks during the period under review, notably a large, persistent outbreak of *Candida auris* in a neonatal unit. Increasingly, its contribution to outbreaks has shifted from epidemiological assistance to molecular investigations.

WHO COLLABORATING CENTRE FOR AMR

As a WHO Collaborating Centre for AMR, the centre participated in the WHO AMR surveillance and quality assessment collaborating centres network, which was formed to support the GLASS implementation (https://www.who.int/glass/reports/en/). The NICD collaborated on activities to strengthen countries' capacity to develop and implement AMR surveillance and provided a WHO/AFRO regional laboratory external quality assessment programme (https://ptschemes.nicd.ac.za/Home/Bacteriology).

RESEARCH ACTIVITIES

CAST-NET

NICD Investigators: NP Govender, GS Greene, R Mashau
Collaborators: University of Minnesota, Epicentre

The CAST-NET project, which aimed to evaluate the effectiveness of the national reflex cryptococcal antigen screen-and-treat

intervention, ended in February 2023. Data were analysed for publication from a selected cohort of >1,700 adults with advanced HIV disease and cryptococcal antigenaemia diagnosed between February 2017 and February 2019 in 27 sub-districts.

Prevalence of AMR genes in animals and humans

NICD Investigators: O Perovic, W Strasheim, A Singh-Moodley, M Lowe
Collaborators: EMC Etter, JM Mokoele, A Jonker (University of Pretoria)

This project was completed in December 2022 and described antibiotic resistance genes present in food, animals, and livestock workers at a commercial pig farm.

ATLAS: surveillance and epidemiology of antimicrobial resistance

NICD Investigators: O Perovic, M Smith, R Kganakga, N Bulbulia, S Jallow, R Mogokotleng, O Taku, M Manavhela
Collaborators: NICD Sequencing Core Facility

This multi-year initiative will develop a scalable surveillance platform using the antimicrobial leadership testing and surveillance (ATLAS) core methodology. The pilot study is being conducted in Ghana, Kenya, Malawi, and Uganda, and is supported by a public-private partnership that expands surveillance capacity to low- and middle-income countries. The centre serves as a central reference laboratory and performs phenotypic and genotypic work. CHARM has received batches of isolates from the pilot sites, completed identification and antimicrobial susceptibility testing, and sent reports to the investigators. The centre has completed isolate testing for 50% of the estimated sample size.

Antimicrobial resistance in Ethiopia among pregnant women and newborns

NICD Investigators: O Perovic, M Smith, P Mashupye
Collaborators: Harvard Medical School, Harvard T.H. Chan School of Public Health, SPHMMC/BIRHAN, Debre Birhan Hospital

A maternal and neonatal colonisation study is being undertaken in Ethiopia, focusing on Gram-negative resistant pathogens (ESBL-producing and carbapenem-resistant Enterobacterales) and Group B *Streptococcus*. All specimens were sent to the centre for culture, identification, antimicrobial susceptibility testing, and WGS. The study was completed in 2022, and data analysis and a manuscript are expected to be finalised in 2023.

Endemic mycoses in South Africa

NICD Investigators: R. Mapengo, S Ndimande, NP Govender, T Maphanga
Collaborators: University of North Carolina at Chapel Hill, Institut Pasteur, Northern Arizona University, Ampath

The centre analysed electronic pathology laboratory data from all public laboratories and one large private laboratory in South Africa from 2010–2020 to describe laboratory-diagnosed cases of endemic and imported mycoses. Diagnostic specimens processed at the centre were also included. We identified 682 cases, of which 307 were proven, 279 were probable, and 96 were possible. A majority of cases had an unspecified endemic mycosis (207/682, 30.4%), followed by sporotrichosis (170/682, 24.9%), emergomycosis (154/682, 22.6%), histoplasmosis (133/682, 19.5%), blastomycosis (14/682, 2.1%), and (imported) talaromycosis (4/682, 0.6%).

The centre performed a detailed phenotypic description and antifungal susceptibility testing of 16 human- and 2 veterinary- isolates of *Histoplasma* from South Africa in its culture collection. The Illumina NextSeq platform was used for short-read sequencing to evaluate the phylogenomic and population structure diversity of these isolates. An analysis is underway to compare these to genome sequences from global strains. The centre has characterised a large culture collection of *Emergomyces africanus* clinical isolates (n=93) by phenotypic description, antifungal susceptibility testing (including n=78 tested against a novel agent, manogepix), and WGS.

FUNGAL SURV: fungal disease surveillance and capacity in southern Africa

NICD Investigators: NP Govender, S Jallow, R Mashau, TM Mwamba, R Mpembe, T Maphanga, S Naicker, G Greene
Collaborators: Africa CDC, National Departments of Health for Angola, Botswana, Eswatini, Lesotho, Mozambique, Namibia, Zambia, and Zimbabwe

This project aims to improve the capacity to perform surveillance, identification, and genomic epidemiology on fungal pathogens in southern Africa. During the reporting period, the centre began work to set up a regional network for fungal genomic surveillance, collaborating with Ministry of Health-supported national reference laboratories to ensure the sustainability of surveillance activities.

Laboratory training was conducted at NICD for partner countries, and initial batches of isolates were shared for identification, antimicrobial susceptibility testing, and WGS.

IMPRINT: A global health research group for HIV-associated fungal infections

NICD Investigators: NP Govender, R Mpembe, T Maphanga, S Naicker
Collaborators: University of the Witwatersrand, University of Cape Town, Botswana-Harvard Partnership, Malawi-Liverpool Wellcome, London School of Hygiene and Tropical Medicine (LSHTM), St George's University of London, Exeter University, Liverpool School of Tropical Medicine, Imperial College London, Tulane University, Hanoi Medical University, Médecins Sans Frontières, and the Drugs for Neglected Diseases Initiative.

IMPRINT is an NIHR-funded Global Health Research Group on HIV-associated Fungal Infections, co-led by LSHTM and NICD/ Wits which aims to improve the diagnosis and treatment of five HIV-associated fungal infections of public health importance (cryptococcosis, PCP, histoplasmosis, talaromycosis, emergomycosis) and to ensure that these improvements are made widely available to populations most commonly affected in Africa and South East Asia. Running from 2022 until 2026, the group brings together leading academic researchers, clinical and public health leaders, non-governmental organisations, and community and patient representatives to address its aims.

TEACHING AND TRAINING

CHARM staff provided and contributed to various teaching and training activities:

- NICD course for registrars;
- Mycology in-person workshop for registrars;
- Regional training on identification and characterisation of fungal pathogens;
- MBBCh Graduate Entry Medical Programme - GEMP (University of the Witwatersrand);
- MMed (Pathology) molecular course (University of the Witwatersrand);
- BHSc Molecular Medicine III (innate and adaptive immunology) (University of the Witwatersrand);
- MSc Vaccinology (University of the Witwatersrand);
- DTM&H (University of the Witwatersrand);
- MSc Epidemiology and Biostatistics (University of the Witwatersrand);
- BHSc Biochemistry (vaccines) (University of Johannesburg);
- MPH (University of Pretoria); and
- PhD, MSc, MTech, MSc or MPH (SAFETP), and MMed supervision.

POST-GRADUATE STUDENTS

Seven students were enrolled for post-graduate studies as follows:

- MSc Med: 1
- MSc Epi: 2
- PhDs: 4

Three students graduated during the review period. These comprised the following:

- MPH: 1
- MSc: 2

RESEARCH OUTPUT

Journal Articles

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CONFERENCES

- International: 6
- National: 2

CENTRE FOR HIV AND STIs (CHIVSTI)

CENTRE FOR HIV AND STIs (CHIVSTI)

PROF ADRIAN PUREN
Centre Head

BACKGROUND

Sexually transmitted infections (STIs), including those caused by the human immunodeficiency virus (HIV), types 1 and 2, remain a major public health problem in Africa. Published estimates of the Joint United Nations Programme on HIV/AIDS show that South Africa has the highest burden of HIV infections, with recent estimates of 7.8 million people living with HIV.

The National Institute for Communicable Diseases (NICD) Centre for HIV and STIs (CHIVSTI) has a strong track record in the research disciplines of HIV virology, HIV immunology, HIV/STI epidemiology, HIV/STI diagnostics, and HIV-STI interactions.

CHIVSTI addresses the challenges of HIV and STI diseases through various programmes:

1. Surveillance of disease burden and antimicrobial resistance;
2. Measurement of endpoint infections and detection;
3. Broadly neutralising antibodies as part of prophylactic HIV vaccine and antibody-mediated protection clinical trials;
4. Exploring an HIV "cure" strategy; and
5. Development and implementation of reference diagnostics and implementation science.

CHIVSTI consists of the following four sections:

1. HIV Virology;
2. Cell Biology;
3. HIV Molecular and Serology; and
4. Sexually Transmitted Infections.

The centre also provides a suitable academic environment for successfully supervising undergraduate and postgraduate students and postdoctoral fellows. The centre has well-established links and collaborations with key national and international organisations in HIV and STIs.

SURVEILLANCE

HIV PAEDIATRIC SURVEILLANCE

The centre supports the DoH by analysing and reporting HIV-related data from the NHLS Data Warehouse. This includes secure online distribution, via the NICD's Self Service Portal, of Results for Action (RfA), reports as per the 2019 National HIV guidelines, monthly reports on Early Infant Diagnosis, Paediatric and Adolescent HIV Viral Load (VL) monitoring, Maternal PMTCT HIV VL monitoring, and the validation of UNAIDS 95-95-95 target achievement at the district-level. The centre provides disaggregated monthly and ad hoc reporting for early infant diagnosis (both testing coverage and positivity), paediatric, adolescent, and adult HIV VL (monthly and rolling annual test-level and patient-level numbers of HIV VL done and the suppression rates), and uptake of maternal HIV VL electronic gatekeeping codes (including antenatal, delivery, and postnatal suppression rates). Reporting is provided at the national, provincial, and district levels to the National and Provincial Departments of Health and other stakeholders. Programme data can also be accessed via the NICD HIV M&E

Dashboard, to which 799 users are currently subscribed. Patient-level RfA reporting is also provided, as endorsed by the 2019 National HIV Guidelines and Paediatric Matrix of Intervention. At the end of the 2022/23 financial year, there were 566 RfA report users subscribed for a total of 1 265 district-level reports and 3 789 facility-level reports. 27 222 reports were downloaded during the 12 months: 13 539 district-level RfAs and 13 683 facility-level RfAs.

ADULT HIV SURVEILLANCE IMPLEMENTATION OF THE 2022 ANTENATAL CLINIC (ANC) SURVEY

The 2021 edition of the HIV antenatal care sentinel surveillance was conducted in February – April 2022 due to the delays caused by the COVID-19-associated restrictions. The survey aimed to estimate the prevalence and incidence of HIV among pregnant women attending antenatal care (ANC) at sentinel sites in all districts and provinces in the country, the knowledge of HIV testing, coverage of antiretroviral therapy use, and viral suppression levels among pregnant women living with HIV, the knowledge of, eligibility for, and coverage of pre-exposure prophylaxis use among HIV-negative pregnant women, the coverage of syphilis screening, syphilis seropositivity, and coverage of treatment among positives, as well as the timing of ANC attendance among all pregnant women. The rest of the year was spent cleaning and analysing data, and a preliminary report was presented to the Scientific Advisory Committee. National dissemination is planned for the next financial year.

HIV CASE SURVEILLANCE

HIV case surveillance (CS) is in the development phase. Firstly, the CS aims to develop and implement a data linkage system for people living with HIV (PLHIV), including a matching algorithm that helps to link an individual's data and prevents data duplication, using the existing NICD SDW data source (2 years of retrospective data). Secondly, the CS aims to develop and implement an HIV case surveillance system to prospectively monitor the HIV care continuum for newly diagnosed and existing PLHIV. During the current financial period, the focus has been on developing and testing the surveillance system to capture retrospective data. Once the system is finalised, the focus will be on the implementation phase of the surveillance system. Pilot sites have been selected.

THE RECENCY OF HIV INFECTION SURVEILLANCE

The goal of the recency of HIV infection surveillance project is to demonstrate the integration of rapid HIV recency testing into routine health facility-based HIV Testing Services (HTS) in South Africa. The project aims to:

1. Assess patient and clinic staff perceptions on the acceptability and feasibility of integrating a recent test for recent infection (RTRI) into routine HTS in public sector health facilities;
2. Estimate the proportion of recent infections among newly diagnosed PLHIV using RITA; and
3. To describe demographic, behavioural, and health service-related factors associated with recent and non-recent testing on the RITA.

The project has been implemented, and data collection is ongoing in the following districts: Ekurhuleni, eThekwini, uMgungundlovu, OR Tambo, and Tshwane. Data from the Gauteng districts has been cleaned, and preliminary analyses have been conducted. Further in-depth analyses will be conducted for the Gauteng districts, and the data from the KwaZulu-Natal districts will also be cleaned and analysed.

HUMAN SCIENCES RESEARCH COUNCIL (HSRC) SABSSM V1 STUDY (THE SIXTH SOUTH AFRICAN NATIONAL HIV PREVALENCE, INCIDENCE, BEHAVIOUR, AND COMMUNICATION SURVEY, 2021 (SABSSM V1)

HIV surveillance combines data from several sources to estimate the number of individuals living with HIV, identify who is infected and why, and evaluate the effectiveness of HIV prevention, testing, and treatment services among various population groups. The HSRC conducts the South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey (SABSSM) once every three years for this purpose. In 2021, the HSRC conducted its sixth survey (SABSSM V1). SABSMM V1 is a cross-sectional survey of a household-based, nationally representative sample of adults and children. COVID-19 antibody testing was included to estimate the proportion of infection at the national and provincial levels. The estimated sample size was 50 348 over the nine provinces in South Africa, and data collection is expected to stop at the end of April 2023. Dried blood spot samples were collected for testing. An HIV Enzyme Immunoassay (EIA) was carried out on all specimens. Confirmed positive specimens were tested for HIV-1 viral load and Lag. A total of 45 801 specimens were collected as of March 2023. A 15% positivity rate was recorded. Approximately 15% of the samples with a viral load of ≥1000 copies/ml were tested for drug resistance. A qualitative HIV-1 PCR test was performed on approximately 1% of the samples from infants younger than 2 years old.

HIV DRUG RESISTANCE

HIV drug resistance (HIVDR) surveillance leveraging on routine antiretroviral treatment (ART) programme monitoring in South Africa

This activity is the second of three annual HIV drug resistance surveillance studies on remnant samples obtained from patients

undergoing routine HIV VL testing. Between August and September 2021, 7008 specimens were selected during the first sampling stage. In the second sampling stage, 621 specimens with a VL >1000 copies/mL were selected for testing. Half of the specimens (323, 52%) had detectable ART levels. Dolutegravir was detected in 45 (7%) specimens. HIVDR testing was successful in 538 (87%) specimens. Overall, resistance was detected in 68% of specimens. Non-Nucleoside Reverse Transcriptase (NNRTI) resistance was detected in 66% of specimens compared to 41%, 4%, and 0.2% Nucleoside Reverse Transcriptase (NRT)I, Protease (PRRT), and Integrase (INT) resistance, respectively—one patient with detectable dolutegravir levels presented with dolutegravir resistance. Overall, resistance prevalence was significantly higher in specimens with detectable ART levels (78%) versus those without (56%, $p<0.0001$). The use of residual specimens proved advantageous, allowing for proportion-to-size sampling and reducing specimen collection time and cost. However, its limitation was the need for the availability of clinical and socio-demographic information. The low prevalence of integrase strand transfer inhibitor (INSTI) resistance aligns with the 2019 rollout of dolutegravir in first-line ART and its high genetic barrier to resistance. Routine surveillance efforts, including regimen-specific surveillance, are required to monitor resistance, especially when new regimens are introduced.

SEXUALLY TRANSMITTED INFECTIONS

The Sexually Transmitted Infections (STI) aetiological surveillance continued in 2022/23 in the three primary healthcare centres in Gauteng, KwaZulu-Natal, and the Western Cape. The surveillance is used to validate the current STI syndromic management guidelines. Neisseria gonorrhoeae remained the commonest cause of male urethritis discharge syndrome, while bacterial vaginosis (BV) and vulvovaginal candidiasis are more prevalent in vaginal discharge syndrome. The relative prevalence of Treponema pallidum has increased considerably during this reporting period. The section continues to monitor antimicrobial susceptibility patterns to detect the emergence of extensively drug-resistant Neisseria gonorrhoeae. These data formed part of the 2022 WHO GLASS report. All isolates were susceptible to the cephalosporins Cefixime and Ceftriaxone. The section has been appointed as a regional focal point of the WHO-enhanced Gonococcal Surveillance Programme (eGASP), and data collection started in February 2023. This enhanced programme collects expanded demographic, behavioural, and clinical data on the isolates. This will ensure timely reporting of critical alerts in the country and within the GASP network for action. STI surveillance among a priority population (Men who have sex with men, MSM, cohort) at a clinic in a sentinel Men's Health Centre in central Johannesburg was initiated with the support of the WHO. The overall aim of surveillance is to establish an early warning system in an at-risk priority population to monitor for evolving resistance to extended-spectrum cephalosporins in Neisseria gonorrhoeae and emerging STIs such as lymphogranuloma venereum.

