NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

ANNUAL OVERVIEW

2023/2024


Sterile Insect Technique

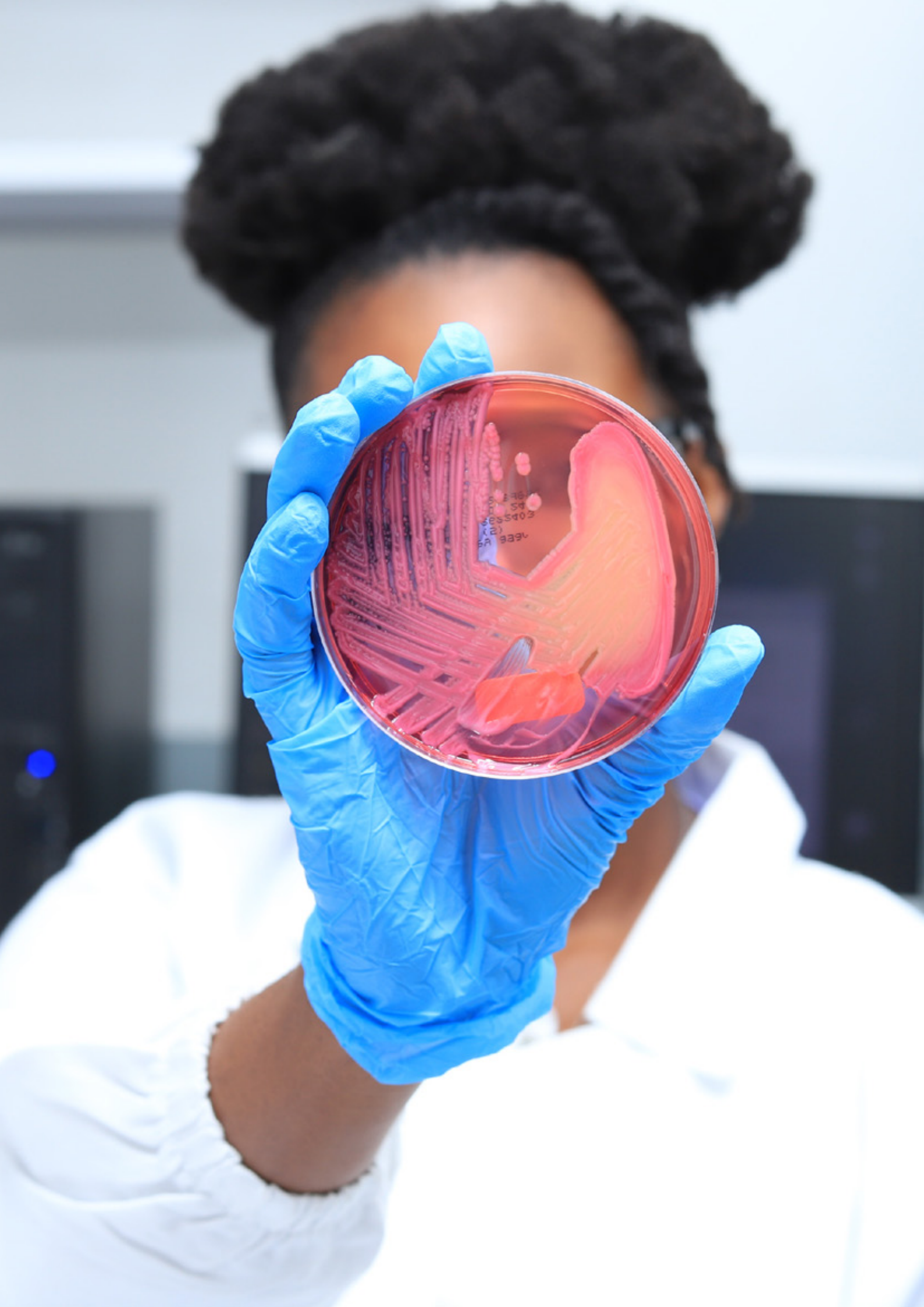
CONTENTS

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 for 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

ESBL	Extended Spectrum Beta-Lactamase
ESKAPE	Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species
FETP	Field Epidemiology Training Programmeme
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	London 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 AFRICA (NGS-SA)
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
RNA	Ribonucleic Acid

RVF	Rift Valley Fever
SABSSM	South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey
SACCESS	South African Collaborative COVID-19 Environmental Surveillance System
SADC	Southern African Development Community
SAFETP	South African Field Epidemiology Training Programmeme
SAHPRA	South African Health Products Regulatory Authority
SAMVAC	South African mRNA Vaccine Consortium
SANAC	South African National AIDS Council
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
SDW	Surveillance Data Warehouse
STI	Sexually Transmitted Infection
SVPL	Special Viral Pathogens Laboratory
TB	Tuberculosis
TPT TB	Preventative Therapy
UNAIDS	Joint United Nations Programmeme 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



PROF. ADRIAN PUREN
Executive Director

EXECUTIVE DIRECTOR'S OVERVIEW

> *The NICD comprises seven disease-focused centres with a range of specialist staff. The NICD maintained its accreditation status for the reporting period.*

The National Institute for Communicable Diseases (NICD) is a national public health institute for South Africa that provides disease surveillance, specialised diagnostic services, outbreak response, public health research, and capacity building to support the government's response to communicable disease threats.

The NICD supports public health responses, including policy advice and technical support to the National Department of Health (NDoH) and many other national and international stakeholders, including the World Health Organization (WHO) and the Africa Centres for Disease Control and Prevention (Africa CDC). The NICD comprises seven disease-focused centres with a range of specialist staff. The NICD maintained its accreditation status for the reporting period for three ISO/IEC standards: ISO/IEC 15189: 2022, ISO/IEC 17025, and ISO/IEC 9001.

CENTRE FOR EMERGING ZOONOTIC AND PARASITIC DISEASES (CEZPD)

The diseases of concern to the Centre include those caused by high-consequence zoonotic pathogens and neglected tropical infections. These diseases are listed as Category One Notifiable Medical Conditions (NMCs), such as viral haemorrhagic fevers (VHFs) (Ebola virus disease, Crimean-Congo haemorrhagic fever, Lassa fever, and Marburg virus disease), anthrax, botulism, yellow fever, plague, Rift Valley Fever (RVF), rabies, mpox, and malaria. The Centre also reports on diseases listed as Category Two NMCs, such as brucellosis, schistosomiasis (or bilharzia), and soil-transmitted helminthic infections (STHs), and Category Three NMCs, such as endemic and non-endemic arboviral infections. The other neglected tropical diseases (NTDs) include leptospirosis, opportunistic parasitic infections, and other emerging zoonoses,

such as Nipah virus disease. The CEZPD operates highly specialised laboratory facilities, including biosafety level three and four facilities, entomology laboratories, and insectaries, including a mass-rearing facility.

The Special Viral Pathogens Laboratory (SVPL) is the national reference laboratory for human rabies in South Africa. The laboratory offers various tests for ante-mortem and post-mortem diagnosis. The SVPL curates a database of epidemiological and clinical information for all confirmed, probable, and suspected rabies cases and contributes to accurate reporting of rabies as a Category One NMC through a passive surveillance approach. The Centre performed 91 tests for suspected rabies cases between 1 April 2023 and 31 March 2024. During the reporting period, outbreaks of rabies in domestic dogs were reported from districts in the KwaZulu-Natal and Eastern Cape Provinces. Additionally, the CEZPD confirmed 14 confirmed human rabies cases from South Africa during the reporting period.

Scabies is an NTD, and in February 2024, CEZPD provided laboratory investigations and support for a suspected scabies outbreak in a mental health facility in the Eastern Cape. A cluster of tanapox cases from the Mpumalanga Province was laboratory-confirmed during the first quarter of 2024.

Eight cases were confirmed by polymerase chain reaction (PCR) testing of lesion swabs and involved individuals who resided or worked in the southern parts of Kruger National Park and an adjacent reserve during February and March 2024. The CEZPD provided laboratory and outbreak investigation support to aid in detecting and reporting this cluster.

The SVPL provides referral diagnostics for Ebola, Marburg, Crimean-Congo haemorrhagic, Lassa, and other *Mammarenavirus* infections and yellow fever through a passive surveillance approach. The SVPL operates High- and Maximum-containment facilities, which allow for the safe and secure handling, testing, and storage of specimens for suspected and confirmed cases of VHF. A total of 164 tests were conducted to investigate suspected cases of VHF from 1 April 2023 to 31 March 2024.

CENTRE FOR ENTERIC DISEASES (CED)

The Centre focuses on six surveillance streams: foodborne diseases, waterborne diseases, routine surveillance (comprising epidemic-prone diseases such as cholera, enteric fever, and listeriosis), rotavirus, diarrhoeal disease syndromic surveillance, and genomic surveillance of priority enteric bacterial pathogens.

The Centre reported 120 laboratory-confirmed cases of enteric fever from eight different Provinces. The majority of cases were from Gauteng (54%, 65/120), followed by the Western Cape (23%, 28/120) and Eastern Cape (6%, 7/120) Provinces. No cases were reported from Limpopo. No cases of enteric fever caused by *Salmonella* Paratyphi A, B, or C have been reported during this period.

Before the current reporting period, a cholera outbreak was declared in South Africa in February 2023. From 1 January through 31 March 2023, 11 confirmed cholera cases were identified (toxigenic *Vibrio cholerae* O1 serotype Ogawa) in Gauteng (Ekhuruleni and City of Johannesburg). The first three cases were imported or import-related cases following travel to Malawi. All subsequent cases acquired infections locally and were classified as indigenous cases. A total of 376 clinical specimens and isolates were tested in the National Cholera Surveillance. Of these, 200 were confirmed as cases of *Vibrio cholerae* and further characterised as toxigenic serogroup O1 *Vibrio cholerae* (196 cases) and non-toxigenic, non-O1 *Vibrio cholerae* (four cases). The CED tested 51 non-human isolates from water and food samples; one was identified as *Vibrio* O1 Inaba and one as V. parahaemolyticus.

A total of 42 were non-toxigenic non-O1 *Vibrio cholerae* and seven were negative for *Vibrio cholera*. A total of 78 laboratory-confirmed cases of listeriosis were reported from eight Provinces. Most cases were from the Western Cape (31%, 24/78), followed by Gauteng (27%, 21/78) and KwaZulu-Natal (23%, 18/78). No cases were reported from the Northern Cape. Persons aged 15-49 years accounted for 44% (34/78) of cases, followed by neonates at 23% (18/78) and 65 years and older at 13% (10/78) of cases.

Diarrhoeal disease sentinel surveillance is active at seven sites in five Provinces. During the reporting period, 635 cases were enrolled (233 from Mpumalanga, 132 from the North West, 135 from Gauteng, 122 from the Western Cape, and 13 from the Free State). Children ≤5 years constituted 69% of cases (438/635), with a median age of 10 months. Patients >5 years comprised 31% (197/635) of enrolments, with a median age of 29 years. Most cases (377/635, 59%) were inpatients. Where results were available, among children up to 15 years of age, 2.2% (9/418) were HIV-infected, while 36% (52/144) of adults 16 years of age or older were HIV-infected. Outcome data was available for 85% (540/635) of the enrolments, with 95% (513/540) of the cases discharged and three deaths reported. Rotavirus was detected in 14% of the specimens screened (91/635), with the highest detection rates and case numbers between July and September 2023.

Through core-genome multilocus sequence typing (cgMLST) analysis of whole genome sequencing (WGS) data of typhoid, clusters were previously identified in the North West (one cluster) and Gauteng (two clusters), and the spread and establishment of the North West Klerksdorp typhoid strain into other Provinces was demonstrated.

During the 2023-2024 reporting period, the Centre responded to 10 food- and waterborne disease outbreaks with epidemiologic and laboratory testing support as needed. A total of 195 foodborne disease outbreaks were reported through NMC or other sources, and 89% (173/195) were followed up; 24% (41/173) did not meet the case definition, while 76% (132/173) were confirmed foodborne disease outbreaks. Gauteng accounted for most of the outbreaks at 29% (38/132), followed by KwaZulu-Natal (27%; 36/132) and the Eastern Cape (14%; 19/132). Many reported outbreaks were not investigated because of insufficient epidemiological data and the absence of clinical, food, and environmental sample collection and testing.

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

CHARM incorporates two national reference laboratories for antimicrobial resistance (AMR) and mycoses 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 Antimicrobial Resistance and Use Surveillance System (GLASS). CHARM's epidemiology team supports priority surveillance projects, conducts outbreak investigations, and is involved in setting up and evaluating public health programmes.

The Centre investigated several healthcare-associated outbreaks during the period under review, notably a large national outbreak of Wickerhamomyces anomalus (previously Candida pelliculosa) from a contaminated medical product widely used by healthcare facilities and the public. The investigation led to the South African Health Products Regulatory Authority issuing a Class 1 Type A recall of this product. Outbreaks of fungal infections are increasingly reported and investigated by the Centre, including a post-cataract surgery fungal infection outbreak in the Western Cape Province and a single case of antifungal-resistant ringworm infection in KwaZulu-Natal Province published in the South African Public Health Bulletin (https://www.phbsa.ac.za/antifungal-resistant-ringworm/).

CENTRE FOR HIV AND STIS (CHIVSTI)

The Centre for HIV and STIs (CHIVSTI) has a strong track record in the disciplines of HIV virology, HIV immunology, HIV/STI epidemiology, HIV/STI diagnostics, and HIV-STI interactions. The Antenatal HIV Survey is a biennial survey for monitoring trends in HIV prevalence, incidence, coverage of HIV testing, viral load suppression, and the syphilis cascade among pregnant women attending antenatal care at 1,589 public sector primary care facilities (sentinel sites). The survey found that HIV prevalence among pregnant women had declined by 2.5 percentage points since the previous survey, representing the first decline in more than a decade. HIV testing and antiretroviral treatment (ART) coverage among pregnant women were nearly universal. Still, there was a decline in the proportion of women who started ART before pregnancy compared to the previous survey. There was also sub-optimal viral suppression (<50 copies/ml) at 74.1%. There was high pre-exposure prophylaxis (PrEP) eligibility but very low coverage among the eligible (6.5%). There was also an increase in the prevalence of syphilis among pregnant women. Since the report's publication, NDoH has been working with partners to scale up PrEP during pregnancy.

The Human Sciences Research Council (HSRC) conducts a 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). The survey ended in April 2023. 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 previously infected and/or vaccinated people at the national and provincial levels. The sample size was 50,348 over the nine Provinces in South Africa, and data collection was stopped at the end of April 2023.

Promising decreases in HIV prevalence, coupled with high community viral load suppression (VLS) (81%), point to the impact of South Africa's National HIV Response. Progress has been made towards South Africa's 95–95–95 adult treatment targets: 90% of adults knew their status, 91% of those diagnosed were on ART, and 94% of those on ART were virally suppressed.

The Sixth South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey continued in 2023 and aimed to address concerns related to the development of drug-resistant HIV in South Africa. This survey also focused on monitoring the emergence of drug resistance to Dolutegravir, an integrase inhibitor that was integrated into the treatment guidelines in 2020.

Among the 51,170 samples collected during the study, 1,172 had unsuppressed viral loads; of these, 1,168 were selected for drug-resistance testing. The preliminary data from the survey revealed that 47% of patients with unsuppressed viral loads carried drug-resistance mutations. Specifically, 1% exhibited resistance to protease inhibitors (PI), 10% had resistance to Nucleoside Reverse Transcriptase Inhibitors (NRTI), 34% had resistance to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI), and 0.8% had resistance to integrase inhibitors.

In 2023-2024, the STI aetiological surveillance continued with the recruitment of patients in the three primary healthcare facilities in Gauteng, KwaZulu-Natal, and the Western Cape. The surveillance is used to validate the current STI syndromic management guidelines. *Neisseria gonorrhoeae* (80%) remained the most typical cause of male urethritis discharge syndrome, while bacterial vaginosis (59%) and vulvovaginal candidiasis (29%) are more prevalent in vaginal discharge syndrome. The relative prevalence of *Treponema pallidum* among patients presenting with genital ulcers was 29%.

CENTRE FOR RESPIRATORY DISEASES AND MENINGITIS (CRDM)

The CRDM houses the National Influenza Centre (NIC) for South Africa, which forms part of the expanded WHO Global Influenza Surveillance and Response System (e-GISRS). The NIC continued to support WHO by serologic and genetic characterisation of influenza viruses to guide the composition of the annual seasonal influenza vaccines, RSV, and SARS-CoV-2. 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 virus isolation, the haemagglutination inhibition assay, whole genome sequencing, and bioinformatics analysis. NIC activities are important in improving the detection, prevention, and control of influenza and other respiratory viruses for pandemic preparedness. CRDM was designated a WHO Coronavirus Network (CoViNet) laboratory in March 2024.

Influenza vaccination guidelines were updated to include updated guidance during COVID-19. In addition, CRDM staff contributed data and expertise to the NAGI RSV working group, which will advise NDoH on introducing newly available prevention approaches for RSV in infants. The Centre is represented by the WHO Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE), which advises the WHO and monitors and evaluates the evolution of SARS-CoV-2. Prof. Cheryl Cohen was appointed vice chair of the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), which periodically reviews the evidence and analyses the implications of emerging variants of concern (VOCs) on the performance of COVID-19 vaccines.

National pneumonia surveillance continued to operate in six Provinces. The programmes describe the burden, risk groups, seasonality, and characteristics of SARS-CoV-2, influenza, RSV, and *Bordetella pertussis*. 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 operated in eight Provinces. Pneumonia and systematic ILI programmes included systematic tuberculosis testing among individuals aged ≥18 years and COVID-19 vaccine effectiveness evaluation.

CENTRE FOR TUBERCULOSIS (CTB)

During the year under review, the CTB continued and refined its laboratory-based TB surveillance programmes. The CTB continued to issue weekly results for action (RfA) reports, covering drug-susceptible and drug-resistant TB, to assist TB programmeme managers and facilities in tracking, tracing, and linking people into care and treatment. The automated quarterly surveillance reports of the number of TB patients diagnosed with laboratory-confirmed pulmonary TB were updated to include the GeneXpert MTB/XDR and the BD Max MDR-TB assays, which the NHLS implemented during the year. Furthermore, linkages between laboratory-confirmed rifampicin-resistant pulmonary TB cases and the Electronic Drug-Resistant Tuberculosis Register (EDRWeb) were implemented to facilitate linkage to care for patients with drug-resistant TB (DR-TB).

The Centre continued to provide monthly reports assessing the implementation of the SMS notification system for TB-nucleic acid amplification tests (TB-NAAT) as part of the National TB Recovery Plan. The CTB, in collaboration with the National TB Programmeme (NTP), analysed Bedaquiline (BDQ) and fluoroquinolone (FLQ) resistance data from July 2019 to November 2023, utilising routine NHLS data. Following the release of new DR-TB reflex testing guidelines in March 2023, there was a notable surge in national BDQ phenotypic drug susceptibility testing (pDST) volumes, with varying provincial coverage. Implementing the new guidelines revealed a higher number of BDQ-resistant FLQ-susceptible (BDQ-R, FLQ-S) TB cases compared to BDQ-R FLQ-resistant (XDR-TB) cases in certain months, underscoring the significance of the new testing approach.

The Centre participated in the NDoH's World TB Day-TB Symposium on BPaL-L and the emergence of BDQ resistance, held in Johannesburg in March 2024, by invitation from the Minister of Health. The CTB reported the emergence of BDQ resistance based on laboratory surveillance of TB drug resistance. The symposium further provided information on the impact of this on the clinical management of drug-resistant TB and identified mitigating interventions to address the emergence of resistance.

CENTRE FOR VACCINES AND IMMUNOLOGY (CVI)

The CVI provides support and expertise in epidemiology and virology of vaccine-preventable viral diseases. The Centre has made great strides in the reporting period to test for other vaccine-preventable viruses in environmental surveillance. The measles outbreak declared in week 40 of 2022 in all Provinces in South Africa, except the Eastern Cape, still showed measles-positive cases during 2023-2024. The review of the measles outbreak surveillance data reporting and factors affecting public health response in Limpopo Province indicated that hospitals had more measles cases notified on the Notifiable Medical Condition Surveillance System (NMCSS) compared to blood samples sent to the laboratory for testing. Primary Healthcare Centres (PHCs) reported fewer measles cases on the NMCSS than the cases that were consulted. Hospitals with Infection, Prevention, and Control (IPC) and Expanded Programmeme for Immunisation (EPI) managers had better data compared to PHCs. The presence of a focal person in the facility substantially improved measles case reporting and case investigation form availability. Sequencing for polioviruses in Acute Flaccid Paralysis (AFP) cases and environmental surveillance from the South African region revealed vaccine-derived polioviruses.

After the measles outbreak in South Africa in 2022/2023, 5,467 South African febrile rash samples were tested under review, with 468 confirmed measles cases (8.56% positivity rate). The number of measles cases detected in 2023 decreased after the measles vaccine campaigns were rolled out in 2023, with a few sporadic measles cases and clusters currently seen. A total of 1,265 rubella cases were reported, constituting 23% of the samples tested at the NICD via febrile rash surveillance. The increase in rubella cases was reported in Western Cape Province in the City of Cape Town in November 2023 and later spread to other districts in the Province. Another increase in Rubella cases was reported in the Pixley Ka Seeme district in the Northern Cape Province. Other Provinces reported a low number of rubella cases. South Africa has approved using measles-rubella-containing vaccines, which will be available at public healthcare facilities. Rubella infections were reported in children aged one to 9 years, with more than 800 children reported being infected.

DIVISION FOR PUBLIC HEALTH SURVEILLANCE AND RESPONSE (DPHSR)

The DPHSR plays a pivotal role in surveillance and response activities related to infectious disease threats in South Africa. The DPHSR comprises the following units: the GERMS-SA surveillance programmeme (which is 21 years old this year), the Provincial Epidemiology Team (PET, consisting of eight epidemiologists based in the Provinces), the NMC Surveillance Unit, and the Outbreak Response Unit (ORU), which hosts the Emergency Operations Centre (EOC). Together, these units, in conjunction with specialists from other NICD centres, contribute to national communicable disease surveillance, pandemic preparedness, and response efforts through real-time alerts and notification of diseases of public health importance, as well as providing technical expertise to national, provincial, and district health departments.

It also facilitates communication and data sharing between the national and provincial health departments and the NICD.

For the year under review, the DPHSR was integral to the continued national and provincial response to the ongoing cholera outbreak, 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 well-co-ordinated and structured data flow, management, and analysis. DPHSR played a crucial role in managing outbreaks of other infectious diseases in response to other epidemics, including benzene/benzine toxicity, conjunctivitis, diphtheria, 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 includes information for targeted public health response, decision-making, and resource allocation. Through the NMC, timeous alerts are issued, and the public health response is initiated. The GERMS-SA collaborates with NICD centres to provide a national active surveillance programmeme for laboratory-confirmed bacterial and fungal infections, complemented by enhanced surveillance at sentinel hospital sites. The collaboration offers a robust platform for monitoring disease trends, which guides public health policy decisions.

NATIONAL CANCER REGISTRY (NCR)

The NCR is responsible for cancer surveillance, which is the systemic collection, storage, analysis, interpretation, and reporting of cancer cases. With the maturation of the Ekurhuleni Population-based Cancer Registry (EPBCR), South Africa now has a robust urban population-based cancer registry, which can be used to correct national pathology-based estimates. For the first time, cancer incidence statistics reported on the GLOBOCAN cancer statistics platform (https://gco.iarc.fr) no longer report data from neighbouring countries but actual South African data. GLOBOCAN 2022 reports data from the national pathology registry, which was scaled using the site and sex-specific percentages of microscopically verified cases obtained from the EPBCR (2018-2021) and applied to the 2022 population. This achievement is an important milestone in cancer surveillance in South Africa.

The NCR continued to provide technical support to the recently launched KwaZulu-Natal Population-Based Cancer Registry. As one of three International Agency for Research in Cancer – Global Initiative for Cancer Registry Development (IARC-GICR) Collaborating Centres (now called Centres of Expertise) for Sub-Saharan Africa, the NCR has been supporting cancer registries within the continent by providing training on record linkage for cervical cancer elimination and childhood cancer registration.

The National Childhood Cancer Registry published its third report on childhood cancer incidence (0-14 years old) for 2020. A total of 1 043 cancers were diagnosed in children aged 0-14 years old in South Africa in 2020. This number of cases equated to an overall age-standardised rate of 62.4 cases per million (95% CI: 51.0-76.0). We found the most common cancer diagnosed in children to be leukaemia, and the second most common cancer was lymphoma. Approximately 40% of the cases (n= 415) were diagnosed in children aged 0-4 years old.

SEQUENCING CORE FACILITY (SCF)

The Sequencing Core Facility (SCF) was established to promote and expedite surveillance and research activities at the NICD to provide accurate, high-quality, and cost-effective next-generation sequencing (NGS) solutions. The SCF currently supports all centres at the NICD on NGS and bioinformatics needs and thus acts as an extension of every centre regarding NGS capacity. The SCF presently houses the following NGS instruments: two Hamilton NGS Star's robots (automated liquid handlers for NGS libraries), Illumina MiSeq, 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 RAM, intermediate storage (117 TB), and long-term storage (2.2 PB) for data analysis. Some key focus areas involve whole genome sequencing (WGS), custom amplicon sequencing, and metagenomics. Research and surveillance activities that depend primarily 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.

In 2023, the SCF sequenced 26,086 genomes, generating ca. 14 TB of data. The distribution of data among the NICD centres are as follows: 56.80% CRDM, of which 35.20% was SARS_COV2, 7.50% CHIVSTI (HIV drug resistance surveillance/research), 15.15% CTB (TB drug resistance surveillance), 10.14% CED (WGS of *Salmonella spp.*), 4.47% CVI (wastewater surveillance), 3.44% CEZPD (Malaria drug resistance and 16s rRNA metagenomic sequencing), and 2.5% CHARM (bacterial and fungal sequencing).

SUPPORT FUNCTION

The collective transversal functions of Division Biosafety and Biosecurity (DBB), Communication, Information Technology, Field Epidemiology, and Occupational Health Services have continued to demonstrate exceptional professionalism and expertise in supporting the NICD mission. The team engages extensively with multiple global partners, from scoping strategies for strengthening public health institutes to advancing biosafety and biosecurity capability, effectively disseminating public health information, and leveraging technology for enhanced data management and analysis. The team continues to nurture the next generation of public health leaders at all levels of the health service, equipping them with the necessary skills and knowledge to address complex health challenges.

COLLABORATION AND KNOWLEDGE-SHARING WITHIN AFRICA

The Regional Diagnostics Demonstration Centre, as the first Regional Centre of Excellence for Biosafety and Biosecurity for the Southern Africa Region, continues to be a benchmark, with its regional subject matter experts providing mentorship for the newly established centres of excellence for the Eastern Africa Region in Dar es Salaam, Tanzania, and more recently in Western Africa in Dakar, Senegal. Dr Lazarus Kuonza was appointed Chairman of the Board of Directors for the African Field Epidemiology Network. He also serves on the advisory board of the Training Programmes in the Epidemiology and Public Health Interventions Network.

As part of managing the NDoH's diagnostic and research permits, the DBB issued permits to transfer 41,182 samples between South Africa and 62 countries, 41 of which were to other African countries. The permit was used 767 times to import 26,014 samples, a twofold increase compared to the previous financial year. This increase bodes well for collaboration and knowledge sharing within the continent.

DR NATALIE MAYET
Deputy Director

DEPUTY DIRECTOR'S OVERVIEW

"NICD continues to nurture the next generation of public health leaders at all levels of the health service equipping them with the necessary skills."

The collective transversal functions of Biosafety and Biosecurity, Communication, Information Technology, Field Epidemiology, and Occupational Health services have continued to demonstrate exceptional professionalism and expertise in supporting the mission of the NICD.

The team engage extensively with multiple partners at a global level from scoping strategy for strengthening public health institutes, advancing biosafety and biosecurity capability, effectively disseminating public health information to leveraging technology for enhanced data management and analysis. We continue to nurture the next generation of public health leaders at all levels of the health service equipping them with the necessary skills and knowledge to address complex health challenges.

DIVISION OF BIOSAFETY AND BIOSECURITY

The Division of Biosafety and Biosecurity (DBB) provides specialised services to the NHLS and NICD for Biorisk Management i.e. Biosafety, Biosecurity and Biocontainment Engineering, in ensuring the safe and secure operations of high and maximum containment laboratory infrastructure and has built internal capacity for biocontainment engineering and biorisk specialists who provide subject matter expertise for Africa and internationally.

DBB manages legislative National Department of Health Diagnostic and Research Permits with 953 copies of the permit issued to transfer 41,182 samples between South Africa and 62 countries, 41 of those being within Africa. The permit was used 767 times for the import of 26,014 samples. This is a twofold increase from last year predominantly imports for Quality Assurance purposes.

The Regional Diagnostic Demonstration Centre (RDDC) as the first Regional Centre of Excellence for Biosafety and Biosecurity (RCoEBB) for the Southern Africa Region continues to be a benchmark with its regional subject matter experts providing mentorship for the newly established centres of excellence for the Eastern Africa Region in Dar es Salaam, Tanzania and more recently in Western Africa (Dakar, Senegal).

Key milestones of engagement include:

National

- Membership of the Biological Weapons Working Committee (BWWC) of the South African Council for the Non-Proliferation of Weapons of Mass Destruction.
- Member of the Biosafety and Biosecurity Technical Working Group for the implementation of the National Action Plan for the International Health Regulations.
- Voting membership on South Africa Bureau of Standards (SABS) technical working committees and sub-committees in the development of Biological Safety Cabinet (BSC) national standards.

Regional

Regional Training and Certification Programmeme for Biosafety and Biosecurity Professionals

- Hosted BSC training, piloting the Regional Training and Certification Programmeme course curriculum, in partnership with Sandia National Laboratories for 10 participants from Gabon and Somalia.
- Facilitated BioRisk Management Level 1 training at the RCoEBB in Tanzania for 23 participants from the 14 countries in the Eastern Africa region.
- Facilitated Biological Waste Management Level 1 training at the RCoEBB in Tanzania for 26 participants from the 14 countries in the Eastern Africa region.
- Hosted an RTCP-BBP Curriculum Review Workshop of the BRM and BWM Level 1 courses at the RDDC. Sixteen African Region Subject Matter Experts, including the Examination Certification Committee (ECC)
- Facilitated the curriculum development of the Maintenance and Management of High Containment Facilities (Biocontainment Engineering) and the Selection, Installation, Maintenance and Certification of Biological Safety Cabinets with 12 experts across Africa.

Regulatory and Certification Framework for Institutions Handling High-Risk Pathogens for the Africa Region:

- Facilitated the TOT for 19 implementers of the Regulatory and Certification Framework for three countries in the North African region.
- Facilitated the Regional Assessor training for the Regulatory and Certification Framework for eight Francophone and West Africa region countries for 20 participants.
- Facilitated the TOT for Implementers of the Regulatory and Certification Framework hosted by the Eastern Africa Regional Co-ordinating Centre for 23 participants from ten 10 countries.
- Facilitated the TOT for Implementers of the Regulatory and Certification Framework for the Central Africa Region in Cameroon, 19 participants, who were subsequently all certified as Implementers of the Framework from the Central African region.
- Co-hosted with the African Biological Safety Association and Health Security Partners, a Biosecurity Symposium for Vaccine R&D and Manufacturing Facilities.
- Co-hosted training on the Tools for Advanced Biorisk Management Training in support of the RDDC with Sandia National Laboratories to support the 16 participants from Africa Regional SMEs.

- Attended a multi-country consultative/ project launch meeting of the Health-Security Partnership Project (HSPA) at the AU Headquarters, Addis Ababa, Ethiopia. The project is a collaboration between the WHO)/ AFRO/Hub, Africa CDC, RKI and six African Union Member States to strengthen surveillance and early warning capabilities.
- Facilitated a Regional Consultative meeting to Review the Report on the Biological Weapons Convention (BWC) Universalisation and National Implementation in African Union States Parties in Kenya.
- Provided support for the World Organisation for Animal Health (WOAH) Fortifying institutional resilience against biological threats project for emergencies. The training courses were offered at the RCoEBB for Malawi - Training on Biosafety and Biosecurity's 30 participants; Zimbabwe-Biosafety and Biosecurity in Animal Health's 28 participants; Regional Biological Waste Management Training in Animal Health laboratories, Level 1 training and exams for 14 participants.
- Co-hosted the Biosecurity and Know Your Collaborator Part II: Biorisk Management Systems Mapping and Implementation Planning Workshop in collaboration with the US Department of State's Biosecurity Engagement Programme (BEP) and Sandia National Laboratories (SNL). Participants included 14 Angolan laboratory professionals from biological facilities.
- Co-hosted design thinking meeting of seven 7 fellows of the Action Accelerator Vehicle (AAV), a collaboration with the Swiss non-profit organisation the Global Health Security Fund in Cape Town.
- Participated in a Validation Workshop of the Regional Guidance for the Development of High Consequence Agents and Toxins (HCAT) List in Zambia. The HCATS Guidance Document will play a significant role in establishing and strengthening biosafety and biosecurity systems in African Union Member States.

International

- Member of the WHO Technical Advisory Group on Biosafety (TAG-B).
- Co-hosted UNSGM Basic Training Course for qualified experts on the UNSGM Roster, the only training of this nature offered in Africa.
- Co-hosted a pre-conference workshop on Strengthening Biosafety and Biosecurity Capabilities Globally at the Global Health Security Conference.
- Participated in a skills training course on 'Sampling and transport of infectious substances' in Berlin, conducted by the Robert Koch Institute in cooperation with the Public Health Agency of Canada. Training was completed with the receipt of an internationally recognised IATA certificate which is valid for 24 months.
- Membership of the Planning Committee supporting the Global Research Agenda for Evidence-Based Biosafety, a collaborative project between Gryphon Scientific and the US Department of State. Attended a workshop for the project with 20 participants on the Focus on Safe Work Practices in Clinical and Diagnostic Laboratories held in South Africa.
- Attended the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction Plenary Meeting held in Rome in Italy.
- The Biorisk Specialist served as an International Federation of Biosafety Associations (IFBA) mentor in the IFBA mentorship programmeme and on the committee developing the adjunct BRM standard for biosafety professionals (adjunct to ISO35001).