STRENGTHENING SURVEILLANCE FOR CONGENITAL SYPHILIS IN SOUTH AFRICA

Congenital syphilis (CS) is a preventable medical condition that results from the mother-to-child transmission of Treponema pallidum (T. pallidum) infection. The infection has severe consequences for the foetus, resulting in early foetal deaths and stillbirths, neonatal deaths, preterm and low birthweight births, symptomatic disease, and asymptomatic infections. CS is a category 2 notifiable medical condition (NMC), meaning that healthcare practitioners are required to notify any cases detected within seven days of detection. The mother-to-child transmission of syphilis has been earmarked for elimination. Therefore, tracking the country's progress towards eliminating CS is necessary. During the year, the centre, in collaboration with the NMC team, continued to implement enhanced case-based surveillance of CS. The centre also worked with the NMC programme to develop a combined electronic and paper-based case notification and case investigation form that will allow providers to report cases and document maternal and infant histories associated with the CS case. The combined form underwent user testing and will be launched early in the new year. An analysis of cases notified during 2022 was undertaken, and data were submitted to the NDoH for inclusion in the Global AIDS Monitoring (GAM) report. During the calendar year, a total of 832 cases of CS were notified. This represented a 232% increase from the previous year. This increase was due to a proliferation of the congenital syphilis burden, as evidenced by rises in the maternal syphilis burden and an increase in the proportion of genital ulcers that were due to syphilis.

NATIONAL REFERENCE LABORATORY FUNCTION EVALUATION OF HIV/DUAL HIV AND SYPHILIS AND SYPHILIS ONLY RAPID KITS

The South African government provides extensive HIV rapid testing as the key entry point to its care and treatment programmes. On an annual basis, 8-10 million tests are performed. The National Tender advertised by the Treasury takes place every three years, and the NICD is mandated to evaluate rapid test kits for the tender. Eliminating mother-to-child transmission (EMTCT) of HIV and syphilis has also become a global health priority. It is estimated that there are 1.4 million new maternal HIV infections and 988 000 new maternal syphilis infections yearly. Syphilis testing and treatment coverage among pregnant women is low in many countries. The use of a dual HIV/syphilis rapid test (RDT) as the first test in antenatal care (ANC) offers the opportunity to test for both infections with a single finger prick. Results are available quickly, enabling many to start either or both HIV and/or syphilis treatment. For this purpose, the NDoH implemented the use of HIV and Syphilis rapid point-of-care (POC) tests at ANC. Treasury issued the first tender in the last quarter of 2021. The test devices were received in January-February 2022. Ten kits were submitted for evaluation (4 kits were tested as they met the NICD pre-screen evaluation criteria, and six kits were rejected as they did not meet the NICD pre-screen evaluation criteria). In December 2022, the tender was awarded to Tecpro for the STANDARD Q HIV/Syphilis combo rapid and Armada Medical for the First Response Syphilis Anti-TP Card Test Rapid Syphilis Card Test.

POST-MARKET SURVEILLANCE (PMS)

Post-market surveillance of HIV Rapid Test kits is the testing conducted on test kits selected as an outcome of the NDoH tender. Ensuring that the rapid test devices perform according to the selected criteria is critical. The PMS programme is a crucial contribution to ensuring

the quality of HIV rapid testing in South Africa. A limited number of test devices from each new batch are selected for testing to ensure that the specifications for batch verification determined by the NICD are met. This activity aims to perform PMS on test devices used in public health facilities to verify that the test devices will perform accurately. When each batch is tested, a well-characterised panel of 122 specimens is tested. On completion of the batch testing, the NICD generates a report on the batch performance that is submitted to the supplier and DoH. The NICD laboratory has tested 47 new batches before final production and 36 of the same batches post-production for distribution, a total of 142 batches in the current financial year. This equates to 17 324 tests that were completed for the PMS programme.

HIV VACCINES TRIALS ENDPOINT TESTING

We are currently participating in the following trials: 705.0, 118.0, 135.0, 139.0 and 140. HIV diagnostic endpoint testing has drastically reduced from 6547 specimens in the previous financial year to a total of 788 samples in the current financial year.

HIV VIROLOGY

The centre has made major contributions to the characterisation of humoral immune responses to SARS-CoV-2 variants associated with increased transmissibility, neutralisation resistance, and disease severity, which is of public health importance. This work resulted in the publication of nine papers defining new variants. In addition, the centre contributed to the analysis of the proof-of-principle HIV Antibody-Mediated Protection (AMP) trial, the first HIV vaccine trial to provide evidence that antibodies can prevent HIV infection and to define a correlate of protection from HIV.

OUTBREAKS

HIV VIROLOGY

With the emergence of novel SARS-CoV-2 Omicron subvariants during the reporting period, the centre played a pivotal role in assessing viral escape and humoral immune responses in SARS-CoV-2 infected individuals and vaccinees, which had global implications for the design of second-generation vaccines.

POLICY CONTRIBUTIONS

HIV VIROLOGY

Prof Penny Moore continues to serve as the Director for the Global Virus Network (GVN) in South Africa and also now serves as a Taskforce Member: Coronavirus Vaccines R&D Roadmap (CVR): research and development (R&D) roadmap for coronavirus vaccines. Moore also serves on the Scientific Advisory Boards of multiple scientific and capacity-strengthening initiatives.

EPIDEMIOLOGY

The HIV seromolecular laboratories and STI reference laboratory contributed to the implementation of dual HIV syphilis testing planned for the new financial year. The introduction of dual HIV/syphilis testing was a recommendation from the findings of the 2019 edition of the ANC survey, which found that 20% of women screened or tested for syphilis did not have results on record as they would be pending in the laboratory or not documented. Contributions included the evaluation of suitable rapid tests and guidelines.

Dr Tendesayi Kufa-Chakezha is a member of the STI technical working group that contributed to the revision of the congenital syphilis sections of the PMTCT and neonatal care guidelines. Dr Tendesayi Kufa-Chakezha is a member of the WHO virtual Technical Working Group on using routine data for surveillance. In this role, she reviewed and gave input into developing the WHO guidelines for using routine surveillance data.

SEXUALLY TRANSMITTED INFECTIONS

CHIVSTI continues to contribute to the guidelines for managing symptomatic sexually transmitted Infections in South Africa. The centre also participated in the WHO Enhanced Gonococcal Antimicrobial Surveillance (EGASP) Meeting in November 2022 to review the EGASP and the extragenital sampling protocol.

PAEDIATRIC HIV SURVEILLANCE

The centre contributed as a member of the National Paediatric HIV Technical Working Group HIV Treatment Guidelines Update 2022. The centre contributed also as a country member to the Global Alliance to End AIDS in Children work plan and monitoring and evaluation.

DIAGNOSTIC SERVICES

PAEDIATRIC SURVEILLANCE

The centre offers individualised diagnostic support, including a range of serological and nucleic acid tests, for infants, children, and adults for whom the HIV diagnosis is in doubt. The need for such a service has arisen because of the decreased positive predictive value of both rapid diagnostic tests and early infant diagnostic assays, a consequence of a reduced positivity yield in the tested population within the context of potent antiretroviral agents, which have the potential to cause loss of detection. Furthermore, alternative testing platforms and diagnostic algorithms are being evaluated to improve diagnostic accuracy in the field.

SEXUALLY TRANSMITTED INFECTIONS

During the review period, the centre provided the following diagnostic services:

1. Specialised reference testing (in-house and commercial PCR assays) for non-resolving STI syndromes, child abuse cases, and complicated STI cases;
2. Verification of Neisseria gonorrhoeae culture identification and antimicrobial susceptibility testing;
3. Mycoplasma genitalium macrolide and fluoroquinolone resistance testing; and
4. Herpes simplex virus type 2 genotypic acyclovir resistance testing.

RESEARCH ACTIVITIES

HIV Virology

The emergence of SARS-CoV-2 Omicron lineages BA.4 and BA.5 in South Africa

NICD Investigators: C Scheepers, JN Bhiman, N Wolter, A von Gottberg
Collaborators: H Tegally, M Moir, J Everatt, M Giovanetti, E Wilkinson, K Subramoney, S Moyo, DG Amoako, C Baxter, CL Althaus, UK Anyaneji, D Kekana, R Viana, J Giandhari, RJ Lessells, T Maponga, D Maruapula, W Choga, M Matshaba, S Mayaphi, N Mbhele, MP Mbulawa, N Msomi, NGS-SA consortium, Y Naidoo, S Pillay, TJ Sanko, JE San, L Scott, L Singh, NA Magini, P Smith-Lawrence, W Stevens, G Dor, D Tshiabuila, W Preiser, FK Treurnicht, M Venter, M Davids, G Chiloane, A Mendes, C McIntyre, A O'Toole, C Ruis, TP Peacock, C Roemer, C Williamson, OG Pybus, A Glass, DP Martin, B Jackson, A Rambaut, O Laguda-Akingba, S Gaseitsiwe, T de Oliveira

Three lineages (BA.1, BA.2, and BA.3) of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant of concern predominantly drove South Africa's fourth Coronavirus Disease 2019 (COVID-19) wave. We have now identified two new lineages, BA.4 and BA.5, responsible for a fifth wave of infections. The spike proteins of BA.4 and BA.5 are identical and similar to BA.2 except for the addition of 69–70 deletion (present in the Alpha variant and the BA.1 lineage), L452R (present in the Delta variant), F486V, and the wild-type amino acid at Q493. The two lineages differ only outside of the spike region. The 69–70 deletion in spike allows these lineages to be identified by the proxy marker of S-gene target failure on the background of variants not possessing this feature. BA.4 and BA.5 have rapidly replaced BA.2, reaching more than 50% of sequenced cases in South Africa by the first week of April 2022. Using a multinomial logistic regression model, we estimated growth advantages for BA.4 and BA.5 of 0.08 (95% confidence interval (CI): 0.08–0.09) and 0.10 (95% CI: 0.09–0.11) per day, respectively, over BA.2 in South Africa. The continued discovery of genetically diverse Omicron lineages points to the hypothesis that a discrete reservoir, such as human chronic infections and animal hosts, is potentially contributing to the further evolution and dispersal of the virus.

Neutralisation titre biomarker for antibody mediated prevention of HIV-1 acquisition

NICD Investigators: NN Mkhize, T Hermanus, P Kgaudi, C Bekker, H Kaldine, RE Mapengo, L Morris
Collaborators: PE Gilbert, Y Huang, AC deCamp, S Karuna, Y Zhang, CA Magaret, EE Giorgi, B Korber, PT Edlefsen, R Rossenkhan, M Juraska, E Rudnicki, N Kochar, Y Huang, LN Carrp, DH Barouch, A Eaton, E Domin, C West, W Feng, H Tang, KE Seaton, J Heptinstall, C Brackett, K Chiong, GD Tomaras, P Andrew, BT Mayer, DB Reeves, MA Sobieszcyk, N Garrett, J Sanchez, C Gay, J Makhema, C Williamson, JI Mullins, J Hural, MS Cohen, L Corey, DC Montefiori

The Antibody Mediated Prevention trials showed that the broadly neutralising antibody (bnAb) VRC01 prevented the acquisition of human immunodeficiency virus-1 (HIV-1) sensitive to VRC01. Using AMP trial data, here we show that the predicted serum neutralisation 80% inhibitory dilution titre (PT80) biomarker—which quantifies the neutralisation potency of antibodies in an individual's serum against an HIV-1 isolate—can be used to predict HIV-1 prevention efficacy. Similar to the results of nonhuman primate studies, an average PT80

of 200 (meaning a bnAb concentration 200-fold higher than that required to reduce infection by 80% in vitro) against a population of probable exposing viruses was estimated to be required for 90% prevention efficacy against the acquisition of these viruses. Based on this result, we suggest that the goal of sustained PT80 >200 against 90% of circulating viruses can be achieved by promising bnAb regimens engineered for long half-lives. We propose the PT80 biomarker as a surrogate endpoint for the evaluation of bnAb regimens and as a tool for benchmarking candidate bnAb-inducing vaccines.

The durability of chadox1 nCOV-19 (AZD1222) vaccine and hybrid humoral immunity against variants including Omicron BA.1 and BA.4 six months after vaccination: a randomised, phase 1b/2a trial

NICD Investigators: SI Richardson, VS Madzorera, NP Manamela, T Hermanus, T Motlou, N Mzindle, H Kaldine, PL Moore
Collaborators: SA Madhi, G Kwatra, AL Koen, V Baillie, CL Cutland, L Fairlie, SH Padayachee, K Dheda, SL Barnabas, QE Bhorat, C Briner, K Ahmed, PK Aley, S Bhikha, AE Bhorat, A Esmail, E Horne, CK Mukendi, M Masilela, S Oelofse, F Patel, S Rhead, L Rossouw, C Taoushanis, S van Eck, T Lambe, S Gilbert, AJ Pollard, A Izu

COVID-19 vaccine rollout is lagging in Africa, with a high rate of SARS-CoV-2 infection. We aimed to evaluate the effect of SARS-CoV-2 infection before vaccination with the ChAdOx-nCoV19 (AZD1222) vaccine on antibody responses through to 180 days. We did an unmasked posthoc immunogenicity analysis after the first and second doses of AZD1222 in a randomised, placebo-controlled, phase 1b–2a study done in seven locations in South Africa. AZD1222 recipients who were HIV-uninfected were stratified into baseline seropositive or seronegative groups using the serum anti-nucleocapsid (anti-N) immunoglobulin G (IgG) electroluminescence immunoassay to establish SARS-CoV-2 infection before the first dose of AZD1222. Binding IgG to spike (anti-S) and receptor binding domain (anti-RBD) were measured before the first dose (day 0), second dose (day 28), day 42, and day 180. Neutralising antibody (NAb) against SARS-CoV-2 variants D614G, beta, delta, gamma, and A.VOI.V2, and omicron BA1 and BA.4 variants, were measured by pseudovirus assay (day 28, day 42, and day 180). This trial is registered with ClinicalTrials.gov, NCT04444674, and the Pan African Clinical Trials Registry, PACTR202006922165132. Of 185 individuals randomly assigned to AZD1222, we included 91 individuals who were baseline seropositive and 58 who were baseline seronegative, in the final analysis. In the seropositive group, there was little change of anti-S IgG (and anti-RBD IgG) or neutralising antibody (NAb) titres at day 42 compared with at day 28. Anti-S (and anti-RBD) IgG geometric mean concentrations (GMCs) were higher throughout in the seropositive compared with the seronegative group, including at day 180 (GMCs 517·8 (95% CI 411·3–651·9) vs 82·1 (55·2–122·3) BAU/mL). Also, D614G NAb geometric mean titres (GMTs) were higher in the seropositive group than the seronegative group, as was the percentage with titres of at least 185 (80% putative risk reduction threshold (PRRT) against wild-type–alpha COVID-19), including at day 180 (92·0% (74·0–99·0) vs 18·2% (2·3–51·8). Similar findings were observed for beta, A.VOI.V2, and gamma. For delta, BA.1, and BA.4, NAb GMTs and the proportion with titres above the PRRT were substantially higher in the seropositive compared with the seronegative group at day 28 and day 42 but no longer differed between the groups by day 180. A single dose of AZD1222 in the general African population, where COVID-19 vaccine coverage is low and SARS-CoV-2 seropositivity is 90%, could enhance the magnitude and quality of antibody responses to SARS-CoV-2.

Antibody-dependent cellular cytotoxicity against SARS-COV-2 Omicron sub-lineages is reduced in convalescent sera regardless of infecting variant

NICD Investigators: SI Richardson, P Kgagudi, NP Manamela, H Kaldine, EM Venter, T Pillay, BE Lambson, T Hermanus, PL Moore
Collaborators: MA van der Mescht, W Burgers, N Ntusi, V Ueckermann, TM Rossouw, MT Boswell

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron BA.4 and BA.5 variants caused major waves of infections. Here, we assess the sensitivity of BA.4 to binding, neutralisation, and antibody-dependent cellular cytotoxicity (ADCC) potential, measured by FcγRIIIa signalling, in convalescent donors infected with four previous variants of SARS-CoV-2, as well as in post-vaccination breakthrough infections (BTIs) caused by Delta or BA.1. We confirm that BA.4 shows high-level neutralisation resistance regardless of the infecting variant. However, BTIs retain activity against BA.4, albeit at reduced titres. BA.4 sensitivity to ADCC is reduced compared with other variants but with smaller fold losses compared with neutralisation and similar patterns of cross-reactivity. Overall, the high neutralisation resistance of BA.4, even to antibodies from BA.1 infection, provides an immunological mechanism for the rapid spread of BA.4 immediately after a BA.1-dominated wave. Furthermore, although ADCC potential against BA.4 is reduced, residual activity may contribute to observed protection from severe disease.

EPIDEMIOLOGY

Evaluating the acceptability of pre-exposure prophylaxis (PReP) and yield of dual syphilis/HIV rapid test kit amongst men attending voluntary male medical circumcision (VMMC) services

NICD Investigators: T Kufa-Chakezha, A Puren, R Kularatne

The NDoH has decided to incorporate additional services into VMMC services as part of scaling Men's Health Services in the country. This study aimed to evaluate the acceptability and performance of a dual HIV/syphilis rapid test and determine the acceptability of and eligibility for PrEP referral among men attending six VMMC services and their public health care providers in Gauteng province. Of 716 males enrolled, 590 were

HIV-negative, of whom 68% were willing to use PrEP and 31.2% were eligible for PrEP. Of 625 men who responded to questions on the acceptability of dual HIV/ syphilis testing, 96% were willing to test for syphilis. The yield of active syphilis was 1.5%, higher than the 1% WHO threshold for considering dual HIV/syphilis testing.

CELL BIOLOGY

PERINATAL HIV-1 INFECTION AND THE ROLE OF FCΓ RECEPTORS

NICD Investigators: J Ebonwu, M Paximadis, C T Tiemessen
Collaborators: R Lassauniere (Statens Institut, Copenhagen, Denmark), L Kuhn (Columbia University, USA), G E Gray (SAMRC)

Cell surface (Fc) gamma receptors (FcγRs), which bind the Fc region of immunoglobulin G (IgG) antibodies, play an important role in linking the innate and adaptive immune systems. Immune mechanisms mediated through cross-linking of cell surface FcγRs include ADCC, antibody-dependent cellular phagocytosis (ADCP), antibody production, B-cell activation, antigen presentation, and cytokine production. Functionally-relevant genetic variants, including single nucleotide polymorphisms (SNPs) and copy number variation (CNV), have been characterised in low-affinity FcγRs and associated with different diseases. Functional consequences for FcγR variants beyond the two common variants - FcγRIIa-H166R and FcγRIIIa-F176V - during HIV-1 infection and acquisition in vivo have not been largely investigated. In this study, we report associations between all the known functional FCGR polymorphisms and HIV-1 acquisition in black South African children born to women living with HIV. FCGR genotypic data from 395 children living with HIV-1 were compared with 312 HIV-1-exposed uninfected children. We found that the commonly studied FCGR2A and FCGR3A polymorphisms did not associate with HIV-1 acquisition, however, less studied gene variants were associated with the risk of infant HIV-1 acquisition. These included FCGR3A gene duplication, FcγRIIb-232TT, and FcγRIIIb-HNA1a – with functional implications for ADCC, cellular activation, and neutrophil phagocytosis, respectively. These findings add insights into the role of FcγRs in the risk of HIV-1 acquisition that inform preventative HIV vaccines (passive or active immunisation). Ongoing investigations are required to confirm these findings, understand underlying mechanisms, and further explore the role of FcγRs in the context of HIV paediatric/adult cure strategies.

TEACHING AND TRAINING

HIV DRUG RESISTANCE

HIV drug resistance training was completed for four staff members from the Namibian Institute of Pathology, one PHIA trainee from Mozambique, and two Ugandan trainees.

HIV VIROLOGY

1. Kholiwe Nozamile, a Master's student from North-West University, co-supervised by Dr Hazel Mufhandu and Prof Penny Moore, visited the HIV Virology Section for a month to learn the HIV-1 pseudovirus neutralisation assay, mutagenesis, plasmid minipreps, and sequencing.
2. Dr Jinal Bhiman gave a lecture to the University of Cape Town BSc Hons students as part of their Vaccinology module, entitled "B-cell immunology relevant to vaccinology and measuring B cells", on May 31, 2022.
3. Dr Jinal Bhiman presented a 2-hour lecture entitled "Emerging and current viral threats: Pandemic/Avian Influenza and Coronaviruses" to the Virology PH III 2022 class at the Faculty of Health Sciences, University of the Witwatersrand, on September 6, 2022.
4. Two students from North-West University spent a further few weeks in the HIV Virology Section to learn techniques needed for their degree projects. MSc student, Kholiwe Mbadu, completed her mutagenesis of VRC01-resistant HIV-1 subtype C gp160 plasmids to make them sensitive to the antibody. Oarabile Ditsele, an honours student, learnt how to carry out the SARS-CoV-2 neutralisation assay by growing viruses and testing them against antibodies.

PAEDIATRIC SURVEILLANCE

1. Postgraduate training on infant diagnosis and paediatric HIV surveillance for rotating registrars.
2. Postgraduate lecture on paediatric HIV surveillance for Clinical Care Platform (online).
3. Training for the DoH and District partner staff on the use of HIV surveillance data for clinical action.

SEXUALLY TRANSMITTED INFECTIONS

The centre contributed to the three-week training course for registrars covering STI management and laboratory methodologies. During the reporting period, the section also participated in training medical scientists during their internship at the NICD. The intern scientist in the section completed his attachment and registered with the HPCSA.

Sequencing Core facility

The NICD Sequencing Core Facility (SCF) was established in 2016 to promote and expedite research and surveillance activities at the

NICD to provide accurate, high-quality, and cost-effective next-generation on sequencing (NGS) solutions. The SCF currently supports all centres at the NICD in terms of NGS and bioinformatics needs and thus acts as an extension of every centre with regard to NGS capacity. The SCF currently houses the following NGS instruments: two Hamilton NGS Star robots (automated liquid handlers for NGS libraries), an Illumina MiSeq, an Illumina Nextseq 1000, three Illumina Nextseq 2000, and a PacBio sequel IIe. In addition to NGS, the SCF has a dedicated high-performance computing (HPC) cluster. Specifications of the HPC cluster include a head node, eight compute nodes (272 CPU cores), three TB of RAM, intermediate storage (117 TB), and long-term storage (0.5 PB) for data analysis. Since its inception in 2016, the SCF has sequenced 100 771 genomes and plays a vital role in developing NGS solutions for research and surveillance activities at the NICD. Some key focus areas involve whole genome sequencing (WGS), custom amplicon sequencing, and metagenomics. Research and surveillance activities that depend largely on the NGS include TB and HIV drug resistance surveillance, HIV antibody research, vaccine validation molecular epidemiology, viral zoonosis studies, fungal pathogens, and outbreak response.

For the year 2022, the SCF sequenced 44 484 genomes, which generated 19 TB of data. The distribution of data amongst the NICD centres is as follows: 75.02% CRDM, of which 71.67% was SARS-COV2, 5.09% CHIVSTI (HIV drug resistance surveillance/research), 3.98% CTB (TB drug resistance surveillance), 7.25% CED (WGS of Salmonella spp.), and the remaining 8.66% distributed among the other NICD centres.

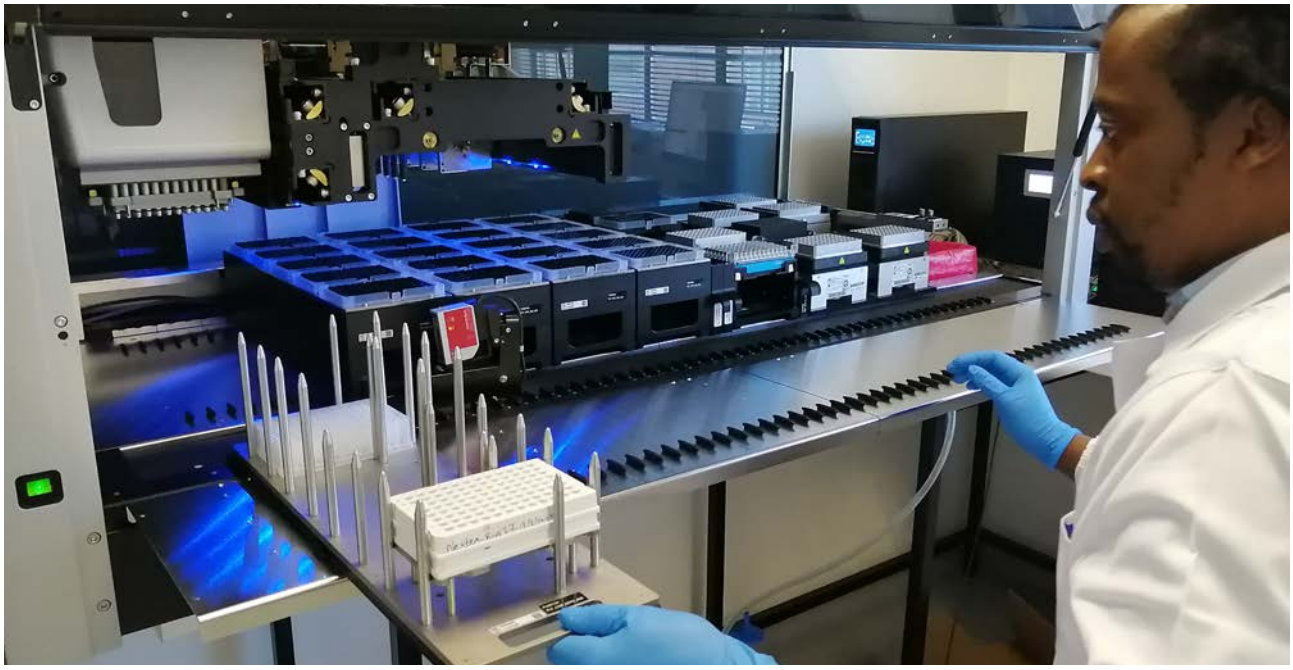

Figure 1: Hamilton NGS STAR.

The increased NGS capacity was a direct result of upgrading both our existing Hamilton NGS STARs with 96 multiple probe heads (MPH), which provide the much-needed increased capacity. This allows library preparations to increase from 96 libraries per day to 192 libraries per day, providing a combined high throughput capacity of preparing 384 NGS libraries in a day.

Further capacity was created by upgrading two illumina Nextseq 550 instruments to illumina Nextseq 2000's. This upgrade was made possible through the funding provided by Africa CDC/PGI. The benefit of upgrading to Nextseq 2000 instruments was faster runtimes (19-29 hours per run), reduction in sequencing costs, and the use of high-throughput applications (increased number of samples per run) for surveillance and research activities. Current projects that benefit from high-throughput applications include the 10x genomics projects (single-cell sequencing), WGS, metagenomics, metatranscriptomics, and RNA-seq projects. The SCF continues to support the NICD centres in terms of NGS capacity by producing high-quality data using state-of-the-art sequencing platforms, which encompass both long and short-read technologies coupled with HPC solutions for the analysis of computationally intensive data.

PROFESSIONAL DEVELOPMENT

POSTGRADUATE STUDENTS

Thirty-seven students were enrolled in postgraduate studies as follows:

1. MSc: 23
2. MPH: 2
3. PhD: 7

4. BSc (Hons): 3
5. MMed: 2

Mentor: 1 Gilead Research Scholar

Eight students graduated in the period under review. These comprised the following:

1. PhD: 1
2. MSc: 7

RESEARCH OUTPUT

Journal Articles

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1. International: 28
2. National: 24
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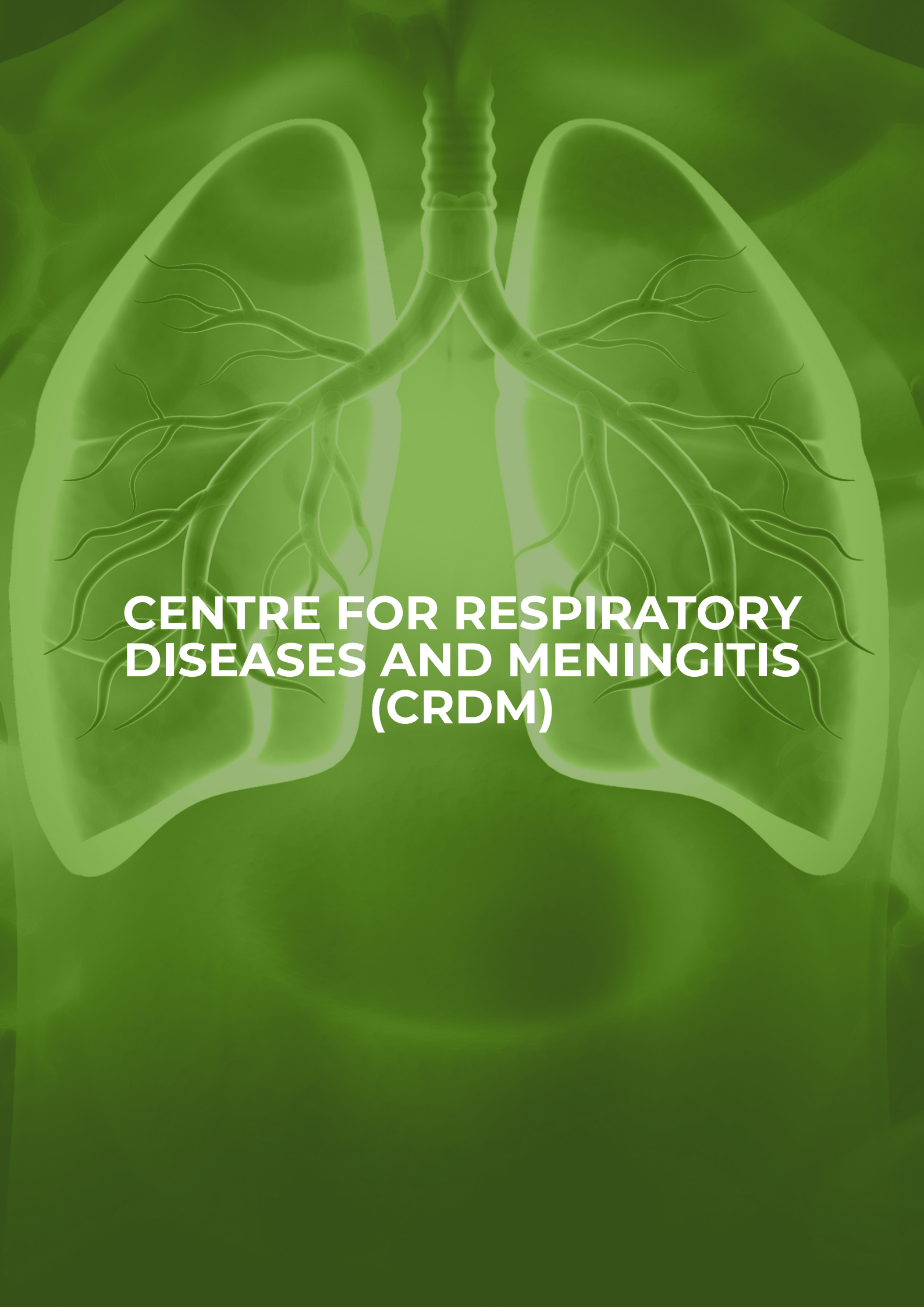

CENTRE FOR RESPIRATORY DISEASES AND MENINGITIS (CRDM)

CENTRE FOR RESPIRATORY DISEASES AND MENINGITIS (CRDM)

PROF CHERYL COHEN
Centre Head

BACKGROUND

The Centre for Respiratory Diseases and Meningitis (CRDM) conducts surveillance, diagnostic testing, outbreak support, and research in the field of communicable respiratory diseases and meningitis for South Africa and the African continent. The centre generates data and provides expertise to the NDoH and healthcare providers, as well as regional and international collaborators, to assist with planning public health policies and programmes and responding to respiratory and meningitis disease outbreaks. CRDM is a source of capacity-building and formal training within South Africa and the African region. During the period under review, the centre de-escalated response activities to the COVID-19 pandemic and supported responses to increases in pertussis and respiratory syncytial virus (RSV) circulation following the relaxation of COVID-19 restrictions. The centre is responsible for six 'category one' notifiable medical conditions (NMCs): acute rheumatic fever, COVID-19, diphtheria, meningococcal disease, pertussis, and respiratory disease caused by a novel respiratory pathogen, as well as two 'category two' NMCs: *Haemophilus influenzae* type b (Hib) disease and legionellosis. In addition to other important diseases, such as influenza, RSV, and pneumococci, these are monitored through ongoing syndromic and laboratory-based surveillance programmes, and the NMC programme.