RESEARCH OUTPUT

Journal articles

1. Stuart D. Blacksell, Sandhya Dhawan, Marina Kusumoto, Kim Khanh Le, Kathrin Summermatter, Joseph O'Keefe, Joseph Kozlovac, Salama Suhail Almuhairi, Indrawati Sendow, Christina M. Scheel, Anthony Ahumibe, Zibusiso M. Masuku. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory SARS-CoV-2. Applied Biosafety, https://bit.ly/43KJjNs
2. The Biosafety Research Road Map: The Search for Evidence to Support Practices in Human and Veterinary Laboratories. Applied Biosafety, https://bit.ly/3WWC5Ui
3. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory-Bacillus anthracis and Brucella melitensis. Applied Biosafety, https://bit.ly/3WRYaTX
4. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory- Shigella spp. Applied Biosafety, https://bit.ly/3WYABci
5. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory-Foot and Mouth Disease Virus. Applied Biosafety, https://doi.org/10.1089/apb.2022.0041
6. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory- Zoonotic Avian Influenza and Mycobacterium tuberculosis. Applied Biosafety, https://doi.org/10.1089/apb.2022.0038
7. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory- Crimean Congo Haemorrhagic Fever Virus and Lassa Virus. Applied Biosafety, https://doi.org/10.1089/apb.2022.0044
8. The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory-Mpox/Monkeypox Virus. Applied Biosafety, https://doi.org/10.1089/apb.2022.0045
9. Research Paper Contribution: Laboratory accidents and biocontainment breaches - Policy options for improved safety and security. Research Paper, London: Royal Institute of International Affairs, https://doi.org/10.55317/9781784135904

Conference Presentations

- Four local conferences
- Three international conferences

COMMUNICATIONS

The Communications Unit is central to the dissemination of strategic communication to showcase the NICD`s value proposition. The launch of the Public Health Bulletin for South Africa and its website was a milestone achievement for the unit.

The NICD website contains a substantial collection of information that is reviewed and updated regularly. For the 2023/24 financial year, 427,000 users visited the website. This is a 244% increase compared to the previous financial year baseline of 124,000 users. Social media platforms have proven to be valuable sources of information for the public, and the number of followers/subscribers continues to steadily grow. LinkedIn followers have increased by 45%, YouTube subscribers by 22%, X (formerly known as Twitter) by 1.98%, and Facebook and Instagram by 1.14% and 0.60% respectively.

The NICD continues to build a good rapport with the media and has published the quarterly Science Focus, highlighting the Institute's research projects showcasing the 191 peer-reviewed publications. The NICD Pulse continues to be a resource delivering relevant content to internal stakeholders.

The Communicable Diseases Communiqué, transitioned to the Public Health Bulletin of South Africa (PHBSA), aimed at providing current and actionable disease surveillance information for all diseases relevant to South Africa, this can be sourced on the PHBSA website https://www.phbsa.ac.za/f.

INFORMATION TECHNOLOGY

The 2023-2024 period witnessed the NICD Information Technology Department's unwavering commitment to driving technological advancements and enhancing operational efficiency within the organisation. The department embarked on a transformative journey in developing its strategy and driving innovation.

The enhancement of the Notifiable Medical Conditions system was central to the department's functions during this period. The introduction of the Merge Portal, underpinned by state-of-the-art artificial intelligence algorithms to integrate clinical and laboratory data and the team developed additional Case Investigation forms for Rift Valley Fever, Animal Bites, and Congenital Rubella.

The IT Department spearheaded the development of Power BI dashboards tailored for monitoring outbreaks, including those for cholera and antimicrobial resistance. These dashboards are intended to provide real-time data and bring efficiency to the data visualisation process. The team have transitioned the OHASIS reports into PowerBI making these real-time reports more accessible to users.

There are nine ongoing projects and 53 completed projects that include support for the integration of the Forensic Chemistry Laboratories into the NHLS systems and OHASIS support for the NIOH.

The development of a comprehensive Risk Assessment System and the deployment of the ESET antivirus solution exemplified the department's commitment to risk mitigation and cybersecurity practices.

IT operations managed 2,060 ticket logs with a success rate of 97%. There was a notable improvement in service availability of 90% uptime as compared to 82% of the previous year. Despite the achievements the IT Department faced significant resource constraints, that posed challenges regarding delayed project execution.

THE SOUTH AFRICAN FIELD EPIDEMIOLOGY TRAINING PROGRAMMEME (SAFETP)

The South African Field Epidemiology Training Programmeme (SAFETP) uses an established applied epidemiology curriculum, providing an accredited Master of Science (MSc) degree from either the University of Pretoria or the University of the Witwatersrand with mentored practical field experience. In addition to the Advanced tier, SAFETP offers the Frontline and Intermediate tiers. The Frontline tier launched in 2016, is a three-month in-service training programme and the first step in the three-tiered FETP model of training whilst the Intermediate tier launched in November 2021, is a nine-month, in-service programme designed for surveillance officers and public health professionals.

To date, the programmeme has trained more than 130 graduates who are employed in various sectors including the private sector, public health institutes, Africa CDC, US CDC and WHO. Currently, the programmeme has 21 residents. More than 400 abstracts have been presented at major scientific conferences.

The significant output of SAFETP was the graduation of 24 FETP Intermediate trainees, 31 Frontline Trainees and a total of 69 health professionals trained in Provinces in using applied epidemiology methods to improve surveillance capacity.

OUTBREAKS

The residents responded to more than 30 outbreaks in this reporting period. The outbreaks investigated include cholera, mumps, measles, influenza, bilharzia,

conjunctivitis and rabies.

The SAFETP Director, in collaboration with the African Field Epidemiology Network (AFENET) and other FETPs, is working on regional policies on advocacy and resource mobilisation for the network.

TRAINING – ADVANCED PROGRAMMEME

In the year under review, 14 residents from the 2021 cohort graduated with a Master of Science in Epidemiology conferred by the University of Pretoria and the University of Witwatersrand.

Dissertations ranged from the Knowledge, Attitudes, and Practices of Healthcare Workers regarding the Notification and Investigation of Foodborne Disease Outbreaks to evaluation of various surveillance systems; The association between underlying comorbidities and in-hospital mortality among COVID-19; Exposure to arbovirus infections among patients seeking primary health care and Prevalence of vaginal candidiasis at sentinel clinics et.al.

INTERMEDIATE TRAINING

The second FETP-Intermediate cohort of 11 healthcare professionals graduated in October 2023. The training was delivered through a partnership with the Mpumalanga Department of Health, the US Centers for Disease Control and Prevention (US CDC), and the Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ). The cohort conducted a group project focusing on "Knowledge, Attitude, and Practices of Healthcare Workers in Reporting a Notifiable Medical Condition, Ehlanzeni District, Mpumalanga Province, South Africa, 2023".

The cohort output included outbreak reports, surveillance system evaluations, scientific abstracts, and conference presentations.

The Intermediate FETP Cohort 3 in KwaZulu-Natal Province commenced in August 2023 and is ongoing with 13 healthcare professionals from the Province. SAFETP facilitated FETP-Intermediate Mentors Training for the KZN cohort in August for 15 mentors. Five workshops were conducted in this reporting period.

FRONTLINE TRAINING

In this reporting period, SAFETP completed the three-month training Frontline training for 35 healthcare professionals, this included training for the Eastern Cape, Eswatini, and the first cohort of 12 participants was enrolled for the Western Cape Province in February 2024 that including Environmental Health Practitioners, Infection Prevention and Control Co-ordinators, Occupational Health and Safety Nurses, NMC surveillance officer, and Communicable Disease Control Co-ordinators.

Additional Training

- In addition to Frontline training, the SAFETP team facilitated a basic epidemiology short course for Tshwane University of Technology third- and fourth-year students in the School of Environmental Health.
- A scientific writing workshop was conducted and facilitated by trained mentors and graduates; 10 draft manuscripts were developed.
- In July, the Bloomberg Data for Health Initiative in collaboration with NICD hosted a Training Trainers workshop for Data to Policy (D2P). Seven participants attended the workshop.
- The SAFETP team attended the IDSR Training of Trainers workshop co-ordinated by the National Department of Health and WHO in August aimed at standardising training materials and plans for Provinces to implement IDSR.
- In September SAFETP facilitated a scientific writing workshop for the Eastern Cape Province for 40 participants which included Frontline & Intermediate training graduates.

PROFESSIONAL DEVELOPMENT

Dr Lazarus Kuonza was appointed as the Chairman of the Board of Directors for AFENET and also serves on the Advisory Board of TEPHINET.

RESEARCH OUTPUT

Journal Articles

1. Gavhi F, De Voux A, Kuonza L, Motaze NV. Evaluation of the rubella surveillance system in South Africa, 2016–2018: A cross-sectional study. Plos one. 2023 Jun 23;18(6):e0287170.
2. Mashele SA, Zwane TB, Kuonza L, Muchengeti MM, Motsuku L. Risk factors for breast cancer among women in Ekurhuleni Metropolitan Municipality, Gauteng Province of South Africa, 2017-2020: a case-control study. ecancermedicalscience. 2023;17.
3. Tshabane C, Kuonza L, Mdose H, Musekiwa A, Motaze NV. Estimation of shedding time in laboratory-confirmed COVID-19 cases in South Africa: a population-based record linkage study, March-December 2020. The Pan African Medical Journal. 2023;46.
4. Chitaka A, Zwane T, Kuonza L, Naicker N, Tlotleng N, Wilson K. Diabetes mellitus mortality by major occupation category in South Africa. Public Health Bulletin South Africa. 2023. 20(1)
5. Mapiye M, Ravhuhali K, de Voux A, Kufa-Chakezha T. Evaluation of the congenital syphilis notification surveillance system in South Africa. Public Health Bulletin South Africa. (2023).
6. Ntshiqa T, Musekiwa A, Manesen R, Mdose H, Ngoma N, Kuonza L, Dlamini T, Reddy C, Williams S. Knowledge, Attitudes, Practices, and Acceptability of Medical Male Circumcision among Males in Traditionally Circumcising Rural Communities of Alfred Nzo District, Eastern Cape, South Africa. International Journal of Environmental Research and Public Health. 2023 Nov 21;20(23):7091.
7. Mahlare E, Ramutshila E, Musekiwa A, Kuonza L, Mabuto T. Knowledge, attitudes and practices of oral HIV pre-exposure prophylaxis (PrEP) among healthcare workers in the Ekurhuleni District, South Africa. South African Medical Journal. 2023 Dec 1;113(12):1548-56.

Conference Presentations

- International conferences: 15
- Local conferences: 21

OCCUPATIONAL HEALTH SERVICES

- Risk assessments for all Centres have been updated and reviewed by the SHE department and a web-based tool is under development to standardise the risk assessment process.
- Medical Surveillance continues with baseline medicals being done for staff and annual medicals for employees. TB screening using symptom monitoring is done quarterly for all at-risk staff and baseline chest X-rays for all new staff. Medicals for employees working on projects, e.g. wastewater collection, are done as per risks of the project.
- Occupational health is also closely involved with Ill Health management where people are not able to perform duties due to ill health.
- Thirty-six swabs were taken for COVID-19 testing, five of whom tested positive for SARS-CoV-2. 73 Immunity checks were completed and 63 vaccines were administered including Hep B x 30; Twinrix x 6; Polio x 9; Measles x 5; Rabies x 5; Typhoid x 2, and Yellow Fever x 6.
- There were 14 injuries on duty and 12 near misses during this financial year, significantly less than in previous years where the average was 40 injuries per year.
- There is ongoing assistance with formal training programmes at induction for new staff, as well as for First Aid and Fire Wardens.

DATA-2 POLICY INITIATIVE

The Data for Health (D4H) initiative partnered with the National Institute for Communicable Diseases (NICD) in South Africa in November 2019 to implement the Data for Impact (DI) activities in the country. The goals of the project are to build capacity to use scientific data to guide and support programme decision-making and policy development. There are three components to the D4H programmeme including:

- Data to Policy (D2P)
- Public Health Bulletin (PHB)
- Scientific Communication (SC)

D2P briefs have advanced in that six policy briefs that were compiled in the first cohort, four (i.e., cervical cancer vaccination, HIV screening tool, schistosomiasis, and rubella surveillance) have had their recommendations advanced towards policy changes. There is the continued advancement of the Public Health Bulletin and Unit 1 of the second D2P cohort has been completed with topics that include the loss of follow-up among TB patients in South Africa; neonatal mortality in a Gauteng tertiary hospital; insufficient blood supply in the South African National Blood Service; Meningococcal meningitis mortality – tertiary education institutions; Hepatitis C mortality in South Africa and Diabetes-related mortality among those in Gauteng TB programmes.

DEPUTY DIRECTOR

The Deputy Director remained as the focal point for liaison with multiple stakeholders at local, regional and international levels and there was a concerted effort to strengthening partnerships to drive collective sustainability.

The priority with the NDOH this year was the implementation of IDSR with joint capacity-building initiatives and the roll-out of integrated surveillance on the notifiable medical condition surveillance platform. The NICD was also involved in planning for the drafting of the National Action Plan for Health Security and the Deputy Director presented the Pandemic Preparedness Response Plan under Pillar 10 at the second Presidential Health Compact.

There was an increasing demand for the integration of surveillance data beyond that of communicable disease and this resulted in participation in the development of the framework for NCD/Mental Health/Injury Surveillance in Morocco hosted by Africa CDC and the presentation at a plenary session in Mpumalanga on Injury Surveillance and Integration hosted by the Institute for Health and Social Sciences. There were also presentations for the National Cancer Alliance and at the Diabetes Summit aimed at exploring diabetes surveillance in the context of IDSR.

The office holds several Board memberships in the Social and Health Sciences focusing on Injury and violence prevention and burns surveillance; the Surveillance Outbreak Response Management and Analysis System Foundation (SOMAS) and the Southern African Centre for Infectious Disease Surveillance (SACIDS) as a One Health consortium.

The NICD had the honour of hosting the Director of the Africa CDC and Regional Collaborating Centre representatives in August to explore opportunities for further engagement and collaboration. Engagement with Africa CDC continues with the drafting of the Research Agenda Framework for Africa in Cape Town, the design of the AES programmeme for the continent, NICD hosting a delegation from Africa CDC and the Southern Regional Collaborating Centre to evaluate the NICD to be a Centre of Excellence as an NPHI. The Deputy Director Co-chaired the NPHI session at the third CPHIA conference in Zambia and was on the panel for the AWARE programmeme for early warning and detection systems.

At a global level, we hosted a delegation from RKI with various centres pursuant to the capacity determination for strengthening surveillance as part of the Health Security partnership with RKI and Africa CDC.

The Deputy Director had the privilege to present at the World Health Summit on "How institutions are adapting to the new technology-driven opportunities to change their approach to work in health security". The visit also presented the opportunity to network at the WHO Berlin Hub and explore opportunities for collaboration.

A highlight of the year was the donations collected by the NICD and handed over to the Pholosho Primary School in Alexandra and the interaction with learners on building capacity for hygiene and hand-washing techniques.

The Deputy Director is involved in drafting multiple funding proposals with the NDOH for advancing Integrated Disease Surveillance and Response (IDSR) and for the pandemic preparedness fund for the country. Other funding proposal engagements include those with the USAID-Right to Care; US CDC; US CDC Foundation; Bloomberg Philanthropies; PEPFAR and the British High Commission.

Conference presentations

- International: 8
- Local: 5

RESEARCH OUTPUT

Journal Articles

1. Modernizing Global Health Security to Prevent, Detect, and Respond- Book Chapter

CENTRE FOR EMERGING ZOONOTIC AND PARASITIC DISEASES (CEZPD)

DR JACQUELINE WEYER
Centre Head

CENTRE FOR EMERGING ZOONOTIC AND PARASITIC DISEASES (CEZPD)

"The CEZPD supported responses through laboratory analysis of suspected cases and assistance in case investigations in various zoonotic disease outbreaks. A national database of known odyssean malaria cases is maintained by CEZPD."

BACKGROUND

The Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD) is a national and regional hub of expertise for reference laboratory testing, surveillance, research, and training in the fields of viral and bacterial zoonoses and parasitic diseases.

The diseases of concern to the Centre include those caused by high-consequence zoonotic pathogens but also neglected tropical infections.

These diseases include:

- Diseases listed as Category One notifiable medical conditions (NMCs) such as viral haemorrhagic fevers (VHFs) (i.e., Ebola virus disease, Crimean-Congo haemorrhagic fever, Lassa fever and Marburg virus disease), anthrax, botulism, yellow fever, plague, Rift Valley fever (RVF), rabies, mpox and malaria;
- Diseases listed as Category Two NMCs: brucellosis, schistosomiasis (or bilharzia) and soil-transmitted helminthic infections (STHs);
- Category Three NMCs: endemic and non-endemic arboviral infections;
- Other neglected tropical diseases (NTDs) including leptospirosis and opportunistic parasitic infections, and other emerging zoonoses such as Nipah virus disease.

The CEZPD supports public health responses including policy advice and technical support to the National Department of Health (NDoH) and many other national and international stakeholders including the World Health Organization (WHO) and Africa Centres for Disease Control and Prevention (Africa CDC). To respond to its mandate, the CEZPD operates ISO15189:2022 and ISO17025:2018 accredited laboratories, biosafety level 3 (high containment) and level 4 (maximum containment) facilities, entomology laboratories and insectaries including a mosquito mass-rearing facility.

SURVEILLANCE

HUMAN RABIES SURVEILLANCE

The CEZPD 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 ISO15189:2022 accredited tests. The SVPL curates a database of epidemiological and clinical information for all confirmed, probable and suspected rabies cases and contributes to accurate reporting of rabies as a Category One NMC through a passive surveillance approach. A total of 91 tests were performed for suspected rabies cases between 1 April 2023 and 31 March 2024. See section on Outbreaks.

SURVEILLANCE SUPPORTING MALARIA ELIMINATION IN SOUTH AFRICA ANTIMALARIAL

Artemisinin-resistant malaria parasites with gene deletions in the histidine-rich protein 2 (*hrp*2) and histidine-rich protein 3 (*hrp*3) genes rendering them invisible to HRP2-based falciparum-specific rapid diagnostic tests, are rapidly expanding across Africa. The Laboratory for Antimalarial Resistance Monitoring and Malaria Operational Research (ARMMOR) therefore expanded its surveillance to include the non-endemic Province of Gauteng, which reported more cases (all imported) than the endemic Provinces of Mpumalanga and KwaZulu-Natal in 2023. While none of the 1,538 specimens analysed carried any validated artemisinin resistance molecular marker, a small portion of malaria isolates (<1%) had a single deletion in either the *hrp2* or *3* genes. These surveillance data suggest that the recommended point-of-care-diagnostic (HRP2-based falciparum-specific rapid diagnostic test) and current first-line treatment are still effective in South Africa. However, the presence of parasite isolates with non-validated artemisinin resistance markers and single *hrp2/3* gene deletions in South Africa, and the presence of malaria parasites with validated artemisinin resistance markers in many neighbouring countries, is a major cause for concern. If these resistant parasites become established in South Africa, malaria-related morbidity and mortality will sharply increase due to the country's largely non-immune population, pushing back the elimination targets.

MONITORING THE OCCURRENCE AND DISTRIBUTION OF MALARIA VECTORS AND INSECTICIDE RESISTANCE

The Vector Control Reference Laboratory (VCRL) monitored and mapped *Anopheles* mosquito species including the occurrence and phenotypic intensity of insecticide resistance in specific malaria vector populations, in the KwaZulu-Natal, Mpumalanga, and Limpopo Provinces. Several resistance phenotypes were detected in the major malaria vector *Anopheles arabiensis*, especially in northern KwaZulu-Natal, but they are currently of low intensity and do not 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) showed the perennial presence of several malaria vector species, indicating continued high risk and receptivity for malaria.

This is especially important because the insecticide regimen indicated for malaria vector control in endemic districts is undergoing a shift away from the use of DDT to next-generation insecticides, and because South Africa's malaria elimination campaign requires accurate vector distribution maps for forward micro-planning and outbreak response.

PLAGUE SURVEILLANCE

The Special Bacterial Pathogens Reference Laboratory (SBPRL) performed diagnostic testing for plague in susceptible rodent populations in the Nelson Mandela Bay (Coega-area) and eThekwini municipalities, to alert public health authorities to the possibility of increased human plague risk. No rodents collected during the reporting period 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, which allows for the safe and secure handling, testing and storage of specimens for suspected and confirmed cases of VHF. A total of 164 tests were conducted to investigate suspected cases of VHF from 1 April 2023 to 31 March 2024.

NEGLECTED TROPICAL DISEASES - LABORATORY-BASED PILOT SURVEILLANCE PROJECT FOR SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHIASIS (STH)

Pilot surveillance for *Schistosoma* species and STHs (including *Ascaris lumbricoides*, *Trichuris trichiura*, *Necator americanus*, and *Ancylostoma duodenale*) was initiated in January 2024. This included submission and retesting of stool and urine specimens at the NICD Parasitology Reference Laboratory (PRL). From January to March 2024, 278 urine and stool specimens for schistosoma ova and soil-transmitted helminths were assessed. All positive samples were characterised as *S. haematobium* (with three showing dual infection with *S. mansoni*). Molecular analysis is to be undertaken with a focus on the detection of hybrid schistosome species.

CEZPD Medical Entomology Museum (MEM)

OUTBREAKS

The CEZPD supported responses through laboratory analysis of suspected cases and assistance in case investigations in various zoonotic disease outbreaks. Odyssean malaria is acquired when infective Anopheles mosquitoes are accidentally transported to non-endemic areas, where they transmit the parasites. In February 2024, a case of odyssean malaria in the Tshwane District, Gauteng Province was investigated by CEZPD staff and a team from the Gauteng Department of Health. A national database of known odyssean malaria cases is maintained by CEZPD.

Figure 1: *Site investigation during an odyssean malaria outbreak included examination of water bodies for Anopheles larvae.*

During the reporting period, ongoing outbreaks of rabies in domestic dogs were reported from districts in KwaZulu-Natal and the Eastern Cape Provinces. The CEZPD confirmed a total of 14 confirmed human rabies cases from South Africa during the reporting period. Scabies is an NTD, and in February 2024, CEZPD provided laboratory investigations and support for a suspected scabies outbreak in a mental health facility in the Eastern Cape. A cluster of tanapox cases were laboratory confirmed from the Mpumalanga Province during the first quarter of 2024.

A total of eight cases were confirmed by PCR testing of lesion swabs and involved individuals residing and/or working in the southern parts of the Kruger National Park and an adjacent reserve, during February and March 2024. The CEZPD provided laboratory and outbreak investigation support in aid of the detection and reporting of this cluster.

POLICY CONTRIBUTIONS

The CEZPD serves on several national and regional boards, committees and advisory groups including the WHO Global Outbreak and Response Network (GOARN) Steering Committee and Research Subcommittee; Africa CDC Southern Africa Regional Integrated Laboratory and Surveillance Network (SA-RISLNET); E8 Vector Control Technical Working Group, Research Subcommittee and Malaria Molecular Surveillance Co-ordinating group (as Co-Chair); the South African Malaria Elimination Committee (SAMEC) Vector Control Subcommittee and Case Management Technical Working Group; Steering Committee of the Tanzanian Malaria Surveillance Initiative; National Institute of Health Innovation Equity Forum, Natural Science Collection Facility Co-ordinating Committee; National Rabies Advisory Group; Joint External Evaluation Technical Working Group for Biosafety and Biosecurity (as Technical Lead); ASSAf Standing Committee on Biosafety and Biosecurity and National One Health Steering Committee (as Co-Chair). The Centre contributed to reviewing and development of policies, guidelines, operating procedures and strategies including the following:

- The Malaria Elimination Strategic Plan for South Africa for 2024-2028;
- The updated WHO Technical Guidelines and Recommendations for Malaria Vector Control Methods and Technologies;
- The national and provincial malaria control policies and programmes in the southern African region as part of the Elimination 8 (E8) Initiative;
- The National Malaria Treatment and Diagnosis Guidelines;
- The Master Plan for Elimination of NTDs in South Africa;
- The National Department of Health, NTD Group, Schistosomiasis mass drug administration planning for KwaZulu-Natal Province;
- The National Guidelines for the Recognition and Management of Viral Haemorrhagic Fevers in South Africa;
- The National Guidelines for the Prevention of Rabies in Humans in South Africa; and
- The National Action Plan for Health Security in South Africa (NAPHS).

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 PRL provided specialised diagnostic services for parasites of medical importance employing conventional methods, PCR and sequencing. A total of 332 diagnostic tests were performed. The majority (53%, 61/115) of malaria PCR tests were positive. Interesting and unusual parasites identified included *Taenia serialis, Leishmania tropica, Leishmania infantum, Trypanosoma brucei gambiense, Bertiella species, Mansonella perstans, Plasmodium vivax and Gedoelstia species*. *Babesia* species from the first case of babesiosis reported in South Africa was confirmed at PRL. Malaria microscopy quality assurance checks for the malaria control programme (MCP) microscopists, totalled 1,351.

The PRL, with financial support from the Global Fund and the E8 countries, maintained and managed the Regional Malaria Slide Bank and Proficiency Testing scheme for supporting malaria laboratory diagnosis in southern African countries. Cabo Verde and Equatorial Guinea were included in the last 12 months. 16,219 Slides in 44 batches were manufactured for microscopist training and external quality assessment by participating regional laboratories. Three PT surveys were conducted, and one comprehensive training slide set was prepared and supplied to each country.

Figure 2: *Staff members from the Parasitology Reference Laboratory preparing the malaria and other blood parasites slide training set.*

The SBPRL provided specialised diagnostic services for zoonotic bacterial pathogens causing diseases including anthrax, plague, leptospirosis, botulism and brucellosis. There were 46 probable cases of leptospirosis and five laboratory-confirmed cases of brucellosis. No cases of anthrax, botulism, or plague from South Africa were detected during the reporting period.

The SVPL confirmed a single case of CCHF in October 2023 from the North West Province of South Africa. The SVPL confirmed 14 human rabies cases from 1 April 2023 to 31 March 2024 (according to time of death), reported from the Eastern Cape, KwaZulu-Natal and Limpopo Provinces. No cases of mpox were diagnosed in South Africa during the reporting period. Following heightened vigilance for Nipah virus disease during an outbreak of this disease in India in 2023, SVPL provided a reference laboratory investigation for suspected cases but no cases were confirmed in South Africa. SVPL and the Electron Microscopy Laboratory (EML) confirmed a cluster of tanapox cases (n=8) in South Africa (Figure 3). The EML also assisted in the description of a case of rhinosporidiosis, and the ultrastructural characterisation of cilia for the diagnoses of several cases of suspected primary ciliary dyskinesia.

A total of 4,403 *Anopheles* mosquitoes were referred to the VCRL from sentinel sites in the KwaZulu-Natal, Mpumalanga, and Limpopo Provinces. The presence of five malaria vector species - *Anopheles arabiensis*, *An. merus*, *An. vaneedeni*, *An. funestus* and *An. parensis* – which contributes to ongoing residual malaria transmission in South Africa -was identified amongst these collections.

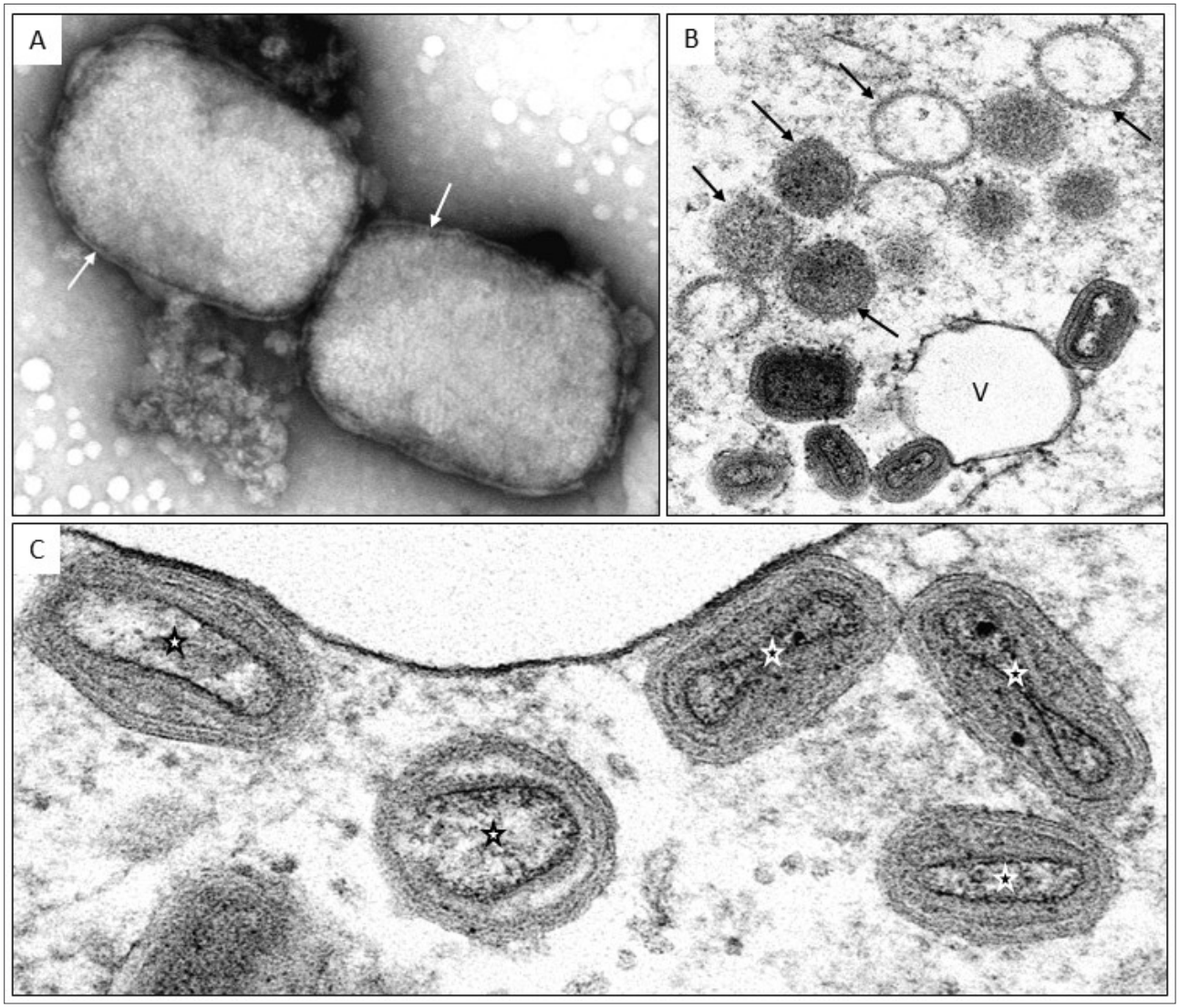


Figure 3: *Transmission electron micrographs of tanapox virions (approximately 240 x 300 nm). A) negatively-stained whole virions surrounded by outer membranes (arrows); B) sectioned tissue showing developmental stages (arrows) of virions in host cell cytoplasm, with maturing virions associated with a vacuole (V); C) various planes of section through mature virions that are still intracellular. The DNA cores are indicated by stars.*

RESEARCH ACTIVITIES

The CEZPD engages in research of zoonoses and parasitic diseases of public health importance to South Africa and the region. Here follows a synopsis of selected research activities (also refer to research outputs under section 8):

Strengthening Malaria Genomic 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)

Over 5,000 samples from five countries belonging to the E8 initiative have been sequenced and analysed using the next-generation targeted amplicon sequencing platform. Markers of artemisinin resistance were detected in isolates from three of the five countries, triggering additional testing in these countries to confirm artemisinin resistance. While most infections were due to *Plasmodium falciparum*, co-infections with either *P. ovale* or *P. malariae* were detected in all participating countries. Investigations are underway to confirm the prevalence of these non-falciparum infections to inform diagnostic policy. There appeared to be limited local transmission in many areas, supporting calls for strengthening surveillance along shared international borders to reduce malaria importation.

New Standardised Methods for Insecticide Resistance Detection in Malaria Vector Mosquitoes

NICD investigators: B Brooke, M Samuel, A Matamba, T Mashatola

Collaborators: V Corbel (Institute for Research & Development, France), R Yadav (WHO Pesticide Evaluation Scheme)

Insecticide resistance in *Anopheles* malaria vectors is extremely common in Sub-Saharan Africa and has a significant effect on malaria control operations in several parts of southern Africa including the malaria-endemic districts of South Africa. To manage this problem, tests for insecticide resistance in *Anopheles* populations are under constant development. In light of this, VCRL contributed to a major international initiative to renew and/or redesign the standard WHO bioassays for insecticide resistance detection, analysis, interpretation and operational decision-making. This project included the production of official WHO training videos that were filmed at the NICD under the technical guidance of VCRL personnel.

Figure 4: *Preservation of an Anopheles malaria mosquito collected in the Jozini area of northern KwaZulu-Natal.*

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)

In a project designed to evaluate the feasibility of the Sterile Insect Technique (SIT) for malaria vector control in South Africa, preliminary results and data analysis on the impact of limited-scale sterile male mosquito releases completed at a field site in 2022 showed a significant reduction of the local *An. arabiensis* population density. Funding was secured for the SIT project to resume pilot field trials in KZN in preparation for a cluster randomised control trial in 2024. The SIT project is also in the preparatory phase for upcoming additional sterile male releases to gather sufficient data to inform the next large-scale field trial.

Development of Immunoreagents and Assays for the Investigation of the Viral Haemorrhagic Fevers, Lassa Fever and Ebola Virus Disease

NICD investigators: N Moolla, J Weyer

Collaborators: M Killick and W Prinz (University of the Witwatersrand)

Eleven nucleoprotein monoclonal antibody (mAb) producing hybridoma cell lines were generated. The mAbs all recognise native Ebola virus-derived nucleoprotein, and recombinant nucleoprotein for Bundibugyo virus (BDBV) and Sudan virus (SUDV), two other virus species in the genus *Orthoebolavirus*, which are known to cause Ebola virus disease (EVD). Functional characterisation of the mAbs is underway with an interest in their utility in the development of a rapid lateral flow-based assay for EVD diagnosis.

Echinococcus Genotypes in a Paediatric Surgical Population in Eastern Cape Province, South Africa, 2019-2022

NICD investigators: B Moodley, C Sriruttan-Nel, J Frean

Collaborators: K Pedersen, Y Manickchund (Department of Pediatric Surgery, Frere Hospital, Eastern Cape)

Cystic echinococcosis (CE) or hydatid disease is a zoonotic disease caused by the larval stage of the cestode *Echinococcus* species. Humans are accidental intermediate hosts and become infected after ingestion of the cestode eggs. The symptoms are usually associated with the target organ which is most commonly the liver (70%) and the lungs (20%). In South Africa, CE is prevalent but has not been well studied. Tests were conducted on hydatid samples from humans to confirm the presence of the parasite and determine the genotype. Over the 38-month study period, samples were collected from 25 CE patients who were either undergoing a PAIR (puncture, aspiration, injection, re-aspiration) procedure or a laparotomy/ laparoscopic removal.

There were 55% females in the study population and the median age was seven years (range 2-12 years). All patients had liver cysts, including 3 who had additional organ involvement. Of the 25 cases, 13 (52%) tested positive by microscopy and 17 (68%) by PCR. Seven (28%) of cases were negative by both methods. There were five cases for which the samples were microscopy-negative and PCR-positive and one case which was microscopy-positive and PCR-negative. All PCR-positive samples were identified as *Echinococcus granulosus* sensu stricto genotype G1 by sequence analysis.

Newly identified lyssaviruses from South Africa

NICD Investigators: N Viljoen, J Coertse, J Weyer

Collaborators: W Markotter (University of Pretoria)

Two potentially novel, rabies-related lyssaviruses, were identified from bats in Limpopo Province, South Africa. Matlo bat lyssavirus (MBLV) was identified in two *Miniopterus natalensis* (Natal long-fingered) bats in 2015 and 2016, and Phala bat lyssavirus (PBLV) was identified in a *Nycticeinops schlieffeni* (Schlieffen's) bat in 2021. MBLV was most closely related to *Lyssavirus caucasicus* (WCBV), whereas PBLV was most closely related to *Lyssavirus formosa* (TWBLV-1) and Taiwan bat lyssavirus 2 (TWBLV-2). Taken together, the findings suggested that, while PBLV is likely a new lyssavirus species, MBLV is likely related to WCBV. This study contributed to knowledge of the diversity of lyssaviruses which may cause rabies in South Africa.

TEACHING AND TRAINING

The CEZPD supported diverse teaching and training activities during the reporting period. These activities encompassed a wide range of workshops, training courses, and curriculum development initiatives. These efforts were aimed at enhancing the capabilities of healthcare professionals pathologists and laboratory staff, not only within South Africa but also across Africa.

Notable training efforts included refresher courses on malaria microscopy and stool parasitology for various programmes and provincial programmes in South Africa, specialised next-generation sequencing training for E8 Genomic Fellows and Africa CDC, and co-ordination of and lectures for the Diploma in Tropical Medicine and Hygiene (DTM&H) programmes for local and international students. CEZPD staff contributed to lecturing for several University of Pretoria and University of the Witwatersrand programmes.

The CEZPD contributed significantly to curriculum development, collaborating with organisations such as the Africa CDC and the University of San Francisco-California to enhance programmes related to biorisk management, and malaria leadership and management. During the period under review, CEZPD staff supervised or co-supervised 46 post-graduate students (12 BSc Hons; 20 MSc/MTech/MPH and 13 PhD students) registered at different national and international universities. Overall, the CEZPD's activities in teaching, training, and curriculum development underscore its dedication to capacity building and knowledge dissemination, positioning itself as a key player in the advancement of knowledge and expertise in the field of zoonotic and parasitic diseases.

PROFESSIONAL DEVELOPMENT, AWARDS AND HONOURS

Dr J Raman was invited and completed the Science of Defeating Malaria Leadership Course held at Cheikh Anta Diop University, Senegal with a certificate awarded from Cheikh Anta Diop University, Senegal and Harvard University, America. (18-23 June 2023). Ms K Govender was awarded an MSc (University of Pretoria) in September 2023. Dr J Rossouw was appointed as Africa-Regional Subject Matter Expert (Af-SME) for Biorisk Management by the Africa CDC.

RESEARCH OUTPUT

Journal Articles

The CEZPD contributed to the publication of 28 manuscripts in peer-reviewed journals during the reporting period:

1. Biedenkopf N, Bukreyev A, Chandran K, Di Paola N, Formenty PBH, Grifths A, Hume A, Mühlberger E, Netesov SV, Palacios G, Pawęska JT, Smither S, Takada A, Wahl V and Kuhn JH. Renaming of genera Ebolavirus and Marburgvirus to Orthoebolavirus and Orthomarburgvirus, respectively, and introduction of binomial species names within family

Filoviridae. Archives of Virology 2023; 168:220. DOI:10.1007/s00705-023-05834-2.

2. Birkhead M, Otido S, Mabaso T, Mopeli K, Tlhapi D, Verwey C and Dangor Z. Ultrastructure for the diagnosis of primary ciliary dyskinesia in South Africa, a resource-limited setting. Front. Pediatr. 2023; 11:1247638. DOI:10.3389/fped.2023.1247638.

3. Birkhead M, Grayson W, Grobbelaar A, Msimang V, Moolla N, Mathee A, Blumberg L, Marshall T, Morobadi D, Popara M and Weyer J. Tanapox, South Africa, 2022. Emerg Infect Dis.2023; 29(6): 1206. DOI:10.3201/eid2906.230326.

4. Coertse J, Mortlock M, Grobbelaar A, Moolla N, Markotter W and Weyer J. Development of a Pan-Filoviridae SYBR Green qPCR assay for biosurveillance studies in bats. Viruses 2023; 15:987. DOI:10.3390/v15040987.

5. Craik A, Gondwe M, Mayindi N, Chipungu S, Khoza B, Gómez-Olivé X, Tollman S, Frean J, Tomlinson LA and Fabian J. Forgotten but not gone in rural South Africa: Urinary schistosomiasis and implications for chronic kidney disease screening in endemic countries. Wellcome Open Res. 2023; 8:68. DOI:10.12688/wellcomeopenres.18650.3.

6. Dahan-Moss YL, Munhenga G, Kaiser ML, Riddin M, Matamba A, Ramashia W, Rasikhanya W, Sekgele W, Langa Z, Shanahan M, Burke A, Noeth K, Lobb L, Mashatola T, Oliver S, Mouatcho J, Tshikae P, Raswiswi E, Mabika L, Dlamini D, Mabaso N, Manyawo Z, Ntshangase N, Sibambo S, Nkosi B, Govere J, Silawu B, Chibi P, Mkhabela L, Ndlovu F, Mgwenya T, Koekemoer LL, Brooke B. Malaria Vector Surveillance Report, South Africa, January - December 2022. Public Health Bulletin South Africa. National Institute for Communicable Diseases. 2024 (February):1-16.

7. Frean J and Ross M. African trypanosomiasis: lessons for occupational health practitioners. Occupational Health Southern Africa 2023; 29(2): 88-89.

8. Geldenhuys M, Ross N, Dietrich M, de Vries JL, Mortlock M, Epstein JH, Weyer J, Pawęska JT and Markotter W. Viral maintenance and excretion dynamics of coronaviruses within an Egyptian rousette fruit bat maternal colony: considerations for spillover. Scientific Reports 2023; 13(1): 15829. DOI:10.1038/s41598-023-42938-w.

9. Gwarinda HB, Tessema SK, Raman J, Greenhouse B and L-M Birkholtz. Population structure and genetic connectivity of Plasmodium falciparum in pre-elimination settings of Southern Africa. Frontiers in Epidemiology 2023; 3:122707L. DOI: 10.3389/fepid.2023.1227071

10. Jeanrenaud ACSN, Letinic BD, Mollett J, Brooke BD and Oliver SV. The effect of pollution on the competitive dynamics of Anopheles arabiensis Patton, 1905 and Culex quinquefasciatus Say, 1823 (Diptera: Culicidae). African Entomology 2023; 31: e10656. DOI: 10.17159/2254-8854/2023/a10656.

11. Johnson SAM, Asmah R, Awuni JA, Tasiame W, Mensah GI, Paweska JT, Weyer J, Hellferscee O and Thompson PN. Evidence of Rift Valley fever virus circulation in livestock and herders in Southern Ghana. Viruses 2023; 15(6): p1346. DOI:10.3390/v15061346.

12. Koekemoer LL, Hajkazemian M, Zawada JW, Mirzaie M, Dahan-Moss YL and Emami SN. Data-driven networking of global transcriptomics and male sexual development in the main malaria vector, Anopheles funestus. Sci Rep. 2023;13(1):16798. DOI: 10.1038/s41598-023-43914-0.

13. Kolo FB, Adesiyun AA, Fasina FO, Harris BN, Rossouw J, Byaruhanga C, Geyer HDW, Blumberg L, Frean J and Van Heerden H. Brucellosis seropositivity using three serological tests and associated risk factors in abattoir workers in Gauteng Province, South Africa. Pathogens 2024; 13(1): 64. DOI: 10.3390/pathogens13010064.

14. Lau C and Frean J. Remembering Professor Peter A. Leggat, AM, ADC (1961-2023). Trop Med Infect Dis. 2024 Jan 24;9(2):28. DOI:10.3390/tropicalmed9020028.

15. Mabona M, Zwane T, Raman J, Kuonza L, Mhlongo B and Phafane P. Evaluation of the malaria surveillance system in KwaZulu-Natal Province, South Africa, 2022: a focus on DHIS2. Malaria Journal 2024; 23:47. DOI:10.1186/s12936-024-04873-72024.

16. MacDonald JW, Frean JA, Ratabane JM, Moodley B, Mannaru K and Holz GE. A case of babesiosis in a returning traveller. S Afr J Infect Dis. 2024;39(1), a588.

17. Markotter W, De Vries L and Paweska J. Wing Tattoos: A cost-effective and long-lasting method for marking bats. Acta Chiropterologica 2023; 25(1):198-202. DOI:10.3161/15081109ACC2023.25.1.012.

18. Mayet H, Reddy DL, Alvarez T, Atiya Y, Govender NP, Birkhead M, Maphanga T and Pather S. Case report of nasal rhinosporidiosis in South Africa. Emer. Infect. Dis. 2024; 30 (4): 766-769. DOI:10.3201/eid3004.240018.

19. Niain'ny Felamboahangy L, Kaiser ML, Zengenene MP, Okumu F, Munhenga G and Koekemoer LL. Optimisation of laboratory-rearing parameters for Anopheles funestus larvae and adults. Acta Trop. 2023; 238:106785. DOI:10.1016/j.actatropica.2022.106785.

20. Odero JO, Nambunga IH, Wangrawa DW, Badolo A, Weetman D, Koekemoer LL, Ferguson HM, Okumu FO and Baldini F. Advances in the genetic characterisation of the malaria vector, Anopheles funestus, and implications for improved surveillance and control. Malar J. 2023 Aug 8;22(1):230. DOI:10.1186/s12936-023-04662-8.

21. Raman J. Editorial: Women in infectious diseases epidemiology. Frontiers in Epidemiology 2024; 3:1351528. DOI:10.3389/fepid.2023.1351528.

22. Raman J and Barnes KI. Ensuring prompt detection and effective treatment of all malaria infections in South Africa. South African General Practitioner 2023; 4(2):54-57. DOI: 10.36303/SAGP.0173.

23. Rants'o TA, Koekemoer LL and van Zyl RL. Bioactivity of select essential oil constituents against life stages of Anopheles arabiensis (Diptera: Culicidae). Exp Parasitol. 2023; 251:108569. DOI:10.1016/j.exppara.2023.108569.

24. Rants'o TA, Koekemoer LL and van Zyl RL. The insecticidal activity of essential oil constituents against pyrethroid-resistant Anopheles funestus (Diptera: Culicidae). Parasitol Int. 2023; 95:102749. DOI:10.1016/j.parint.2023.102749.

25. Ross M, Frean J. Occupational malaria: lessons for occupational health practitioners. Occupational Health Southern Africa 2023; 29(3): 141-143

26. Saxena SK, Ansari S, Maurya VK, Kumar S, Jain A, Paweska JT, Tripathi AK and Abdel-Moneim AS. Re-emerging human monkeypox: A major public-health debacle. Journal of Medical Virology 2023; 95(1): e27902. DOI: 10.1002/jmv.27902.

27. Tine R, Herrera S, Badji MA, Daniel K, Ndiaye P, Gueye CS, Tairou F, Slutsker L, Hwang J, Anash E and Littrel M on behalf of the Malaria Operational Research Partnership. Defining operational research priorities to improve malaria control and elimination in Sub-Saharan Africa: results from a country-driven research prioritization setting process. Malaria Journal 2023; 22:219. DOI: 10.1186/s12936-023-04654-8.

28. Quan V, Frean J, Weyer J, Rossouw J, Oosthuizen M. and Blumberg, L. Zoonosis as a cause of acute febrile illness at a One Health interface in rural South Africa: it's the little five, not the big five. Inter. J. Infect. Dis. 2023; 130: S36. DOI: 10.1016/j.ijid.2023.04.083.

29. van Meer V, Pawęska JT, Swanepoel R, Grobbelaar A, Bastos AD. Genome sequencing of historical encephalomyocarditis viruses from South Africa links the historical 1993/4 Savanna elephant (Loxodonta africana) outbreak to cryptic Mastomys rodents. Pathogens. 2024; 13(3):261. DOI:10.3390/pathogens13030261.

30. Viljoen N, Ismail A, Weyer J and Markotter W. A rabies-related lyssavirus from a Nycticeinops schlieffeni bat with neurological signs, South Africa. Microbiology Resource Announcement 2023;12(11): e00621-23. DOI: 10.1128/MRA.00621-23.

31. Viljoen N, Weyer J, Coertse J and Markotter W. Evaluation of taxonomic characteristics of Matlo and Phala bat rabies-related Lyssaviruses identified in South Africa. Viruses 2023; 15(10):2047. DOI: 10.3390/v15102047.

32. Viljoen N, Burt F and Weyer J. Coding-complete genome of human alphaherpesvirus 1 isolated from a case of fulminant hepatitis. Microbiology Resource Announcements 2023; 12(10): e00355-23. DOI: 10.1128/MRA.00355-23.

Conferences

During the year under review, staff from the Centre made 54 contributions to international, national and local congresses. Centre for Emerging Zoonotic and Parasitic Diseases

CENTRE FOR ENTERIC DISEASES (CED)

PROF. NICOLA PAGE
Acting Centre Head

CENTRE FOR ENTERIC DISEASES (CED)

BACKGROUND

The Centre is responsible for providing timeous, locally relevant information to facilitate the understanding, management and prevention of enteric diseases in the South African population. The Centre focuses on six research streams, including:

1. **Foodborne diseases**, globally recognised as a threat to food safety and security.
2. **Waterborne diseases**, affecting substantial portions of the population in instances where unsafe water is utilised, and often associated with large outbreaks.
3. **Category One notifiable medical conditions** (NMC) under routine surveillance, comprising epidemic-prone diseases such as cholera, enteric fever and listeriosis.
4. **Rotavirus,** a vaccine-preventable disease in South Africa.
5. **Diarrhoeal disease** syndromic surveillance in selected sites, monitoring important viral, bacterial and parasite enteric pathogen prevalence.
6. **Genomic surveillance** of priority enteric bacterial pathogens, detecting unknown outbreaks and establishing disease clusters.

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

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

SURVEILLANCE

NATIONAL CHOLERA SURVEILLANCE

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

In the reporting period, a total of 376 clinical specimens and isolates were tested at the CED. Of these, 200 were confirmed as cases of *Vibrio cholerae,* and further characterised as toxigenic serogroup O1 *Vibrio cholerae* (196 cases) and non-toxigenic, non-O1 *Vibrio cholerae* (four cases). Fifty-one non-human isolates from water and food samples were also tested, one was identified *as Vibrio cholerae* 01 Inaba and one as *Vibrio parahaemolyticus*, 42 were non-toxigenic non-O1 *Vibrio cholerae* and seven were negative for *Vibrio cholerae.*

NATIONAL ENTERIC FEVER SURVEILLANCE

A total of 120 laboratory-confirmed cases of enteric fever were reported from eight different Provinces. The majority of cases were from Gauteng (54%, 65/120) followed by Western Cape (23%, 28/120), and Eastern Cape (6%, 7/120) Provinces. No cases were reported from Limpopo. No cases of enteric fever caused by *Salmonella* Paratyphi A, B or C have been reported during this period. Updates on clusters previously identified in several Provinces through genomic surveillance are provided in the following section.

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, comprehensive food history and isolate referral for WGS.

Seventy-eight laboratory-confirmed cases of listeriosis were reported from eight Provinces. Most cases were from Western Cape (31%, 24/78) followed by Gauteng (27%, 21/78) and KwaZulu-Natal (23%, 18/78). No cases were reported from the Northern Cape. Persons aged 15-49 years accounted for 44% (34/78) of cases, followed by neonates at 23% (18/78) and 65 years and older at 13% (10/78) of cases.

ACUTE DIARRHOEAL DISEASE SURVEILLANCE

Diarrhoeal disease sentinel surveillance is active at seven sites in five Provinces. During the reporting period, 635 cases were enrolled (233 from Mpumalanga, 132 from North West; 135 from Gauteng, 122 from Western Cape, and 13 from Free State). Children ≤5 years constituted 69% of cases (438/635) with a median age of 10 months. Patients >5 years comprised 31% (197/635) of enrolments, with a median age of 29 years. Most cases (377/635, 59%) were inpatients. Where results were available, among children up to 15 years of age, 2.2% (9/418) were HIV-infected, while 36% (52/144) of adults 16 years or older, were HIV-infected. Outcome data was available for 85% (540/635) of the enrolments, with 95% (513/540) of the cases discharged and three deaths reported.

Rotavirus was detected in 14% of the specimens screened (91/635) with detection rates and case numbers highest between July and September 2023. Multiplex PCR testing for other enteric viruses, bacteria and parasites was also performed. Excluding rotavirus, the most common enteric viruses detected were adenovirus (88/531; 17%; enteric and respiratory human adenovirus), norovirus (73/531; 14%) and astrovirus (23/531; 4%). *Shigella* spp. was the most common enteric bacterial pathogen identified (82/478; 17%) followed by Campylobacter spp. (41/478; 9%) and *Salmonella* spp. (19/478; 4%). The most common parasite detected was *Cryptosporidium* spp. (27/432; 6%).

Rotavirus, norovirus and shigellosis remain the three most common causes of diarrhoea in hospitalised children under five years, a finding consistent with reports in many low- and middle-income countries. Unlike children and adolescents, a large proportion (slightly more than a third) of adults hospitalised or seeking treatment for diarrhoea are HIV-infected.

OUTBREAKS

The Centre's staff regularly follow up on alerts of suspected enteric disease outbreaks reported through the NMC system and other sources. In addition, the routine use of whole-genome sequencing (WGS) as a surveillance tool enables the detection of clusters (small localised outbreaks) and targeted epidemiological investigation of cases by the NDoH and assists in our understanding of the complex epidemiology of some of the endemic enteric diseases. The Centre provides epidemiological and laboratory support for outbreak investigation as required.

ENTERIC FEVER (TYPHOID FEVER)

Through core-genome multilocus sequence typing (cgMLST) analysis of WGS data, clusters were previously identified in North West (one cluster) and Gauteng (two clusters) and the spread and establishment of the North West Klerksdorp typhoid fever cluster strain into other Provinces was demonstrated. The first case of enteric fever caused by the Klerksdorp strain was identified in the North West Province in November 2020. As of 31 March 2024, there were 95 confirmed cases across six Provinces (GP= 45, NW=37, MP=6, KZN=3; FS=2; WC=2). The most recent case identified in North West Province occurred in February 2023 and the additional 11 cases identified during the reporting period were all from Gauteng Province. In the North West and Gauteng Provinces, males predominate (73% of cases) with a median age of 26 and 25 years, respectively. It is likely that different concurrent patterns of transmission were responsible for the initial cases and subsequent spread of the Klerksdorp cluster strain.

No new cases belonging to either Gauteng cluster have been identified in the current reporting period, suggesting that these clusters are no longer active. The first Gauteng cluster consisted of 32 cases, detected from January 2020 through October 2022; and the second Gauteng cluster consisted of 12 cases detected from June 2020 through April 2022. Contamination of municipal water is very unlikely to be the source of infection in any of the clusters described, and the ongoing challenge in 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. Centre staff members (Dr Linda Erasmus and Mr Phuti Sekwadi) responded to intermittent media queries and gave interviews on the topic as needed.

CHOLERA

Several African countries (including Malawi, Mozambique and Zimbabwe) have reported cholera outbreaks over the last year highlighting the risk of imported cases in South Africa. Prior to the current reporting period, a cholera outbreak was declared in South Africa in February 2023. From 1 January through 31 March 2023, 11 confirmed cholera cases were identified (toxigenic *Vibrio cholerae* O1 serotype Ogawa) in Gauteng (Ekhuruleni and City of Johannesburg). The first three cases were imported or import-related cases following travel to Malawi. All subsequent cases acquired infection locally and were classified as indigenous cases.

From 1 April 2023 to 31 March 2024, a cumulative total of 1,605 suspected cholera cases were notified through the NMC system from nine Provinces. From 7 May through 25 July 2023, 188 laboratory-confirmed cholera cases were identified. Gauteng Province accounted for the majority of the cases (n=165), mostly from Hammanskraal in Tshwane; Free State Province had 11 cases primarily affecting Vredefort/ Parys, Fezile Dabe District; North West Province

reported six cases and Limpopo Provinces had four cases. Mpumalanga and KwaZulu-Natal Provinces identified one case each.

A single case was confirmed in North West Province in October 2023 and a further case was identified in Eastern Cape Province in December 2023. In the first quarter of 2024, 10 laboratory-confirmed cholera cases were reported; nine from Limpopo Province and one case from Gauteng Province. The first three cases were imported following travel to Zimbabwe, while no travel history was reported in the other cases. One case from Limpopo Province was serotyped as *Vibrio cholerae* O1 Inaba, while nine of the cases were serotyped as *Vibrio cholerae* O1 Ogawa. Antimicrobial susceptibility testing was performed on 148 *Vibrio cholerae* isolates and all were susceptible to azithromycin and ciprofloxacin.

The CED has supported the NDoH in cholera case investigation, field investigation and contact tracing activities, provided technical advice to the National DoH, maintained and updated the cholera outbreak line list of all the suspected and confirmed cases and attended the cholera outbreak MNORT meetings. Testing of stool specimens/isolates at the CED laboratory, including culture, serotyping and PCR, is ongoing. Centre staff members (Drs Juno Thomas, Linda Erasmus, Nicola Page and Mr Phuti Sekwadi) responded to media queries and gave radio and TV interviews on the topic.

SELECTED FOODBORNE DISEASE OUTBREAKS

Investigation of foodborne disease outbreak in a home for the intellectually and physically disabled persons, Gauteng in August 2023

On 31 August 2023, a visiting doctor at a home for elderly persons living with intellectual and physical disabilities reported a suspected foodborne disease outbreak involving 24 residents. Two residents were admitted to hospital, one of whom demised. Specimens were collected from symptomatic residents (n=6) and food retention samples (including boiled eggs and chicken meals) were sent to a private laboratory for screening of foodborne pathogens. All clinical specimens tested positive for *Salmonella enteritidis*, and the isolates were confirmed at CED as *Salmonella enteritidis*. The laboratory results for the food samples were not shared. The facility conducted extensive investigations and reinforced infection control measures throughout its food preparation processes. No new cases were reported after 31 August.

Foodborne disease outbreak of Salmonella enteritis among inmates at an event in Western Cape, October 2023

Between 1 and 6 October 2023, 12 inmates fell ill with gastroenteritis while attending an event at a Western Cape correctional facility. During transit to the Western Cape on 30 September, inmates from a correctional facility in KwaZulu-Natal consumed cooked food from a visitor. The onset of illness occurred during transit. None of the inmates at Western Cape correctional facility reported any illness. Ten stool samples were collected and tested at the George NHLS laboratory. One patient was admitted to hospital with no fatalities. *Salmonella* species were isolated from nine of the 10 samples and CED confirmed *Salmonella enteritidis*. Food samples of the implicated food items were not available for testing.

Suspected foodborne disease outbreak at a restaurant, Cape Town, Western Cape, February 2024

On 8 February, a suspected foodborne disease outbreak affecting patrons and staff at a restaurant in the Western Cape was reported. During investigations, 20 cases were identified (12 staff; eight patrons) with onset between 31 January and 9 February. Meals consumed at the restaurant between 7 and 8 February were suspected to be the vehicle of infection. Environmental assessments were conducted, and surface swabs and food samples were collected for laboratory analysis. Clinical specimens were collected from cases, of symptomatic and asymptomatic staff members. Two specimens were tested at a private lab with Shigella/EIEC detected by

PCR. A further 60 specimens were screened at CED for viruses, bacteria and parasites. Shigella/EIEC targets were detected in 63% (38/60) of symptomatic and asymptomatic persons and Shiga-toxin-producing *Escherichia coli* targets in 3% (2/60) of specimens. No enteric pathogens were detected from the environmental swabs, although high coliform counts were noted on three of the 13 food samples collected. Epidemiological investigations were conducted by the Western Cape DoH outbreak response team.

OTHER FOOD- AND WATERBORNE DISEASE OUTBREAKS

During the 2023/2024 reporting period, the centre responded to 10 reported outbreaks with epidemiologic and laboratory testing support as needed. 195 Foodborne disease outbreaks were reported to NICD/CED through NMC or other sources. Eighty-nine percent (173/195) were followed up, 24% (41/173) did not meet the case definition, and 76% (132/173) were confirmed foodborne disease outbreaks. Gauteng accounted for most of the outbreaks at 29% (38/132) followed by KwaZulu-Natal (27%; 36/132) and Eastern Cape (14%; 19/132). Clinical specimens were collected in 39% (52/132) of the outbreaks. Pathogens were isolated in 38% (20/52) of the outbreaks. Non-typhoidal *Salmonella* was the most common pathogen isolated (50%; 10/20). Many reported outbreaks were not investigated further due to insufficient epidemiological data and the absence of clinical/food/environmental sample collection and testing. Improper storage and temperature abuse of food are commonly identified as a likely contributing factor in reported outbreaks.

POLICY CONTRIBUTIONS

The summary of cholera diagnosis and case management 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 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:

- Specialised rotavirus testing and rotavirus typing
- Specialised testing for other enteric viruses, including astrovirus, norovirus and sapovirus
- Specialised adenovirus typing for diarrhoea cases, acute hepatitis of unknown cause cases during 2023/24 and conjunctivitis outbreaks
- Specialised molecular screening for enteric pathogens (including multiplex PCR)
- Specialised testing for *Vibrio cholerae*, including phenotypic and molecular testing
- Specialised phenotypic characterisation and molecular testing for diarrhoeagenic *E. coli*, including Shiga toxin-producing *E. coli*
- Specialised testing for *Salmonella* species, including serotyping
- Specialised testing for *Listeria* species
- WGS for enteric bacterial pathogens where indicated

TEACHING AND TRAINING

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

- **Undergraduate and post-graduate teaching:** Field Epidemiology Training Programmeme (FETP); MSc Epidemiology and Biostatistics, MSc Vaccinology and Diploma in Tropical Medicine and Hygiene (DTM&H) courses at the University of Witwatersrand; registrar training courses hosted by the NICD; NICD intern medical scientist rotational training.
- **Postgraduate supervision:** Staff from the centre supervised five PhD students, three MSc students, one MMed student and one MPH

student. Four intern medical scientists were trained in the centre.

- **Trainer:** Welcome Connecting Science course, South African Society of Travel Medicine course.

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

PROFESSIONAL DEVELOPMENT

- Post-graduate candidates: two centre staff members (one for MSc and one for MPH).

RESEARCH OUTPUT

Journal Articles

1. Gallichan S, Ramalwa N, Thomas J, Feasey NA, Smith AM. 2023. Salmonella Enteritidis clades in South Africa: why we should be paying more attention. Frontiers in Tropical Diseases 4:1152422 (doi: 10.3389/fitd.2023.1152422)
2. Carey ME, Dyson ZA, Argimón S, Cerdeira L, Yeats C, Aanensen D, Mboowa G, Baker S, Tessema SK, Smith AM, Okeke IN, Holt KE. 2023. Unlocking the potential of genomic data to inform typhoid fever control policy: Supportive resources for genomic data generation, analysis, and visualization. Open Forum Infectious Diseases 10 (Suppl. 1): S38-S46 (https://doi.org/10.1093/ofid/ofad044)
3. Smith AM, Erasmus LK, Tau NP, Smouse SL, Ngomane HM, Disenyeng B, Whitelaw A, Lawrence CA, Sekwadi P, Thomas J. Enteric fever cluster identification in South Africa using genomic surveillance of Salmonella enterica serovar Typhi. Microb Genom. 2023 Jun;9(6):mgen001044 (doi: 10.1099/mgen.0.001044)
4. Fellows T, Page N, Fix A, Flores J, Cryz S, McNeal M, Iturriza-Gomara M, Groome MJ. Association between Immunogenicity of a Monovalent Parenteral P2-VP8 Subunit Rotavirus Vaccine and Fecal Shedding of Rotavirus following Rotarix Challenge during a Randomised, Double-Blind, Placebo-Controlled Trial. Viruses. 2023 Aug 25;15(9):1809
5. Page NA, Netshikweta R, Tate JE, Madhi SA, Parashar UD, Groome MJ; South African Intussusception Surveillance Group. Microorganisms Detected in Intussusception Cases and Controls in Children <3 Years in South Africa From 2013 to 2017. Open Forum Infect Dis. 2023 Sep 4;10(9):ofad458
6. Johnstone SL, Erasmus L, Thomas J, Groome MJ, du Plessis NM, Avenant T, de Villiers M, Page NA. Epidemiology and aetiology of moderate to severe diarrhoea in hospitalised patients ≥5 years old living with HIV in South Africa, 2018-2021: A case-control analysis. PLOS Glob Public Health. 2023 Sep 8;3(9):e0001718
7. Myataza A, Thomas J, Smith AM. 2023. Characterisation of Salmonella enterica serovar Isangi from South Africa, 2020-2021. BMC Infectious Diseases 23:791 (https://doi.org/10.1186/s12879-023-08786-9)
8. Stenhouse GE, Keddy KH, Bengtsson RJ, Hall N, Smith AM, Thomas J, Iturriza-Gomara M, Baker KS. 2023. The genomic epidemiology of shigellosis in South Africa. Nature Communications 14:7715 (http://dx.doi.org/10.1038/s41467-023-43345-5)
9. Antoni S, Nakamura T, Cohen AL, Mwenda JM, et al (including Page NA). Rotavirus genotypes in children under five years hospitalised with diarrhea in low and middle-income countries: Results from the WHO-co-ordinated Global Rotavirus Surveillance Network. PLOS Glob Public Health. 2023 Nov 28;3(11):e0001358 (doi: 10.1371/journal.pgph.0001358)

10. Mohy A, Page N, Boyce W, Gomez JA. Economic Evaluation of Rotavirus Vaccination in Children Aged Under Five Years in South Africa. Clin Drug Investig. 2023 Nov;43(11):851-863 (doi: 10.1007/s40261-023-01312-4)

11. Wieters I, Johnstone S, Makiala-Mandanda S, Poda A, et al (including Page NA). Reported antibiotic use among patients in the multicenter ANDEMIA infectious diseases surveillance study in Sub-Saharan Africa. Antimicrob Resist Infect Control. 2024 Jan 25;13(1):9 (doi: 10.1186/s13756-024-01365-w)

12. Chhabra P, Tully DC, Mans J, Niendorf S, et al., (including Page NA). Emergence of Novel Norovirus GII.4 Variant. Emerg Infect Dis. 2024 Jan;30(1):163-167 (doi: 10.3201/eid3001.231003)

13. Davids M, Johnstone S, Mendes A, Brecht G, Avenant T, du Plessis N, de Villiers M, Page N, Venter M. Changes in Prevalence and Seasonality of Pathogens Identified in Acute Respiratory Tract Infections in Hospitalised Individuals in Rural and Urban Settings in South Africa; 2018-2022. Viruses. 2024 Mar 5;16(3):404 (doi: 10.3390/v16030404)

14. Sekwadi P, Smith AM, Maruma W, Mongologa G, Tsele G, Ngomane HM, Tau N, Smouse SL, Disenyeng B, Sebiloane M, Johnston L, Erasmus L, Thomas J. 2024. A prolonged outbreak of enteric fever associated with illegal miners in the City of Matlosana, South Africa, November 2020-September 2022. Open Forum Infectious Diseases 2024 Feb 28;11(3):ofae118 (https://doi.org/10.1093/ofid/ofae118)

15. Rafetrarivony LF, Rabenandrasana MAN, Hariniaina ER, Randrianirina F, Smith AM, Crucitti T. 2024. Antimicrobial susceptibility profile of Neisseria gonorrhoeae from patients attending a medical laboratory, Institut Pasteur de Madagascar between 2014-2020: Phenotypical and genomic characterisation in a subset of Neisseria gonorrhoeae isolates. Sex Transm Infect. 2024 Jan 17;100(1):25-30 (https://doi.org/10.1136/sextrans-2023-055878)

16. Smith AM, Sekwadi P, Erasmus LK, Lee CC, Stroika SG, Ndzabandzaba S, Alex V, Nel J, Njamkepo E, Thomas J, Weill F-X. 2023. Imported cholera cases, South Africa, 2023. Emerg Infect Dis. 2023 Aug;29(8):1687-1690 (https:// 10.3201/eid2908.230750)

17. Carey ME, Dyson ZA, Ingle DJ, Amir A, et al (including Smith AM). Global diversity and antimicrobial resistance of typhoid fever pathogens: Insights from a meta-analysis of 13,000 Salmonella Typhi genomes. eLife 2023 Sep 12;12:e85867 (https://doi.org/10.7554/eLife.85867)

Conferences

Three presentations were delivered at international conferences and one national conference by centre staff members.

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

PROF. VINDANA CHIBABHAI
Centre Head

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

"CHARM functions as a World Health Organization (WHO) AMR collaborating centre and is the national focal point for WHO's global AMR surveillance system"

BACKGROUND

CHARM incorporates two national reference laboratories for antimicrobial resistance (AMR) and mycoses, accredited to ISO 15189: 2012 requirements and houses the pathogenic bacteria and fungi national stock culture collection. It functions as a World Health Organization (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

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 and C Cohen

Collaborators: A Dramowski, C Mackay, R Phayane T Mailula, O Mekgoe, C Kapongo and Dr Maphosa

Through tier one of this project, the Centre conducted a 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 2020-2023 received to be cleaned and analysed. Tier two focused on a detailed characterisation of neonatal infections at six secondary-level institutions (provincial/regional neonatal units). A manuscript accepted and to be published through Lancet Microbe. In a new sub-study, (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 pathogens were analysed for publication.