SURVEILLANCE

GROUP FOR ENTERIC, RESPIRATORY AND MENINGITIS SURVEILLANCE – SOUTH AFRICA (GERMS-SA)

This programme conducts national, laboratory, and population-based active surveillance for invasive pneumococcal (IPD), meningococcal, and Hib disease to evaluate the ongoing impact of the pneumococcal conjugate vaccine and the Hib conjugate vaccine, as well as the impact of the COVID-19 pandemic on these pathogens. IPD surveillance data were submitted to the global Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) Project, which investigated the global change in IPD and pneumococcal meningitis incidence following PCV10/13 introduction. Future investigations from this collaboration will include modelling the impact of new and future PCV formulations, the heterogeneity of PCV impact, and cost-benefit analysis for childhood immunisation. Data were also shared regularly with the Invasive Respiratory Infections Surveillance Initiative (IRIS) to contextualise GERMS data relative to those from other countries in the context of COVID-19. Data on antimicrobial resistance were shared with the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS), which monitors antimicrobial resistance in common bacteria and invasive fungi and antimicrobial consumption (AMC) in humans. Furthermore, data on *S. pneumoniae, H. influenzae and N. meningitidis meningitis* cases were shared with the WHO at a WHO-facilitated workshop for developing strategic plans for defeating meningitis by 2030 in November 2022 (Brazzaville, Congo). The centre also supported diagnostic testing and outbreak response for suspected cases of meningitis from other African countries. Surveillance for Group A and Group B *Streptococcus* continued, aiming to generate evidence to contribute to vaccine development and decision-making for the introduction of future vaccines or other control interventions.

SYNDROMIC SURVEILLANCE FOR RESPIRATORY ILLNESS (SRI/ILI/VIRAL WATCH)

National pneumonia surveillance continued to operate in six provinces. The programmes aim to describe the burden, risk groups, seasonality, and characteristics of COVID-19, influenza, RSV, and *Bordetella pertussis*. Two new hospitals, Tambo Memorial Hospital in Gauteng and Khayelitsha District Hospital in the Western Cape, were added in September 2022 and December 2022, respectively.

Systematic surveillance for outpatient influenza-like illness (ILI) and suspected pertussis is ongoing at outpatient public sector clinics in four provinces. The Viral Watch surveillance network of general practitioners continues to operate in eight provinces. Pneumonia and systematic ILI programmes were expanded to include systematic tuberculosis testing as well as COVID-19 vaccine effectiveness evaluations. In addition, all syndromic programmes provide information on the timing of influenza and RSV seasons and COVID-19 waves and provide data on influenza virus circulation and strains for decision-making around annual influenza vaccine composition as well as annual estimates of influenza vaccine effectiveness. Data were also provided describing risk factors for severe COVID-19 and vaccine effectiveness estimates for COVID-19 vaccines to provide a platform for SARS-CoV-2 genomic surveillance to monitor circulating strains and emerging variants of concern.

Following the decrease in circulation of influenza, RSV, and pertussis and out-of-season circulation of RSV and influenza reported in 2020 and 2021, surveillance data from these programmes showed a return to winter seasonality in 2022 for influenza, with RSV preceding the influenza season. In 2022, an increase in *B. pertussis* circulation was reported from July 2022 to March 2023, with the majority of cases reported from the Western Cape Province. RSV also circulated at high levels in 2022.

OUTBREAKS

COVID-19

CRDM continued to play a leading role in the response to the COVID-19 pandemic in South Africa as the response was de-escalated following reductions in the burden of severe disease. CRDM represented the National COVID-19 Incident Management Team for the epidemiology and laboratory streams. The centre produced regular COVID-19 surveillance reports, including the Weekly Epidemiological Brief, the Weekly Testing Summary, the COVID-19 Reproductive Number, and the SARS-CoV-2 Genomic Surveillance Update.

As a WHO COVID-19 international regional reference laboratory, CRDM continued to provide technical support and training to many African countries. In collaboration with other centres within the NICD, the centre conducted SARS-CoV-2 testing, including PCR, sequencing, serology, and viral culture. CRDM staff consulted on numerous expert committees and working groups for WHO, the Africa Centres for Disease Control (Africa CDC), and the WHO African Region (AFRO).

CRDM conducted ongoing COVID-19-related research activities, including burden of disease, transmission, sero-epidemiology, and viral sequencing. CRDM staff participated in numerous media engagements aimed at informing the public about COVID-19 risks and how to reduce transmission, as well as providing updates on the epidemic's progression. Cheryl Cohen was a member of the Ministerial Advisory Committee on COVID-19 Vaccines and the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC). Anne von Gottberg was vice-chair of the WHO Technical Advisory Group on SARS-CoV-2 evolution. CRDM staff contributed to the Emergency Operations Centre and National Incident Management Team by providing data, epidemiology, laboratory, and clinical expertise nationally and for the continent.

PERTUSSIS

Following little to no circulation of *B. pertussis* in 2020 until the first half of 2022, an outbreak of pertussis was reported from the Western Cape, with the number of cases reported from July 2022 higher than the numbers reported during the peak in 2018. CRDM provided alerts for clinicians, responded to media queries regarding the increase in cases, and produced monthly communiqués.

POLICY CONTRIBUTIONS

Data on the COVID-19 pandemic was used to advise on several policy recommendations, such as those of the COVID-19 Ministerial Advisory Committees and NDoH, including topics such as de-escalation of the COVID-19 response, planning for emerging SARS-CoV-2 variants, and the COVID-19 vaccine programme. Influenza vaccination guidelines were updated to include updated guidance at the time of COVID-19. Updated pertussis preparedness guidelines were released in December 2022. Anne von Gottberg continued to act as chairperson of the National Advisory Group on Immunisation (NAGI). In addition, CRDM staff have contributed data and expertise to a NAGI pertussis vaccine advisory group since 2019, and this advisory was finalised and submitted to NAGI in 2022.

DIAGNOSTIC SERVICES

CRDM routinely offers advanced molecular testing for several respiratory and meningitis-causing pathogens using a variety of in-house and commercial platforms, including meningitis/encephalitis, respiratory and pneumonia multi-pathogen panels. The Centre also offers serotyping/grouping of vaccine-preventable bacterial pathogens and subtyping for influenza and RSV.

NATIONAL INFLUENZA CENTRE

CRDM houses the National Influenza Centre (NIC) for South Africa, which forms part of the WHO Global Influenza Surveillance and Response System (GISRS Plus). The NIC continued to support the WHO by providing serology data and genetic characterisation of influenza viruses to guide the composition of the annual seasonal influenza vaccines. The NIC provided technical assistance and capacity building to other countries in the region to strengthen the diagnosis and characterisation of respiratory viruses, including training on PCR, virus isolation, the haemagglutination inhibition assay, whole genome sequencing, and bioinformatics analysis. NIC activities play an important role in improving the detection, prevention, and control of influenza and other respiratory viruses for pandemic preparedness.

RESEARCH ACTIVITIES

A *Streptococcus pneumoniae* lineage usually associated with pneumococcal conjugate vaccine (PCV) serotypes is the most common cause of serotype 35B invasive disease in South Africa, following routine use of PCV.

NICD investigators: KM Ndlangisa, M du Plessis, L de Gouveia, et al. Microbial Genomics. 2022 April;8(4):000746.

This study describes the epidemiology of non-vaccine serotype 35B in South Africa before and after the introduction of PCV. This serotype has become one of the emerging non-PCV serotypes in South Africa following PCV introduction, and its dominance appears to be driven by a pre-existing lineage (GPSC5/CC172), which, in South Africa, was previously dominated by PCV serotype 23F prior to the introduction of PCV. These findings contribute to the general understanding of pneumococcal molecular epidemiology in the PCV era as well as the international effort to characterise replacement serotypes.

Clinical severity of omicron lineage BA.2 infection compared with BA.1 infection in South Africa.

NICD investigators: N Wolter, W Jassat, DATCOV-Gen Author Group, A von Gottberg, C Cohen. Lancet 2022 Jul 9; 400(10346):93–6.

Clinical severity of SARS-CoV-2 Omicron BA.4 and BA.5 lineages compared to BA.1 and Delta in South Africa.

NICD investigators: N Wolter, W Jassat, S Walaza, R Welch, H Moultrie, MJ Groome, et al. Nature Communications 2022 Oct 4;13(1):5860.

Two high-impact papers were published describing the epidemiology of new lineages of the SARS-CoV-2 Omicron variant of concern.

Following the emergence of the SARS-CoV-2 Omicron variant of concern and associated lineages (BA.1, BA.2, BA.4 and BA.5), we conducted early analyses to assess the severity of the new VOC and thereby guide the public health response. Our data indicated a reduced risk of hospital admission among S-gene target failure (SGTF)-infected individuals (a proxy for Omicron VOC) when compared to non-SGTF-infected individuals diagnosed during October–November 2021, and a reduced risk of severe disease among SGTF-infected individuals when compared to earlier Delta-infected individuals.

Seroprevalence of severe acute respiratory syndrome coronavirus 2 after the second wave in South Africa in human immunodeficiency virus-infected and uninfected persons: a cross-sectional household survey.

NICD investigators: N Wolter, S Tempia, A von Gottberg, JN Bhiman, S Walaza, J Kleynhans, et al. Clinical Infectious Disease Journal 2022 Aug 24;75(1): e57–68.

The Healthcare Utilisation and Seroprevalence (HUTS) study aimed to estimate SARS-CoV-2 seroprevalence by HIV status and identify epidemiological characteristics associated with seropositivity. We conducted a cross-sectional household survey spanning the second pandemic wave (November 2020–April 2021) in three communities. The study showed that by the end of the second wave, just under half of the population had a prior infection with SARS-CoV-2, a much larger burden of infection than indicated by the enumeration of laboratory-confirmed cases. People living with HIV who were not virally suppressed were less likely to be seropositive compared to HIV-uninfected individuals.

SARS-CoV-2 incidence, transmission, and reinfection in a rural and an urban setting: results of the PHIRST-C cohort study, South Africa, 2020–21.

NICD investigators: C Cohen, J Kleynhans, A von Gottberg, N Wolter, JN Bhiman, et al. Lancet Infectious Diseases. 2022 Jun;22(6):821–34.

SARS-CoV-2 seroprevalence after third wave of infections, South Africa.

NICD investigators: J Kleynhans, S Tempia, N Wolter, A von Gottberg, JN Bhiman, A Buys, et al. Emerging Infectious Diseases 2022 May 1;28(5):1055–8.

SARS-CoV-2 transmission, persistence of immunity, and estimates of Omicron's impact in South African population cohorts.

NICD investigators: S Tempia, J Kleynhans, A von Gottberg, C Cohen, N Wolter, et al. Science Translational Medicine 2022 Aug 24;14(659).

Here we highlight three important papers published describing the detailed epidemiology and transmission of SARS-CoV-2 in South Africa from a novel cohort study.

During the Prospective Household Study of SARS-CoV-2, Influenza, and Respiratory Syncytial Virus Community Burden, Transmission Dynamics, and Viral Interaction in South Africa (PHIRST-C), households were followed up from July 2020 through August 2021 to collect twice weekly respiratory specimens for the detection of influenza, RSV and SARS-CoV-2, and blood was collected at 12 time points from July 2020 through March 2023 for the detection of SARS-CoV-2 antibodies. 85% of SARS-CoV-2 infections were asymptomatic; index cases, irrespective of whether they were symptomatic, could infect household members. SARS-CoV-2 seroprevalence was tracked in the study population through each SARS-CoV-2 infection wave, and differences were assessed by site and age. Comparing seroprevalence estimates to national surveillance data, 95% of infections were not detected through national surveillance, and an estimated 0.5-2% of infections resulted in hospitalisation, and 0.1-0.6% in death. Using modelling, the Omicron BA.1/2 variant's fitness advantage over the Delta variant was demonstrated, and Omicron BA.1/2 likely infected between 44-81% of the population. Hybrid immunity (natural infection and vaccination) and repeated prior infections reduced the risk of Omicron BA.1/2 infection by 30% and 85%, respectively.

Case-fatality and sequelae following acute bacterial meningitis in South Africa, 2016 through 2020.

NICD investigators: S Meiring, C Cohen, L de Gouveia, M du Plessis, V Quan, J Kleynhans, et al. International Journal of Infectious Diseases 2022 Sep 1;122:1056–66.

Providing country-specific estimates of case-fatality and sequelae from bacterial meningitis is important to evaluate and monitor progress towards the World Health Organization's roadmap to "defeating meningitis by 2030". In South Africa, a middle-income country, over one in three individuals with bacterial meningitis die. A total of 24% of survivors reported sequelae, and 5% died within 2 months of hospital discharge. HIV (particularly in individuals with low cluster of differentiation [CD4] T cell counts) was a risk factor for death.

Risk factors for severe coronavirus disease 2019 among human immunodeficiency virus-infected and -uninfected individuals in South Africa, April 2020-March 2022: data from sentinel surveillance.

NICD investigators: S Walaza, S Tempia, A von Gottberg, N Wolter, JN Bhiman, A Buys, et al. Open Forum Infect Dis 2022 Nov 2;9(12):ofac578

Using existing syndromic surveillance programmes for influenza-like-illness and severe respiratory illness at sentinel sites in South Africa, risk factors associated with COVID-19 hospitalisation and mortality were assessed. Older age was strongly associated with COVID-19 hospitalisation and mortality. Additionally, prior or current tuberculosis and severe HIV immunosuppression were associated with increased risk of COVID-19-associated hospitalisation. Compared to the Delta variant, the Omicron variant (BA.1 and BA.2) was associated with reduced risk of mortality and Beta was associated with decreased risk of hospitalisation. Active syndromic surveillance combining clinical, laboratory and genomic data can be used to describe the epidemic timing, epidemiological characteristics of cases, early detection of variants of concern and their impact on disease severity and outcome; and it presents a viable surveillance approach in settings where national surveillance is not possible. It may also be a sustainable option for moving beyond the pandemic phase when testing for SARS-CoV-2 is reduced. Elderly people with tuberculosis or people with HIV, especially severely immunosuppressed, should be prioritised for vaccination.

TEACHING AND TRAINING

- Training at various sites in South Africa for surveillance and COVID-19 special studies.
- Laboratory training workshops for SARS-CoV-2, influenza, and RSV detection and further characterisation and sequencing (Africa).
- Advisory, technical, and epidemiological support in-country and on the continent for SARS-CoV-2, influenza, RSV, and bacterial meningitis.
- Training and MSc and PhD supervising efforts as part of an international research training grant (D43) from the United States National Institutes of Health (NIH) and Fogarty International Center (FIC) sub-award through the University of Pittsburgh. The grant provides young South African public health and academic investigators from historically disadvantaged backgrounds with the multidisciplinary tools needed to conduct cutting-edge research in public health genomic and metagenomic epidemiology of respiratory and invasive bacterial and fungal diseases. Nine students (5 PhD, 4 MSc) were enrolled in the programme in 2022.
- Wits university lectures and course facilitation, postgraduate supervision of MSc and PhD students (joint staff contributions).

POSTGRADUATE STUDENTS

Eleven students were enrolled for postgraduate studies as follows:

- Masters: 4
- PhD: 7

One student graduated with a PhD.

RESEARCH OUTPUT

Journal Articles

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CONFERENCES

- International: 19 presentations
- Local: 1 presentation

Figure 1: CRDM team, World Pneumonia Day 2022

CENTRE FOR TUBERCULOSIS (CTB)

CENTRE FOR TUBERCULOSIS (CTB)

DR SHAHEED VALLY OMAR
Centre Head

BACKGROUND

The Centre for Tuberculosis' (CTB) core function is to execute TB surveys and population research, conduct laboratory-based public health surveillance of TB, and contribute to the advancement of TB epidemiology, diagnostics, and treatment, thereby guiding South African policy. In addition, the centre houses the National TB Reference Laboratory and is a member of the WHO TB Supranational Reference Laboratory network for the sub-Saharan region. The centre has made significant contributions towards both National and Global TB policies and guidelines in collaboration with the NDoH and WHO. For the year under review, CTB provided critical support for the National TB Programme, including supporting the development of the National Strategic Plan for HIV, TB, and STIs 2023-2028, the National TB Programme's TB Strategic Plan 2023-2028, and the TB Recovery Plan.