Healthcare-associated Infection (HAI) Outbreak Detection and Response

NICD investigators: NP Govender, L Shuping, H Ismail, Andani Marumo

Collaborators: S Abrahams, L Mnqokoyi, B Banda, F Khan and A Thomas

The Centre conducted a surveillance system evaluation of a real-time alert system, using a custom-built mobile application, to prospectively detect outbreaks of healthcare-associated bloodstream infections among neonates. An internal report was completed and the publication of an external report is planned for 2024.

Antimicrobial Resistance Surveillance

NICD investigators: O Perovic, NP Govender, L Shuping, H Ismail, M Smith, R Mpembe, Ruth Mogokotleng, S Jallow and Caroline Maluleka

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 *Escherichia coli* invasive infections. Isolated and demographic data collection were finalised in September.
- Community-based surveillance for urinary tract infections (UTI) was completed at Alexandra Community Health Centre in Johannesburg. Surveillance findings were presented to the Ministerial Advisory Committee on AMR and a report was submitted to the National Department of Health (NDoH) National Essential Medicines List (EML) Committee. A manuscript is in preparation for a journal publication in 2024.
- Electronic laboratory surveillance: annual data were compiled on bloodstream infections caused by the ESKAPE bacterial pathogens and more recently *Candida*. Public and private-sector pathology data were made 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 is available at the facility level. These surveillance data were published as part Surveillance for Antimicrobial Resistance and Consumption of Antibiotics in South Africa (2018-2022) report by the National Department of Health in March 2024 (https://knowledgehub.health.gov.za/content/antimicrobial-resistance) (Antimicrobial Resistance | Department of Health Knowledge Hub)

- CHARM, a co-ordinating centre for AMR WHO GLASS reporting assigned by NDoH, and has submitted the required data for 2022 on the WHO site.
- Wastewater-based surveillance for ESKAPE pathogens: a pilot study was initiated for six months 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, C Maluleka

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 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 national outbreak of *Wickerhamomyces anomalus* (previously *Candida pelliculosa*) from a contaminated medical product widely used by healthcare facilities and the public. The investigation led to the South African Health Products Regulatory Authority (SAHPRA) issuing a Class 1 Type A recall of this product. Outbreaks of fungal infections are increasingly reported and investigated by the centre, including a post-cataract surgery fungal infection outbreak in the Western Cape Province and a single case of antifungal-resistant ringworm infection in KwaZulu-Natal Province published in the South African Public Health Bulletin (https://www.phbsa.ac.za/antifungal-resistant-ringworm/).

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 programmeme (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 and 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 and M Manavhela, H Shirinda

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. Supported by a public-private partnership that expands surveillance capacity to low and middle-income countries, the pilot study is being conducted in Ghana, Kenya, Malawi and Uganda. 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 and 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 have been accepted by IJID, https://doi.org/10.1016/j.ijid.2024.107035

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 two 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) through phenotypic description, antifungal susceptibility testing (including n=78 tested against a novel agent, manogepix) and WGS.

Antimicrobial resistance of bacteria in human, animals and environment (One Health Approach) in South Africa

NICD investigators: Ruth Mogokotleng, Olga Perovic and Sabelle Jallow

Collaborators: University of the Witwatersrand

This project aims to highlight the critical need for employing effective genomic surveillance studies for AMR in bacteria. Such a platform will provide detailed data essential for ongoing surveillance efforts in addressing the challenge of antimicrobial resistance with a focus on One Health and to expose the urgent need for global measures addressing the spread of MDR and highly pathogenic variants. AMR genes and resistance mechanisms found may guide the essential medicines list in South Africa and guide the choice of empirical therapy. In addition, the data generated will assist local and national health authorities with health policy planning; IPC practices; and antimicrobial stewardship programmes. The Centre performed phenotypic testing (Species identification and Antimicrobial susceptibility testing) and moleculary testing using polymerase chain reaction (PCR) and whole genome sequencing (WGS). Laboratory testing, data analysis and manuscript writing is underway.

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, and 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 of 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 a 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 initially 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 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)
- PhD, MSc, MTech, MSc (SAFETP), and MMed supervision

Post-graduate students

Seven students were enrolled for post-graduate studies through the centre, specifically one each for MSc Med, two MSc Epi and four PhDs. Three students graduated during the review period, namely one with MPH and two MSc.

RESEARCH OUTPUT

Journal articles

1. Paccoud O, Shuping L, Mashau R, Greene G, Quan V, Meiring S, Govender NP; for GERMS-SA. Impact of prior cryptococcal antigen screening on in-hospital mortality in cryptococcal meningitis or fungaemia among HIV-seropositive individuals in South Africa: a cross-sectional observational study. Clin Microbiol Infect. 2023 Aug;29(8):1063-1069. doi: 10.1016/j.cmi.2023.04.016. Epub 2023 Apr 21. PMID: 37086780.
2. Naicker SD, Shuping L, Zulu TG, Mpembe RS, Mhlanga M, Tsotetsi EM, Maphanga TG, Govender NP; MMed, FC Path SA, for GERMS-SA. Epidemiology and susceptibility of Nakaseomyces (formerly Candida) glabrata bloodstream isolates from hospitalised adults in South Africa. Med Mycol. 2023 Jun 5;61(6): myad057. doi: 10.1093/mmy/myad057. PMID: 37336590.
3. Shuping L, Maphanga TG, Naicker SD, Mpembe R, Ngoma N, Velaphi S, Nakwa F, Wadula J, Jaglal P, Govender NP. High Prevalence of Candida auris Colonization during Protracted Neonatal Unit Outbreak, South Africa. Emerg Infect Dis. 2023 Sep;29(9):1913-1916. doi: 10.3201/eid2909.230393. PMID: 37610276; PMCID: PMC10461653.
4. Kekana D, Naicker SD, Shuping L, Velaphi S, Nakwa FL, Wadula J, Govender NP; for GERMS-SA1. Candida auris Clinical Isolates Associated with Outbreak in Neonatal Unit of Tertiary Academic Hospital, South Africa. Emerg Infect Dis. 2023 Oct;29(10):2044-2053. doi: 10.3201/eid2910.230181. PMID: 37735719; PMCID: PMC10521600.
5. Bolton, L., Bekker, A., Govender, N., van Schalkwyk, C., Whitelaw, A. and Dramowski, A., 2023. Neonatal sepsis: Challenges in data access, harmonisation and analysis to inform empirical antibiotic recommendations in South African neonatal units. *Southern African Journal of Public Health*, pp.42-44
6. Magobo RE, Ismail H, Lowe M, Strasheim W, Mogokotleng R, Perovic O, Kwenda S, Ismail A, Makua M, Bore A, Phayane R, Naidoo H, Dennis T, Ngobese M, Wijnant W, Govender NP; for Baby GERMS-SA1. Outbreak of NDM-1- and OXA-181-Producing *Klebsiella pneumoniae* Bloodstream Infections in a Neonatal Unit, South Africa. Emerg Infect Dis. 2023 Aug;29(8):1531-1539. doi: 10.3201/eid2908.230484. PMID: 37486166; PMCID: PMC10370860.
7. Sati H, Alastruey-Izquierdo A, Perfect J, Govender NP, Harrison TS, Chiller T, Sorrell TC, Bongomin F, Oladele R, Chakrabarti A, Wahyuningsih R, Colombo AL, Rodriguez-Tudela JL, Beyrer C, Ford N. HIV and fungal priority pathogens. Lancet HIV. 2023 Nov;10(11):e750-e754. doi: 10.1016/S2352-3018(23)00174-1. Epub 2023 Oct 9. PMID: 37827187; PMCID: PMC7615271.

8. Bongomin F, Ekeng BE, Kwizera R, Salmanton-García J, Kibone W, van Rhijn N, Govender NP, Meya DB, Osaigbovo II, Hamer DH, Oladele R, Denning DW. Fungal diseases in Africa: Closing the gaps in diagnosis and treatment through implementation research and advocacy. J Mycol Med. 2023 Nov;33(4):101438. doi: 10.1016/j.mycmed.2023.101438. Epub 2023 Oct 19. PMID: 38358796.

9. Mabena FC, Olwagen CP, Phosa M, Ngwenya IK, Van der Merwe L, Khan A, Mwamba TM, Mpembe R, Magobo RE, Govender NP, Velaphi SC, Madhi SA. Bacterial and Candida Colonization of Neonates in a Regional Hospital in South Africa. Pediatr Infect Dis J. 2024 Mar 1;43(3):263-270. doi: 10.1097/INF.0000000000004177. Epub 2023 Nov 20. PMID: 38381956.

10. Nzimande SP, Govender NP, Maphanga TG. *In vitro* manogepix susceptibility testing of South African *Emergomyces africanus, Emergomyces pasteurianus*, and *Blastomyces emzantsi* clinical isolates. Antimicrob Agents Chemother. 2023 Dec 14;67(12):e0110423. doi: 10.1128/aac.01104-23. Epub 2023 Nov 16. PMID: 37971237; PMCID: PMC10720492.

11. Perovic O, Singh-Moodley A, Lowe M. In Vitro Activity of Ceftolozane-Tazobactam against *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* Obtained from Blood Cultures from Sentinel Public Hospitals in South Africa. Antibiotics (Basel). 2023 Feb 453:(3)12;24. doi: 10.3390/antibiotics12030453. PMID: 36978322; PMCID: PMC10044232.

12. Osaigbovo II, Govender NP, Jordan AM, Bongomin F, Meya DB, Kanyua A, Mashedi OM, Koffi D, Loyse A, Sturny-Leclère A, Gangneux JP, Denning DW, Chiller T, Cornely OA, Oladele RO. The Nairobi Declaration 2023: A commitment to address deadly yet neglected fungal diseases in Africa. Med Mycol. 2024 Jan 9;62(1):myad141. doi: 10.1093/mmy/myad141. PMID: 38154488.

13. Mayet H, Reddy DL, Alvarez TB, Atiya Y, Govender NP, Birkhead M, Maphanga T, Pather S. Case Report of Nasal Rhinosporidiosis in South Africa. Emerg Infect Dis. 2024 Apr;30(4):766-769. doi: 10.3201/eid3004.240018. PMID: 38526207; PMCID: PMC10977841.

14. Höft MA, Duvenage L, Salie S, Keeton R, Botha A, Schwartz IS, Govender NP, Brown GD, Hoving JC. The pathogenesis of experimental Emergomycosis in mice. PLoS Negl Trop Dis. 2024 Jan 10;18(1):e0011850. doi: 10.1371/journal.pntd.0011850. PMID: 38198478; PMCID: PMC10805315.

15. Lass-Flörl C, Kanj SS, Govender NP, Thompson GR 3rd, Ostrosky-Zeichner L, Govrins MA. Invasive candidiasis. Nat Rev Dis Primers. 2024 Mar 21;10(1):20. doi: 10.1038/s41572-024-00503-3. PMID: 38514673.

16. Getnet Amsalu , Christine Tedijanto Wen , Olga Perovic , Addisalem Gebru , Bezawit M. Hunegnaw , Fisseha Tadesse , Marshagne Smith, Addisalem Fikre , Delayehu Bekele , Lisanu Taddesse , Grace Chan , Carriage of antimicrobial resistant Enterobacterales among pregnant women and newborns in Amhara, Ethiopia, International Journal of Infectious Diseases (2024), doi: https://doi.org/10.1016/j.ijid.2024.107035

Technical reports and guidelines:

- A case of antifungal-resistant ringworm infection in KwaZulu-Natal Province was published in the South African Public Health Bulletin (https://www.phbsa.ac.za/antifungal-resistant-ringworm/).
- CHARM participated in the publication of a media article regarding sepsis: https://theconversation.com/what-is-sepsis-how-to-spot-manage-and-prevent-it-203802
- Published a review article for clinicians regarding Echinocandins in the treatment of invasive candidiasis (including Candida auris): Infectious Diseases Update Volume 12 No 3 2023

Conferences

CHARM members contributed to six international, and two national conferences during the year under review.

CENTRE FOR HIV AND STIs (CHIVSTI)

PROF. ADRIAN PUREN
Centre Head

CENTRE FOR HIV AND STIs (CHIVSTI)

"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."

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 Programmeme 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.

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

- Surveillance of disease burden and antimicrobial resistance;
- Measurement of endpoint infections and detection;
- Broadly neutralising antibodies as part of prophylactic HIV vaccine and antibody-mediated protection clinical trials;
- Exploring an HIV "cure" strategy; and
- Development and implementation of reference diagnostics and implementation science.
- CHIVSTI consists of the following four sections:

- HIV Virology; Cell Biology; HIV Molecular and Serology Sexually Transmitted Infections

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

SURVEILLANCE

VIROLOGY

The HIV & SARS-CoV-2 Virology Section in the Centre has made significant contributions in elucidating the immune responses in individuals with hybrid SARS-CoV-2 immunity and people living with HIV, which resulted in three publications. The Centre has contributed to analysing passive immunisation HIV studies, including pharmacokinetic and viral escape analyses in high-risk adult and paediatric cohorts in South Africa. These studies resulted in contributions to seven publications.

EPIDEMIOLOGY

ANC SURVEY

The Antenatal HIV survey is a biennial survey for the monitoring trends in HIV prevalence, incidence, coverage of HIV testing, viral load suppression and the syphilis cascade among pregnant women attending antenatal care at 1,589 public sector primary care facilities (sentinel sites). The survey found that HIV prevalence among pregnant women had declined by 2.5% points since the previous survey, representing the first decline in more than a decade. HIV testing and ART coverage among pregnant women was nearly universal. Still, there was a decline in the proportion of women who started ART before pregnancy compared to the previous survey. There was also sub-optimal viral suppression (<50 copies/ml) at 74.1%. There was high PrEP eligibility but very low coverage among the eligible (6.5%). There was also an increase in the prevalence of syphilis among pregnant women. Since the report's publication, the NDoH has been working with partners to scale up PrEP during pregnancy. PEPFAR/CDC has funded a follow-up qualitative study to determine the barriers and facilitators of PrEP use among pregnant women.

CONGENITAL SYPHILIS SURVEILLANCE

Congenital syphilis is a category two notifiable medical condition. The period under review saw the appointment of a new surveillance officer (shared with two other NICD centres – CED and CVI) to support follow-up of cases that did not have case investigation forms submitted at reporting; the development and user testing of a combined case notification form and case investigation form; the analysis and submission for publication the case investigation form data describing gaps in the prevention of mother-to-child-transmission of syphilis; as well as a presentation of data from this enhanced case surveillance at the Conference on Retroviruses and Opportunistic Infections. The analysis of the case investigation form data showed there were gaps at all steps of the maternal syphilis treatment cascade – 16% of mothers who gave birth to infants with CS were unbooked, 13% of mothers were not tested during pregnancy, 28% were tested,but the timing of testing was suboptimal, and 56% did not receive adequate treatment for syphilis. The NDoH rolled out rapid dual HIV/syphilis testing to improve the frequency of syphilis testing coverage of testing and reduce the time to treatment.

CASE-BASED SURVEILLANCE

Firstly, the case surveillance (CS) project aims to develop and implement a data linkage system for PLHIV, including a matching algorithm that helps link an individual's data and prevents data duplication, using the existing NICD Surveillance Data Warehouse (SDW) data source (two years of retrospective data). Secondly, the CS aims to develop and implement an HIV case surveillance system to prospectively monitor

the HIV care continuum of newly diagnosed and existing PLHIV. During the current financial period, the focus has been on developing a tablet version of the surveillance system; conducting beta-testing at three facilities located in KwaZulu-Natal (one in eThekwini district and two in uMgungundlovu district); and implementing technical updates identified during the beta-testing period. For the beta-testing phase, 10 healthcare workers used CS to monitor patients. Overall, CS was well received and will be crucial in improving patient management for PLHIV. The next phase for the CS will be the pilot phase, which will be implemented in more facilities in eThekwini and uMgungundlovu districts.

RECENCY OF HIV INFECTION SURVEILLANCE

The protocol for the recency of the HIV infection surveillance project has been amended. The goal of the recency of HIV infection surveillance project has been amended to utilise a laboratory-based recency assay to identify recent HIV infections in South Africa. The amended aims of the project are to: assess the acceptability and feasibility of integrating LAg Avidity EIA into routine HTS in public sector health facilities; estimate the proportion of recent infections among newly diagnosed PLHIV using the RITA; and to describe among patients presenting for HIV testing, demographic and health service related factors associated with previous HIV testing/diagnosis history, and recent and long-term testing on the RITA. The amended protocol has the following changes: use of a centralised laboratory testing approach instead of point-of-care testing; use of LAg Avidity EIA testing instead of the rapid test for recent infection; implementation only in KwaZulu-Natal (eThekwini and uMgungudlovu districts); and use of LabTrak to determine CD4 count or viral testing history.

HIV SERO-MOLECULAR

HSRC SABSSM V1 Study (The Sixth South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey, 2021 (SABSSM V1)

The HSRC conducts a South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey (SABSSM) once every three years for this purpose. In 2021, the HSRC conducted their sixth survey (SABSSM V1). The survey ended in April 2023. SABSSM 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 sample size was 50,348 over the nine Provinces in South Africa, and data collection was expected to stop at the end of April 2023. Dried Blood Spot (DBS) samples were collected for testing. Laboratory testing was completed in July 2023. A total of 51,170 specimens were received. 50,213 Specimens were tested on the HIV Screen EIA test, 8,658 specimens were tested on the confirmatory HIV EIA test, and 8,219 specimens were tested for Viral load.

A total of 7, 144 specimens were tested for HIV recency using the Maxim Limiting Antigen Avidity assay. On 27 November 2023, the HSRC launched the key findings of the 6th National Survey. The overall national estimate for HIV prevalence for all ages in 2022 was 12.7% (95% CI: 12.0-13.4), translating to 7.8 million (95% CI: 7.2–8.4). The HIV prevalence was 1.3% lower than the estimate found in 2017, which was 14.0% (95%CI:13.2-14.8), translating to 7.9 million (95% CI: 7.2–8.6). This represented 107,000 fewer people living with HIV in 2022. Promising decreases in HIV prevalence, coupled with high community VLS (81%), points to the impact of South Africa's National HIV Response. Progress has been made toward South Africa's 95-95-95 adult treatment targets: 90% of adults knew their status, 91% of those diagnosed were on ART, and 94% of those on ART were virally suppressed.

Surveillance of HIV Drug Resistance in Adult Patients through Routine ART Programmeme Monitoring in South Africa, 2023

A surveillance study conducted in South Africa aimed to assess the prevalence of HIV drug resistance (HIVDR) among adult patients receiving antiretroviral therapy (ART). The study utilised remnant plasma specimens and viral load data from routine monitoring to estimate the extent of HIVDR in 2023. 19,398 Remnant specimens were collected, and 791 samples were selected for further testing. Genotyping procedures successfully detected resistance to at least one drug class in 53.7% of cases, with non-nucleoside reverse transcriptase inhibitors (NNRTIs) being the most prevalent form of resistance (50.7%). Resistance to nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs) were observed in 25.2%, 2.2%, and 2.3% of specimens, respectively.

Drug level testing (DLT) was conducted for all 791 specimens, with 36.8% of cases showing detectable ART levels. Detectable drug levels are representative of ART exposure. Specimens with ART exposure exhibited higher rates of resistance compared to those without. For specimens with detectable INSTI levels, 10.5% showed INSTI resistance, while only 0.8% of specimens without detectable drug levels displayed this resistance. Similarly, among specimens with detectable PI levels, 32.6% exhibited PI resistance, compared to only 0.7% in specimens without detectable drug levels. Among specimens with detectable NNRTI levels, 84.0% presented with NNRTI resistance, with a prevalence of 45.0% in specimens without detectable drug levels.

The study highlights the importance of ongoing monitoring of HIVDR to guide treatment guidelines and ensure the effectiveness of ART programmes. Efforts to optimise treatment adherence, promote early diagnosis, and provide access to effective antiretroviral drugs are crucial in minimising the development and transmission of drug-resistant HIV strains. The findings contribute to understanding HIVDR patterns in South Africa and can inform strategies to improve treatment outcomes for HIV-positive individuals.

THE SIXTH SOUTH AFRICAN NATIONAL HIV PREVALENCE, INCIDENCE, BEHAVIOUR, AND COMMUNICATION SURVEY (SABSSMVI)

The Sixth South African National HIV Prevalence, Incidence, Behaviour, and Communication Survey continued in 2023 and aimed to address concerns related to the development of drug-resistant HIV in South Africa. This survey also focused on monitoring the emergence of drug resistance to Dolutegravir, an integrase inhibitor that was integrated into the treatment guidelines in 2020.

Among the 51,170 samples collected during the study, 1,172 had unsuppressed viral loads, and 1,168 were selected for further drug resistance testing. The preliminary data from the survey revealed that 47% of patients with unsuppressed viral loads carried drug-resistance mutations. Specifically, 1% exhibited resistance to protease inhibitors (PI), 10% had resistance to Nucleoside Reverse Transcriptase inhibitors (NRTI), 34% had resistance to Non-nucleoside Reverse Transcriptase inhibitors (NNRTI), and 0.8% had resistance to integrase inhibitors.

In summary, the data obtained from this survey provides essential information on the prevalence of drug resistance mutations among individuals with unsuppressed viral loads in South Africa. This knowledge is necessary for guiding HIV treatment practices, improving patient outcomes, and developing effective public health interventions to combat drug-resistant HIV in the country.

HIVDR SURVEY AMONG ALL PEOPLE RECEIVING ART (ADULTS, ADOLESCENTS AND CHILDREN) (ACQUIRED HIVDR ADR)

Preliminary Report on HIV Drug Resistance Surveillance in Eritrea

According to a 2016 report, HIV prevalence in Eritrea has significantly decreased from 2.14% in 2003 to 0.36% in 2019. Antiretroviral therapy (ART) has been introduced, with approximately 95% of ART patients receiving first-line treatment consisting of nucleoside reverse transcriptase inhibitors (NRTIs) and non-NNRTIs, particularly tenofovir or dolutegravir-based regimens. The report indicates that among patients on ART, the prevalence of resistance to NNRTIs was 7.1%. Acquired drug resistance (ADR) was observed among people living with HIV (PLHIV), with a prevalence of 30.1% to any antiretroviral (ARV), 30.1% to NNRTIs, and 18.5% to NRTIs.

A cross-sectional survey was conducted to assess the prevalence of HIV drug resistance (HIVDR) in Eritrea. A total of 863 samples were received for analysis. Viral load suppression was observed in 92.4% of the samples analysed, and 66 (7.6%) samples had a viral load greater than 1,000 copies/ml, referred for HIV genotyping. Specifically, the polymerase region was amplified in 46 samples for protease (PR) and reverse transcriptase (RT) analysis and 59 samples for integrase (IN) analysis. Among the 46 sequences analysed for specific drug resistance mutations (SDRMs), 63.0% had at least one SDRM. None of the 46 sequences analysed for protease showed protease inhibitor (PI) SDRMs.

Among the 46 reverse transcriptase (RT) sequences, 32.6% exhibited NRTI SDRMs, and 63.0% had NNRTI SDRMs. Additionally, 32.6% of RT sequences showed resistance to both NRTIs and NNRTIs. None of the sequences analysed exhibited SDRMs for all three drug classes (NRTI, NNRTI, and PI). Of the 59 integrase (IN) sequences analysed, 3.4% contained integrase strand transfer inhibitor (INSTI) SDRMs.

It is important to note that these findings are based on a population sample and require further analysis to establish their representativeness. The final report, which will incorporate a more extensive analysis, is expected to offer more comprehensive and conclusive results regarding the prevalence and patterns of HIV drug resistance in Eritrea.

PAEDIATRIC SURVEILLANCE

The Centre provides aggregated 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 viral load done and suppression rates), and uptake of maternal HIV VL electronic gatekeeping codes (including antenatal, delivery and postnatal suppression rates). Reporting is provided at National, Provincial, District and Facility levels to the National and Provincial Departments of Health and other stakeholders, including South African National AIDS Council (SANAC), as part of reporting for the Global Alliance to End AIDS in Children.

These reports highlight programmematic achievements and trends and support the HIV treatment programmeme by highlighting areas that require targeted interventions and assisting with the effective monitoring thereof.

SEXUALLY TRANSMITTED INFECTIONS (STI)

In 2023-24, the aetiological surveillance continued with the recruitment of patients in the three primary healthcare facilities in Gauteng, KwaZulu-Natal and the Western Cape. The surveillance is used to validate the current STI syndromic management guidelines. *Neisseria gonorrhoeae* (80%) remained the most typical cause of male urethritis discharge syndrome, whilst bacterial vaginosis (59%) and vulvovaginal candidiasis (29%) are more prevalent in vaginal discharge syndrome. The relative prevalence of *Treponema pallidum* among patients presenting with genital ulcers was 29%. The section continues

to monitor antimicrobial susceptibility patterns to detect the emergence of extensively drug-resistant *Neisseria gonorrhoeae*. All isolates were susceptible to the cephalosporins cefixime and ceftriaxone. We have detected an increase in azithromycin-resistant isolates. As a WHO Enhanced Gonococcal Surveillance Programmeme (eGASP) site, the isolates' demographic, behavioural and clinical data collected in 2023 have been uploaded on the GLASS EGASP platform. Critical alerts have been reported in the country and within the EGASP network for action.

STI surveillance among a priority population (MSM cohort) at a sentinel Men's Health Centre clinic in Melville was initiated in 2023 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. Pharyngeal *Neisseria gonorrhoeae* infection was detected in 1.5% of participants with a 17.6% syphilis seropositivity rate.

OUTBREAKS

VIROLOGY

The Centre continued to play a pivotal role in assessing viral escape and humoral immune responses in SARS-CoV-2 infected individuals and vaccinees and defining correlates of protection, which have global implications for developing second-generation vaccines.

POLICY CONTRIBUTIONS

VIROLOGY

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

EPIDEMIOLOGY

The Centre took part in developing and introducing dual HIV/syphilis testing in the country, including training materials and guidelines. This policy shift was informed by the rising congenital syphilis cases documented by the Centre through the enhanced Congenital Syphilis surveillance and the increasing maternal syphilis prevalence as noted by the 2019 and 2022 ANC surveys.

PAEDIATRIC SURVEILLANCE

Guideline for Vertical Transmission Prevention of Communicable Infections 2023 (contributing member of Vertical Transmission Prevention Technical Working Group).

Global Alliance to End AIDS in Children by 2030 – The South African Country Plan (contributing member of Global Alliance Technical Working Group).

SEXUALLY TRANSMITTED INFECTIONS (STI)

CHIVSTI continued to make contributions to the National Department of Health STI Technical Working Group and provides support for the introduction of dual HIV/ Syphilis rapid diagnostic tests at antenatal care clinics. We also participated in the GARDP-Zoliflodacin Meeting in July 2023 to discuss the introduction of Zoliflodacin in low- and middle-income countries.

DIAGNOSTIC SERVICES

NATIONAL REFERENCE LABORATORY FUNCTION:

POST-MARKET SURVEILLANCE

Post-market surveillance (PMS) of HIV Rapid Test kits is testing conducted on test kits selected as an outcome of the NDoH tender. Ensuring the rapid test devices perform according to the chosen criteria is critical. The PMS programmeme is crucial to ensuring the quality of HIV rapid testing 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. A well-characterised panel of 122 specimens is tested when each batch is tested. On completion of the batch testing, the NICD generates a report on the batch's performance, which is submitted to the supplier and NDoH. The NICD laboratory has tested 47 new batches before final production, and 36 of the same batches post their production for distribution, totalling 142 batches in the current financial year.

HIV VACCINES TRIALS ENDPOINT TESTING

We currently participate in the following trials: HVTN 305, 118, 135, 139, 140, 605 and 705. HIV diagnostic endpoint testing has drastically reduced since December 2022. Four hundred twenty-seven samples were received in this reporting period compared to 788 specimens in 2022-2023. In the 2021-2022 reporting period, 6,547 specimens were received for endpoint testing. The work volume has decreased considerably.

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 on account 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 diagnostics algorithms are evaluated to assist diagnostic accuracy in the field.

SEXUALLY TRANSMITTED INFECTIONS (STI)

Specialised reference testing (in-house and commercial PCR assays) for non-resolving STI syndromes, child abuse cases and complicated STI cases.

- Verification of *Neisseria gonorrhoeae* culture identification and antimicrobial susceptibility testing.
- *Mycoplasma genitalium* macrolide and fluoroquinolone resistance testing.
- Herpes simplex virus type 2 genotypic acyclovir resistance testing.
- WHO Clinic-based evaluations of STI POCTs

The STI Section participated in a WHO multi-country validation study of the performance of molecular-based point-of-care (POC) tests (GeneXpert platform) for selected STIs in a variety of primary healthcare settings (PHCs). The study focused on screening 'women at risk' for gonorrhoea, chlamydia and trichomonas in four countries – South Africa, Guatemala, Morocco and Australia. In South Africa, on-site POC testing was performed at Khayelitsha Site C Youth Clinic near Cape Town. In contrast, reference STI NAAT testing was conducted at NICD on the Panther instrument (Aptima-Combo and Aptima TV assays). The validation study results (publications listed below under "Research outputs") showed that these POC tests were clinically acceptable for diagnosing these STIs by non-laboratory trained personnel at PHCs.

RESEARCH ACTIVITIES

VIROLOGY

Neutralisation profiles of HIV-1 viruses from the VRC01 Antibody Mediated Prevention (AMP) trials

NICD Investigators: Mkhize NN, Kaldine H, van Dorsten RT, Lambson B, Modise T, Kgagudi P, Mapengo RE, Moore PL, Morris L

Collaborators: Yssel AEJ, Woodward AS, Davis W, Beaume N, Matten D, York T, Westfalls DH, Giorgi EE, Korber B, Anthony C, Bekker V, Domin E, Eaton A, Deng W, DeCamp A, Huang Y, Gilbert PB, Gwashu-Nyangiwe A, Thebus R, Ndabambi N, Mielke D, Mgodi N, Karuna S, Edupuganti S, Seaman MS, Corey L, Cohen MS, Hural J, McElrath MJ, Mullins JI, Montefiori D, Williamson C

HIV-1 viruses from the Antibody Mediated Prevention (AMP) trials, obtained in 2016-2020, represent our most recent panel of transmitted viruses in the population. Reference virus strains currently used to evaluate broadly neutralising antibodies (bnAb) for passive immune trials and assess the quality of vaccine-induced antibody responses were collected between 1998 and 2010. As HIV-1 evolves, virus panels may need to be updated occasionally. Sequences were obtained from participants infected with HIV-1 from both the African (HVTN 703/HPTN081) and the Americas/European (HVTN 704/HPTN085) AMP trials. These viruses were then tested in a neutralisation assay with eight bnAbs under clinical development. Comparing the neutralisation coverage with older viruses, we found that recent viruses have become more resistant to VRC07-523LS and CAP256.25 antibodies. Predictive modelling identified triple bnAb combinations that would effectively neutralise HIV-1 strains from different geographical regions. Reference panels that include recently transmitted HIV-1 strains provide essential information that can be used to design bnAb combinations to consider for prevention studies.

Despite delayed kinetics, people living with HIV achieve equivalent antibody function after SARS-CoV-2 infection or vaccination

NICD Investigators: Motsoeneng BM, Manamela NP, Kaldine H, Kgagudi P, Hermanus T, Ayres F, Makhado Z, Moyo-Gwete T, Moore PL, Richardson SI

Collaborators: van der Mescht MA, Abdullah F, Boswell MT, Ueckermann V, Rossouw TM, Madhi SA

The kinetics of Fc-mediated functions following SARS-CoV-2 infection or vaccination in people living with HIV (PLWH) are not known. We compared SARS-CoV-2 spike-specific Fc functions, binding, and neutralisation in PLWH and people without HIV (PWOH) during acute infection (without prior vaccination) with either the D614G or Beta variants of SARS-CoV-2 or vaccination with ChAdOx1 nCoV-19. Antiretroviral treatment (ART)-naïve PLWH had significantly lower levels of IgG binding, neutralisation, and antibody-dependent cellular phagocytosis (ADCP) compared with PLWH on ART. The magnitude of antibody-dependent cellular cytotoxicity (ADCC), complement deposition (ADCD), and cellular trogocytosis (ADCT) was differentially triggered by D614G and Beta. The kinetics of spike IgG-binding antibodies, ADCC, and ADCD were similar, irrespective of the infecting variant between PWOH and PLWH. However, compared with PWOH, PLWH infected with D614G had delayed neutralisation and ADCP.

Furthermore, Beta infection resulted in delayed ADCT, regardless of HIV status. Despite these delays, we observed improved co-ordination between binding and neutralising responses and Fc functions in PLWH. In contrast to D614G infection, binding responses in PLWH following ChAdOx-1 nCoV-19 vaccination were delayed. At the same time, neutralisation and ADCP had similar timing of onset but lower magnitude, and ADCC was significantly higher than in PWOH. Despite delayed and differential kinetics, PLWH on ART develop comparable responses to PWOH, supporting the prioritisation of ART rollout and SARS-CoV-2 vaccination in PLWH.

Anticipating viral escape – resistance to active and passive immunisation

NICD Investigators: Moore PL

Collaborators: Williamson C, Lynch RM

Active and passive immunisation strategies are challenged by the extraordinary diversity of HIV and the need for high titers of neutralising antibodies to

confer protective immunity. This review summarises recent studies and the barriers these interventions will need to overcome to prevent viral resistance.

Recent findings: Studies from the antibody-mediated prevention trial identified a measure of protective titers, finding that higher titers than anticipated will be needed to prevent infection. This benchmark has advanced our ability to predict combinations of broadly neutralising antibodies (bNAbs) that will provide optimal coverage. To limit escape, these combinations should ensure that at least two antibodies bind most viruses. The characterisation of currently circulating viruses has revealed increased resistance to some bNAbs, highlighting the need for continued surveillance, especially in under-studied populations and subtypes.

Active vaccination will face similar challenges in combating diversity, although, despite successes in germline targeting, this approach is not yet able to elicit bNAbs.

Summary: Cumulatively, these studies highlight the need to target multiple antibody epitopes for maximum coverage and restrict escape pathways. Successful immunisation strategies should anticipate viral escape and devise strategies to counteract this.