SURVEILLANCE

ROUTINE SURVEILLANCE REPORTING AND REQUEST FOR ACTION ALERTING

Surveillance findings continue to be regularly analysed and reported to the national and provincial TB programmes. The weekly results for action (RfA) reports cover both drug-susceptible and drug-resistant TB. Quarterly reporting of the number of TB patients (drug-susceptible and drug-resistant) nationally and further stratified by province and sub-district is ongoing, with automated reports being emailed to the relevant stakeholders at regular intervals. The updated 2021 definition for Pre-XDR and XDR has been incorporated into the quarterly reports, and this definition will be used for all future reports. The definitions are yet to be incorporated into the weekly RfA reports. Terms and conditions (Ts and Cs) have been added to the reports in line with the POPI Act. Integration of the NHLS laboratory data and EDR.web has been developed, enabling improved estimates of the total burden of drug-resistant TB in South Africa.

GLOBAL FUND SURVEILLANCE SUPPORT

With support from the Global Fund, enhanced TB surveillance reports were developed for 12 priority TB districts to support the targeting of local interventions and improve the TB programme. The enhanced reports include detailed facility-level epidemiological, geospatial, and trajectory analyses. Reports for 2022 Q1–Q4 have been distributed and presented to stakeholders.

SMS NOTIFICATIONS FOR XPERT ULTRA LABORATORY TESTS

In August 2022, the NICD, with the support of the NHLS, implemented the automated sending of SMS notifications of Xpert laboratory test results to people undergoing investigation for presumptive TB as part of the TB Recovery Plan. The purpose of the TB SMS notifications is to strengthen systems for the linkage of people diagnosed with TB to appropriate treatment, thereby reducing the initial loss by prompting patients to return to the health care facility when their results are available. The NICD provides monthly reports, disaggregated by sex, age, province, facility, laboratory, and Xpert result, on the implementation of the SMS notification system. While the proportion of Xpert tests with valid patient cell phone numbers steadily increased from 21% in August 2022 to 38% in March 2023, there is considerable provincial heterogeneity.

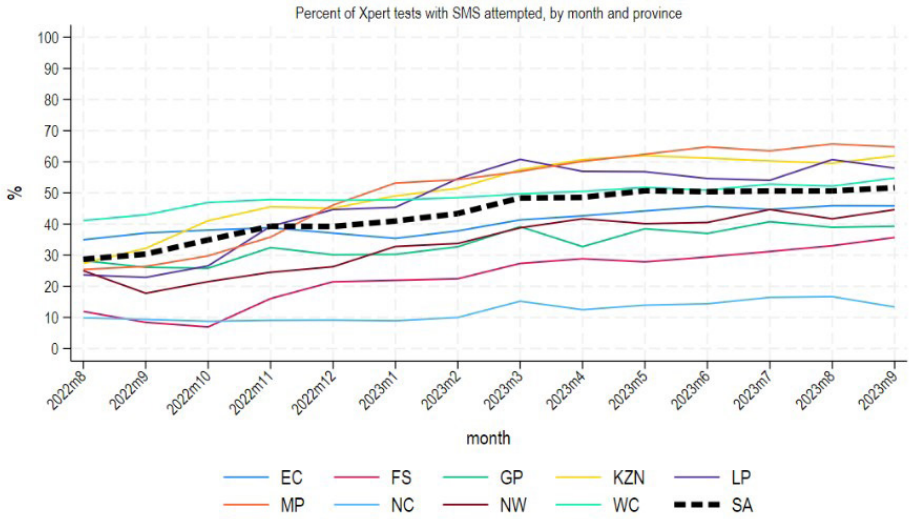

Figure 1: Proportion of Xpert tests with SMS notification delivered, by month and province.

JOINT ASSESSMENT OF THE TUBERCULOSIS DIAGNOSTIC NETWORK OF THE REPUBLIC OF SOUTH AFRICA

The NICD CTB was instrumental in supporting the implementation of the USAID Diagnostic Network Assessment, including conducting spatial analyses of the population access, coverage, and sample referral transport patterns of Xpert tests conducted through the NHLS. In 2022, NHLS performed ±2.5 million Xpert TB tests, submitted from 4,206 facilities and processed at 162 laboratories. One of the general findings suggested that the NHLS has an organised and structured TB diagnostic network in place with clearly defined tiers with specific roles and responsibilities and is led by a strong National TB Reference Laboratory.

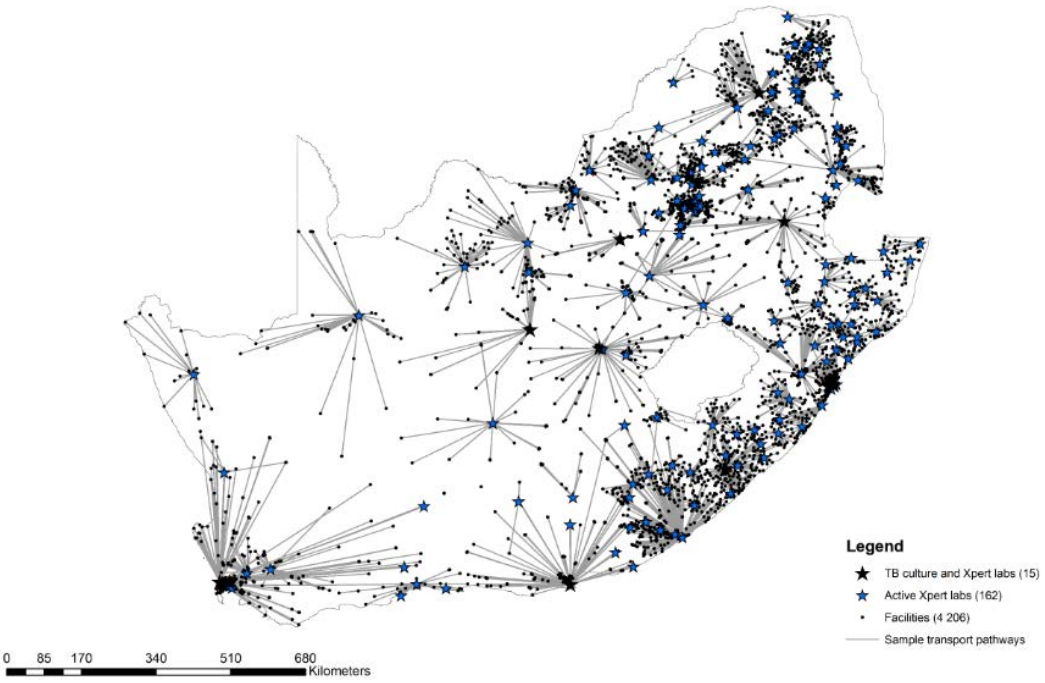

Figure 2: Spatial analysis of the NHLS TB Diagnostic Network predominant Xpert specimen transport patterns, 2022.

GERMS SURVEILLANCE

The TB section of the GERMS surveillance focuses on participants with rifampicin-susceptible TB diagnosed at hospitals. This effort allows for the detection of isoniazid (INH) mono resistance and monitoring the relative contribution of HIV/ART, TB preventative therapy (TPT), and pathways to care in reducing incidences and achieving the expectations of the NDoH strategic plan. Surveillance was expanded to include hospitals in seven provinces (previously five). Five hundred and eighty-three (583) samples were received from the seven provinces, of which 397 were culture-positive and 51 (13%) were found to be resistant to INH.

MODERNISING TB SURVEILLANCE

The development of the TB module on the NMC system has been an important advancement on the public health surveillance and response front. The NMC-TB module allows the user to capture cases electronically. Public health responders can thereafter view these cases in near real-time. The electronic capturing of TB patients removes the need for paper-based notification and reduces notification time and capture errors. This will ultimately reduce the initial loss to follow-up among TB patients. The NMC-TB module will integrate clinical and laboratory notifications to provide a more accurate measure of the TB burden in South Africa. Internal and external piloting of the NMC-TB module has been completed, and feedback from the piloting is currently being incorporated.

DIAGNOSTIC SERVICES

SPECIALISED REFERENCE MYCOBACTERIOLOGY – NATIONAL AND SUPRANATIONAL REFERENCE LABORATORY ACTIVITIES

Proficiency testing panels for second-line drug susceptibility testing (including Bedaquiline (BDQ)) were prepared by the centre and sent to the NHLS laboratories performing DR-TB Reflex testing. On the regional front, we have provided support to Namibia in terms of performing drug susceptibility testing for patients who have a poor response to a drug-resistant TB regimen. CTB also assisted the NHLS QA division in the standardisation of Auramine smear microscopy to conform to the Global Laboratory Initiative (GLI).

ADVANCING DIAGNOSTICS, EPIDEMIOLOGY, AND TREATMENT

As part of the Advancing Diagnostics, Epidemiology, and Treatment function of the centre, several new cutting-edge diagnostic technologies were evaluated during this period, including next-generation target sequencing technologies for predicting drug resistance. The centre has been instrumental in the implementation of the GeneXpert MTB/XDR assay, which aims to significantly improve turnaround time for the detection of drug-resistant tuberculosis, thereby providing comprehensive information for the adequate clinical management of patients. The centre has been listed as the first Performance Evaluation Laboratory (PEL) for the evaluation of TB NAT for in vitro diagnostics by the WHO Prequalification Unit.

RESEARCH ACTIVITIES

Microbiological and epidemiological surveillance of tuberculosis in South Africa: Application of whole genome sequencing to enhance microbiological and epidemiological surveillance of drug-resistant tuberculosis in South Africa

NICD Investigators: F Ismail, SV Omar, H Said, L Joseph, H Moultrie, J Mwansa, E Kachingwe
Collaborator: Centre for Disease Control, South Africa / USA

This research activity aims to assess Whole Genome Sequencing (WGS) as the primary phylogenetic investigation tool for longitudinal surveillance of transmission in selected regions with relatively high burdens of MDR-TB, improving the detection of high-risk cluster transmissions with outbreak potential, and demonstrating the effective use of WGS to improve surveillance by comprehensive detection of drug resistance to guide national policy. Furthermore, the study aims to validate the diagnostic performance of target next-generation sequencing (tNGS) assays in predicting drug resistance to first-line, second-line, and new anti-TB drugs and diagnostic performance among smear-positive and negative samples. The study is currently in year 4, and a total of 1127 rifampicin-resistant samples were collected between April 2022 and March 2023; 860 (76.3%) from the City of Cape Town (CoC) and 267 (23.7%) from the City of Johannesburg (CoJ). The primary findings of the diagnostic performance of tNGS have been shared with the WHO to support policy recommendations.

Multi-centre clinical trial to assess the performance of culture-free, end-to-end targeted NGS (TNGS) solutions for the diagnosis of Drug-Resistant TB (DR-TB)

NICD Investigators: SV Omar, F Ismail
Collaborator: Foundation for Innovative New Diagnostics, Geneva, Switzerland

This fund-sponsored multi-site study includes India, Georgia, and South Africa. The study aims to determine the diagnostic accuracy

of culture-free, end-to-end targeted NGS (tNGS) Solutions for the Diagnosis of Drug Resistant TB, which can offer higher throughput and greater accuracy across more TB drugs than current WHO-endorsed molecular assays, and a significantly faster time-to-result than phenotypic drug susceptibility testing (DST). A total of 262 TB patients were screened and 182 participants enrolled. Laboratory processing and data collation were completed during this reporting year.

Investigating the usefulness of the new QuantiFERON-TB Plus assay in diagnosing latent TB infection and progression to active TB disease among healthcare workers in high-incidence settings

NICD Investigators: SV Omar, F Ismail, J Mwansa
Collaborator: TB Directorate – National Department of Health & Aurum Institute

This project, which is a collaboration with the Aurum Institute and the NDoH, is designed to understand and provide a baseline of the prevalence of latent TB infection (LTBI), as well as the progression from latent to active TB among HCWs. Additionally, it will seek to assess the feasibility of using QuantiFERON-TB Plus amongst HCWs in a routine healthcare setting in the country. Due to the impact of COVID-19 on activities, the study sites were revised, and activities were re-initiated in 2022. During this period, participant follow-up visits were completed, and the qualitative study component was initiated to determine the feasibility and acceptability of LTBI testing.

Pretomanid resistance surveillance programme

NICD Investigators: SV Omar, F Ismail
Collaborator: TB Alliance

Pretomanid is a new nitroimidazooxazine antimycobacterial drug. One of the United States (US) Food and Drug Administration (FDA) post-marketing requirements (PMRs) specifies that a 5-year resistance surveillance study should be conducted after the introduction of pretomanid to the market to monitor changes in *Mycobacterium tuberculosis* susceptibility to pretomanid. The primary goal is to conduct a study over a 5-year period to determine pretomanid minimum inhibitory concentrations (MICs) of a sample of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Mycobacterium tuberculosis* complex (MTB) isolates. The centre has successfully submitted year 2 data during this reporting period.

Calibration of antimicrobial susceptibility testing methods and breakpoints against EUCAST reference standards for Bedaquiline, clofazimine, levofloxacin, and linezolid

NICD Investigators: SV Omar, D Ngcamu, M Motsei, L Joseph
Collaborator: University of Cambridge

The purpose of the calibration portion of this study is to propose quality control (QC) ranges/targets and epidemiological cut-offs (ECOFFs) for the European Committee on Antimicrobial Susceptibility Testing (EUCAST) Middlebrook 7H9 broth (7H9) microdilution (BMD) reference method and to calibrate surrogate methods, the results of which would be submitted to the EUCAST Subcommittee on Antimycobacterial Susceptibility Testing (EUCAST-AMST) for review. All QC isolate runs will be included in the calculations for essential agreement between BMD and the mycobacteria growth indicator tube (MGIT). During this period, we have completed the pilot and phase one component of the study, and the final phase is planned for mid-2023.

Molecular, clinical, and phenotypic monitoring of Bedaquiline resistance in drug-resistant tuberculosis in South Africa

NICD Investigators: SV Omar, L Joseph
Collaborator: Janssen Pharmaceuticals

Bedaquiline (BDQ) is a key component in the shortened regimen for drug-resistant tuberculosis. This study aims to investigate the changes in the prevalence of BDQ resistance following the increased uptake of the drug in the high-burden districts in South Africa. Whole genome sequencing was completed for 2048 isolates from six high-burden districts across three Provinces in South Africa.

Clinical decision-making using a rapid, point-of-care targeted sequencing assay at art clinics in southern Africa for the identification of drug- resistant tuberculosis directly from sputum samples

NICD Investigators: SV Omar, L Joseph
Collaborator: Bern University

The study aims to determine the utility of targeted next-generation sequencing (tNGS) directly from clinical samples. The results from the study will be used to guide clinical decision-making for individualising DR-TB treatment regimens. Sputum samples from 34 participants meeting the eligibility criteria for the study have been processed using tNGS and drug resistance reports have been submitted to the clinic for further follow-up.

POLICY CONTRIBUTIONS

NATIONAL POLICY

- National TB Recovery Plan.
- National Strategic Plan for HIV, TB, and STIs 2023-2028.
- National Guidelines on the Treatment of Tuberculosis Infection.

NATIONAL POLICY

- WHO consolidated guidelines on tuberculosis: Module three tests for tuberculosis infection.
- WHO Rapid Communication: TB antigen-based skin tests for the diagnosis of TB infection.
- WHO Policy statement: Optimised broth microdilution plate methodology for drug susceptibility testing of Mycobacterium tuberculosis complex.

TEACHING AND TRAINING

- Training was provided on both reference mycobacteriology testing and public health aspects of TB to rotating registrars and intern medical scientists from university-based medical microbiology and public health departments in South Africa. CTB staff provided formal lectures to undergraduate medical students and medical microbiology registrars at the University of Pretoria and post-graduate students at the University of Witwatersrand. Several post-graduate students were hosted at the centre to be trained and perform advanced testing, which supported their research. The CTB has taken responsibility for the NICD's three-week Communicable Diseases Rotation.

POSTGRADUATE STUDENTS

Four students were enrolled for postgraduate studies as follows:

- PhD: 2
- MSc: 2

Professional development, awards, and honours:

- Two Intern medical scientists passed National Assessment
- Two are in-training

RESEARCH OUTPUT

Journal Articles

1. Antimycobacterial Susceptibility Testing Group. Updating the approaches to define susceptibility and resistance to anti-tuberculosis agents: implications for diagnosis and treatment. European Respiratory Journal. https://doi.org/10.1183/13993003.00166-2022.
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13. Norbet Ndjeka, Jonathan R Campbell, Graeme Meintjies *et al.* Treatment outcomes 24 months after initiating short, all-oral bedaquiline-containing or injectable-containing rifampicin-resistant tuberculosis treatment regimens in South Africa: a retrospective cohort study. Lancet Infect Dis 2022. https://doi.org/10.1016/S1473-3099(22)00811-2.
14. Pai Helen, Ndjeka Norbert, Mbuagbaw Lawrence *et al.* Bedaquiline safety, efficacy, utilization and emergence of resistance following treatment of multidrug-resistance tuberculosis patients in South Africa: a retrospective cohort analysis. BMC Infectious Diseases. https://doi.org/10.1186/s12879-022-07861-x.
15. Rachel M Wake, Nazir A Ismail, Shaheed V Omar *et al*. Prior Pulmonary Tuberculosis Is a Risk Factor for Asymptomatic Cryptococcal Antigenemia in a Cohort of Adults with Advanced Human Immunodeficiency Virus Disease. Open Forum Infectious Diseases. https://doi.org/10.1093/ofid/ofac202.
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WORLD TB DAY ACTIVITIES

The centre successfully utilised social media messaging as a tool for our World TB Day activities. With strategic planning and engagement, we leveraged various social media platforms through our strong communications unit to raise awareness about tuberculosis, educate the community, and mobilise action. Our campaign included compelling visual content designed to align with STOPTB and WHO global messaging. This demonstrated the effectiveness of utilising digital platforms to disseminate vital information in the digital era.

ACKNOWLEDGEMENTS

The CTB thanks the NICD/NHLS for funding and operational support and PEPFAR through the CDC, under terms of agreement 1U19GH000571, the Global Disease Detection Program (U2GPS001328), the Global Fund, and the NIAID (1R01 AI089349 and AI080737) for funding support.

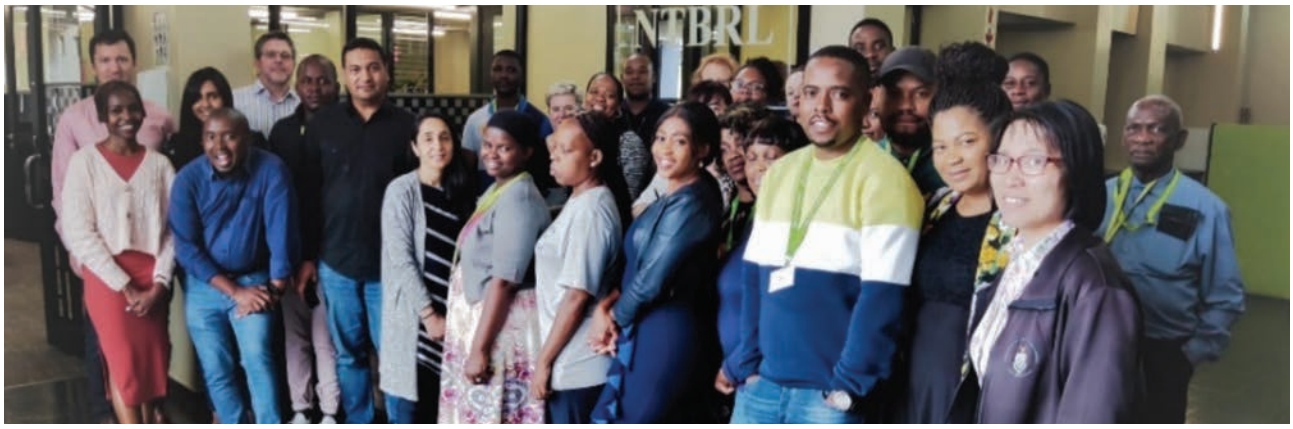

Figure 3: Centre for TB 2022/3.

CENTRE FOR VACCINES AND IMMUNOLOGY (CVI)

CENTRE FOR VACCINES AND IMMUNOLOGY (CVI)

DR NISHI PRABDIAL-SING
Centre Head

BACKGROUND

The CVI supports the NDoH with expert knowledge and function in the epidemiology and virology of vaccine-preventable diseases. As timelines for eradication and elimination reach closer, the centre conducts rigorous testing or surveillance for poliovirus, measles, rubella, tetanus, and viral hepatitis. The centre also performs environmental surveillance by testing wastewater for poliovirus and SARS-CoV2. Research is focused on whole genome sequencing for poliovirus, SARS-CoV2, and viral hepatitis.

The CVI provides laboratory testing for polio, measles, and rubella at its national and regional reference laboratories and supports outbreak response within the country and in neighbouring countries. The centre also provides new developments and validations of laboratory testing to improve turn-around times, sensitivity and specificity, and quantitative analyses.

In the review period, the centre had declared measles outbreaks in all provinces in South Africa, except the Eastern Cape. The centre is currently testing measles-suspected and measles-positive cases in the country, providing test positivity rates per province, including population demographics and geographically mapped locations of the cases. The centre continues to support sub-Saharan African countries with the detection and sequencing of polioviruses in AFP cases to detect vaccine-derived or wild-type virus in the region, as well as conducting testing and close monitoring of environmental surveillance from South Africa and neighbouring countries. The SARS-CoV2 environmental surveillance detects and maps SARS-CoV2 distribution in sewage, with close monitoring of SARS-CoV2 levels and viral variants.

SURVEILLANCE ACTIVITIES

MEASLES/RUBELLA SURVEILLANCE

The centre is the national and WHO regional reference laboratory for measles and rubella testing and surveillance. CVI provides serological testing for these diseases and molecular testing for measles in support of the measles and rubella strategic framework 2021-2030.

Laboratory results (detection of measles-specific IgM antibodies, avidity of anti-measles IgG antibodies, RT-PCR, and genotyping) are used in conjunction with epidemiologic case investigations in diagnosing acute measles infections. A total of 6 664 South African febrile rash samples were tested during the period under review, with 995 confirmed measles cases (14.9% positivity rate). In May 2022, 11 cases of measles were detected in Gauteng (Tshwane Metro, Johannesburg Metro, Ekurhuleni Metro, West Rand, and Sedibeng), of which 4 were epidemiologically linked. Two more cases were detected in the Free State and the Western Cape provinces. Measles genotype B3 was detected in 7 of the cases; 5 sequences formed a cluster, while 2 were unrelated to this transmission chain. From September 2022 (week 40), measles cases were detected in the Greater Sekhukhune district of Limpopo, and shortly thereafter outbreaks were declared in 8 provinces (Limpopo, Mpumalanga, North West, Gauteng, Free State, Western Cape, Northern Cape, and KwaZulu-Natal). Measles virus genotype D8 was detected in these outbreaks, and the sequences were identical to or closely related to the Zimbabwe 2022 outbreak strains.

Zambia and Zimbabwe sent throat swabs to the NICD for genotyping during their measles outbreaks in 2022. Measles genotype B3 was detected in the Zambian outbreak samples (linked to the DRC), while genotype D8 was detected in the Zimbabwe outbreak samples. Only 34 rubella cases were identified via febrile rash surveillance. Very few rubella cases have been detected since the SARS-CoV-2

pandemic, but this likely reflects lower transmission because of social distancing and lockdown measures. In the period under review, South Africa met the WHO indicator of a non-measles, non-rubella discard rate of ≥2/100,000 population.

As part of the WHO regional quality assurance programme, the centre retests approximately 10% of serum samples from 11 Southern and Eastern African countries, namely Botswana, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, eSwatini, Zambia, and Zimbabwe. Although only seven countries sent samples, 515 samples were tested, and there was good concordance between the inter-laboratory measles IgM and rubella IgM results.

POLIO SURVEILLANCE

The poliovirus national laboratory serves eight Southern African countries for acute flaccid paralysis (AFP) surveillance: Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, eSwatini, and South Africa, and seven countries for environmental surveillance: Angola, Botswana, Malawi, Mozambique, Namibia, eSwatini, and South Africa. The poliovirus regional reference laboratory is only one of two in Africa providing sequence analysis of polioviruses supporting additional African countries in the region.

ACUTE FLACCID PARALYSIS SURVEILLANCE

During the period under review, 5 536 samples were processed for poliovirus isolation: 935 from South Africa and 4 601 from the other seven countries. Between January and March 2023, the non-polio AFP detection rate in children under the age of 15 in the country was 2.1/100,000 population, just above the WHO target of 2/100,000 but below the national target of 4/100,000. No polioviruses of programmatic importance were identified in South Africa. Wild poliovirus type 1 was detected in seven cases in Mozambique following importation from Malawi. The date of onset of the last wild type 1 case from Mozambique was August 2022. Vaccine-derived poliovirus type 1 (VDPV1) was identified in 29 cases and two contacts (five cases and one contact from Malawi and 24 cases and one contact from Mozambique). Vaccine-derived poliovirus type 2 (VDPV2) was identified in five cases from Mozambique.

For those countries for which we provide a sequencing function, VDPV1 was identified in 199 samples: the Congo (1), Madagascar (27), and the Democratic Republic of the Congo (171). VDPV2 was identified in 367 samples from Burundi (3), Mali (2), and the Democratic Republic of the Congo (362).

ENVIRONMENTAL SURVEILLANCE

During the period under review, 1 016 samples were processed for poliovirus isolation: 123 from South Africa and 893 from the other six countries. Sabin/Sabin-like viruses of types one and three were identified in seven sites in three provinces of South Africa, and no polioviruses of programmatic importance were identified. VDPV2 was identified at two sites in Botswana and 1 site in Malawi.

Polio sequencing from other countries confirmed VDPV1 at one site in the Democratic Republic of the Congo (n = 2), 20 sites in Madagascar (n = 176), two sites in the Ivory Coast (n = 2) and one site in Uganda (n = 6). VDPV2 was identified in five sites in the Democratic Republic of the Congo (n = 10), 1 site in Uganda (n = 3) and two sites in Zambia (n = 3).

SARS-COV2 ENVIRONMENTAL SURVEILLANCE

The NICD partnered with the National Institute for Occupational Health (NIOH), Lumegen Laboratories, GreenHill Laboratories, Praecautio, Waterlab, Durban University of Technology (DUT), and the Council for Scientific and Industrial Research (CSIR) in the South African Collaborative COVID-19 Environmental Surveillance (SACCESS) network to detect and geographically locate SARS-CoV-2 distribution in sewage.

In total, 413 wastewater samples were processed for SARS-CoV-2 surveillance from sites in Gauteng, the Western Cape, the Free State, KwaZulu-Natal, the Eastern Cape, and the Northern Cape. SARS-CoV-2 was identified in 392 samples (95%). This was quantitated using optimised methodology to obtain copies of SARS-CoV-2 RNA/ml of wastewater.

Quantitative PCR had documented increases and subsequent decreases in viral load in wastewater correlating with clinical caseloads in each metropolitan area. In addition to testing, NICD collated and reported results from 73 additional sites from SACCESS partners. Reports are compiled and shared with stakeholders every Friday and published online (https:// wastewater.nicd.ac.za/). Mutation characteristics of the SARS-CoV-2 variants C.1.2, Delta, and Omicron lineages BA.5.3.1, BA.5.2, BA.5.2.6, BA.5.3.5, BA.5, BA.2.75, BQ.1, and XBB.1.5 have been successfully detected in wastewater using next-generation sequencing. SARS-CoV-2 is considered non-infectious from sewage samples, but the viral RNA remains detectable in raw sewerage. Sewage monitoring may provide accessory information to the NDoH for planning geographically localised interventions.

TETANUS

The centre collates and classifies tetanus cases reported through the NMC system. In the reporting period, five tetanus cases were notified and confirmed. Five cases were notified and are awaiting classification. No neonatal tetanus cases were reported. The WHO declared South Africa had eliminated maternal and neonatal tetanus in 2002, with the country's rate of neonatal tetanus below the threshold of less than one case per 1 000 live births in every district annually.

VIRAL HEPATITIS

The centre remains committed to achieving the viral hepatitis elimination goals by 2030. CVI performs passive laboratory-based surveillance for hepatitis A, B and C, using data from the NHLS corporate data warehouse (CDW) and Notifiable Medical Conditions (NMC).

HEPATITIS A

During the period under review, 2 425 hepatitis A cases were confirmed with a positive hepatitis A IgM antibody test throughout NHLS laboratories nationally. A significant increase in hepatitis A cases was seen in three districts in the Western Cape Province and one district in the Northern Cape Province in 2022. Both provinces were alerted for a public health response.

HEPATITIS B

Between April 1, 2022, and February 28, 2023, NHLS laboratories tested 668 313 cases for HBsAg, of which 28 222 (4.2%) tested positive. Of these, the majority (20 475, 72.5%) were among the age group of 25 to 49 years, and 83 cases (0.3%) were in children under 1 year old. Hepatitis B data was shared with the NDoH (in joint reporting format) and at the national advisory group on immunisation (NAGI) meetings held during this period.

HEPATITIS C

From April 1, 2022, to February 28, 2023, 117 751 patients were tested for hepatitis C virus exposure with a hepatitis C antibody test. Of the 3 257 (2.77%) positive results, only 749 patients had a hepatitis C viral load test, of which 74% (749) were positive. The number of people with active hepatitis A infection has increased due to the inclusion of data from high-risk programmes. The gaps in patient care and testing algorithms must be addressed to achieve the goal of eliminating viral hepatitis by 2030. Hepatitis C genotyping information showed the circulation of genotypes 1 to 5 in South Africa.

RESEARCH ACTIVITIES

Establishing a national COVID-19 wastewater surveillance pilot

NICD Investigators: K McCarthy, S Rachinda, M Yousif, N Ndlovu, C Iwu-Jaja, S Taukobong, M Macheke
Collaborators: CSIR, DUT, Greenhill/Praecautio, Lumegen, MRC-BRIP, MRC-TB, NICD, NIOH, Praecautio, Waterlab/UP

Some of the important activities were conducted and/or co-ordinated by the NICD, according to contractual agreements, namely:

- The development of standard operating procedures for SARS-CoV-2 detection and quantification in wastewater;
- The determination of the presence and quantity of SARS-CoV-2 in wastewater at predefined sites (which initially increased in number and then decreased over the duration of the grant);
- The conducting of inter-laboratory comparison and quality assurance tests among partner laboratories;
- The sequencing of SARS-CoV-2 and analysis of sequence results with regard to variants of concern;
- The creation of a wastewater dashboard for public dissemination of SARS-CoV-2 levels in wastewater (https://wastewater.nicd.ac.za/);
- Engagement with urban health specialists to support the interpretation of results in relation to the built environment and social determinants of health.

The NICD co-funded all activities through the provision of key staff members and the purchase of reagents, consumables, and courier services for samples processed at the NICD. Water Research Commission (WRC) funding secured testing by partner laboratories, the employment of additional NICD laboratory staff, and the development of the wastewater dashboard. The sequencing of SARS-CoV-2 was co-funded by the Bill and Melinda Gates Foundation (BMGF).

Through funding provided by the WRC (Project 2020/2021-00669) and the NICD, the Centre for Vaccines and Immunology (CVI/NICD) established a COVID-19 wastewater surveillance project that supported 10 laboratories to test over 4 000 wastewater samples for SARS-CoV-2 during a 2-year period. Detection, quantitation, and sequencing of the SARS-CoV-2 genome were conducted. Key findings

included 1) the good and sometimes excellent correlation of SARS-CoV-2 levels in wastewater with clinical case load by district; 2) the accurate determination of SARS-CoV-2 variants and lineages using sequencing results and bioinformatics pipelines; 3) early warning of the 4th wave of SARS-CoV-2 in Gauteng Province in November-December 2021; and 4) refinements in methodological sequencing approaches.

Our findings support recommendations regarding the configuration of Wastewater-Based Epidemiology (WBE) surveillance networks in low and middle-income countries (that sentinel site surveillance is a suitable model) and that investment in WBE in these contexts is meaningful as findings reduce uncertainty regarding the temporal and spatial distribution of SARS-CoV-2. The surveillance network and findings from this WRC-funded pilot have ensured that South Africa is among the global leaders in WBE research and have generated data to support the awarding of four subsequent grants related to the expansion of WBE to other pathogens.

Correlating SARS-CoV-2 variants from wastewater with clinical cases in South Africa

NICD Investigators: M Yousif
Collaborators: Bill and Melinda Gates Foundation and Scripps Research

In this project, we showed how wastewater can be used to effectively characterise SARS-CoV-2 predominance in the population and identify changes in viral evolution, as evidenced by emerging variants from sentinel wastewater treatment plants in urban metros. This demonstrates the utility of wastewater genomics surveillance to complement clinical surveillance efforts in a middle-income setting. We also identified the potential strengths and limitations of genomic wastewater surveillance for SARS-CoV-2 in the South African context.

The project was a pilot study aimed at detecting and sequencing SARS-CoV-2 from wastewater samples from South African treatment plants and comparing sequence data with SARS-CoV-2 variants from patients whose specimens have undergone routine or epidemiologically targeted sequencing. We also aimed to share our findings with policymakers and document how these data inform public health decision-making.