Homologous Ad26.COV2.S vaccination results in reduced boosting of humoral responses in hybrid immunity but elicits antibodies of similar magnitude regardless of prior infection

NICD Investigators: Moyo-Gwete T, Richardson SI, Hermanus T, Spencer H, Manamela NP, Ayres F, Makhado Z, Motlou T, Moore PL

Collaborators: Keeton R, Tincho MB, Benede N, Ngomti A, Baguma R, Chauke MV, Mennen M, Adriaanse M, Skelem S, Gogo A, Garrett N, Bekker L, Gray G, Ntusi NAB, Riou C, Burgers WA

The impact of previous SARS-CoV-2 infection on the durability of Ad26.COV2.S vaccine-elicited responses, and the effect of homologous boosting have not been well explored. We followed a cohort of healthcare workers for six months after receiving the Ad26.COV2.S vaccine and a further one month after they received an Ad26.COV2.S booster dose. We assessed longitudinal spike-specific antibody and T cell responses in individuals who had never had SARS-CoV-2 infection, compared to those who were infected with either the D614G or Beta variants before vaccination. Antibody and T cell responses elicited by the primary dose were durable against several variants of concern over the six month follow-up period, regardless of infection history. However, six months after the first vaccination, antibody binding, neutralisation, and ADCC were as much as 33-fold higher in individuals with hybrid immunity than those without no prior infection. Antibody cross-reactivity profiles of the previously infected groups were similar at six months, unlike at earlier time points, suggesting that the effect of immune imprinting diminishes by six months – notably, an Ad26.COV2.S booster dose increased the magnitude of the antibody response in individuals with no prior infection to similar levels as those with previous infection. The magnitude of spike T cell responses and proportion of T cell responders remained stable after homologous boosting, concurrent with a significant increase in long-lived early differentiated CD4 memory T cells.

Thus, these data highlight that multiple antigen exposures, whether through infection and vaccination or vaccination alone, result in similar boosts after Ad26.COV2.S vaccination.

CELL BIOLOGY

Early antiretroviral treated children and adolescents with perinatally-acquired HIV-1 infection: understanding viral control on treatment, reservoir size, and effects on the microbiome

NICD investigators: M Paximadis, S Shalekoff, S Loubser, M Tshabalala, S Mncube, S Reddy, C T Tiemessen

Collaborators: L Kuhn (Columbia University, USA), R Strehlau R (Rahima Moosa Mother and Child Hospital, Johannesburg), GM Aldrovandi (University of California, USA), AC Ka'e and J Fokam (Chantal BIYA International Reference Centre for Research on HIV/AIDS Prevention and Management (CIRCB), Yaounde, Cameroon).

Early ART initiation in infants with perinatally-acquired HIV-1 associates with better control of the virus (as measured by plasma viral loads), smaller reservoir size (as measured by cellular HIV DNA), less virus diversity, and better immunological response. The pooled prevalence of archived-drug resistance mutations (ADRMs) is generally high in paediatric populations, and timing and duration of suppression with ART are key determinants of HIV-1 reservoir size. Viral suppression and non-suppression on ART tracks with levels of various cytokines indicative of ongoing immunological activity. Interestingly, a study evaluating the oral microbiome of ART-treated children with HIV-1 at median age 11 years - showed less microbial diversity and relative abundances of taxa in children with HIV-1 compared to uninfected controls, but no association of earlier ART initiation with microbiota profile in the context of HIV-1 infection.

Proximal factors, including current ART regimen, were associated with contemporaneous profile of oral microbiota; this may have masked associations with factors such as age at ART initiation.

EPIDEMIOLOGY

Implementation of the research study "Evaluation of the feasibility and acceptability of Dual HIV/syphilis testing and PrEP referral among males attending VMMC services

NICD investigator(s): Tendesayi Kufa-Chakezha, Beverley Singh, Ewalde Cutler, Venessa Maseko, Zinhle Brukwe, Adrian Puren

Collaborators: Ocean Tobaiwa (CHAI), Philip Dorrell (CHAI), Erushka Pillay (CHAI) Yogan Pillay (CHAI), Khumbulani Moyo (Right to Care), Lindokuhle Zondi (Right to Care), Sean Patrick (University of Pretoria)

Data collection for this project was completed in 2021 but analysis and dissemination were completed during the year. The analysis found that rapid dual HIV/syphilis testing was acceptable to men attending VMMC services and the yield was high at 1.5%. While performance of the syphilis component, it was improved for recent syphilis infection.

Individual patient meta-analysis on etiology of genital ulcer, vaginal discharge and urethral discharge syndromes in Sub-Saharan Africa

NICD investigator(s): Tendesayi Kufa, Thabitha Mathega,

Collaborators: Julia Michalow (Imperial College), Magdalene K Walters (Imperial College), Olanrewaju Edun (Imperial College), Max Wybrant (Imperial College), Bethan Davies (Imperial College), Sungai T Chabata (CeSHHAR), Frances M Cowan (CeSHHAR), Anne Cori (Imperial College), Marie-Claude Boily (Imperial College), Jeffrey W Imai-Eaton (Imperial College)

Data collation and analysis were started and completed during the year. The CHIVSTI contributed individual patient data and the meta-analysis found that contributions of gonorrhoea and chlamydia towards male and female discharge have remained the same over time and are similar across many countries in Sub- Saharan Africa.

SEXUALLY TRANSMITTED INFECTIONS (STI)

GARDP ZOLIFLODACIN PHASE 3 CLINICAL TRIAL

The Centre was the regional laboratory for the Phase 3 multi-centre, randomised, open-label, non-inferiority trial to evaluate the efficacy and safety of a single, oral dose of zoliflodacin compared to a combination of a

single intramuscular dose of ceftriaxone and a single oral dose of azithromycin in the treatment of patients with uncomplicated gonorrhoea. Recruitment started in April 2021 and was completed in February 2023, with South Africa having a total of 452 patients, which is one of the highest recruiting sites. The preliminary results shared in November found that oral zoliflodacin demonstrated statistical non-inferiority of microbiological cure at the urogenital site when compared to the current global standard of care regimen. Zoliflodacin was found to be generally well tolerated and no serious adverse events or deaths were recorded in the trial.

TEACHING AND TRAINING

VIROLOGY

Hosted PhD students, Rokhaya Faye and Adji Astou from GIISER-Senegal and Institute Pasteur Dakar, Senegal from 17 April to 12 May 2023 who were trained on the Rapid Amplification, transfection and production of immunoglobulin (RATP-Ig) monoclonal antibody isolation workflow.

Rufaro Chivaura from the Mutala Trust - Infectious Disease Research Laboratory in Harare, Zimbabwe visited the lab from 2-19 May 2023 to train on the HIV Neutralization Assay.

Prof. Penny Moore and Dr Nono Mkhize gave lectures to Wits MSc Vaccinology students on HIV & COVID-19 on 19 September 2023.

Prof. Penny Moore gave a lecture as part of the NICD three-week Registrar rotation on 16 October 2023, entitled: "HIV Vaccines: where are we?".

Prof .Penny Moore was invited to give a virtual talk on HIV infection to students during Karolinksa Institute's Viral Diseases Course together with Benedict Chambers (Centre for Infectious Medicine, MedH), on 18 October, entitled: "HIV Vaccine Development - state of the field".

Prof. Penny Moore gave lectures to Graduate Entry Medical Programmeme (GEMP) students on Active vs Passive Immunity and Immunological challenges of HIV, and Dr Simone Richardson gave a lecture on Innate Immunity, on 12 and 15 February 2024.

HIV Sero-Molecular:

- Trained eight intern scientists in June 2023 for two weeks
- One intern Scientist under contract for two years, due to submit a portfolio to HPCSA in September 2024

Paediatric Surveillance:

- Post-graduate training and lectures on infant diagnosis and paediatric HIV surveillance for registrars
- Training for the Department of Health and District partner staff on the use of HIV surveillance data for clinical action

SEXUALLY TRANSMITTED INFECTIONS (STI)

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 the training of medical scientists during their internship at the NICD.

The Centre participated in the Africa CDC Funded Antimicrobial Resistance training organised by CHARM for the Ethiopian Public Health Institute's delegates on 22 May 2023.

Dr Etienne Müller attended eGASP whole genome sequencing (WGS) training in Örebro, Sweden from 9-17 March 2024 to prepare for future decentralisation of WGS activities from Sweden to South Africa (NICD).

PROFESSIONAL DEVELOPMENT

- 41 (2 MMed, 1 MPA, 8 PhD, 19 MSc, 11 BSc [Hons])
- 18 (5 PhD, 7 MSc, 6 BSc [Hons])

RESEARCH OUTPUT

Journal Articles

1. Benede N, Tincho MB, Walters A, Subbiah V, Ngomti A, Baguma R, Butters C, Hahnle L, Mennen M, Skelem S, Adriaanse M, Facey-Thomas H, Scott C, Day J, Spracklen TF, van Graan S, Balla SR, Moyo-Gwete T, Moore PL, MacGinty R, Botha M, Workman L, Johnson M, Goldblatt D, Zar HJ, Ntusi NAB, Zuhlke L, Webb K, Riou C, Burgers WA, Keeton RS. (2024) Distinct T cell polyfunctional profile in SARS-CoV-2 seronegative children associated with endemic human coronavirus cross-reactivity. iScience. 27:1.

2. Butters C, Benede SB, Moyo-Gwete T, Richardson SI, Rohlwink U, Shey M, Ayres F, Manamela NP, Makhado Z, Balla SR, Madzivhandila M, Ngomti A, Baguma R, Facey-Thomas H, Abrahams D, Spracklen TF, Faleye A, Day J, van der Ross H, Riou C, Burgers WA, Scott C, Zuhlke L, Moore PL, Keeton RS, Webb K. (2024) Comparing the immune abnormalities in MIS-C to healthy children and those with inflammatory disease reveals distinct inflammatory cytokine production and a monofunctional T cell response. Clinical Immunology. 259, 109877.

3. Da Costa Dias B, Sekgele W, Nhlapo D, Mahlangu MP, Venter JME, Maseko DV, Müller EE, Greeves M, Botha P, Radebe F, Kufa T, Kularatne RS. Extragenital Sexually Transmitted Infections Among High-Risk Men Who Have Sex With Men in Johannesburg, South Africa. Sex Transm Dis. 2024 Apr 1;51(4):245-250. doi: 10.1097/OLQ.0000000000001927. Epub 2024 10 January. PMID: 38534082.

4. Frank D, Kufa T, Dorrell P, Kularatne R, Maithufi R, Chidarikire T, Pillay Y, Mokgatle M. Evaluation of the national clinical sentinel surveillance system for sexually transmitted infections in South Africa: Analysis of provincial and district-level data. South African Medical Journal. 2023 Jul 1;113(7):1275-82.

5. Haeri Mazanderani AF, Murray TY, Johnson LF, Ntloana M, Silere-Maqetseba T, Guo S, Sherman GG. Eliminating Vertical Transmission of HIV in South Africa: Establishing a Baseline for the Global Alliance to End AIDS in Children. Diagnostics. 2023;13:2563. https://doi.org/10.3390/diagnostics13152563.

6. Hunt GM, Yousif M, Levin L, Ledwaba J, Steegen K, Kufa T, Zwane H, Kalimashe M, Kana V, Aynalem G, Perlman J, Ayalew K, Kindra G, Diallo K, Carmona S, Sherman G, Raizes EJ. Resistance is common in paediatric patients failing ART in South Africa. J Antimicrob Chemother. 2023 May 3;78(5):1160-1167. doi: 10.1093/jac/dkac443. PMID: 37017009; PMCID: PMC10616358.

7. Jassat W, Mudara C, Ozougwu L, Welch R, Arendse T, Masha M, Blumberg L, Kufa T, Puren A, Groome M, Govender N. Trends in COVID-19 admissions and deaths among people living with HIV in South Africa: analysis of national surveillance data. The Lancet HIV. 2024 Feb 1;11(2):e96-105.

8. Jaumdally S, Tomassichio M, Pooran A, Esmail A, Kotze A, Meier S, Wilson L, Oelofse S, van der Merwe C, Roomaney A, Davids M, Suliman T, Joseph R, Perumal T, Scott A, Shaw M, Preiser W, Williamson C, Goga A, Mayne E, Gray G, Moore PL, Sigal A, Limberis J, Metcalfe J, Dheda K. (2024) Frequency, kinetics and determinants of culturable SARS-CoV-2 in bio-aerosols from ambulatory COVID-19 patients infected with the Beta, Delta or Omicron variants. Nature Communications. 15(1):2003.

9. Ka'e AC, Nanfack A, Santoro MM, Yagai B, Ambada G, Sagnia B, Nka AD, Semengue ENJ, Pabo W, Takou D, Sonela N, Colizzi V; Perno CF, Ceccherini-Silberstein F, Lewin S,

Tiemessen CT, Fokam J. Characterisation of HIV-1 reservoirs in pediatric populations: protocol for a systematic review and meta-analysis. BMJ Open 2023. 13(10): e073672. DOI: 10.1136/bmjopen-2023-073672.

10. Ka'e AC, Nanfack AJ, Ambada G, Santoro MM, Takou D, Semengue ENJ, Nka AD, Bala MLM, Endougou ON, Elong E, Beloumou G, Ndjupsa S, Gouissi DH, Fainguem N, Tchouaket MCT, Sosso SM, Kesseng D, Ndongo FA, Sonela N, Kamta ACL, Tchidjou HK, Ndomgue T, Ndiang STM, Nlend AEN, Nkenfou CN, Montesano C, Halle-Ekane GE, Cappelli G, Tiemessen CT, Colizzi V, Ceccherini-Silberstein F, Perno CF, Fokam J. Inflammatory Profile of Vertically HIV-1 Infected Adolescents Receiving ART in Cameroon: A Contribution Toward Optimal Pediatric HIV Control Strategies. Frontiers in Immunology 2023. 14: 1239877. DOI: 10.3389/fimmu.2023.1239877.

11. Ka'e AC, Santoro MM, Nanfack A, Semengue ENJ, Yagai B, Nka AD, Ambada G, Mpouel M-L, Sagnia B, Kenou L, Sanhanfo M, Pabo W, Takou D, Chenwi CA, Sonela N, Sosso SM, Nkenfou C, Colizzi V, Halle-Ekane GE, Ndjolo A, Ceccherini-Silberstein F, Perno CF, Lewin S, Tiemessen CT, Fokam J. Characterisation of HIV-1 Reservoirs in Children and Adolescents: A Systematic Review and Meta-analysis toward Pediatric HIV Cure. J Pediatrics. 2024; 267:113919. DOI: 10.1016/j.jpeds.2024.113919.

12. Kakooza F, Golparian D, Matoga M, Maseko V, Lamorde M, Krysiak R, Manabe YC, Chen JS, Kularatne R, Jacobsson S, Godreuil S, Hoffman I, Bercot B, Wi T, Unemo M; WGS Study Group. Genomic surveillance and antimicrobial resistance determinants in Neisseria gonorrhoeae isolates from Uganda, Malawi and South Africa. Antimicrob Chemother. 2015-20. J. 2023 Jun 23: doi:10.1093/jac/dkad193. Epub ahead of print. PMID: 37352017.

13. Kana BD, Arbuthnot P, Botwe BK, Choonara YE, Hassan F, Louzir H, Matsoso P, Moore PL, Muhairwe A, Naidoo K, Ndomondo-Sigonda M, Madhi SA. (2023) Opportunities and challenges of leveraging COVID-19 vaccine innovation and technologies for developing vaccine sustainable vaccine manufacturing capabilities in Africa. Lancet ID. S1473-3099(23)00354-7.

14. Karim F, Riou C, Bernstein M, Jule Z, Lutig G, van Graan S, Keeton RS, Upton J, Ganga Y, Khan K, Reedoy K, Mazibuko M, Govender K, Thambu K, Ngcobo, Venter E, Makhado Z, Hanekom W, von Gottberg A, Hoque M, Abdool Karim Q, Abdool Karim SS, Manickchund N, Magula N, Gosnell BI, Lessells RJ, Moore PL, Burgers QA, de Oliveira T, Moosa MS, Sigal A. (2024) Clearance of persistent SARS-CoV-2 associates with increased neutralising antibodies in advanced HIV disease post-ART initiation. Nature Communications. 15(1):2360.

15. Koen AL, Izu A, Baillie V, Kwatra G, Cutland CL, Fairlie L, Padayachee SD, Dheda K, Barnabas SL, Bhorat QE, Briner C, Ahmed K, Bhikha S, Bhiman JN, du Plessis J, Esmail A, Horne E, Hwa SH, Oommen-Jose A, Lambe T, Laubscher M, Malahleha M, Benade G, McKenzie S, Oelofse S, Patel F, Pillay S, Rhead S, Rodel H, Taoushanis C, Tegally H, Thombrayil A, Villafana TL, Gilbert S, Pollard AJ, Madhi SA. (2023) Efficacy of primary series AZD1222 (ChAdOx1 nCoV-19) vaccination against SARS-CoV-2 variants of concern: Final analysis of a randomised, placebo-controlled, phase 1b/2 study in South African adults (COV005). Vaccine. 26;41 (23):3486-3492.

16. Kufa T, Woldesenbet S, Cheyip M, Ayalew K, Kularatne R, Manda S, Lombard C, Puren A. Syphilis screening coverage and positivity by HIV treatment status among South African

pregnant women enrolled in the 2019 antenatal HIV sentinel survey. Scientific reports. 2023 Apr 1;13(1):5322.

17. Kuhn L, Wang T, Li F, Strehlau R, Tobin NH, Violari A, Brooker S, Patel F, liberty A, Shiau S, Arpadi SM, Wadhwa S, Yin MT, Wang S, Tiemessen CT, Aldrovandi GM. Microbiota in the oral cavity of school-age children living with HIV who started antiretroviral therapy at young ages in South Africa. AIDS 2023. 37: 1583-1591. DOI: 10.1097/QAD.0000000000003599.

18. Lemmer Y, Chapman R, Abolnik C, Smith T, Schafer G, Hermanus T, du Preez L, Goosen K, Sepotokele KM, Gers S, Suliman T, Preiser W, Shaw ML, Roth R, Truyts A, Magwaza M, Mahanyana O, Verschoor JA, Moore PL, O'Kennedy MM. Protective efficacy of a plant-produced Beta variant rSARS-CoV-2 VLP vaccine in Golden Syrian hamsters. Vaccine. 42:4, 738-744.

19. Maenetje P, Baik Y, Schramm D, Vangu M, Wallis R, Mlotshwa M, Tiemessen CT, Li Y, Kornfeld H, Churchyard G, Auld SC, Bisson GP. Circulating biomarkers, FeNO, and lung function in patients with HIV and tuberculosis. JID 2024. 229(3): 824-832. DOI: 10.1093/infdis/jiad232.

20. Mahanjana SK, Ledibane T, Sherman GG, Murray TY, Mazanderani AFH. Retrospective review of maternal HIV viral load electronic gatekeeping codes in South Africa. S Afr J HIV Med. 2024;25(1):a1539. https://doi.org/10.4102/sajhivmed.v25i1.1539.

21. Mahomed S, Garrett N, Capparelli EV, Osman F, Mkhize NN, Harkoo I, Gengiah TN, Mansoor LE, Baxter C, Archary D, Yende-Zuma N, Samsunder N, Carlton K, Narpala S, McDermott AB, Doria-Rose NA, Moore PL, Morris L, Abdool Karim Q, Mascola JR, Abdool Karim SS. (2023) Safety and pharmacokinetics of escalating doses of neutralising monoclonal antibody CAP256V2LS administered with and without VRC07-523LS in HIV-negative women in South Africa (CAPRISA 012B): a phase 1, dose-escalation, randomised controlled trial. The Lancet HIV. 10:4, 230-243.

22. Mahomed S, Garrett N, Potloane D, Sikazwe I, Capparelli E, Harkoo I, Gengia TN, Yende-Zuma N, Osman F, Mansoor LE, Archary D, Myeni N, Radebe P, Samsunder N, Doria-Rose NA, Carlton K, Gama L, Koup RE, Narpala S, Serebryannyy L, Moore PL, Williamson C, Pozetto B, Hankins CA, Morris L, Abdool Karim Q, Abdool Karim SS. (2023) Extended Safety and Tolerability of subcutaneous CAP256V2LS and VRC07-523LS in HIV-negative women: Study Protocol for the randomised, placebo-controlled double-blinded, phase 2 CAPRISA 012C trial. BMJ Open. 13: e076843.

23. Mapiye M, Ravhuhali K, de Voux A, Kufa T. Factors associated with an unsuppressed viral load among HIV-positive individuals attending STI services in South Africa, 2019. BMC Infectious Diseases. 2024 Jan 30;24(1):148.

24. Mapiye M, Ravhuhali K, de Voux A, Kufa-Chakezha T. Evaluation of the congenital syphilis notification surveillance system in South Africa (2020) Public Health Bulletin, South Africa. https://www.phbsa.ac.za/wp-content/uploads/2023/11/Congenital-Syphilis-Notification-Surveillance-System-in-South-Africa.pdf.

25. Mbira TE, Kufa T, Sherman GG, Ngandu NK, PHANGISA Study Team. Compliance to Viral Load Monitoring Schedules Among Women Attending Prevention of Vertical HIV Transmission Services Before and During the COVID-19 Pandemic in Ehlanzeni District, Mpumalanga, South Africa. AIDS and Behavior. 2024 Mar;28(3):868-85.

26. Mkhize NN, Yssel AEJ, Kaldine H, van Dorsten RT, Woodward AS, Davis W, Beaume N, Matten D, Lambson B, Modise T, Kgagudi P, York T,

Westfalls DH, Giorgi EE, Korber B, Anthony C, Mapengo RE, Bekker V, Domin E, Eaton A, Deng W, DeCamp A, Huang Y, Gilbert PB, Gwashu-Nyangiwe A, Thebus R, Ndabambi N, Mielke D, Mgodi N, Karuna S, Edupuganti S, Seaman MS, Corey L, Cohen MS, Hural J, McElrath MJ, Mullins JI, Montefiori D, Moore PL, Williamson C, Morris L. (2023) Neutralisation profiles of HIV-1 viruses from the VRC01 Antibody Mediated Prevention (AMP) trials. PLoS Pathogens. 19(6):e1011469.

27. Moore PL, Gray G. (2023) COVID-19 as a catalyst for vaccine manufacturing: a South African experience. Cell Host and Microbe. 31(6): 839-842.

28. Motsoeneng BM, Manamela NP, Kaldine H, Kgagudi P, Hermanus T, Ayres F, Makhado Z, Moyo-Gwete T, van der Mescht MA, Abdullah F, Boswell MT, Ueckermann V, Rossouw TM, Madhi SA, Moore PL, Richardson SI. (2023) Despite delayed kinetics, people living with HIV achieve equivalent antibody function after SARS-CoV-2 infection or vaccination. Frontiers in Immunology. 3 August;14:1231276.

29. Moyo S, Simbayi L, Zuma K, Marinda E, Jooste S, Fortuin M, Singh B, Mabaso M, Reddy T, Parker W, Naidoo I, Manda S, Goga A, Ngandu N, Cawood C, Morris L, Moore PL, Puren A & the NCAS Study Team. (2023) Seroprevalence survey of anti-SARS-CoV-2 antibody and associated factors in South Africa: Findings of the 2020–2021 population based household survey. PLOS Global Public Health. 3(9):e0002358.

30. Moyo-Gwete T, Richardson SI, Keeton R, Hermanus T, Spencer H, Manamela NP, Ayres F, Makhado Z, Motlou T, Tincho MB, Benede N, Ngomti A, Baguma R, Chauke MV, Mennen M, Adriaanse M, Skelem S, Gogo A, Garrett N, Bekker L, Gray G, Ntusi NAB, Riou C, Burgers WA, Moore PL. (2023) Homologous Ad26. COV2.S vaccination results in reduced boosting of humoral responses in hybrid immunity, but elicits antibodies of similar magnitude regardless of prior infection. PLoS Pathogens. 19(11): e1011772.

31. Müller EE, Gumede LYE, Maseko DV, Mahlangu MP, Venter JME, Da Costa Dias B, Nhlapho D, Kularatne RS. Emergence of high-level azithromycin-resistant Neisseria gonorrhoeae causing male urethritis in Johannesburg, South Africa, 2021. Sex Health. 2024 Feb;21(1):NULL. doi: 10.1071/SH23143. PMID: 38029797.

32. Planas D, Peng L, Zheng L, Guivel-Benhassine F, Staropoli I, Porrot F, Bruel T, Bhiman JN, Bonaparte M, Savarino S, de Bruyn G, Chicz RM, Moore PL, Olivier S, Sridhar S. Beta-variant recombinant booster vaccine elicits broad cross-reactive neutralisation of SARS-CoV-2 including Omicron variants. Helliyon. 10(5):e27033.

33. Reeves DF, Mayer BT, decamp AC, Huang Y, Zhang B, Carpp LN, Margaret CA, Juraska M, Gilbert PB, Montefiori DC, Bar KJ, Cardozo-Ojeda EF, Schiffer JT, Rossenkhan R, Edlefsen P, Morris L, Mkhize NN, Williamson C, Mullins JI, Seaton KE, Tomaras GD, Andrew P, Mbodi N, Ledgerwood JE, Cohen MS, Corey L, Naidoo L, Orrell C, Goepfert PA, Casapia M, Sobieszczyk, Karuna ST, Edupuganti S. (2023) High monoclonal neutralisation titers reduced breakthrough HIV-1 viral loads in the Antibody Mediated Prevention trials. 14(1):8299.

34. Seaton KE, Huang Y, Karuna S, Heptinstall JR, Brackett C, Chiong K, Zhang L, Yates NL, Sampson M, Rudnicki E, Juraska M, decamp AC, Edlefsen PT, Mullins JI, Williamson C, Rossenkhan R, Giorgi EE, Kenny A, Angier H, Randhawa A, Weiner JA, Rojas M, Sarzotti-kelsoe M, Zhang L, Sawant S, Ackerman ME, McDermott AB, Mascola JR, Hural J, McElrath MJ, Andrew P, Hidalgo JA, Clark J, Laher F, Orrell

C, Frank I, Gonzales P, Edupuganti S, Mgodi N, Corey L, Morris L, Montefiori D, Cohen MS, Gilbert PB, Tomaras G. Pharmacokinetic serum concentrations of VRC01 correlate with prevention of HIV-1 acquisition. eBiomedicine. 93: 104590.

35. Shephard M, Matthews S, Andrewartha K, Dimech W, Cabuang L, Barbara C, Chen, XS, Cordioli M, Hançali A, Jiang TT, Kularatne R, Meli S, Muller E, Oumzil H, Padovese V, Sandri A, Vargas S, Zahra G, Unemo M, Blondeel K, Toskin I. Quality control and external quality assessment for the independent clinic-based evaluation of point-of-care testing to detect Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis in eight countries. BMC Infect Dis. 2024 29 February;24(Suppl 1):203. doi: 10.1186/s12879-024-09057-x. PMID: 38418947; PMCID: PMC10902926.

36. Shephard M, Matthews S, Kularatne R., Andrewartha K, Blondeel K, Alvarez C, Camey E, Hançali A, Müller E, Haw A, Oumzil H, Golparian D, Ramirez DE, Kiarie J, Kurbonov, F., Mirandola, M., Peeling, R.W., Silva, R., Thwin, S.S., Unemo, M., Toskin I. Independent clinic-based evaluation of point-of-care testing for the screening of Chlamydia trachomatis, Neisseria gonorrhoea and Trichomonas vaginalis in women-at-risk in Australia, Guatemala, Morocco, South Africa. BMC Infect Dis. 2024 4 March;24(Suppl 1):277. doi: 10.1186/s12879-024-09018-4. PMID: 38438953; PMCID: PMC10910521.

37. Singh B, Mthombeni J, Olorunfemi G, Goosen M, Cutler E, Julius H, Brukwe Z, Puren A. Evaluation of the accuracy of the Asanté assay as a point-of-care rapid test for HIV-1 recent infections using serum bank specimens from blood donors in South Africa, July 2018 - August 2021. S Afr Med J. 2023 23 October;113(10):42-48. doi: 10.7196/SAMJ.2023.v113i10.678. PMID: 37881912.

38. Steegen K, van Zyl GU, Claassen M, Khan A, Pillay M, Govender S, Bester PA, van Straaten JM, Kana V, Cutler E, Kalimashe MN, Lebelo RL, Moloi MBH, Hans L. Advancing HIV Drug Resistance Technologies and Strategies: Insights from South Africa's Experience and Future Directions for Resource-Limited Settings. Diagnostics (Basel). 2023 Jun 29;13(13):2209. doi: 10.3390/diagnostics13132209. PMID: 37443603; PMCID: PMC10340187.

39. Tatoud R, Jones B, Dong K, Ndung'u T, Deeks S, Tiemessen CT, and The 2023 Research-for-Cure Academy Fellows. Advancing HIV cure research in low- and middle-income countries requires empowerment of the next generation of scientists. J Virus Eradication 2024. 10(1): 100364. DOI: 10.1016/j.jve.2024.100364.

40. Trkola A, Moore PL. (2023) Vaccinating people with HIV (PWH) – a short-circuit to an effective HIV vaccine. Lancet Infectious Diseases. doi: 10.1016/S1473-3099(23)00481-4.

41. Twesigomwe D, Drogemoller BI, Wright GEB, Adebamowo C, Agongo G, Boua PR, Matshaba M, Paximadis M, Ramsay M, Simo G, Simuunza MC, Tiemessen CT, Lombard Z, Hazelhurst S. Characterisation of CYP2B6 and CYP2A6 Pharmacogenetic Variation in Sub-Saharan African Populations. Clin Pharmacol Ther. 2024; 115(3): 576-594. DOI: 10.1002/cpt.2749.

42. Van de Perre P, Moore PL. Super early treatment for HIV acquired in utero. Lancet HIV. doi: /10.1016/S2352-3018(23)00260-6.

43. Van de Perre P, Scarlatti G, Moore PL, Moles J, Nagot N, Tylleskär T, Gray G, Goga A. (2024) Preventing breastmilk HIV transmission using broadly neutralising monoclonal antibodies: one size does not fit all. Immunity, Inflammation and Disease. 12(3): e1216.

44. Vukovich MJ, Raju N, Kgagudi P, Manamela

N, Abu-Shmais A, Gripenstraw K, Wasdin P, Shen S, Dwyer B, Akoad J, Lynch R, Montefiori D, Richardson S, Moore PL, Georgiev I. (2023) Development of LIBRA-seq for the guinea pig model system as a tool for the evaluation of antibody responses to multivalent HIV-1 vaccines. Journal of Virology. doi: 10.1128/jvi.01478-23.

45. Williamson C, Lynch RM, Moore PL. (2023) Anticipating viral escape – resistance to active and passive immunisation, Current Opinion in HIV & AIDS. 18:6, 342-348.

Presentations

- International congresses: 23
- National congresses and local congresses: 24

CENTRE FOR RESPIRATORY DISEASES AND MENINGITIS (CRDM)

PROF. CHERYL COHEN
Centre Head

CENTRE FOR RESPIRATORY DISEASES AND MENINGITIS (CRDM)

"Following the relaxation of COVID-19 restrictions, increased circulation of pertussis, RSV and influenza infections occurred."

OVERVIEW

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 CRDM generates data and provides expertise to the National Department of Health (NDoH) and healthcare providers, as well as regional and international collaborators, to assist with the planning of public health policies and programmes, and response 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 of review, CRDM de-escalated response activities to the COVID-19 pandemic and supported response to increases in pertussis, respiratory syncytial virus (RSV) and influenza circulation following the relaxation of COVID-19 restrictions.

The Centre is responsible for six 'category one' notifiable medical conditions (NMC): 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. These diseases, in addition to other important diseases, such as influenza, RSV and pneumococcus are monitored through ongoing syndromic and laboratory-based surveillance programmes, as well as the NMC programmeme.

SURVEILLANCE

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

This programmeme 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. In addition, surveillance for Group A and Group B *Streptococcus* continued, aiming to generate evidence to contribute to vaccine development and decision-making for introducing future vaccines or other control interventions. We initiated real-time bacterial genomic surveillance to characterise and track lineages and better assist in outbreak detection, with the goal of also developing methods for sequencing from culture-negative clinical specimens. Surveillance data were 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.

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 SARS-CoV-2, influenza, RSV and *Bordetella pertussis*. 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 included systematic tuberculosis testing among individuals aged ≥18 years and COVID-19 vaccine effectiveness evaluation. In addition, all syndromic programmes provide information on the timing of influenza and RSV seasons and SARS-CoV-2 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, vaccine effectiveness estimates for COVID-19 vaccines, and a platform for SARS-CoV-2 genomic surveillance to monitor circulating strains and emerging variants of concern. Through these programmes circulating respiratory viruses are genetically characterised in real time through whole genome sequencing to monitor virus evolution and identify emerging variants.

OUTBREAKS

NATIONAL

The outbreak of pertussis that was initially reported from the Western Cape in July 2022, continued throughout 2023 and included other Provinces. CRDM provided alerts for clinicians, responded to media queries regarding the increase in cases, and produced monthly communiques.

The Centre also assisted with outbreak response to diphtheria in a correctional services facility in the Western Cape, an influenza outbreak in a school in the Free State, and *ad hoc* testing for suspected avian influenza cases.

INTERNATIONAL

CRDM provided laboratory support for African partners, in response to outbreaks of meningitis, respiratory illness and diphtheria. 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, we conducted expanded SARS-CoV-2 testing including PCR, sequencing, serology and viral culture. CRDM staff consult on numerous expert committees and working groups for WHO, Africa Centres for Disease Control (Africa CDC) and the WHO African Region (AFRO).

CRDM is exploring multi-pathogen target-enrichment-based and metagenomics-based sequencing methods to enable the detection and characterisation of novel and emerging pathogens. In addition, CRDM is working with animal health and environmental health colleagues to be able to rapidly detect and respond to zoonotic infections and outbreaks, such as avian influenza.

POLICY CONTRIBUTIONS

Influenza vaccination guidelines were updated to include updated guidance in the time of COVID-19. Prof. Anne von Gottberg continued to act as chairperson of the National Advisory Group on Immunisation (NAGI). In addition, CRDM staff contributed data and expertise to the NAGI RSV working group which will advise NDoH on the introduction of newly available prevention approaches for RSV in infants.