Our approach to the interpretation of sequence data generated from wastewater samples is unlike the analysis of sequences derived from clinical specimens. Because wastewater contains a mix of RNA fragments from viral particles originating from many infected individuals, the generation of consensus sequences is not meaningful. Our approach allows for the identification of previously described variants in wastewater samples and for the detection of new patterns of mutations suggesting previously undescribed variants. Similarly, this approach has also been used by Crits-Christoph and colleagues (Crits-Christoph *et al*., 2021).

Up to February 15, 2023, a total of 749 wastewater samples from the listed sites underwent RNA extraction, amplification, and sequencing. We used three methods for sequence analysis: (1) The Freyja tool to capture the dynamics of virus evolution and spread. The Freyja tool uses a "barcode" library of lineage-defining mutations to uniquely define all known SARS-CoV-2 lineages and solve for lineage abundance using a depth-weighted, least absolute deviation regression approach. Freyja is free to use and available at https://github.com/andersen-lab/Freyja. (2) An in-house pipeline on the Galaxy platform for mutational analysis. We identified unique or signature mutations for each VOC and/or VOI and used STATA code scripts to look for these mutations in each sample; the presence of those mutations indicated the presence of a VOC or VOI. (3) Using the amino acid data from the Galaxy pipeline, we also constructed a heatmap of mutations to identify patterns of emerging mutations in the spike gene using Excel conditional formatting.

Figure 1 below shows the output of the Freyja tool, illustrating the variants of SARS-CoV-2 identified each month in wastewater.

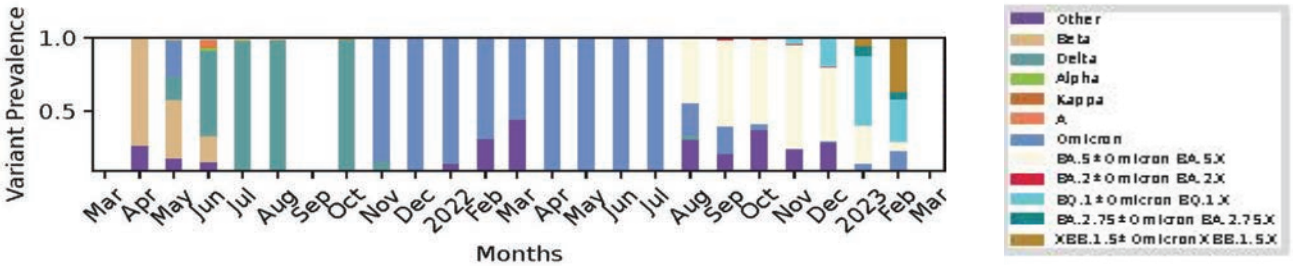

Figure 1: The proportion of SARS-CoV-2 variants in the environmental samples sorted by month and year (April 2021-February 2023) from all South African provinces. The number of samples processed each month, with a coverage >50% are indicated as n.

TEACHING AND TRAINING

Undergraduate

- GEMPII and PHII (viral hepatitis), medicine (medical immunology, vaccinology)

Postgraduate

- Registrar rotation, FETP, MSc, MMed, PhD, MPH

Intern Scientists

- 3 intern scientists over this period

PROFESSIONAL DEVELOPMENT

POSTGRADUATE STUDENTS

Seven students were enrolled for postgraduate studies as follows:

- MSc: 2,
- PhD: 4,
- FETP: 1

GRADUATIONS

Three students graduated in the period under review. These comprised the following:

- PhD: 1
- Intern scientist: 1
- MSc: 1

OTHER ACTIVITIES

The centre continued with its key support to NICD COVID-19 activities including routine surveillance by Dr S Malfeld. Dr K McCarthy and Dr M Yousif gave multiple media interviews related to COVID-19.

1. Dr K McCarthy, Dr M Yousif and Dr R. Said gave media interviews related to the wastewater dashboard.
2. Dr K McCarthy, N Prabdial-Sing, and Jack Manamela gave media interviews related to the measles outbreak.
3. Dr S Malfeld attended a WHO training course for measles and rubella molecular detection, genotyping, sequencing, and phylogenetic analysis, November 14-23, 2022, in Maputo, Mozambique.
4. Lerato Seakamela and Wayne Howard attended the 29th Informal Consultation of the Global Polio Laboratory Network (GPLN), WHO, in the International Conference Center Geneva (CICG), Geneva, Switzerland, December 24-25, 2022.

RESEARCH OUTPUT

Journal Articles

1. Alleman MM, Jorba J, Riziki Y, Henderson E, Mwehu A, Seakamela L, Howard W, Albert Kadiobo Mbule AK, Nsamba RN, Djawe K, Yapi MD, Mengouo MN, Gumede N, Ndoutabe M, Kfutwah AKW, Senouci K, Burns CC. Vaccine-derived poliovirus serotype 2 outbreaks and response in the Democratic Republic of the Congo, 2017–2021, Vaccine,2023.
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1. Jack Morubula Manamela, Measles outbreak in Limpopo and Mpumalanga provinces, October 2022, Communicable Diseases Communiqué October 2022, Vol. 21 (10).
2. Chenoa Sankar, South African Measles outbreak 2022, December 2022, Communicable Diseases Communiqué December 2022, Vol. 21 (12).
3. Jack Morubula Manamela, Measles outbreak in Tshwane district, Gauteng province, July 2022, Communicable Diseases Communiqué July 2022, Vol number 21 (7).
4. Susan Malfeld, Tetanus cases from 01 January to 15 August 2022, Communicable Diseases Communiqué August 2022, Vol. 21 (8).

Book chapter

5. McCarthy K, Moonasar P, Mendelson M, Naidoo R, Chetty K, Furumele T. COVID-19 and Health Emergencies. In (Eds) MP Matsoso, U Chikte, L Makubalo, Y Pillay, R (Bob) Fryatt. Health Reforms 2015 - 2020: The Road Ahead. Johannesburg: Trackstar Trading 111 (Pty) Ltd, 2022. ISBN 978-0-6397-2368-6.

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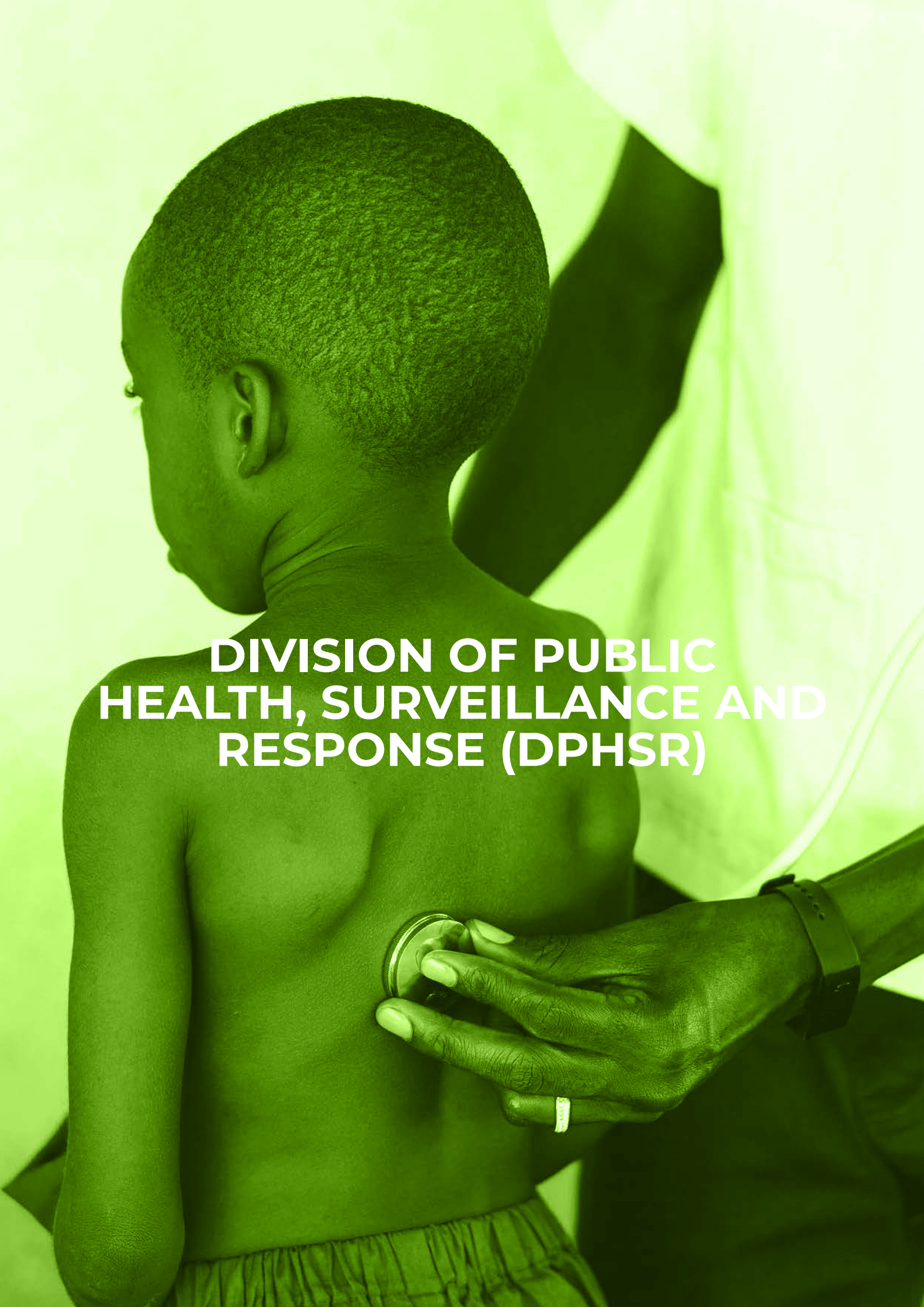
1. International: 4
2. National: 6

Image 1: CVI commemorated Africa Vaccination and World Immunisation Week, 24th -28thApril 2022.

Image 2: CVI hosted World Hepatitis Day on 28thof July 2022, baring the slogan "Hepatitis Can't Wait".



DIVISION OF PUBLIC HEALTH, SURVEILLANCE AND RESPONSE (DPHSR)

DIVISION OF PUBLIC HEALTH, SURVEILLANCE AND RESPONSE (DPHSR)

DR MICHELLE GROOME
Centre Head

BACKGROUND

The DPHSR plays a pivotal role in surveillance and response activities related to infectious disease threats in South Africa. The DPHSR incorporates the GERMS-SA surveillance programme, the Provincial Epidemiology Team (PET), consisting of eight epidemiologists based in the provinces, the Notifiable Medical Conditions (NMC) Surveillance Unit, and the Outbreak Response Unit (ORU), which hosts the Emergency Operations Centre (EOC). Together, these, in conjunction with the NICD specialist centres teams, contribute to national communicable disease surveillance, pandemic preparedness, and response efforts by providing systems for the rapid alert and notification of diseases of public health importance, as well as providing technical expertise to national, provincial, and district departments of health. It also facilitates communication and data sharing between the national and provincial health departments and the NICD.

During the past year, the DPHSR was integral to the continued national and provincial COVID-19 pandemic response, providing epidemiological expertise and maintaining data platforms to monitor trends in cases, tests, hospitalisations, and deaths. Epidemiological support from the EOC, ORU, and PET led to a well-co-ordinated and structured data flow, data management, and analysis. Decreases in COVID-19-related hospitalisations and deaths led to a loosening of restrictions in South Africa and a slow return to "normal" population movement and activities. DPHSR played a key role in managing outbreaks of other infectious diseases in response to other epidemics, including lassa fever, mpox, measles, cholera, and rabies cases. Event-based surveillance was expanded, and EOC staff conducted training on emergency management locally and in several other African countries.

The NMC surveillance system provides co-ordinated collection, collation, analysis, interpretation, and dissemination of public and private sector NMC data through a real-time surveillance system and provides information for targeted public health response, decision-making, and resource allocation. Noteworthy changes to the NMC include the listing of mpox, rubella, and congenital rubella syndrome as category 1 NMCs and a new hospital surveillance function that replaces the DATCOV platform, in addition to other system improvements. Lastly, the GERMS-SA collaborates with NICD centres to provide a national active surveillance programme for laboratory-confirmed bacterial and fungal infections, complemented by enhanced surveillance at sentinel hospital sites. This provides a robust platform for monitoring disease trends, which guides public health policy decisions.

SURVEILLANCE

Approximately 250 microbiology laboratories in the public and private sectors participate in the GERMS-SA laboratory surveillance programme and send specimens matching the GERMS-SA case definitions to NICD centres for further characterisation. Data are boosted through the NHLS Corporate Data Warehouse, where all isolates matching the case definitions are included in the GERMS-SA databases. This provides the minimum burden of disease for each pathogen, reflecting over 275,000 cases over the last 19 years. Within this network, an enhanced surveillance component operates at 25 sentinel public sector sites nationally, where nurse surveillance officers collect clinical information and outcome data on patients relating to specific pathogens. The GERMS-SA core team also supports the operational side of syndromic surveillance programmes, including pneumonia and influenza-like illnesses (with CRDM), diarrhoea (with CED), and rifampicin-sensitive TB (with CTB).

The NMC reporting application was initially rolled out in 2018 and facilitates real-time notification for the prompt diagnosis of NMCs. This strengthens NMC surveillance, as required by the International Health Regulations (2005). NMCs are reported electronically through mobile applications on Android, Huawei, and iPhone, and a web-based application. Electronic notification is preferred, although paper-based forms can still be used. As of March 2023, there were 18,367 active users, with the average user's monthly engagement increasing to 371 in March 2023 compared to 200 in April 2022. In the year under review, the NMC surveillance system received 59,757 notifications, of which 12% (n=6 940) were Category 1 NMC and 98% (n=52 817) were Category 2. The most common Category 1 notifications were clinical and laboratory notifications of malaria cases (62%), followed by measles cases (16%), reflecting the ongoing measles outbreak. Common Category 2 notifications included pulmonary tuberculosis (40%), followed by bilharzia (24%). New NMC categories were gazetted in February 2023, which saw the inclusion of mpox, rubella, and congenital rubella syndrome as Category 1 NMCs. Hospital surveillance for Category 1 NMCs was launched in March 2023. Electronic case investigation forms (CIFs) are being added to the NMC surveillance system to remove the need to complete paper CIFs after electronic notification; these forms are currently available on the web but not yet on mobile. To date, mpox and congenital syphilis CIFs have been published, while other forms are in various stages of development.

The PET continued to provide COVID-19 data management, analysis, report writing, and report dissemination support to the provincial departments of health. In collaboration with national and provincial stakeholders, the provinces undertook a rapid review of COVID-19 hospital-based mortality. PET's involvement in the provincial COVID-19 mortality reviews included the co-ordination of data collection, data analysis, and report writing. In the North West province, the use of technology to enhance disease surveillance was evidenced by the development and publication of public health surveillance dashboards. Routine surveillance dashboards (malaria and TB notifications; HIV/TB Phuthuma weekly indicators) and outbreak response dashboards (measles, COVID-19) were produced and published to inform and support public health action and decision-making. The ORU strengthened event-based surveillance (EBS) for communicable diseases, drafted an EBS framework, and now produces a weekly EBS bulletin that provides updates on current local, regional, and international infectious disease threats for the NICD and NDoH stakeholders.

OUTBREAKS

The ORU provided epidemiological support and technical expertise to the NDoH and provinces related to several outbreak preparedness and response activities of national importance, such as the imported lassa fever outbreak in the KwaZulu-Natal province in May 2022, the mpox outbreak from May to September 2022, the ongoing measles outbreak that started in late 2022, and the cholera outbreak in Gauteng in February 2023. ORU continued to provide epidemiological support and expertise on COVID-19 outbreak response and data management activities to the Minister of Health at the national and provincial levels, including NICD stakeholders. The EOC co-ordination the NICD COVID-19 pandemic response After Action Review (AAR) in November 2022 and has drafted a correction action plan with recommendations for improvement. This includes the strengthening of internal stakeholder relationships and collaboration.

The PET provided technical support for local outbreak preparedness and response activities in the provinces, including the mpox outbreak, the measles outbreak that was declared in eight of the nine provinces, and the cholera outbreak that was reported in Gauteng, Free State, Mpumalanga, KwaZulu-Natal, North West, and Limpopo. The PET supported outbreak investigation and report writing for local outbreaks, including a multidrug-resistant *Acinetobacter baumannii* cluster in a neonatal intensive care unit at a regional facility, a lassa fever outbreak, and human rabies and foodborne illness outbreaks reported in the different provinces.