Prof. Anne von Gottberg continued to act as vice-chair of the WHO Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) which advises WHO and monitors and evaluates the evolution of SARS-CoV-2. Prof. Cheryl Cohen was appointed vice chair of the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) which periodically reviews the evidence and analyses the implications of emerging variants of concern (VOCs) on the performance of COVID-19 vaccines.

DIAGNOSTIC SERVICES

CRDM provides testing services that may not be available at NHLS laboratories, offering support when required. The Centre also offers serotyping/grouping of vaccine-preventable bacterial pathogens and subtyping for influenza and RSV. The centre is currently exploring culture-free, sequencing methods to assist in pathogen detection and characterisation directly from clinical specimens.

NATIONAL INFLUENZA CENTRE (NIC) AND WHO CORONAVIRUS NETWORK (COVINET)

CRDM houses the NIC for South Africa, which forms part of the expanded WHO Global Influenza Surveillance and Response System (e-GISRS). The NIC continued to support WHO by serologic testing and genetic characterisation of influenza viruses, to guide the composition of the annual seasonal influenza vaccines, RSV and SARS-CoV-2. 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 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. CRDM was designated a WHO Coronavirus Network (CoViNet) laboratory in March 2024.

RESEARCH ACTIVITIES

Moyes J, Tempia S, Walaza S, McMorrow ML, Treurnicht F, Wolter N, von Gottberg A, Kahn K, Cohen AL, Dawood H, Variava E, Cohen C. The burden of RSV-associated illness in children aged < 5 years, South Africa, 2011 to 2016. BMC Med [Internet]. 2023 Apr 11 [cited 2023 Jul 4];21(1):139. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37038125

Moyes J, Tempia S, Walaza S, McMorrow ML, Treurnicht F, Wolter N, von Gottberg A, Kahn K, Cohen AL, Dawood H, Variava E, Cohen C. The economic burden of RSV-associated illness in children aged < 5 years, South Africa 2011-2016. BMC Med. 2023 Apr 13;21(1):146.

Moyes J, Tempia S, Walaza S, McMorrow ML, Cohen AL, Treurnicht F, Hellferscee O, Wolter N, Von Gottberg A, Dawood H, Variava E, Kahn K, Madhi SA, Cohen C. The attributable fraction of respiratory syncytial virus among patients of different ages with influenza-like illness and severe acute respiratory illness in a high HIV prevalence setting, South Africa, 2012-2016. Int J Infect Dis 2023 May 20;134:71-7.

Maternal vaccines and infant monoclonal antibodies are available globally for the prevention of respiratory syncytial virus (RSV) infection in young children. Accurate burden estimates will assist national policymakers regarding the introduction of these technologies into South Africa.

A set of three papers describes (i) the attributable fraction (AF) of RSV in people of all ages (ii) the national burden of RSV in young children (adjusted for the AF) and (iii) the economic burden of RSV infection in children. The AF of RSV was highest in infants admitted to the hospital (95% (95% Confidence interval (CI) 91%-98%), lower in older children aged 1-4 years (83% (95% CI 71%-91%), decreasing with age and then increasing to 81% (0-97%) in adults aged ≥65 years. Similar trends were seen in mild (outpatient illness) although smaller variances overall.

The AF-adjusted mean annual burden and cost burden of RSV illness were similarly highest in the young infants, specifically those aged < 3 months of age with an incidence of 18361/100 0000 in the 2-month-old age group. The mean annual cost burden of RSV in children < 5 was $ 137 204 393 of which 76% were healthcare system costs. An intervention aimed at young infants would reduce the burden of illness and the associated costs of RSV illness, specifically the hospitalisation costs.

Kleynhans J, Dall'Amico L, Gauvin L, Tizzoni M, Maloma L, Walaza S, Martinson NA, von Gottberg A, Wolter N, Makhasi M, Cohen C, Cattuto C, Tempia S. Association of close-range contact patterns with SARS-CoV-2: a household transmission study. Elife [Internet]. 2023 Jul 18;12: e84753.

Households are an important location for SARS-CoV-2 transmission. We used wearable proximity sensors to measure face-to-face interactions between household members after SARS-CoV-2 was identified in the household. We assessed the association of contact parameters with SARS-CoV-2 transmission and found factors associated with SARS-CoV-2 acquisition to be index cases with higher SARS-CoV-2 viral loads and female contacts. No contact parameters were associated with acquisition for any of the duration, frequency, cumulative time in contact, or average duration in contact with the SARS-CoV-2 index case. Our findings may be due to study limitations, that droplet-mediated transmission during close-proximity contacts plays a smaller role than airborne transmission of SARS-CoV-2 in the household, or due to high contact rates in households.

Moosa F, du Plessis M, Weigand MR, Peng Y, Mogale D, de Gouveia L, Nunes MC, Madhi SA, Zar HJ, Reubenson G, Ismail A, Tondella ML, Cohen C, Walaza S, von Gottberg A, Wolter N. Genomic characterisation of *Bordetella pertussis* in South Africa, 2015-2019. Microb Genomics 2023 Dec 1;9(12).

Pertussis remains a public health concern in South Africa, with an increase in reported cases and outbreaks in recent years. Whole genome sequencing was performed on 32 *Bordetella pertussis* isolates sourced from three different surveillance programmes in South Africa between 2015 and 2019. All isolates were the globally-disseminated sequence type 2 and no pertactin-deficient or other mutations in vaccine antigen genes were identified (as has been described in other countries). Increases in case numbers are probably not due to evolutionary changes in the genome but possibly due to other factors such as the cyclical nature of *B. pertussis* disease, waning immunity due to the use of acellular vaccines and/or population immunity gaps.

Wolter N, Tempia S, von Gottberg A, Bhiman JN, Walaza S, Kleynhans J, Moyes J, Aitken S, Magni S, Yun J, Fellows T, Makamadi T, Weiner R, Cawood C, Martinson N, Lebina L, Cohen C. Healthcare utilisation during the first two waves of the COVID-19 epidemic in South Africa: A cross-sectional household survey. PLoS One Sep 14;18(8):e0290787.

Healthcare utilisation surveys contextualise facility-based surveillance data for burden estimates. We conducted a cross-sectional healthcare utilisation survey in households in three communities from three Provinces (KwaZulu-Natal, Western Cape, and North West) during the first year of the COVID-19 pandemic. From November 2020 through April 2021, we enrolled 5,804 households and 23,003 individuals. Any respiratory illness was reported by 1.6% of individuals; 0.7% reported ILI only, 0.8% reported SRI

only, and 0.1% reported both ILI and SRI. Less than half of ILI episodes and only 71% of SRI episodes were medically attended during the first two COVID-19 waves in South Africa, and therefore facility-based data may underestimate the disease burden during the COVID-19 pandemic.

Cohen C, Kleynhans J, Moyes J, McMorrow ML, Treurnicht FK, Hellferscee O, Wolter N, Martinson NA, Kahn K, Lebina L, Mothlaoleng K, Wafawanaka F, Gómez-Olivé FX, Mkhencele T, Mathunjwa A, Carrim M, Mathee A, Piketh S, Language B, von Gottberg A, Tempia S. Incidence and transmission of respiratory syncytial virus in urban and rural South Africa, 2017-2018. Nat Commun [Internet]. 2024 Dec 1;15(1):116.

To describe RSV incidence and transmission, we conducted a prospective cohort study in rural and urban communities in South Africa during 2017-2018. Nasopharyngeal swabs were collected twice weekly for 10 months annually and tested for RSV using PCR. We tested 81,430 samples from 1,116 participants in 225 households (follow-up 90%). 32% (359/1116) of individuals had ≥1 RSV infection; 10% (37/359) had repeat infection during the same season, 33% (132/396) of infections were symptomatic, and 2% (9/396) sought medical care. Incidence was 47.2 infections/100 person-years and highest in children <5 years (78.3). Symptoms were the most commong in individuals aged <12 and ≥65 years. Individuals 1-12 years accounted for 55% (134/242) of index cases. Within two South African communities, the RSV attack rate was high, and most infections were asymptomatic. Young children were more likely to introduce RSV into the home, and to be infected.

TEACHING AND TRAINING

- Training at various sites in South Africa for surveillance.
- 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 Centre (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. Six students (5 PhD, 4 MSc) were enrolled in the programme in 2020.
- Wits University lectures and course facilitation, post-graduate supervision of MSc and PhD students (joint staff contributions).

Postgraduate students

- Currently enrolled: Masters 1; PhD 7
- Students graduated/passed: Hons 1; Masters 3; PhD 1

RESEARCH OUTPUTS (PUBLICATIONS 2023/2024)

1. Grant R, Sacks JA, Abraham P, Chunsuttiwat S, Cohen C, Figueroa JP, Fleming T, Fine P, Goldblatt D, Hasegawa H, MacIntrye CR, Memish ZA, Miller E, Nishioka S, Sall AA, Sow S, Tomori O, Wang Y, Van Kerkhove MD, Wambo MA, Cohen HA, Mesfin S, Otieno JR, Subissi L, Briand S, Wentworth DE, Subbarao K. When to update COVID-19 vaccine composition. Nat Med [Internet]. 2023 Apr 1 [cited 2023 Jul 4];29(4). Available from: https://pubmed.ncbi.nlm.nih.gov/36807683/
2. Hawkins PA, Chochua S, Lo SW, Belman S, Antonio M, Kwambana-Adams B, von Gottberg A, du Plessis M, Cornick J, Beall B, Breiman RF, Bentley SD, McGee L, The Global Pneumococcal Sequencing Consortium. A global genomic perspective on the multidrug-resistant *Streptococcus pneumoniae* 15A-CC63 sub-lineage following pneumococcal

conjugate vaccine introduction. Microb genomics [Internet]. 2023 Apr 1 [cited 2023 Jul 4];9(4):mgen000998. Available from: https://pubmed.ncbi.nlm.nih.gov/37083600/

3. Moyes J, Tempia S, Walaza S, McMorrow ML, Treurnicht F, Wolter N, von Gottberg A, Kahn K, Cohen AL, Dawood H, Variava E, Cohen C. The burden of RSV-associated illness in children aged < 5 years, South Africa, 2011 to 2016. BMC Med [Internet]. 2023 Apr 11 [cited 2023 Jul 4];21(1):139. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37038125

4. Moyes J, Tempia S, Walaza S, McMorrow ML, Treurnicht F, Wolter N, von Gottberg A, Kahn K, Cohen AL, Dawood H, Variava E, Cohen C. The economic burden of RSV-associated illness in children aged < 5 years, South Africa 2011-2016. BMC Med [Internet]. 2023 Apr 13 [cited 2023 Jul 4];21(1):146. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37055799

5. Jassat W, Abdool Karim SS, Ozougwu L, Welch R, Mudara C, Masha M, Rousseau P, Wolmarans M, Selikow A, Govender N, Walaza S, von Gottberg A, Wolter N, Terrence Pisa P, Sanne I, Govender S, Blumberg L, Cohen C, Groome MJ. Trends in cases, hospitalizations, and mortality related to the Omicron BA.4/BA.5 Subvariants in South Africa. Clin Infect Dis [Internet]. 2022 Apr 17 [cited 2023 Jul 4];76(8):1468–75. Available from: https://pubmed.ncbi.nlm.nih.gov/36453094/

6. Carbonell-Estrany X, Simões EA, Bont LJ, Paes BA. Prioritising respiratory syncytial virus prevention in low-income and middle-income countries (Cheryl Cohen part of RSV Prevention Collaborators). Lancet Glob Heal [Internet]. 2023 May 1 [cited 2023 Jul 4];11(5):e655–7. Available from: https://pubmed.ncbi.nlm.nih.gov/37061306/

7. Staadegaard L, Del Riccio M, Wiegersma S, El Guerche-Séblain C, Dueger E, Akçay M, Casalegno JS, Dückers M, Caini S, Paget J. (Nicole Wolter is part NIC collaborators). The impact of the SARS-CoV-2 pandemic on global influenza surveillance: Insights from 18 National Influenza Centers based on a survey conducted between November 2021 and March 2022. Influenza Other Respi Viruses [Internet]. 2023 May 1 [cited 2023 Jul 4];17(5):e13140. Available from: https://pubmed.ncbi.nlm.nih.gov/37180840/

8. Jamieson L, Van Schalkwyk C, Nichols BE, Meyer-Rath G, Silal S, Pulliam J, Blumberg L, Cohen C, Moultrie H, Jassat W. Differential in-hospital mortality and intensive care treatment over time: Informing hospital pathways for modelling COVID-19 in South Africa. Musuka GN, editor. PLOS Glob public Heal [Internet]. 2023 May 17 [cited 2023 Jul 4];3(5):e0001073. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37195977

9. Moyes J, Tempia S, Walaza S, McMorrow ML, Cohen AL, Treurnicht F, Hellferscee O, Wolter N, Von Gottberg A, Dawood H, Variava E, Kahn K, Madhi SA, Cohen C. The attributable fraction of respiratory syncytial virus among patients of different ages with influenza-like illness and severe acute respiratory illness in a high HIV prevalence setting, South Africa, 2012-2016. Int J Infect Dis [Internet]. 2023 May 20 [cited 2023 Jul 4];134:71–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37211271

10. Ismael N, van Wyk S, Tegally H, Giandhari J, San JE, Moir M, Pillay S, Utpatel C, Singh L, Naidoo Y, Ramphal U, Mabunda N, Abílio N, Arnaldo P, Xavier J, Amoako DG, Everatt J, Ramphal Y, Maharaj A, de Araujo L, Anyaneji UJ, Tshiabuila D, Viegas S, Lessells R, Engelbrecht S, Gudo E, Jani I, Niemann S, Wilkinson E, de Oliveira T. Genomic epidemiology of SARS-CoV-2 during the first four waves in Mozambique. PLOS Glob public Heal [Internet]. 2023 Mar 6 [cited 2023 Oct 4];3(3):e0001593. Available from: https://pubmed.ncbi.nlm.nih.gov/36963096/

11. Weiner R, Magni S, Maakamadi T, Fellows T, Aitken S, Yun J, Tempia S, von Gottberg A, Bhiman J, Walaza S, Moyes J, Cawood C, Martinson N, Lebina L, Cohen C, Wolter N. Knowledge, attitudes, practices and intention to get vaccinated against COVID-19: results from a cross-sectional survey in three peri-urban communities in South Africa. Pan Afr

Med J [Internet]. 2023 Jul 12 [cited 2023 Oct 4];45(120). Available from: https://pubmed.ncbi.nlm.nih.gov/37745916/

12. Kleynhans J, Dall'Amico L, Gauvin L, Tizzoni M, Maloma L, Walaza S, Martinson NA, von Gottberg A, Wolter N, Makhasi M, Cohen C, Cattuto C, Tempia S. Association of close-range contact patterns with SARS-CoV-2: a household transmission study. Elife [Internet]. 2023 Jul 18 [cited 2023 Sep 14];12. Available from: https://pubmed.ncbi.nlm.nih.gov/37461328/

13. Magobo RE, Ismail H, Lowe M, Strasheim W, Mogokotleng R, Perovic O, Kwenda S, Ismail A, Makua M, Bore A, Phayane R, Naidoo H, Dennis T, Ngobese M, Wijnant W, Govender NP. Outbreak of NDM-1- and OXA-181-Producing *Klebsiella pneumoniae* Bloodstream Infections in a Neonatal Unit, South Africa. Emerg Infect Dis [Internet]. 2023 Aug 1 [cited 2023 Oct 4];29(8):1531–9. Available from: https://pubmed.ncbi.nlm.nih.gov/37486166/

14. Mandomando I, Mwenda JM, Nakamura T, de Gouveia L, von Gottberg A, Kwambana-Adams BA, Antonio M, Messa A, Litt D, Seaton S, Weldegebriel GG, Biey JNM, Serhan F. Evaluation of Laboratories Supporting Invasive Bacterial Vaccine-Preventable Disease (IB-VPD) Surveillance in the World Health Organization African Region, through the Performance of Coordinated External Quality Assessment. Trop Med Infect Dis [Internet]. 2023 Aug 14 [cited 2023 Oct 4];8(8):413. Available from: https://pubmed.ncbi.nlm.nih.gov/37624351/

15. Wolter N, Tempia S, von Gottberg A, Bhiman JN, Walaza S, Kleynhans J, Moyes J, Aitken S, Magni S, Yun J, Fellows T, Makamadi T, Weiner R, Cawood C, Martinson N, Lebina L, Cohen C. Healthcare utilization during the first two waves of the COVID-19 epidemic in South Africa: A cross-sectional household survey. PLoS One [Internet]. 2023b Aug 25 [cited 2023 Sep 14];18(8):e0290787. Available from: https://pubmed.ncbi.nlm.nih.gov/37624826/

16. Bingham J, Tempia S, Moultrie H, Viboud C, Jassat W, Cohen C, Pulliam JRC. Estimating the time-varying reproduction number for COVID-19 in South Africa during the first four waves using multiple measures of incidence for public and private sectors across four waves. Anjorin AA, editor. PLoS One [Internet]. 2023 Sep 22 [cited 2023 Oct 4];18(9):e0287026. Available from: https://pubmed.ncbi.nlm.nih.gov/37738280/

17. Jassat W, Reyes LF, Munblit D, Caoili J, Bozza F, Hashmi M, Edelstein M, Cohen C, Alvarez-Moreno CA, Cao B. Long COVID in low-income and middle-income countries: the hidden public health crisis. Lancet (London, England) [Internet]. 2023 Sep 30 [cited 2023 Oct 4];402(10408):1115–7. Available from: https://pubmed.ncbi.nlm.nih.gov/37652071/

18. Shaw D, Abad R, Amin-Chowdhury Z, Bautista A, Bennett D, *et al* Trends in invasive bacterial diseases during the first 2 years of the COVID-19 pandemic: analyses of prospective surveillance data from 30 countries and territories in the IRIS Consortium. Lancet Digit Heal [Internet]. 2023 Sep 1 [cited 2023 Oct 4];5(9):e582–93. Available from: https://pubmed.ncbi.nlm.nih.gov/37516557/

19. Chiwandire N, Jassat W, Groome M, Kufa T, Walaza S, Wolter N, von Gottberg A, Zar HJ, Reubenson G, Tempia S, Ebonwu J, Govender N, Ntshoe G, Shonhiwa AM, Blumberg L, Cohen C. Changing Epidemiology of COVID-19 in Children and Adolescents Over Four Successive Epidemic Waves in South Africa, 2020-2022. J Pediatric Infect Dis Soc [Internet]. 2023 Apr 18 [cited 2024 Jan 4];12(3):128–34. Available from: https://pubmed.ncbi.nlm.nih.gov/36648247/

20. Farley E, Okeibunor J, Balde T, Donkor IO, Kleynhans J, Wamala JF, Kaboré NF, Balam S, Chamla D, Braka F, Subissi L, Herring B, Whelan MG, Bergeri I, Lewis HC. Short communication-Lessons learnt during the implementation of Unity-aligned SARS-CoV-2 seroprevalence studies in Africa. Influenza Other Respi Viruses [Internet]. 2023 Aug 1 [cited 2024 Jan 3];17(8):e13170. Available from: https://pubmed.ncbi.nlm.nih.gov/37621920/

21. Zhu Y, Almeida FJ, Baillie JK, Bowen AC, Britton PN, et al. International Pediatric COVID-19 Severity Over the Course of the Pandemic. JAMA Pediatr [Internet]. 2023 Oct 1 [cited 2023 Oct 4];177(10):1073–84. Available from: https://pubmed.ncbi.nlm.nih.gov/37603343/

22. Kekana D, Naicker SD, Shuping L, Velaphi S, Nakwa FL, Wadula J, Govender NP. *Candida auris* Clinical Isolates Associated with Outbreak in Neonatal Unit of Tertiary Academic Hospital, South Africa. Emerg Infect Dis [Internet]. 2023 Oct 1 [cited 2023 Oct 4];29(10):2044–53. Available from: https://pubmed.ncbi.nlm.nih.gov/37735719/

23. Yousif M, Rachida S, Taukobong S, Ndlovu N, Iwu-Jaja C, Howard W, Moonsamy S, Mhlambi N, Gwala S, Levy JI, Andersen KG, Scheepers C, von Gottberg A, Wolter N, Bhiman JN, Amoako DG, Ismail A, Suchard M, McCarthy K. SARS-CoV-2 genomic surveillance in wastewater as a model for monitoring evolution of endemic viruses. Nat Commun [Internet]. 2023 Oct 10 [cited 2024 Jan 3];14(1):6325. Available from: https://pubmed.ncbi.nlm.nih.gov/37816740/

24. Martin-Vicente M, Mthiyane H, Jiménez-Sousa MA, Subramoney K, Hellferscee O, Wolter N, Walaza S, Fernández-Rodríguez A, Cohen C, von Gottberg A, Resino S, Martínez I, Treurnicht FK. TNFAIP3-interacting protein 1 polymorphisms and their association with symptomatic human respiratory syncytial virus infection and bronchiolitis in infants younger than one year from South Africa: A case-control study. Int J Infect Dis [Internet]. 2023 Nov 1 [cited 2024 Jan 3];136:107–10. Available from: https://pubmed.ncbi.nlm.nih.gov/37751795/

25. Mokaya J, Mellor KC, Murray GGR, Kalizang'oma A, Lekhuleni C, Zar HJ, Nicol MP, McGee L, Bentley SD, Lo SW, Dube F. Genomic epidemiology of *Streptococcus pneumoniae* serotype 16F lineages. Microb genomics [Internet]. 2023 Nov [cited 2024 Jan 3];9(11):001123. Available from: https://pubmed.ncbi.nlm.nih.gov/37917136/

26. Waterlow NR, Kleynhans J, Wolter N, Tempia S, Eggo RM, Hellferscee O, Lebina L, Martinson N, Wagner RG, Moyes J, von Gottberg A, Cohen C, Flasche S. Transient increased risk of influenza infection following RSV infection in South Africa: findings from the PHIRST study, South Africa, 2016-2018. BMC Med [Internet]. 2023 Nov 15 [cited 2024 Jan 3];21(1):441. Available from: https://pubmed.ncbi.nlm.nih.gov/37968614/

27. Moosa F, du Plessis M, Weigand MR, Peng Y, Mogale D, de Gouveia L, Nunes MC, Madhi SA, Zar HJ, Reubenson G, Ismail A, Tondella ML, Cohen C, Walaza S, von Gottberg A, Wolter N. Genomic characterisation of *Bordetella pertussis* in South Africa, 2015-2019. Microb Genomics [Internet]. 2023 Dec 1 [cited 2024 Jan 3];9(12). Available from: https://pubmed.ncbi.nlm.nih.gov/38117675/

28. Khan K, Lustig G, Römer C, Reedoy K, Jule Z, Karim F, Ganga Y, Bernstein M, Baig Z, Jackson L, Mahlangu B, Mnguni A, Nzimande A, Stock N, Kekana D, Ntozini B, van Deventer C, Marshall T, Manickchund N, Gosnell BI, Lessells RJ, Karim QA, Abdool Karim SS, Moosa MYS, de Oliveira T, von Gottberg A, Wolter N, Neher RA, Sigal A. Evolution and neutralization escape of the SARS-CoV-2 BA.2.86 subvariant. Nat Commun [Internet]. 2023 Dec 6 [cited 2024 Jan 3];14(1):8078. Available from: https://pubmed.ncbi.nlm.nih.gov/38057313/

29. Bents SJ, Viboud C, Grenfell BT, Hogan AB, Tempia S, von Gottberg A, Moyes J, Walaza S, Hansen C, Cohen C, Baker RE. Modeling the impact of COVID-19 nonpharmaceutical interventions on respiratory syncytial virus transmission in South Africa. Influenza Other Respi Viruses [Internet]. 2023 Dec 10 [cited 2024 Jan 3];17(12). Available from: https://pubmed.ncbi.nlm.nih.gov/38090227/

30. Wolter N, Walaza S, von Mollendorf C, von Gottberg A, Tempia S, McMorrow ML, Moyes J, Treurnicht F, Hellferscee O, Moleleki M, Makhasi M, Baute N, Cohen C. Association of HIV Exposure and HIV Infection With In-hospital Mortality Among Hospitalised Infants <1 Year of Age, South Africa, 2016-2018. J Pediatric Infect Dis Soc [Internet]. 2023 Dec 16 [cited 2024

Jan 3];12(12):646–51. Available from: https://pubmed.ncbi.nlm.nih.gov/37952237/

31. Cohen C, Kleynhans J, Moyes J, McMorrow ML, Treurnicht FK, Hellferscee O, Wolter N, Martinson NA, Kahn K, Lebina L, Mothlaoleng K, Wafawanaka F, Gómez-Olivé FX, Mkhencele T, Mathunjwa A, Carrim M, Mathee A, Piketh S, Language B, von Gottberg A, Tempia S. Incidence and transmission of respiratory syncytial virus in urban and rural South Africa, 2017-2018. Nat Commun [Internet]. 2024 Dec 1 [cited 2024 Apr 4];15(1):116. Available from: https://pubmed.ncbi.nlm.nih.gov/38167333/

32. Jassat W, Mudara C, Ozougwu L, Welch R, Arendse T, Masha M, Blumberg L, Kufa T, Puren A, Groome M, Govender N, Pisa P, Govender S, Sanne I, Brahmbhatt H, Parmley L, Wolmarans M, Rousseau P, Selikow A, Burgess M, Hankel L, Parker A, Cohen C. Trends in COVID-19 admissions and deaths among people living with HIV in South Africa: analysis of national surveillance data. lancet HIV [Internet]. 2024 Feb 1 [cited 2024 Apr 4];11(2):e96–105. Available from: https://pubmed.ncbi.nlm.nih.gov/38296365/

33. Lovelock T, du Plessis M, van der Westhuizen C, Janson JT, Lawrence C, Parker A, Pecoraro A, Prozesky H, von Gottberg A, Taljaard J. Non-toxigenic Corynebacterium diphtheriae endocarditis: A cluster of five cases. South African J Infect Dis [Internet]. 2024 Feb 21 [cited 2024 Apr 4];39(1):539. Available from: https://pubmed.ncbi.nlm.nih.gov/38444885/

34. Dall'Amico L, Kleynhans J, Gauvin L, Tizzoni M, Ozella L, Makhasi M, Wolter N, Language B, Wagner RG, Cohen C, Tempia S, Cattuto C. Estimating household contact matrices structure from easily collectable metadata. PLoS One [Internet]. 2024 Mar 14 [cited 2024 Apr 4];19(3): e0296810. Available from: https://pubmed.ncbi.nlm.nih.gov/38483886/

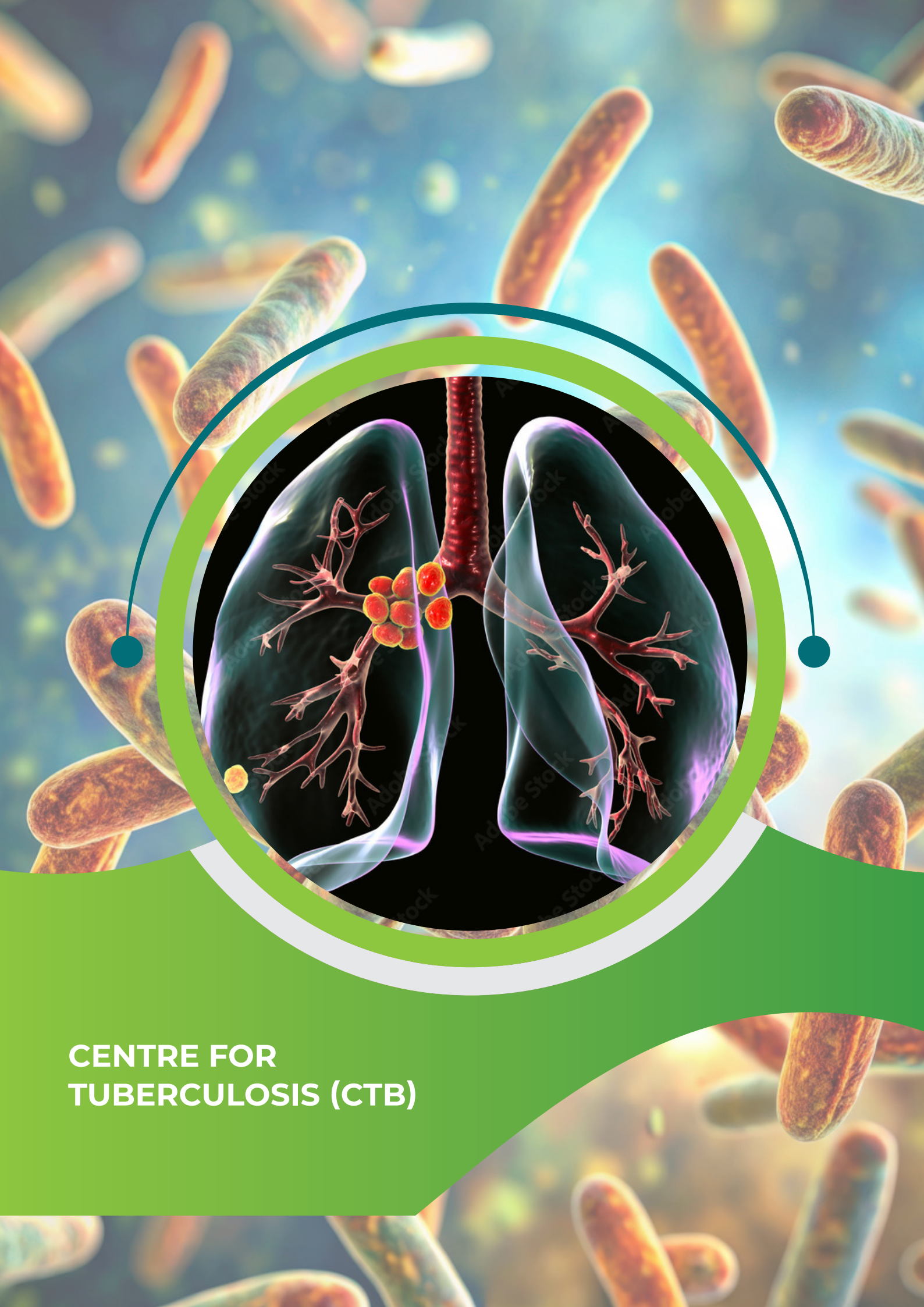
35. Deng S, Guo L, Cohen C, Meijer A, Moyes J, Pasittungkul S, Poovorawan Y, Teirlinck A, van Boven M, Wanlapakorn N, Wolter N, Paget J, Nair H, Li Y, von Gottberg A, Aerssens J, Ispas G, Ahani B, Atwell J, Begier E, Htar TT, Bangert M, Kramer R, Vernhes C, Beutels P, Bont L, Campbell H, Osei-Yeboah R, Wang X, Cohen R, Dos Santos G, Last T, Kumar V, Machin N, Nohynek H, Openshaw P, Pollard A. Impact of Subgroup Distribution on Seasonality of Human Respiratory Syncytial Virus: A Global Systematic Analysis. J Infect Dis [Internet]. 2024 Mar 15 [cited 2024 Apr 5];229(Supplement_1):S25–33. Available from: https://pubmed.ncbi.nlm.nih.gov/37249267/

36. Karim F, Riou C, Bernstein M, Jule Z, Lustig G, van Graan S, Keeton RS, Upton JL, Ganga Y, Khan K, Reedoy K, Mazibuko M, Govender K, Thambu K, Ngcobo N, Venter E, Makhado Z, Hanekom W, von Gottberg A, Hoque M, Karim QA, Abdool Karim SS, Manickchund N, Magula N, Gosnell BI, Lessells RJ, Moore PL, Burgers WA, de Oliveira T, Moosa MYS, Sigal A. Clearance of persistent SARS-CoV-2 associates with increased neutralizing antibodies in advanced HIV disease post-ART initiation. Nat Commun [Internet]. 2024 Mar 15 [cited 2024 Apr 5];15(1):2360. Available from: https://pubmed.ncbi.nlm.nih.gov/38491050/

37. Cohen C, Kleynhans J, von Gottberg A, McMorrow ML, Wolter N, Bhiman JN, Moyes J, du Plessis M, Carrim M, Buys A, Martinson NA, Kahn K, Tollman S, Lebina L, Wafawanaka F, du Toit J, Gómez-Olivé FX, Dawood FS, Mkhencele T, Tempia S. Characteristics of infections with ancestral, Beta and Delta variants of SARS-CoV-2 in the PHIRST-C community cohort study, South Africa, 2020-2021. BMC Infect Dis [Internet]. 2024 Mar 21 [cited 2024 Apr 4];24(1):336. Available from: https://pubmed.ncbi.nlm.nih.gov/38515050/

Conferences

Conferences: 39 presentations



CENTRE FOR TUBERCULOSIS (CTB)

DR SHAHEED VALLY OMAR
Centre Head

CENTRE FOR TUBERCULOSIS (CTB)

"The WHO Prequalification Unit has designated the Centre for Tuberculosis as the first tuberculosis laboratory for performance evaluation in connection with WHO prequalification of in vitro diagnostics."

BACKGROUND

The Centre for Tuberculosis' (CTB) core functions are 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 World Health Organization (WHO) TB Supranational Reference Laboratory network for the Sub-Saharan region. The Centre has made significant contributions toward both National and Global TB policies and guidelines in collaboration with the National Department of Health (NDoH) and WHO.

For the year under review, CTB provided critical support for the National TB Programmeme including supporting the development of the National Strategic Plan for HIV, TB and STIs 2023-2028, the National TB Programmeme's TB Strategic Plan 2023-2028, the TB Recovery Plan, and revision of the National TB diagnostic algorithms.

The WHO Prequalification Unit has designated the Centre for Tuberculosis as the first tuberculosis laboratory for performance evaluation in connection with WHO prequalification of in vitro diagnostics. This listing, effective 20 April 2023, marks a significant milestone in global efforts to enhance tuberculosis diagnostics.

SURVEILLANCE

During the year under review, the CTB continued and refined its laboratory-based TB surveillance programmes. The CTB continued to issue weekly results for action (RfA) reports, covering both drug-susceptible and drug-resistant TB to assist TB programmeme managers and facilities in tracking, tracing and linking people into care and treatment. Our automated quarterly surveillance reports of the number of TB patients diagnosed with laboratory-confirmed pulmonary TB were updated to include the GeneXpert MTB/XDR and the BD Max MDR-TB assays which were implemented by the NHLS during the course of the year. Furthermore, linkages between laboratory-confirmed rifampicin-resistant pulmonary TB cases and the Electronic Drug-Resistant Tuberculosis Register (EDRWeb) were implemented to facilitate linkage to care for patients with drug-resistant TB (DR-TB). The CTB continued to provide monthly reports assessing the implementation of the SMS notification system for TB-nucleic acid amplification tests (TB-NAAT) as part of the National TB Recovery Plan.

With support from the Global Fund, enhanced TB surveillance reports were disseminated for 12 priority TB districts to support the targeting of local interventions to improve the TB programmeme. The enhanced reports include detailed facility-level epidemiological, geospatial, and trajectory analyses.

The CTB led the analyses of the 12 benchmarks contained in the WHO Standard: Universal Access to Rapid TB Diagnostics for South Africa. The results were presented at the EndTB Summit in Paris in November 2023.

The CTB collaborated with the National Health Hotline to develop a TB call centre campaign to support people with laboratory-confirmed TB to access care and treatment. Unfortunately, the TB call centre campaign was terminated in early 2024 due to funding constraints.

ANALYSIS OF BEDAQUILINE RESISTANCE IN SOUTH AFRICA

Bedaquiline (BDQ), the first new TB drug in 40 years (28 December 2012) received accelerated FDA approval for use to treat drug-resistant TB and was first introduced in South Africa as part of the BDQ Compassionate Use Access Programme in March 2013. This drug has become a core drug in most drug-resistant TB regimens.

The CTB, in collaboration with the National TB Programmeme (NTP), analysed BDQ, and fluoroquinolone (FLQ) resistance data from July 2019 to November 2023, utilising routine National Health Laboratory Service (NHLS) data. Following the release of new DR-TB reflex testing guidelines in March 2023, there was a notable surge in national BDQ phenotypic drug susceptibility testing (pDST) volumes, with varying provincial coverage. Implementation of the new guidelines revealed a higher number of BDQ-resistant FLQ-susceptible (BDQ-R, FLQ-S) TB cases compared to BDQ-R FLQ-resistant (XDR-TB) cases in certain months, underscoring the significance of the new testing approach.

The prevalence of BDQ-resistant TB has risen from 3.8% to 6.5% across three Provinces, notably driven by a substantial increase in the Western Cape to 10.2%, compared to the previous cross-sectional study conducted in 2014-2019. To address these findings, the NTP is strategising to mitigate high loss-to-follow-up (LTFU) rates on TB treatment, prioritising areas with the highest LTFU rates and those on BDQ-containing regimens. Additionally, the CTB is devising an implementation plan for targeted next-generation sequencing for BDQ to reduce TAT for BDQ-resistant tests. Simultaneously, the National Clinical Advisory Committee (NCAC) is reviewing potential treatment regimens for patients with BDQ-R FLQ-S TB, with ongoing collaborations with researchers for clinical trials of BDQ-free regimens.

GERMS SURVEILLANCE

The TB section of the GERMS surveillance focuses on participants with rifampicin-susceptible TB diagnosed at hospitals to detect isoniazid (INH) mono resistance and monitor the relative contribution of HIV/ART and TB preventative therapy (TPT). Surveillance was expanded to include hospitals in seven Provinces (previously five). We have completed five years of surveillance (2018-2023). 1,549 Samples were successfully processed, with the majority from Gauteng (36%). There were more male (56%) samples than female samples. Sixty-eight percent of the participants were HIV positive, 63% were on ART and only 3% were on TPT. Seventy-five percent of sputum samples were smear positive and INH resistance was detected in 140 samples (9%), with the highest proportion from the North West Province (31%).

POLICY CONTRIBUTIONS

NATIONAL POLICY

- Clinical Management of Rifampicin Resistant TB: Updated Clinical Reference GuidePrimary Care Management of Rifampicin-Resistant Tuberculosis National Clinical
- Management Training Participant Manual
- National TB Diagnostic Algorithm
- Paediatric TB Diagnostic Algorithm
- National TB Recovery Plan

INTERNATIONAL POLICY

- WHO Consolidated guidelines on tuberculosis: Module 3: diagnosis: rapid diagnostics for tuberculosis detection
- WHO Operational handbook on tuberculosis: Module 3: diagnosis: rapid diagnostics for tuberculosis detection
- WHO Policy statement: Critical concentrations for pretomanid and cycloserine
- Technical manual for culture-based drug susceptibility testing of anti-tuberculosis drugs used in the treatment of tuberculosis
- Dr Shaheed V Omar was nominated by the National TB Programmeme/National Department of Health to represent the directorate at the WHO EndTB Summit in Paris
- Dr Shaheed V Omar was selected to form part of the National TB Programmeme/ National Department of Health delegation to participate during the BRICS TB Summit under the thematic area TB diagnostics

DIAGNOSTIC SERVICES

SPECIALISED REFERENCE MYCOBACTERIOLOGY – NATIONAL AND WHO SUPRANATIONAL REFERENCE LABORATORY ACTIVITIES

Proficiency testing panels for second-line drugs susceptibility testing (including BDQ and Linezolid (LZD)) were prepared by the Centre and sent to the NHLS laboratories performing DR-TB Reflex testing. An extended drug susceptibility testing is provided for all patients not responding to their drug resistant TB regimen. Phenotypic drug susceptibility testing for BDQ and LZD are provided for the private laboratories. We commenced the validation of Pretomanid as per WHO recommended critical concentrations. Drug susceptibility testing for non-tuberculous mycobacteria is also provided on request from clinicians and or pathologists. Testing of clinical isolates will commence in the new financial year.

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.

The laboratory has been designated as the central laboratory for genomics supporting the Bill and Melinda Gates Medical Research Institute for the PAN-TB clinical trial as well as the Otsuka Pharmaceutical Development and Commercialization OPC-167832 clinical trial.

ADVANCING DIAGNOSTICS, EPIDEMIOLOGY AND TREATMENT

As part of the Advancing Diagnostics, Epidemiology and Treatment function of the CTB, several new cutting-edge diagnostic technologies were evaluated during this period, which include targeted next-generation sequencing technologies for predicting drug resistance. The CTB has been instrumental in the implementation of the GeneXpert MTB/XDR assay which aims to significantly improve the turnaround time to detection of drug-resistant tuberculosis, thereby providing comprehensive information for the adequate clinical management of patients. The CTB has been listed as the first Performance Evaluation Laboratory (PEL) for the evaluation of TB-NAAT 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: Farzana Ismail, Shaheed V Omar, Halima Said, Lavania Joseph, Harry Moultrie, Judith Mwansa, Elizabeth 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 targeted 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 5 and a total of 1,349 Rifampicin-resistant samples were collected between April 2023 and March 2024; 932 (69.0%) from the City of Cape Town and 417 (30.9%) from the City of Johannesburg. The primary findings of the proportion of BDQ resistance prompted the investigation of national data and provided a basis for the national BDQ testing. Results were presented to the NDoH and WHO.

Bedaquiline, Pretomanid, and Linezolid Resistance Emergence in Drug-resistant TB Treatment in South Africa (B-Prepared study)

NICD Investigators: Shaheed Vally Omar; Lavania Joseph, Farzana Ismail

Collaborators: Columbia University, Emory University, Albert Einstein College of Medicine

Bedaquiline (BDQ) and pretomanid (Pa) are medications from the first novel TB drug classes created since 1968. Combined with a repurposed medication, linezolid (LZD), these new drugs have provided substantial improvements in survival and cure rates. The emergence of widespread BDQ, Pa or LZD resistance could undermine these drugs' potential. In the study, we will examine the emergence of BDQ, Pa, and LZD resistance in South Africa as treatment with these new drugs is expanded to all drug-resistant TB cases. Samples will be processed for MICs to each of the three drugs and whole genome sequencing. Three hundred and forty-eight samples have been included into the study.

Pan-Africa Network for Genomic Surveillance of Poverty Related Disease and Emerging Pathogens

NICD Investigator: Shaheed V Omar, Harry Moultrie, Lavania Joseph, Halima Said, Farzana Ismail, Thabisile Gwala

Collaborators: PanGens Consortium

The main purpose of this project is to increase Africa's capacity in genomic epidemiology and to conduct genomic epidemiology of drug-resistant tuberculosis and malaria across 12 African countries. The capacity building strategy will include engagement of post-docs, conducting of on-site workshops and development of free training virtual materials. The initiative will expand south-south research collaborations, train the next generation of African scientists with cutting-edge techniques, and develop advances in disease surveillance, contributing to the African Union Agenda. The Pan-Africa Network For Genomic Surveillance Of Poverty Related Disease And Emerging Pathogens is part of the EDCTP3 Programmeme and supported by the European Union.

DriveDx4TB: Accelerating the Introduction of Novel TB Diagnostics

NICD Investigators: Shaheed Vally Omar, Thabisile Gwala, Lavania Joseph, Dumisani Ngcamu and Mamello Motsei

Collaborator: Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland

FIND, the global alliance for diagnostics, and Unitaid recently signed a new US$15.9 million grant to accelerate the introduction of new TB diagnostics, to address access barriers and improve case detection at primary healthcare and community levels. The Drive Diagnostics for Tuberculosis (DriveDx4TB) project is harnessing the power of collaboration to increase TB testing options in primary care clinics and community settings. By working with local communities, as well as manufacturers, in-country partners and the global health organisation Unitaid, DriveDx4TB aims to accelerate the development and implementation of next-generation TB diagnostics. The CTB participated in a closed request for proposals to participate in this activity and after a rigorous peer review assessment, were selected as the most suitable lab to perform the feasibility testing, through laboratory evaluations of the selected diagnostic tools that would influence decision-making on diagnostic projects which would be further evaluated in clinical setting in other project countries.

Pretomanid Resistance Surveillance Programmeme

NICD Investigators: Shaheed V Omar & Farzana 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 five-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 five-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 CTB has successfully submitted year 3 data during this reporting period. Testing of year four samples is in progress.

Calibration of Antimicrobial Susceptibility Testing Methods and Breakpoints Against EUCAST Reference Standards for Bedaquiline, Clofazimine, Levofloxacin, and Linezolid

NICD Investigators: Shaheed Vally Omar, Dumisani Ngcamu, Mamello Motsei & Lavania Joseph

Collaborator: The European Committee on Antimicrobial Susceptibility Testing

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 mycobacteria growth indicator tube (MGIT). During this period, we have completed the pilot and phase 1 components of the study, the final phase is currently in progress.

Molecular, Clinical, and Phenotypic Monitoring of Bedaquiline Resistance in Drug-resistant Tuberculosis in South Africa

NICD Investigators: Shaheed Vally Omar & Lavania 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 prevalence of BDQ resistance following the increased uptake of the drug in the high burden districts in South Africa. Whole genome sequencing and bioinformatics analysis was completed for 2,048 isolates from six high-burden districts across three Provinces in South Africa. Minimum inhibitory concentration (MIC) testing is in progress for isolates harbouring a mutation in any BDQ resistance associated gene.

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: Shaheed Vally Omar & Lavania 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 182 participants meeting the eligibility criteria for the study have been processed using tNGS and drug resistance reports submitted to the clinic for further follow up.

First Insights into Circulating Pre-XDR Mycobacterium Tuberculosis in Four Provinces of South Africa

NICD Investigators: Halima Said, Shaheed V Omar, Farzana Ismail, Lavania Joseph, John Nortje

Collaborator: University of the Witwatersrand, South Africa

A better understanding of drug resistance conferring mutations associated with resistance and transmission of drug resistant strains harbouring these mutations, in particular resistance to FQs and new MDR-TB drugs such as bedaquiline (BDQ), in South Africa is crucial. Using whole genome sequencing, we aimed to investigate the prevalent mutations conferring pre-XDR-MTB strains in four Provinces (Limpopo, North West, Mpumalanga, and Free State) of South Africa over a five-year period (2019–2023) and assess the transmission patterns to understand the circulating strains and transmission clusters.

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, medical microbiology registrars, and epidemiology and biostatistics master's students at the University of Pretoria and post-graduate students at the University of Witwatersrand. Several post-graduate students were hosted at the CTB to be trained and performed advanced testing which supported their research. The CTB has taken responsibility for co-ordination of the NICD three-week Communicable Diseases Rotation. Regional training support was provided for Namibia, Zambia, Somalia, and Ethiopia.

The CTB supported the National and Provincial departments training on drug-resistant TB. Training provided for PhD students from the Medical Research Council/University of Pretoria.

PROFESSIONAL DEVELOPMENT

Post-graduate Supervision

- 2 PhD, 6 MSc and 2 Honours students.

Intern Medical Scientist training

- 3 Intern Medical Scientists graduated and 1 in training.

RESEARCH OUTPUT

1. Aguiar Soares K, Ehrlich J, Camará M, et al. Implementation of WHO guidelines on urine lateral flow LAM testing in high TB/HIV burden African countries. Eur Respir J. 2023 Oct 19;62(4):2300556. doi: 10.1183/13993003.00556-2023.
2. Bingham J, Tempia S, Moultrie H, Viboud C et al. Estimating the time-varying reproduction number for COVID-19 in South Africa during the first four waves using multiple measures of incidence for public and private sectors across four waves. PLoS One. 2023 Sep 22;18(9):e0287026. doi: 10.1371/journal.pone.0287026.
3. Branigan D, Denkinger CM, Furin J et al. Diagnostics to support the scaling up of shorter, safer tuberculosis regimens. Lancet Microbe. 2023 Oct;4(10):e758-e760. doi: 10.1016/S2666-5247(23)00217-3.
4. Brown TS, Tang L, Omar SV et al.. Genotype-Phenotype Characterisation of Serial Mycobacterium tuberculosis Isolates in Bedaquiline-Resistant Tuberculosis. Clin Infect Dis. 2024 Feb 17;78(2):269-276. doi: 10.1093/cid/ciad596.
5. CRyPTIC Consortium. Quantitative measurement of antibiotic resistance in Mycobacterium tuberculosis reveals genetic determinants of resistance and susceptibility in a target gene approach. Nat Commun. 2024 Jan 12;15(1):488. doi: 10.1038/s41467-023-44325-5.
6. Dheda K, Mirzayev F, Cirillo DM, Udwadia Z et al. Multidrug-resistant tuberculosis. Nat Rev Dis Primers. 2024 Mar 24;10(1):22. doi: 10.1038/s41572-024-00504-2.
7. Ghebrekristos YT, Beylis N, Centner CM, Venter R et al. Xpert MTB/RIF Ultra on contaminated liquid cultures for tuberculosis and rifampicin-resistance detection: a diagnostic accuracy evaluation. Lancet Microbe. 2023 Oct;4(10):e822-e829. doi: 10.1016/S2666-5247(23)00169-6.
8. Hamada Y, Quartagno M, Law I et al. Association of diabetes, smoking, and alcohol use with subclinical-to-symptomatic spectrum of tuberculosis in 16 countries: an individual participant data meta-analysis of national tuberculosis prevalence surveys. EClinicalMedicine. 2023 Aug 30;63:102191. doi: 10.1016/j.eclinm.2023.102191.
9. Hamada Y, Quartagno M, Law I, Malik F, Bonsu FA, Adetifa IMO, Adusi-Poku Y, D'Alessandro U, Bashorun AO, Begum V, Lolong DB, Boldoo T, Dlamini T, Donkor S, Dwihardiani B, Egwaga

S, Farid MN, Garfin AMCG, Gaviola DMG et al. Tobacco smoking clusters in households affected by tuberculosis in an individual participant data meta-analysis of national tuberculosis prevalence surveys: Time for household-wide interventions? PLOS Glob Public Health. 2024 Feb 29;4(2):e0002596. doi: 10.1371/journal.pgph.0002596.

10. Jamieson L, Van Schalkwyk C, Nichols BE et al. Differential in-hospital mortality and intensive care treatment over time: Informing hospital pathways for modelling COVID-19 in South Africa. PLOS Glob Public Health. 2023 May 17;3(5):e0001073. doi: 10.1371/journal.pgph.0001073.

11. Meyer-Rath G, Hounsell RA, Pulliam JR, Jamieson L, Nichols BE, Moultrie H, Silal SP. The role of modelling and analytics in South African COVID-19 planning and budgeting. PLOS Glob Public Health. 2023 Jul 3;3(7):e0001063. doi: 10.1371/journal.pgph.0001063.

12. Naidoo K, Perumal R, Cox H et al.. The epidemiology, transmission, diagnosis, and management of drug-resistant tuberculosis-lessons from the South African experience. Lancet Infect Dis. 2024 Mar 22:S1473-3099(24)00144-0. doi: 10.1016/S1473-3099(24)00144-0.

13. Ngcelwane M, Omar SV, Said M et al. New Horizons in the Diagnosis of Tuberculosis of the Spine: The Role of Whole Genome Sequencing. Asian Spine J. 2023 Jun;17(3):511-517. doi: 10.31616/asj.2022.0247.

14. Rambaran S, Maseko TG, Lewis L et al. Blood monocyte and dendritic cell profiles among people living with HIV with Mycobacterium tuberculosis co-infection. BMC Immunol. 2023 Jul 21;24(1):21. doi: 10.1186/s12865-023-00558-z.

15. Reta MA, Said HM, Maningi NE et al. Genetic diversity of Mycobacterium tuberculosis strains isolated from spiritual holy water site attendees in Northwest Ethiopia. A cross-sectional study. New Microbes New Infect. 2024 Mar 8;59:101235. doi: 10.1016/j.nmni.2024.101235.

16. Rupasinghe P, Reenaers R, Vereecken J et al. Refined understanding of the impact of the Mycobacterium tuberculosis complex diversity on the intrinsic susceptibility to pretomanid. Microbiol Spectr. 2024 Mar 5;12(3):e0007024. doi: 10.1128/spectrum.00070-24.

17. Said H, Kachingwe E, Gardee Y et al.. Determining the risk-factors for molecular clustering of drug-resistant tuberculosis in South Africa. BMC Public Health. 2023 Nov 24;23(1):2329. doi: 10.1186/s12889-023-17234-x.

18. Scott LE, Shapiro AN, Da Silva MP et al. Integrating Molecular Diagnostics and GIS Mapping: A Multidisciplinary Approach to Understanding Tuberculosis Disease Dynamics in South Africa Using Xpert MTB/RIF. Diagnostics (Basel). 2023 Oct 10;13(20):3163. doi: 10.3390/diagnostics13203163.

19. Shapiro AN, Scott L, Moultrie H et al. Tuberculosis testing patterns in South Africa to identify groups that would benefit from increased investigation. Sci Rep. 2023 Nov 27;13(1):20875. doi: 10.1038/s41598-023-47148-y.

20. Silal SP, Pulliam JRC, Meyer-Rath G et al. The National COVID-19 Epi Model (NCEM): Estimating cases, admissions and deaths for the first wave of COVID-19 in South Africa. PLOS Glob Public Health. 2023 Apr 24;3(4):e0001070. doi: 10.1371/journal.pgph.0001070.

21. Sonnenkalb L, Carter JJ, Spitaleri A et al. Comprehensive Resistance Prediction for Tuberculosis: an International Consortium. Bedaquiline and clofazimine resistance in Mycobacterium tuberculosis: an in-vitro and in-silico data analysis. Lancet Microbe. 2023 May;4(5):e358-e368. doi: 10.1016/S2666-5247(23)00002-2.

WORLD TB DAY ACTIVITIES

The Centre participated in the National Department of Health's World TB Day – TB Symposium by invitation from the Minister of Health, Dr J Phaahla, on BPaL-L and the emergence of Bedaquiline resistance, held at the Radisson Blu Hotel in Sandton on 23 March 2024.

Dr Shaheed V Omar and Dr Harry Moultrie were invited speakers to provide an update of the emergence of Bedaquiline Resistance based on our laboratory surveillance of TB drug resistance. The symposium further provided the impact this may have on the clinical management of drug-resistant TB as well as identifying mitigating interventions to address the emergence of resistance.

ACKNOWLEDGEMENTS

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

Centre for Tuberculosis 2024

CENTRE FOR VACCINES AND IMMUNOLOGY (CVI)

DR NISHI PRABDIAL-SING
Centre Head

CENTRE FOR VACCINES AND IMMUNOLOGY (CVI)

> *"The centre has made great strides in the reporting period to test for other vaccine-preventable viruses in our environmental surveillance."*

BACKGROUND

The CVI supports the NDoH with expert knowledge and expertise in the epidemiology and virology of vaccine-preventable viral diseases. Eradication of poliovirus is imminent and elimination of measles, rubella, and viral hepatitis is closer. Vigorous efforts from CVI testing and surveillance remain paramount to meet WHO targets.

The Centre has made great strides in the reporting period to test for other vaccine-preventable viruses in our environmental surveillance. Detection and sequencing of poliovirus and SARS-CoV-2 have been performed in wastewater. Research on whole genome sequencing for poliovirus, SARS-CoV-2, and viral hepatitis is continuing.

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, quantitative analyses and next-generation sequencing.

The measles outbreak declared from week 40 in 2022 in all Provinces in South Africa, except the Eastern Cape, still showed measles-positive cases during 2023-2024. From our review of the measles outbreak surveillance data reporting and factors affecting public health response in Limpopo Province, our findings indicated that hospitals had more measles cases notified on the Notifiable Medical Condition Surveillance System (NMCSS) compared to blood

samples sent to the laboratory for testing. PHCs reported fewer measles cases on the NMCSS than the cases that were consulted. Hospitals with IPC and EPI managers had better data compared to PHCs. The presence of a focal person in the facility substantially improved measles case reporting and CIF availability. From our support to Sub-Saharan African countries with the detection and sequencing of polioviruses in AFP cases and environmental surveillance samples, vaccine-derived polioviruses were detected in the region.

SURVEILLANCE

MEASLES/RUBELLA SURVEILLANCE

The Centre provides measles and rubella testing and surveillance as a WHO national and regional reference laboratory. Serological testing for these diseases and molecular testing for measles supports the measles and rubella strategic framework 2021-2030.

The Centre provides measles test positivity rates per Province, including population demographics and geographically mapped locations of the cases. 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.

After the measles outbreak in South Africa in 2022/2023, a total of 5,467 South African febrile rash samples were tested during the period under review, with 468 confirmed measles cases (8.56% positivity rate). The number of measles cases detected in 2023 decreased after the measles vaccine campaigns were rolled out in 2023 with a few measles sporadic cases and clusters seen currently.

About 1,265 Rubella cases, which constituted 23% of the total number of samples tested at the NICD, via febrile rash surveillance. The increase in rubella cases was reported in Western Cape, in the City of Cape Town, in November and later started spreading to other districts in the Province. Another increase in rubella cases was reported in the Pixley Ka Seme District in Northern Cape Province. Other Provinces reported a low number of rubella cases. South Africa has approved the use of measles-rubella-containing vaccines which will be available at public healthcare facilities. Rubella infections were reported in children aged 1-9 years with more than 800 children reported to be infected.

As part of the WHO regional quality assurance programmeme, 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. In the past year, 1,201 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 nine countries in the region for acute flaccid paralysis (AFP) surveillance: Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, Eswatini, Seychelles and South Africa, and nine countries for environmental surveillance, eight as above excluding Lesotho and including Zimbabwe. 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, 5,088 samples were processed for poliovirus isolation; 912 were from South Africa and 4,176 from the other eight countries. Between January and March 2024, the non-polio AFP detection rate in children under the age of 15 years in the country was 2.1/per 100,000 population, just above the WHO target of 2/100,000 but below the national target of 4/100,000. No polioviruses of programmematic importance were identified in South Africa. Vaccine-derived poliovirus type 1 (VDPV1) was identified in three cases from

Mozambique, and vaccine-derived poliovirus type 2 (VDPV2) was identified in two cases (one case from Mozambique and one other case from Angola) and five contacts from Mozambique. The date of onset for the recent VDPV2 in Angola is 14 February 2024, while the onset date for the VDPV2 in Mozambique is 28 September 2023.

For those countries that we provide a sequencing function, VDPV1 was identified in 121 samples: Democratic Republic of the Congo (73), and Madagascar (48). VDPV2 was identified in 202 samples from Burkina Faso (4), Burundi (2), Cote d'Ivoire (28), Mali (30), Democratic Republic of the Congo (106), Republic of South Sudan (10), Tanzania (11), Zambia (6) and Zimbabwe (5).

ENVIRONMENTAL SURVEILLANCE

During the period under review, 1,184 samples were processed for poliovirus isolation: 176 from South Africa and 1,008 from the other eight countries. Sabin viruses of types 1 or 3 were identified in four sites in three Provinces of South Africa and no polioviruses of programmematic importance were identified.

VDPV1 was detected in one site from Zimbabwe and VDPV2 was detected in three sites from Angola, three sites from Botswana and four sites from Zimbabwe.

Polio sequencing from other countries confirmed VDPV1 in 16 sites in Madagascar (n = 242), and VDPV2 in five sites in Burundi (n = 45), 11 sites in Cote d'Ivoire (n = 379), one site in Congo (n = 6), two sites in Liberia (n = 37), seven sites in Democratic Republic of the Congo (n = 38), two sites in Rwanda (n = 41), one site in Sierra Leone (n = 1), five sites in Tanzania (n = 49) and four sites in Zambia (n = 12).

ENVIRONMENTAL SURVEILLANCE FOR SARS-COV-2

The surveillance for SARS-CoV-2 continued in the period under review. A total of 2,053 wastewater samples were processed for SARS-CoV-2 surveillance from sites in Gauteng, Western Cape, Free State, KwaZulu-Natal, Eastern Cape, North West, Limpopo, Mpumalanga, and Northern Cape Provinces. SARS-CoV-2 was identified in 1,137 samples (55%) using optimised sensitive digital PCR assays. From the samples that tested positive, and were sequenced, 837 sequences were generated.

The programmeme is currently using Exatype software for quality checks and single nucleotide polymorphisms (SNPs). After this, four other tools are used for analysis as follows:

1. Mapping of reads to reference genome using BWA;
2. Sorting using Samtools;
3. SNP calling using iVar; and
4. Run Freyja demix using Freyja.

The sequencing has continued to highlight key events or changes in circulating variants, including the emergence of novel genotypes. Reports are compiled and shared with stakeholders every week on the NICD website.

TETANUS

The Centre collates and classifies tetanus cases reported through the NMC system. In the reporting period, 18 tetanus cases were reported in three districts, Capricorn District in Limpopo Province and two cases in Ehlanzeni District in Mpumalanga Province. Fourteen cases of tetanus were reported in adults and one case with age unknown. One death was reported in one of the adult cases. 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, April 1, 2023, and March 31, 2024, 2,570 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 Western Cape Province in the City of Cape Town, Cape Winelands, West Coast, and Garden Route districts. Sub-genotype IB was detected in the Western Cape region. Four other metros also reported an increased number of hepatitis A cases, the City of Johannesburg (198 cases), the City of Tshwane (339), Ekhurhuleni and eThekwini reported 189 cases. Both Provinces were alerted for a public health response.

HEPATITIS B

Between 1 April and 31 March 2024, national NHLS laboratories tested 1,140,243 cases for HBsAg, of which 40,394 (3.5%) tested positive. Of these, the majority (28,945, 71.66%) were among the age group of 25 to 49 years, and 115 cases (0.3%) were in children under one year old. Hepatitis B data was shared with the NDoH (in joint reporting format).

HEPATITIS C

From 1 April to 31 March 2024, 213,309 patients were tested for hepatitis C virus exposure with a hepatitis C antibody test. Of the 7,583 (3.6%) positive results, only 971 (12.8%) patients had a hepatitis C viral load test, of which 69.1% (671) were positive. The number of people with active hepatitis C infection has increased due to the inclusion of data from programmes of high-risk data. 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.

OUTBREAKS

Two measles clusters were detected recently (week one to week 9, 2024, with one in Gauteng Province where five children were affected in the City of Johannesburg and another cluster was reported in Steve Tshwete subdistricts in Mpumalanga, with seven laboratory-confirmed measles cases. Another measles outbreak was detected in Northern Cape Province in a childcare centre with two cases admitted to the hospital. No deaths were reported. Most of the children affected were aged 5-14 years. In all the reported clusters and outbreaks the Department of Health at the districts or subdistrict level intervened by implementing targeted vaccination campaigns.

RESEARCH ACTIVITIES

STRENGTHENING SURVEILLANCE FOR KEY VACCINE-PREVENTABLE DISEASES

NICD Investigators: Kerrigan McCarthy, Mukhlid Yousif, Nkosenhle Ndlovu, Emmanuel Phalane, Mokgaetji Macheke, Sipho Gwala, Natasha Singh, Thabo Mangena, Mantshali Motaung, Lebohang Rabotapi, Lethabo Monametsi, Fiona Els, Chenoa Sankar, Sibonginkosi Maposa

Key activities conducted included:

- Development of assays for the optimisation of detection of SARS-CoV-2, Influenza A and B, Hepatitis A and E, Measles and Rubella
- Compilation of the SOPs for the assays
- Development of a sample collection and handling SOP
- SOP for the training of field sample collectors

This research project is funded by the Bill and Melinda Gates Foundation (BMGF). The NICD co-funded all activities through the provision of key staff members, laboratory space some reagents and consumables, and courier services for samples processed at the NICD.

INTEGRATED ENVIRONMENTAL SURVEILLANCE IMPLEMENTATION IN SOUTH AFRICA

NICD Investigators: Mukhlid Yousif Kerrigan McCarthy, Nkosenhle Ndlovu, Emmanuel Phalane, Mokgaetji Macheke, Sipho Gwala, Natasha Singh, Thabo Mangena, Mantshali Motaung, Lebohang Rabotapi, Lethabo Monametsi, Fiona Els, Chenoa Sankar, Sibonginkosi Maposa.

Key achievements under this project include:

- Successful expansion of the wastewater epidemiology sentinel sites network. The programmeme has now grown to 44, spread across the whole country (Table 1 below). The sites that are monitored at least once a week. There are 24 sentinel and 20 sites that are part of closed catchments, following effluent to wastewater treatment works.

Table 1: *Wastewater surveillance programmeme sites in South Africa*

Provinces	Municipalities	Wastewater Treatment Plants (sites)
Eastern Cape	Nelson Mandela Bay Metropolitian Municipality	East Bank, Mdansane, Brickfield and KwaNobuhle
Free State	Mangaung Metropolitian Municipality	Sterkwater (Dewetsdorp Pad) and Bloemspruit
Gauteng	Johannesburg Metropolitian Municipality	Northern Works and Goudkoppies and six more in a closed catchment that includes Chris Hani Baragwanath Hospital and Bushkoppies Wastewater Treatment Works
	Ekurhuleni Metropolitian Municipality	Vlakplaats and Hartbeesfontein and seven more in a closed catchment that includes Tembisa Hospital, Midstream, Olifantsfontein Water Treatment Works and Tembisa Mall
	City of Tshwane Metropolitian Municipality	Rooiwal and seven more sites in a closed catchment that includes Dasport and Kalafong Hospital
KwaZulu-Natal	eTekwini Metropolitian Municipality	Northern and Central
	uMkhanyakude District Municipality	Jozini and Manguzi
Limpopo	Vhembe District Municipality	Musina (town) and Nancefield
Mpumalanga	Nkomazi Local Municipality	Komatipoort
	Mbombela Local Municipality (Silulumanzi concession)	Silulumanzi
North West	Mahikeng Local Municipality	Mahikeng and Mmabatho
	Rustenburg Local Municipality	Rustenburg and Boitekong
Northern Cape	Cape Town Metropolitian Municipality	Homevale
Western Cape	Sol Plaatjie Local Municipality	Borchards Quarry and Zandvliet

- Development of a public-facing dashboard sharing the results from routine testing. The dashboard is expected to go live, in early 2025.

ENVIRONMENTAL SURVEILLANCE ANALYTICS: VALIDATION, APPLICATION, AND INTERVENTIONS FOR PUBLIC HEALTH

NICD Investigators: Kerrigan McCarthy, Mukhlid Yousif, Fiona Els, Chenoa Sankar, Sibonginkosi Maposa

Collaborators: Gillian Maree (Gauteng City – Region Observatory), Prof. Kathleen O'Reilly (London School of Hygiene and Tropical Medicine)

This work is seeking to support comprehensive data collection to support the development of models to support the application of wastewater-based surveillance for public health. Notable achievements in the review period include:

- Knowledge products (a photo essay on wastewater-based epidemiology, conference presentations).
- A stakeholder meeting that included local municipalities to raise awareness and build consensus.
- Establishment of an international consortium of scientists, epidemiologists and modelling experts.

TEACHING AND TRAINING

- Undergraduate: GEMPII and PHII (viral hepatitis), medicine (medical immunology, vaccinology)
- Post-graduate: Registrar rotation, FETP, MSc, MMed, PhD, MPH
- Intern Scientists: Four intern scientists over this period

PROFESSIONAL DEVELOPMENT

- Postgraduate Students: Seven (2 MSc, 4 PhD, 1 FETP)
- Graduations: Three (1 MSc, 1 PhD, 1 Intern Scientist)

TEACHING AND TRAINING

JOURNAL ARTICLES

1. Moonsamy, S., Pillay, P. and Prabdial-Sing, N. September 2023. Hepatitis B infection status among South Africans attending public health facilities over five years: 2015 to 2019. PLOS Glob Public Health, 3 (9): e0000992.
2. Iwu-Jaja C, Ndlovu NL, Rachida S, Yousif M, Taukobong S, Macheke M, Mhlanga L, van Schalkwyk C, Pulliam JRC, Moultrie T, le Roux W, Schaefer L, Pocock G, Coetzee LZ, Mans J, Bux F, Pillay L, de Villiers D, du Toit AP, Jambo D, Gomba A, Groenink S, Madgewick N, van der Walt M, Mutshembele A, Berkowitz N, Suchard M, McCarthy K; SACCESS network. The role of wastewater-based epidemiology for SARS-CoV-2 in developing countries: Cumulative evidence from South Africa supports sentinel site surveillance to guide public health decision-making. Sci Total Environ. 2023 Jul 26;903:165817. doi: 10.1016/j.scitotenv.2023.165817. Epub ahead of print. PMID: 37506905.
3. Mukhlid Yousif, Said Rachida, Setshaba Taukobong, Nkosenhle Ndlovu, Chinwe Iwu-Jaja, Wayne Howard, Shelina Moonsamy, Nompilo Mhlambi, Sipho Gwala, Joshua I Levy, Kristian G Andersen, Cathrine Scheepers, Anne von Gottberg, Nicole Wolter, Jinal N Bhiman, Daniel Gyamfi Amoako, Arshad Ismail, Melinda Suchard, Kerrigan McCarthy. SARS-CoV-2 genomic surveillance in wastewater as a model for monitoring evolution of endemic viruses. Nat Commun 14, 6325 (2023). https://doi.org/10.1038/s41467-023-41369-5.
4. Shaw, A.G., Troman, C., Akello, J.O… McCarthy, K., Yousif, M. et al. Defining a research agenda for environmental wastewater surveillance of pathogens. Nat Med 29, 2155–2157 (2023). https://doi.org/10.1038/s41591-023-02457-7.