The EOC is currently supporting the NDoH in establishing a public health EOC (PHEOC) for all hazards, while the EOC based at the NICD will be operationalised for infectious diseases only. To date, this has included the review and sharing of documents relevant to the process, attendance at a workshop to assess the KwaZulu-Natal PHEOC capacity, attendance and input at a national PHEOC assessment and action plan review/validation workshop, and input into national PHEOC contingency planning. The EOC secured funding through the WHO to strengthen current activities conducted by the EOC and to support the WHO and the NDoH in cascading EOC capacity to the provinces. With this funding, the EOC expanded its human resource capacity, allowing for the review and improvement of existing plans, policies, and procedures and the development of online EOC training materials. The NICD-EOC team plans to continue supporting the NDoH and WHO-led projects towards the establishment of functional national and provincial PHEOCs and to further develop training material for a broader range of emergency management topics.

POLICY CONTRIBUTIONS

- DPHSR contributed to the revisions of various National Guidelines as well as the development of preparedness and response plans and risk assessments for South Africa in response to the multi-country mpox outbreak and the imported case of lassa fever.
- The inclusion of mpox, rubella, and congenital rubella syndrome as Category 1 NMCs allows for the monitoring of the cases of mpox in South Africa and will strengthen rubella surveillance. This is of particular importance in light of the planned introduction of a rubella-containing vaccine in the childhood expanded programme of immunisation in South Africa in 2024, which will enable post-implementation effectiveness and impact studies.

- The Long COVID study informed our understanding of the long-term sequelae of COVID-19, and the team participated in the clinical technical working group, contributing to guidelines, training HCWs on Long COVID, and informing them on the health services required for Long COVID sufferers.
- Findings from the hospital-based COVID-19 mortality reviews were presented at respective provincial platforms, including provincial COVID-19 Incident Management Team meetings and clinician forums.
- Hospital surveillance for Category 1 NMC will allow for the collection of real-time epidemiological data on severe cases of Category 1 NMC for public health action, especially in an outbreak or future pandemic.
- As part of the ongoing Data to Policy (D2P) project, funded by Bloomberg Philanthropies in collaboration with the CDC Foundation, three DPHSR staff members led projects that were presented at the D2P Policy Forum held in February 2023 and culminated in policy briefs on the following:
  - The implementation of mass drug administration of praziquantel towards the elimination of schistosomiasis in South Africa.
  - The enhancement of rabies control to eliminate dog-associated human rabies in the Eastern Cape Province through animal bite surveillance with post-exposure prophylaxis tracking.
  - Improved rubella notification and collection of baseline data for evaluating the effectiveness of the rubella.
- Dr Groome is a member of the steering committees for the African Region Monitoring Vaccine Effectiveness (AFRO-MoVE) Network and the Global Outbreak Alert and Response Network.

RESEARCH ACTIVITIES

The DPHSR conducted several research activities in collaboration with NICD centres and national and international partners including:

The Long-Term Sequelae Following the COVID-19 Infection in South Africa

NICD Investigators: W Jassat, L Blumberg
Collaborators: ISARIC
Funder: Bill and Melinda Gates Foundation

To establish the presence of long-term complications in COVID-19 survivors and guide the rehabilitation of COVID-19 survivors. This was a longitudinal cohort: a qualitative survey (part of a multi-centre international study co-ordinated by ISARIC). Telephonic interviews were conducted at 1-, 3-, 6-, and 12-months post-discharge from the hospital following an acute COVID-19 infection. A standardised tool developed by ISARIC was used. The Long COVID study informed our understanding of the long-term sequelae of COVID-19 in South Africa.

Effectiveness of COVID-19 Vaccines Against Hospitalisation in Adults in South Africa Using Administrative Data from a Health Insurer

NICD Investigators: M Groome, C Cohen, S Johnstone, N Chiwandire
Collaborators: Government Employee Medical Scheme (GEMS), Insight Actuaries & Consultants
Funder: Bill and Melinda Gates Foundation

To estimate vaccine effectiveness against laboratory-confirmed COVID-19 hospitalisation, stratified by age group, time since vaccination, and vaccine product for the delta, omicron BA.1, and omicron BA.4/5 periods among (1) adults ≥18 years old (excluding healthcare workers) and (2) HIV-infected individuals. This was a test-negative case-control study using retrospective medical aid data. Results were presented at the WHO-convened meeting, COVID-19 Vaccine Effectiveness in Africa and SE Asia, in Cape Town, South Africa, March 27-28, 2023.

TEACHING AND TRAINING

DPHSR staff provided and contributed to the teaching, training, and supervision of intern scientists, SAFETP residents, public health medicine registrars, and microbiology registrars from various South African universities. Staff provided lectures for undergraduates and postgraduates in the Faculty of Health Sciences, at the University of the Witwatersrand, and at other South African universities. Ongoing teaching and training are provided on NMCs and the use of the NMC platform, as well as on current infectious disease outbreaks. For example, DPHSR staff provided training during the national mpox training and webinars conducted in collaboration with NDoH, CEZPD, and other stakeholders on general epidemiology and the background of mpox, contact tracing, clinical presentation, and case management.

Building on a collaboration with Georgetown University, the EOC developed training materials to use as a platform to engage with different stakeholders. This led to the rollout of online training sessions in order to establish a cohort of personnel who would understand the operations of the EOC as well as develop a base for surge staff identification. These sessions were attended by 108 participants. The EOC team is involved in the establishment of the provincial EOC in the Northern Cape province.

This included the conceptualisation of the EOC and the sharing of relevant documents needed for developing an EOC. The Northern Cape Department of Health, through their assigned WHO focal point, invited the EOC team to conduct an EOC executive-level training with senior management in the province. This training was the first of its kind to be conducted in South Africa. The EOC manager supported phase one of the AVHOC-SURGE initiative, which aims to train 3,000 emergency responders across Africa, as an expert facilitator of the module on PHEOC. This is a joint initiative by the Africa CDC and the WHO AFRO. This invitation to act as a facilitator is a testament to the capacity that exists at the NICD. He is also an active member of the WHO GOARN Online Gaming for Enhanced Outbreak Response Working Group.

PROFESSIONAL DEVELOPMENT

GRADUATIONS

Seven students graduated during the period under review:

- PhD: 1
- MPH: 1
- BCom Supply Chain Management: 1
- Bachelor of Business Administration: 2
- Diploma in Management Project Management: 1
- Diploma in Business Management: 1

POSTGRADUATE STUDENTS

Eight students are currently enrolled, comprising the following:

- PhD: 3
- MPH: 3
- MM Governance and Management: 1
- MSc Epidemiology and Biostatistics: 1

RESEARCH OUTPUT

Journal Articles

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NATIONAL CANCER REGISTRY (NCR)

NATIONAL CANCER REGISTRY (NCR)

DR MAZVITA MUCHENGETI
Centre Head

BACKGROUND

The National Cancer Registry (NCR) is responsible for cancer surveillance, which includes the systemic collection, storage, analysis, interpretation, and reporting of cancer cases. National pathology-based cancer surveillance and the implementation of population-based cancer registration are the primary roles of the NCR. The NCR also undertakes childhood cancer surveillance as one of its primary roles. Within NHLS/NICD, the NCR is the only unit specialising in non-communicable disease surveillance. The information provided by the national pathology-based cancer registry delivers insight into the cancer landscape in South Africa for the prioritisation of cancers of public health importance.

There were two notable accolades for the NCR during this financial year. The first was the launch of the second sentinel population-based cancer registry and the KwaZulu-Natal population-based cancer registry (KZN PBCR) in the KZN province on February 28, 2023. This was done in collaboration with the University of KwaZulu-Natal. The NCR provides technical support to the KZN PBCR and, as part of the launch, met with key stakeholders and data sources to encourage reporting in KZN. The second accolade was the formal inauguration of the NCR as one of three International Agencies for Research in the Cancer Global Initiative for Cancer Registry Development (IARC-GICR) Collaborating Centres for Sub-Saharan Africa (SSA) on November 22, 2022. This initiative is currently funded by Vital Strategies, an implementation partner of Bloomberg Philanthropies. As a collaborating centre, NCR will expand the support offered by the African Cancer Registry Network (AFCRN) to cancer registries within the continent, with a special focus on record linkage training for cervical cancer elimination and childhood cancer registration. The inauguration was attended by several key stakeholders from the DoH and civil society.

The Men of African Descent Carcinoma of the Prostate (MADCaP) Consortium, of which the NCR is a part, announced the "Dr Elvira Singh Travel Fellowship" for early career researchers in honour of the late Dr Singh. Dr Singh was also posthumously awarded the Cancer Association of South Africa AG Oettlé Memorial Award for her outstanding contribution to cancer research in South Africa in October 2022 (https://cansa.org.za/oettle-memorial-award-2022-to-doctor-elvira-singh/).

SURVEILLANCE

PATHOLOGY-BASED CANCER REGISTRY

In the year under review, we published the 2020 cancer incidence report on the NCR website (https://www.nicd.ac.za_wp-content/uploads/2023/04/The-National-Pathology-Cancer-Incidence-Report-2020.pdf). In 2020, there was a 10.4% decrease in the number of cancer cases compared to 2019. This reduction in the number of cancers diagnosed was expected as an effect of the COVID-19 pandemic lockdowns. Data on cancers diagnosed in 2021 and 2022 is currently being coded and cleaned. The pathology-based registry faced some challenges. Currently, the post of data manager is unfilled. Ms Patricia Kellett, who was responsible for data cleaning and maintaining the pathology registry database for the past 22 years, retired at the end of July 2022. This post remains frozen and unfilled due to the current austerity measures. Additionally, it was identified that there was outstanding data from two private laboratories, PathCare and Lancet. The transfer of outstanding reports only took place in February 2022; coding and quality checking of the outstanding reports are still ongoing, thereby delaying the 2021 report. The NICD IT team is updating the NCR app to allow double-coding to improve quality control.

Image 1: IARC-GICR collaborating centre inauguration held at NICD PRF Auditorium, Johannesburg, South Africa (November 2022). Left to right: Natasha Abraham (NCR), Kibachio Mwangi (WHO), Sandhya Singh (DoH), Dr Kamy Chetty (NHLS), Dr Mazvita Muchengeti (NCR), Dr Magdalena Paczkowski (Vital Strategies), Sizeka Mashele (NCR), Prof Adrian Puren (NICD), Dr Freddie Bray (IARC).

EKURHULENI POPULATION-BASED CANCER REGISTRY (EPBCR)

This report details the fifth year of population-based cancer registration in the Ekurhuleni metropolitan municipality, Gauteng province, South Africa. This includes cancers that were diagnosed between January 1 and December 31, 2021. Data collection for these cancers was conducted in 2021 and 2022. The overall case finding and data collection for the year 2021 was 4631 (compared to 3131 in 2020). Regardless of the challenges encountered, such as the COVID-19 pandemic restrictions, the Charlotte Maxeke Johannesburg Academic Hospital fire, and frequent power cuts, the results of the 2021 EPBCR reports are significant. The increase in reported cancer cases from 2020 to 2021 reflects some restoration of cancer services and surveillance with the progressive relaxation of COVID-19 restrictions in 2021. The most common cancers registered were prostate, colorectal, and lung cancers among males and breast, cervix, and colorectal cancers among females. Among children (0-14 years old), the most common cancers were Central Nervous System cancers, soft tissue sarcomas, retinoblastoma, and nephroblastoma, respectively.

The EPBCR manager, Ms Lactatia Motsuku, resigned on the 31st of August 2022. A new manager, Ms Babongile Ndlovu, was appointed on 1st December 2022. Six out of eight surveillance officers are still on yearly contracts, with renewal subject to the availability of funds from the DoH. There is also a need for funding for surveillance officers at the KZN PBCR. This presents a threat to the continuity of population-based cancer surveillance.

CHILDHOOD CANCER REGISTRY

The National Childhood Cancer Registry published its second report on childhood cancer incidence (0-14 years old) for the year 2019. A total of 961 cancers were diagnosed in children aged 0-14 years old in South Africa in 2019. This equated to an overall age-standardised rate of 57.7 cases per million (95%CI: 46.8-70.8). We found the most common cancer group diagnosed to be leukaemia, and the second most common cancer was lymphoma. Approximately 40% of the cases (n=376) were diagnosed in children aged 0-4 years old. Our results are comparable to those of registries within the African region and to global trends. Annual reports of childhood cancers are the first step towards improving the reporting of childhood cancers and raising awareness of the incidence of childhood cancers. Efforts are ongoing to receive data from all possible sources.

POLICY CONTRIBUTIONS

The NCR staff participated in the Data to Policy (D2P) Forum and presented their project titled "Let's Eliminate Cancer - A Call for Inclusive School-Based Vaccination Against HPV" on the 7th of February 2023, at the NICD.

RESEARCH ACTIVITIES

South African HIV Cancer Match Study (SAM)
NCR Investigators: M Muchengeti, C Metekoua, V Olago, T Tombe-Nyahuma
Collaborators: University of Bern: M Egger, E Rohner, Y Ruffieux
Swiss Tropical Public Health Institute: J Bohlius, T Dhokotera, M Davidovic

Funders: The SAM Study is supported by the National Institutes of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) under the award number U01AI069924 (Principal Investigators: Matthias Egger and Mary-Ann Davies). It has also received funding from the Swiss National Science Foundation and the Swiss Cancer Research Foundation

The SAM study is a national cohort of HIV-positive people created from NHLS HIV data (HIV tests, CD4 count, and HIV viral load tests) and linked probabilistically to the National Cancer Registry to determine the spectrum and risk of cancer in the HIV population. The HIV data has been updated to include 2015–2019 data, and the deduplication and linkage with NCR from 2004–2019 HIV data are complete. The quality checks and validation of the linkage are in progress. A steering group meeting of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Southern Africa was held at Kloofzicht, South Africa (14-16 November 2022). Two NCR staff members presented at this meeting: Carole Metekoua and Dr Mazvita Muchengeti. Carole Metekoua has successfully registered for a PhD, which will focus on non-Hodgkin lymphomas in the SAM study.

Johannesburg Cancer Case-control Study (JCS) and Evolving Risk Factors for Cancer in African Populations (ERICA-SA)

NCR Investigators: M Muchengeti, WC Chen, M Mothlale, MG Singini
Collaborators: D Bradshaw, CG Mathew, CB de Villiers, T Waterboer, R Newton, F Sitas
Funders: The study is supported by the South African Medical Research Council (with funds received from the South African National Department of Health) and the UK Medical Research Council (with funds from the UK Government's Newton Fund) (MRCRFA-SHIP 01-2015).

The JCS is a case-control study of newly diagnosed (< 6 months) black cancer patients (1995- 2016), with over 26 000 patients interviewed and over 20 000 blood samples stored to examine genetic, emerging, and/or novel risk factors for cancer. Two students, Dr Mwiza Singini and Dr Melitah Motlhale, completed their PhD studies within the ERICA study, and they have commenced post-doctoral fellowships linked to the Johannesburg Cancer Study at IARC in Lyon, France.

TEACHING AND TRAINING

NCR hosted a Breast Cancer Awareness Day training for NICD staff with the Pink Drive in October 2022. NCR appointed an "advocacy team," and the team completed the UICC Advocacy for Resources for Cervical Cancer Elimination training. Dr Muchengeti was appointed to the AFCRN Research Committee. Dr Muchengeti participated in a six-week fellowship with the National Cancer Institute (NCI), based at the National Institute of Health (NIH), Maryland, USA, to foster new collaborations. NCR hosted seven medical students from the University of Pretoria for three weeks in October as part of their programme to develop cancer research interest among medical students, done in partnership with the University of Utah.

IARC-GICR COLLABORATING CENTRE FOR SUB-SAHARAN AFRICA

South Africa was nominated as a regional collaborating centre for sub-Saharan Africa for "childhood cancers" and "record linkage" by the Global Initiative for Cancer Registry (GICR) Development. As part of the IARC-GICR collaborating centre activities, the NCR conducted an online training on record linkage of cervical cancer screening registers with population-based cancer registries for 65 participants from 12 sub-Saharan African countries. Additionally, childhood cancer registration training for registrars from various population-based registries in Tanzania was also undertaken.

PROFESSIONAL DEVELOPMENT

POSTGRADUATE STUDENTS

Eight post-graduate students were enrolled, comprising the following:

- PhD: 4
- MSc:4

GRADUATIONS

Three students graduated during the period under review:

- PhD: 3

RESEARCH OUTPUT

Publications

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CONFERENCES

- International: 5
- Local: 2

NOTES

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RP 205/2023
ISBN: 978-0-621-51272-4