5. 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, April 2023.

6. Davlantes E, Greene SA, Tobolowsky FA, Biya O, Wiesen E, Abebe F, Weldetsadik MB, Eboh VA, Chisema MN, da Conceição Mário B, Tinuga F, Bobo PM, Chigodo CK, Sethy G, Hellström JM, Goundara AM, Burny ME, Mwale JC, Jorba J, Makua KS, Howard W, Seakamela L, Okiror S, Thompson A, Ali A, Samba D, Agbo C, Kabamba L, Kazoka A, Zomahoun DL, Manneh F, Abdelrahim K, Kamugisha C, Umar AS. Update on Wild Poliovirus Type 1 Outbreak - Southeastern Africa, 2021-2022. MMWR Morb Mortal Wkly Rep. 2023 Apr 14;72(15):391-397. doi: 10.15585/mmwr.mm7215a3. PMID: 37053125; PMCID: PMC10121257.

7. Morais A, Morais J, Felix M, Neto Z, Madaleno V, Umar AS, Panda N, Lemma F, Chivale JAL, Cavalcante DG, Davlantes E, Ghiselli M, Espinosa C, Whiteman A, Iber J, Henderson E, Bullard K, Jorba J , Burns CC, Diop O, Gumede N, Seakamela L, Howard W, Frawley A. Genetic and epidemiological description of an outbreak of circulating vaccine-derived poliovirus type 2 (cVDPV2) in Angola, 2019–2020, Vaccine, 2023.

COMMUNICABLE DISEASES COMMUNIQUÉ

1. Poliomyelitis Update, April 2023, Vol.22(4)
2. Measles In Limpopo, June 2023, Vol.22(6)
3. Hepatitis E, June 2023, Vol.22(6)
4. Hepatitis A, August 2023, Vol.22(8)
5. Hepatitis C Seroprevalence In South Africa, August 2023, Vol.22(8)
6. Review Of Measles Outbreak Surveillance Data Reporting And Factors Affecting Public Health Response In Limpopo Province - August 2023, September 2023, Vol.22(9).
7. Increase In Rubella (German Measles) Cases In Western Cape Province, October 2023, Vol.22(10)
8. Measles Rubella Surveillance, November 2023, Vol.22(11)

PRESENTATIONS

- International: 11
- National: 4

Poliovirus Intratypic Differentiation Workshop hosted by WHO, facilitated by WHO, CDC and NICD, from 5-9 June 2023.

DIVISION FOR PUBLIC HEALTH SURVEILLANCE AND RESPONSE (DPHSR)

DR SUSAN NZENZE
Centre Head

DIVISION FOR PUBLIC HEALTH SURVEILLANCE AND RESPONSE (DPHSR)

> *DPHSR was integral to the continued national and provincial response to the ongoing cholera outbreak, providing epidemiological expertise and maintaining data platforms to monitor trends in cases.*

BACKGROUND

The DPHSR plays a pivotal role in surveillance and response activities related to infectious disease threats in South Africa.

The DPHSR comprises the following units: the GERMS-SA surveillance programmeme (which is 21 years old this year), 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 units in conjunction with the NICD specialist centres' teams, contribute to national communicable disease surveillance, pandemic preparedness and response efforts through real-time alerts and notification of diseases of public health importance, as well as providing technical expertise to national, and 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 response to the ongoing cholera outbreak, 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. DPHSR played

a key role in managing outbreaks of other infectious diseases in response to other epidemics including benzene/benzine toxicity, conjunctivitis, diphtheria, 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. Through the NMC timeous alerts are issued and the public health response is initiated. Lastly, the GERMS-SA collaborates with NICD centres to provide a national active surveillance programmeme 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

In the last 20 years, NHLS microbiology laboratories and those in the private sector have participated in the GERMS-SA laboratory surveillance programmeme and sent specimens matching the GERMS-SA case definitions to NICD centres for further characterisation. Through the NHLS Corporate Data Warehouse, full case counts from NHLS laboratories are added to our GERMS-SA databases for all isolates matching our case definitions. This provides the minimum burden of disease for each pathogen, reflecting more than 30,000 cases over the last 20 years. At 30 sentinel public sector sites nationally, nurse surveillance officers enhance our surveillance by collecting 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 smaller site-specific studies with CHARM and CVI.

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 2024, there were 24,829 authorised users, the mean number of active users per month in 2023 was 368 compared to 279 in 2022. The number of active users in March 2024 was the same as in March 2023 (371), indicating some stability. In the year under review (2023), the NMC surveillance system received 165,595 notifications (excluding COVID-19), of which 23% (n= 38,869) were Category 1 NMC and 77% (n=123,726) were Category 1.

The most common Category 1 notifications were clinical and laboratory notifications of malaria cases (40%), followed by measles cases (18%), reflecting the ongoing measles outbreak. Common Category 2 notifications included pulmonary tuberculosis (55%), followed by extra-pulmonary tuberculosis (18%). 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 support the provincial departments of health with public health surveillance data management, analysis, report writing, and report dissemination. The Western Cape and North West PET, demonstrated the use of technology to improve disease surveillance by the development and publication of bespoke public health surveillance

dashboards. Routine surveillance dashboards (measles, malaria and TB notifications; HIV/TB Phuthuma weekly indicators) and outbreak response dashboards (mumps) were produced and published to inform and support public health action and decision-making. In Mpumalanga, the provincial epidemiologist assisted in threshold setting for Hepatitis A. 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 and communications support, and technical expertise to the NDoH and Provinces related to several outbreak preparedness and response activities of national importance, such as cholera, measles, mumps, *Wickerhamomyces anomalus* and several suspected foodborne disease outbreaks. In addition, the ORU continued its stellar work of co-ordinating the clinical hotline for infectious disease queries. The most significant development in the last year was the ORU being a significant stakeholder in the development of the national integrated disease surveillance and response strategy (IDSR) on behalf of the National Department of Health (NDoH). Additionally, the ORU adopted and adapted the Africa Centres for Disease Control and Prevention (Africa CDC) framework for EBS, again on behalf of the NDoH. This marked a significant step in the formalisation of a longstanding practice by the ORU to identify outbreaks at their infancy, and will form part of the overall IDSR strategy. To implement the media-monitoring component of EBS, the ORU was able to secure funding for additional staff capacity through the United States Centres for Disease Control and Prevention (US CDC).

ORU continues to interact with other public health agencies globally and are active members of the World Health Organization (WHO) Global Outbreak Alert and Response Network (GOARN).

The EOC continues 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. The EOC secured funding through the US CDC to strengthen current activities conducted by the EOC and to support 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. The NICD-EOC team plans to continue supporting the NDoH project towards the establishment of functional national and provincial PHEOCs and to further develop training material for a broader range of emergency management topics. Additionally, the EOC as a representation of ORU, participated in the National Pandemic Preparedness Planning Module One workshop for South Africa, hosted by WHO.

The PET provided technical support for local outbreak preparedness and response activities in the Provinces, including the mumps outbreak reported from two 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 mysterious disease outbreak in uThukela District, linked to Benzene/Benzine toxicity, Conjunctivitis outbreak in KwaZulu-Natal, Diphtheria in a prison in the Western Cape, and several foodborne illness outbreaks occurring in schools reported in the different Provinces.

POLICY CONTRIBUTIONS

The DPHSR contributed to the development and drafting of the national integrated disease surveillance and response strategy.

Ms Genevie Ntshoe was appointed as a member of the cholera task force responsible for reviewing and updating the national cholera guidance documents.

Dr Susan Nzenze, Ms Lehlohonolo Kumalo, Dr Ruvimbo Chingonzoh and Ms Janine Bezuidenhoudt were trained as trainers for the data2policy programmeme and are mentoring the second cohort of Data2Policy (D2P) participants which includes several staff from the DPHSR (Vanessa Quan, Susan Meiring, Genevie Ntshoe, Moipone Shonhiwa, Poncho Phafane, Zandile Nukeri and Zikhona Jojozi).

RESEARCH ACTIVITIES

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

A Review of Legal Instruments for Emergency Management and Outbreak Response in South Africa: NICD perspective

NICD Investigators: Nevashan Govender

Collaborators: Sayuri Pillay (University of Witwatersrand)

To discuss the development and the extent of the roles and responsibilities of existing ORU and the National EOC in South Africa. To identify gaps in the current outbreak response and EOC legal structure in South Africa. To ascertain if the ORU/ EOC at the NICD is legally mandated. In addition, to provide recommendations for the ideal Public Health Emergency Operation Centre (PHEOC) set-up, in terms of legislation, functions and others, for all the relevant stakeholders involved.

Burnout and mental health resilience among frontline workers providing Pandemic Response in South Africa NICD

NICD Investigators: Nevashan Govender

Collaborators: Inge Kleinhans (Sefako Makgatho Health Sciences University)

To describe the knowledge, attitudes and practices of frontline staff regarding burnout and mental health resilience as well as to provide a situational analysis that can inform policy and strengthen the overall wellness of employees within the workplace.

Prevalence and Distribution of Protozoal Enteropathogens in South Africa between 2016 and 2021

NICD Investigators: Nevashan Govender, Bhavani Moodley, Charlotte Sriruttan

Collaborators: Inge Kleinhans (Sefako Makgatho Health Sciences University)

A descriptive, retrospective and cross-sectional analysis of secondary data from the NHLS Corporate Data Warehouse (CDW). We assessed the prevalence and distribution of selected protozoal enteropathogens (*Cryptosporidium, Entamoeba histolytica* and *Giardia lamblia*) in public-health sector patients in South Africa from 2016 to 2021.

The Epidemic of Knowing: An Ethnographic Study of Biomedical Knowledge Production in the South African COVID-19 Epidemic

NICD Investigators: Nevashan Govender

Collaborators: Praveer Patel (University of Johannesburg)

To study how biomedical knowledge is being produced through the surveillance of the COVID-19 pandemic. To achieve this will look at how digital technology such as various COVID-19 dashboards and social media are used as tools for research and for

sharing knowledge as COVID-19 has emphasised the importance of digital technology.

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 post-graduates 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 a request basis, as well as on current infectious disease outbreaks such as national cholera webinars. Several staff were trained as trainers on WHO IDSR (NMC Surveillance officer, Provincial Epidemiologists and two ORU Epidemiologists); two ORU staff were trained on event-based surveillance by Africa CDC; and two ORU staff were trained on hotline co-ordination and operationalisation for event-based surveillance also by Africa CDC.

Two staff from the ORU assigned to EOC duties, made history as the first two fellows from South Africa to graduate from the prestigious Public Health Emergency Management Fellowship offered by the US CDC in Atlanta. Among 25 fellows from 17 countries, their presence in this diverse programmeme enriched the learning experience, fostering a global community of emerging experts in public health emergency management. This achievement marks a significant step forward for South Africa in the global public health stage, inspiring future participants and creating lasting impacts on emergency management in the country and beyond. Since returning to South Africa, they have assisted the NDoH project towards the establishment of provincial PHEOCs in Mpumalanga, KwaZulu-Natal, the Eastern Cape and Western Cape.

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

Twenty students are currently enrolled, comprising of the following:

- PhD in public Health (1)
- PhD in Public Health (Epidemiology) (1)
- PhD in Environmental Health (1)
- Master in Public Health: 1 Master in Business Administration
- MSc Epidemiology and Biostatistics: (1)
- MM Governance (1)
- Bachelor of Commerce in Project Management (2)
- Bachelor of Commerce in Public Administration (1)
- Bachelor of Arts in Environmental Health (1)
- Bachelor of Commerce in Project Management (1)
- Postgraduate Diploma in Public Health (3)
- Diploma in Public Health (2)
- Diploma in Business Administration (1)
- Diploma in TB and HIV management (1)
- Postgraduate Diploma in Public Health (1)

RESEARCH OUTPUT

Journal Articles

1. Ziad A Memish 1, Lucille Blumberg 2, Amal Saif Al-Maani 3, Rama Baru 4, Eve Dube 5, George F Gao 6, Daniel B Jernigan 7, Yee-Sin Leo 8, Joseph Sriyal Malik Peiris 9, Jakir Hossain

B Masud 10, Jodie McVernon 11, Justice Nonvignon 12, Folasade Tolulope Ogunsola 13, Helen Reese 14, Rana Muhammad Safdar 15, Kumnuan Ungchusak 16, Lothar H Wieler 17, David Heymann; Moving cholera vaccines ahead of the epidemic curve. Lancet. 2024 Jan 13;403(10422):127-129.doi: 10.1016/S0140-6736(23)02244-4. Epub 2023 Oct 17.

2. Francis B Kolo 1, Abiodun A Adesiyun 2, Folorunso O Fasina 1, Bernice N Harris 3, Jennifer Rossouw 4, Charles Byaruhanga 1, Hermanus De Wet Geyer 4, Lucille Blumberg 4, John Frean 4 5, Henriette van Heerden 1;Brucellosis Seropositivity Using Three Serological Tests and Associated Risk Factors in Abattoir Workers in Gauteng Province, South Africa, Pathogens. 2024 Jan 9;13(1):64.doi: 10.3390/pathogens13010064.

3. Jassat W, Mudara C, Ozougwu L, Welch R, Arendse T, Masha M, Blumberg L, Kufa T, Puren A, Groome M, Govender N, Pisa P, Govender S, Sanne I, Brahmbhatt H, Parmley L, Wolmarans M, Rousseau P, Selikow A, Burgess M, Hankel L, Parker A, Cohen C. Trends in COVID-19 admissions and deaths among people living with HIV in South Africa: analysis of national surveillance data; Lancet HIV. 2024 Feb;11(2):e96-e105. doi: 10.1016/S2352-3018(23)00266-7.

4. Collins Iwuji 1 2, Catherine E Martin 3, Diantha Pillay 3, Patience Shamu 3, Susan Nzenze 3, Mercy Murire 3, Laura Ashleigh Cox 3, Alec Miners 4, Carrie Llewellyn 5, Saiqa Mullick 3, Implementation preferences for the management of sexually transmitted infections in the South African health system: a discrete choice experiment; Sex Transm Infect, 2024 Jan 17;100(1):10-16. doi: 10.1136/sextrans-2023-055816.

5. James A Banaski Jr 1 2, Nevashan Govender 3, Michelle J Groome 3 4, Ryan Houser 1 5, Ashley Greiner 6, Sharanya Krishnan 7, Brenna Means 1 5, Ryan Remmel 1 8, Ileana Vélez Alvarado 1 5, Claire J Standley 1 9; Introducing www.epidemic-em.org: A collection of online resources and training materials for strengthening use of Emergency Operations Centers for epidemic response, Disaster Med Public Health Prep, 2024 Feb 23:1-16. doi: 10.1017/dmp.2024.36.

6. Maxwell Mabona 1 2 3, Thembekile Zwane 4, Jaishree Raman 5 6 7, Lazarus Kuonza 4, Babongile Mhlongo 8, Poncho Phafane 8 9; Evaluation of the malaria case surveillance system in KwaZulu-Natal Province, South Africa, 2022: a focus on DHIS2, Malar J, 2024 Feb 14;23(1):47. doi: 10.1186/s12936-024-04873-7. https://doi.org/10.1186/s12936-024-04873-7

7. Andrew C K Lee 1, Bjorn G Iversen 2, Sadaf Lynes 3, Jean-Claude Desenclos 4, Janine E Bezuidenhoudt 5, Gerd M Flodgren 2, Thidar Pyone 6, The state of integrated disease surveillance globally: synthesis report of a mixed methods study, Public Health, 2024 Mar:228:85-91. doi: 10.1016/j.puhe.2024.01.003. Epub 2024 Feb 9. https://doi.org/10.1016/j.puhe.2024.01.003

8. Sung Hee Ko 1, Pierce Radecki 1, Frida Belinky 1, Jinal N Bhiman 2 3, Susan Meiring 2, Jackie Kleynhans 2 4, Daniel Amoako 2 5, Vanessa Guerra Canedo 1, Margaret Lucas 1, Dikeledi Kekana 2, Neil Martinson 6 7, Limakatso Lebina 6, Josie Everatt 2, Stefano Tempia 2 4, Tatsiana Bylund 1, Reda Rawi 1, Peter D Kwong 1, Nicole Wolter 2 8, Anne von Gottberg 2 8, Cheryl Cohen 2 4, Eli A Boritz 1, Rapid Emergence and Evolution of SARS-CoV-2 Variants in Advanced HIV Infection, bioRxiv, 2024 Jan 6:2024.01.05.574420. doi: 10.1101/2024.01.05.574420.

9. Article Erratum: Investigation of two suspected diarrhoeal-illness outbreaks in Northern Cape and KwaZulu-Natal Provinces, South Africa, April–July 2013: The role of rotavirus has just been published and is available at the following link: https://sajid.co.za/index.php/sajid/article/view/597

10. Carter ED, Stewart DE, Rees EE, Bezuidenhoudt JE, Ng V, Lynes S, Desenclos JC, Pyone T, Lee ACK. Surveillance system integration: reporting the results of a global multicountry survey. Public

Health. 2024 Apr 10;231:31-38. doi: 10.1016/j.puhe.2024.03.004. Epub ahead of print. PMID: 38603977.

11. Lee ACK, Iversen BG, Lynes S, Desenclos JC, Bezuidenhoudt JE, Flodgren GM, Pyone T. The state of integrated disease surveillance globally: synthesis report of a mixed methods study. Public Health. 2024 Mar;228:85-91. doi: 10.1016/j.puhe.2024.01.003. Epub 2024 Feb 9. PMID: 38340506.

12. Moshibudi Poncho Phafane et al. Factors associated with mortality among laboratory-diagnosed drug-resistant tuberculosis patients on treatment, KwaZulu-Natal Province, 2017-2019. Pan African Medical Journal. 2024;47:181. [doi: 10.11604/pamj.2024.47.181.34571]

.

NATIONAL CANCER REGISTRY (NCR)

DR MAZVITA MUCHENGETI
Centre Head

NATIONAL CANCER REGISTRY (NCR)

"GLOBOCAN 2022 reports data from the national pathology registry which was scaled using the site and sex-specific percentages of microscopically verified cases obtained from the EPBCR. This is an important milestone in cancer surveillance in South Africa."

BACKGROUND

The National Cancer Registry (NCR) is responsible for cancer surveillance, which is the systemic collection, storage, analysis, interpretation, and reporting of cancer cases. National pathology-based cancer surveillance, childhood cancer surveillance and the implementation of population-based cancer registration are the primary roles of the NCR. Within the NHLS/NICD, the NCR is the only unit conducting non-communicable disease surveillance. The information provided by the national pathology-based cancer registry informs the prioritisation of cancers of public health importance by the National Department of Health.

With the maturation of the Ekurhuleni Population-based Cancer Registry (EPBCR), South Africa now has a robust urban population-based cancer registry which can be used to correct national pathology-based estimates. For the first time, cancer incidence statistics reported on the GLOBOCAN cancer statistics platform (https://gco.iarc.fr) no longer report data from neighbouring countries but actual South African data. GLOBOCAN 2022 reports data from the national pathology registry which was scaled using the site and sex-specific percentages of microscopically verified cases obtained from the EPBCR (2018-2021) and applied to the 2022 population. This is an important milestone in cancer surveillance in South Africa.

The NCR continued to provide technical support to the recently launched KZN PBCR. As one of three International Agency for Research in Cancer – Global Initiative for Cancer Registry Development (IARC-GICR), Collaborating Centres (now called Centres of Expertise) for Sub-Saharan Africa, the NCR has been supporting cancer registries within the continent by training them on record linkage for cervical cancer elimination and childhood cancer registration.

Dr Mazvita Muchengeti was appointed as Head of Department for the NCR from 1 April 2023, and Dr Judith Mwansa-Kambafwile as senior epidemiologist from 1 November 2023.

SURVEILLANCE

PATHOLOGY-BASED CANCER REGISTRY

In the year under review, both the 2021 and 2022 cancer incidence reports were published on the NCR website (https://www.nicd.ac.za/centres/national-cancer-registry/). In 2021, there was a slight increase of 0.8% in the number of cancer cases compared to 2020. This was the beginning of the recovery of the healthcare system from the effect of the 2020 COVID-19 pandemic lockdowns. Compared to 2021, there was an 11.7% increase in cancer cases reported in 2022. A further comparison of the pre-COVID pandemic numbers to the subsequent years shows an initial dip and then a peak in the number of cancer cases reported in 2022, surpassing the pre-COVID pandemic cases (87,321 in 2019 versus 89,589 in 2022). Data on cancers diagnosed in 2023 is currently being coded and cleaned. Due to the current austerity measures, the Data Manager post has remained unfilled since the 2022/2023 financial year.

EKURHULENI POPULATION-BASED CANCER REGISTRY (EPBCR)

This is the sixth year of population-based cancer registration in the Ekurhuleni metropolitan municipality, Gauteng Province. The published report includes cancers diagnosed between 1 January 1 and 31 December 2022. The overall case finding and data collection for 2022 was 4,116 (compared to 4,631 in 2021). There was an increase in the number of reported cancer cases from 2020 to 2021, indicating the restoration of cancer services and surveillance with the progressive relaxation of COVID-19 restrictions in 2021. However, the registry encountered some challenges in the period under review as reflected in the decrease in reported cases. These include delays in filling vacant surveillance officer posts due to prevailing cost-containment measures.

The most common cancers reported were prostate, colorectal, and lung cancers among males and breast, cervix, and colorectal cancers among females. Among children (0-14 years), the most common cancers were lymphomas, leukaemias and central nervous system cancers respectively. Retinoblastoma and nephroblastoma were the fourth most common cancers in children.

Funding for the six surveillance officer posts has run out. The contracts are being extended by a further six months at a time. Two surveillance officer posts are yet to be filled pending the outcome of the cost-containment evaluation. There is also a need for funding for surveillance officers at the KwaZulu-Natal PBCR. This presents a threat to the continuity of population-based cancer surveillance.

CHILDHOOD CANCER REGISTRY

The National Childhood Cancer Registry published its third report on childhood cancer incidence (0-14 years old) for the year 2020. A total of 1,043 cancers were diagnosed in children aged 0-14 years old in South Africa in 2020. This equated to an overall age-standardised rate of 62.4 cases per million (95%CI: 51.0-76.0). We found the most common cancer diagnosed in children to be leukaemia, and the second most common cancer was lymphoma. Approximately 40% of the cases (n=415) 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 hosted a Cancer Surveillance Workshop in August 2023 to review the current cancer surveillance status in South Africa, discuss challenges, and explore collaborative opportunities with key stakeholders. Dr Muchengeti and Mr Sizeka Mashele participated in stakeholder meetings on the adoption of the WHO cervical cancer elimination strategy for South Africa.

Dr Muchengeti and Dr Mwansa-Kambafwile are Technical Leads of the Surveillance and Data Analytics Technical Working Groups of the newly formed US-South Africa Cancer Care and Research Alliance (US-SACCRA). The first US-SACCRA TWG Leadership Meeting (Online Retreat) was held in the last quarter of the reporting period.

Dr Muchengeti was appointed to the Advisory Group to recommend priorities for the International Agency for Research in the Cancer Monographs during 2025-2029 and the National Advisory Group on Immunisation (NAGI) for Human Papillomavirus vaccination.

RESEARCH ACTIVITIES

South African HIV Cancer Match Study (SAM)

NCR Investigators: Natasha Abraham, Carole Metekoua, Tinashe Tombe-Nyahuma, Judith Mwansa-Kambafwile and Mazvita Muchengeti.

Collaborators: Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, Swiss Tropical and Public Health Institute, Allschwil, Switzerland, University of Basel, Basel, Switzerland, University of Witwatersrand, School of Public Health, South Africa.

Funders: International epidemiology databases to evaluate AIDS (IeDEA), National Institutes of Health, USA, Swiss National 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. Currently, the cohort is being updated to include data up to 2021. The linkage and deduplication of the HIV data and the NCR data are underway. The ethics renewal application is also in progress.

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

NCR Investigators: Mazvita Muchengeti, Wenlong Carl Chen.

Collaborators: Freddy Sitas, Debbie Bradshaw, Chris Mathews, Tim Waterboer, Gary Clifford, Melitah Motlhale, Mwiza Singini, Valerie McCormack.

Funders: South African Medical Research Council and the UK Government's Newton Fund through the UK Medical Research Council.

The JCS is a case-control study of newly diagnosed (< six months) black cancer patients (1995-2016), with over 26,000 patients interviewed and more than

20,000 blood samples stored to examine genetic and emerging and/or novel risk factors for cancer.

TEACHING AND TRAINING

The NCR continued to offer cancer surveillance lectures to students of the SAFETP programme and University of the Witwatersrand. The Centre also hosted undergraduate medical students from the University of Pretoria for three weeks in October 2023 as part of their programmeme to develop cancer research interest among medical students, done in partnership with the University of Utah. Public health medicine specialists also rotated through the Centre during their scheduled rotations at the NICD. The rest of the training activities are covered under the section below (IARC-GICR Centre of Expertise Sub-Saharan Africa).

The NCR, in collaboration with the Living with Cancer organisation, launched the first patient led cancer registry in South Africa on World Dancer Day 2024. During the period under review, the NCR held a prostate cancer awareness campaign and co-hosted a colorectal awareness event with the Global Colon Cancer Association. The NCR also supported the Breast Cancer Awareness Day hosted by the Pink Drive.

IARC-GICR CENTRE OF EXPERTISE FOR SUB-SAHARAN AFRICA

As part of the IARC-GICR Centre of expertise activities, the NCR conducted an in-person training for cervical cancer record linkage during the first quarter of the financial year. Fifteen participants from South Africa, Tanzania, Ethiopia, Kenya, Zimbabwe, Zambia and Nigeria were trained.

In the last quarter of the financial year, the NCR conducted an online training with 153 participants from across Sub-Saharan African countries and Europe. The NCR also hosted a virtual scientific writing workshop that was attended by 15 participants from seven Sub-Saharan countries.

PROFESSIONAL DEVELOPMENT

- **POST-GRADUATE STUDENTS:** There were five PhD and seven master's students in training in the period under review.
- **GRADUATIONS:** Five students graduated (1 PhD, 2 Masters,1 Honours and 1 Bachelors) in the period under review.

RESEARCH OUTPUT

Journal publications

1. Chiwambutsa SM, Ayeni O, Kapungu N, Kanji C, Thelingwani R, Chen WC, Mokone DH, O'Neil DS, Neugut AI, Jacobson JS, Ruff P, Cubasch H, Joffe M, Masimirembwa C.Effects of genetic polymorphisms of drug metabolizing enzymes and co-medications on tamoxifen metabolism in black South African women with breast cancer.Clin Pharmacol Ther. 2023.
2. Ruffieux Y, Muchengeti M, Olago V, Dhokotera T, Bohlius J, Egger M, Rohner E. Age and Cancer Incidence in 5.2 Million People With Human Immunodeficiency Virus (HIV): The South African HIV Cancer Match Study. Clin Infect Dis 2023
3. Sharma K, Machalek DA, Toh ZQ, Amenu D, Muchengeti M, Ndlovu AK, Mremi A, Mchome B, Vallely AJ, Denny L, Rees H, Garland SM. No woman left behind: achieving cervical cancer elimination among women living with HIV. Lancet HIV 2023
4. Metekoua C, Ruffieux Y, Olago V, Dhokotera T, Egger M, Bohlius J, Rohner E, Muchengeti M. Decreasing Incidence of Conjunctival Squamous Cell Carcinoma in People with HIV in South Africa. J Natl Cancer Inst. 2023.
5. Liu B, Abraham N, Chitsike I, Sylvie CGL, Kambugu J, Stévy NMA, et al. Enhancing information on stage at diagnosis for childhood cancer in Africa. Pediatr Blood Cancer. 2023. doi:10.1002/pbc.30555
6. Chen WC, Brandenburg JT, Choudhury A, Hayat M, Sengupta D, Swiel Y, Babb de Villiers C, Ferndale F, Aldous C, Soo CS, Lee S, Curtis

C, Newton R, Waterboer T, Sitas F, Bradshaw D, Abnet CC, Ramsay M, Parker MI, Singh E, Lewis CM, Mathew CG (2023) Genome-wide association study of oesophageal squamous cell cancer identifies shared and distinct risk variants in African and Chinese populations. The American Journal of Human Genetics, https://doi.org/10.1016/j.ajhg.2023.08.007

7. Dhokotera TG, Muchengeti M, Davidović M, Rohner E, Olago V, Egger M, Bohlius J. Gynaecologic and breast cancers in women living with HIV in South Africa: A record linkage study. Int J Cancer. 2023 Sep 8. doi: 10.1002/ijc.34712.. PMID: 37682630.

8. Engels EA, Shiels MS, Barnabas RV, Bohlius J, Brennan P, Castilho J, Chanock SJ, Clarke MA, Coghill AE, Combes JD, Dryden-Peterson S, D'Souza G, Gopal S, Jaquet A, Lurain K, Makinson A, Martin J, Muchengeti M, Newton R, Okuku F, Orem J, Palefsky JM, Ramaswami R, Robbins HA, Sigel K, Silver S, Suneja G, Yarchoan R, Clifford GM. State of the science and future directions for research on HIV and cancer: Summary of a joint workshop sponsored by IARC and NCI. Int J Cancer. 2023 Sep 15. doi: 10.1002/ijc.34727. PMID: 37715370.

9. Mapanga W, Ayeni OA, Chen WC, Jacobson JS, Neugut AI, Ruff P, Cubasch H, O'Neil DS, Buccimazza I, Čačala S, Stopforth LW, Farrow HA, Nietz S, Phakathi B, Chirwa T, McCormack VA, Joffe M. The South African breast cancer and HIV outcomes study: Profiling the cancer centres and cohort characteristics, diagnostic pathways, and treatment approaches. PLOS Glob Public Health. 2023 Oct 24;3(10):e0002432. doi: 10.1371/journal.pgph.0002432. PMID: 37874786; PMCID: PMC10597516.

10. Ramadhar A, Miller PN, Muchengeti M, Kagura J, Chu K, Gaskill C. Gastric cancer in Sub-Saharan Africa - a systematic review of primary data. Ecancermedicalscience. 2024 Mar 7;18:1680. doi: 10.3332/ecancer.2024.1680. PMID: 38566758; PMCID: PMC10984845.

11. Mashele SA, Zwane TB, Kuonza L, Muchengeti MM, Motsuku L. Risk factors for breast cancer among women in Ekurhuleni Metropolitan Municipality, Gauteng Province of South Africa, 2017-2020: a case-control study. Ecancermedicalscience. 2023 Aug 25;17:1593. doi: 10.3332/ecancer.2023.1593. PMID: 37799951; PMCID: PMC10550293.

12. Stuart KV, Shepherd DJ, Lombard A, Hollhumer R, Muchengeti M. Incidence and epidemiology of conjunctival squamous cell carcinoma in relation to the HIV epidemic in South Africa: a 25-year analysis of the National Cancer Registry (1994-2018). Br J Ophthalmol. 2024 Jan 29;108(2):175-180. doi: 10.1136/bjo-2022-322456. PMID: 36517211.

CONFERENCE PRESENTATIONS

Oral Presentations:

- Genome-wide association study identifies common variants associated with breast cancer in South African Black women. Authors: Hayat M, Chen WC, Ramsay M, Mathew CG, Brandenburg JT and ERICA-SA study. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023.Presenter: Brandenburg JT.
- A genome-wide association study of cervical cancer in the Black South African women. Authors: Kamiza A, Chen WC, Brandenburg JT, Ramsay M and Mathew CG. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023. Presenter: Kamiza A.
- Prevalence of monoclonal gammopathies detected by mass spectrometry and their risk factors among black Africans in Soweto, Johannesburg, South Africa. Authors: Lee D, Bertamini L, El-Khoury H, Chen WC, Marinac C and Ghobrial I. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023. Presenter: Lee D.
- Network for Oncology Research in Africa. Genetics and Biology of African Breast Cancer. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023. Presenter: WC Chen.

- Monitoring of cancer screening and prevention in Sub-Saharan Africa. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023. Presenter: M. Muchengeti
- The South African HIV Cancer Match Study. AORTIC Conference 2023, Dakar, Senegal. 2-6 November 2023. Presenter: M. Muchengeti
- London Global Cancer Week. AFCRN session. Monitoring cervical cancer screening and prevention 15 November 2023. Presenter: S.Mashele
- South African Society of Medical Oncology (SASMO) in collaboration with South African Stem Cell Transplant Society (SASCeTS) Conference. Cancer in People living with HIV. Plenary Session. March 2024. Presenter: M.Muchengeti
- UROGIN HPV conference, Sweden. March 2024. Screening and treatment for cervical precancer in People with HIV in LMICs. Presenter: M.Muchengeti

Poster Presentations

- Epidemiological risk factors for African Oesophageal-Squamous cell carcinoma in South Africa: A case-control comparison from the Johannesburg Cancer Study. Authors: Chen WC, Bradshaw D, Babb de Villiers C, Mathew CG, Muchengeti M and Sitas F. Presenter: Chen WC.
- Somatic mutation profiles in non-tobacco smoking and non-alcohol drinking South African Black female oesophageal-squamous cell carcinoma patients. Authors: Ferndale L, Chen WC, Mpangase P, Brandenburg JT, Aldous C and Mathew CG. Presenter: Ferndale L.
- Trends on hormone-related cancers by ethnicity: a report from the South African national cancer registry (1994 -2021) L Khoali, C Metekoua, P Kellett and M Muchengeti. Presenter: L.Khoali.
- NORA network in-person conference from 31 October to 2 November 2023 in Dakar, Senegal. Cervical cancer screening collaboration in Sub-Saharan Africa: insights from IARC-GICR centre, Johannesburg, 2022-2023. Sizeka Mashele.

NOTES

NOTES

NOTES

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

GET IN TOUCH

Physical Address
1 Modderfontein, Sandringham
Johannesburg, South Africa, 2192

Postal Address
Private Bag X8, Sandringham
2131 Johannesburg,
South Africa

Tel: (011) 386 6400
Fax: (011) 882 0596
www.nicd.ac.za

RP248/2024
ISBN: 978-1-77997-204-0