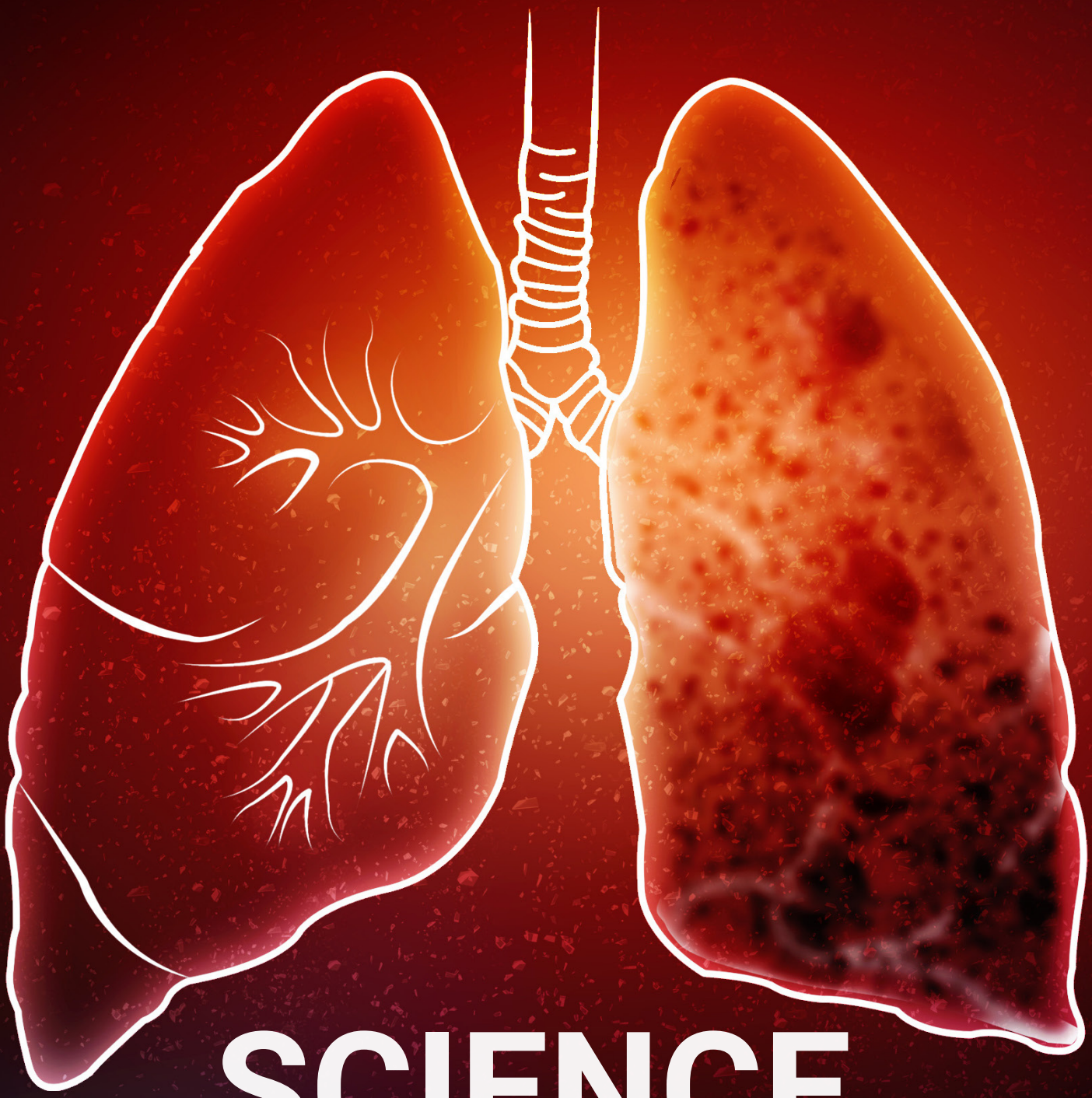
Issue 20 - March 2022

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



SCIENCE FOCUS

The Science Focus acknowledges NICD members of staff who have published in peer-reviewed journals. This publication is a compilation of scientific publications where an NICD staff member is either the first or last author.

Editor's Note

Significant research achievements from experts at the National Institute for Communicable Diseases (NICD) are highlighted in the Science Focus. Over and above notable statistical findings, the number of peer-reviewed articles produced, the top published authors and high impact factor score articles are also incorporated.

The edition starts with a collaboration between Drs Shaheed Vally Omar, Harry Moultrie and Farzana Ismail from the Centre for Tuberculosis. Their study assessed the epidemiological and genetic characteristics, and clinical outcomes of resistance to bedaquiline in patients treated for rifampicin-resistant tuberculosis. Interestingly the research revealed that bedaquiline resistance was associated with poorer treatment outcomes and that resistance could be prevented through novel combination therapies, current treatment optimisation and patient support.

The top published author for the quarter, Prof Nelesh Govender, starts off the edition with 'Global guideline for the diagnosis and management of rare yeast infections: an initiative of the ECMM in cooperation with ISHAM and ASM.' With rare or uncommon yeast infections on the rise, this insightful read points out key features of the epidemiology, diagnosis, antifungal susceptibility, and treatment outcomes of those infected with *Geotrichum* and *Saprochaete* infections.

Next, Prof Cheryl Cohen, a frequent research contributor and author, reveals findings from a population cohort study that involves risk factors associated with COVID-19 deaths among patients diagnosed with HIV and TB. In collaboration with the Western Cape Department of Health, nearly 3.5 million patients were included in the study that brought interesting findings to light and revealed that those living with HIV and tuberculosis were associated with increased COVID-19 mortality.

Drs Anthony Smith and Juno Thomas collaborated on a publication published in Emerging Infectious Diseases. Here they describe the molecular epidemiology of cholera in 'Emergence of *Vibrio cholerae* O1 Sequence Type 75, South Africa, 2018 - 2020.' Mrs Antoinette Grobbelaar, Dr Jacqueline Weyer and Prof Janusz Paweska conducted a survey around mammarenaviruses of rodents in South Africa and Zimbabwe. Over 5,000 rodents of 33 species were collected (for unrelated purposes) for 30 years between 1964 and 1994, and where then surveyed for group-specific indirect immunofluorescence antibody to mammarenaviruses.

Celebrated author, Mark Twain said that it is wiser to find out than to suppose. Kudos to the NICD researchers who continue to push the envelope for the sake of certainly, and in doing so publish important public health papers in high-impact publications. These publications include The Lancet, Clinical Infectious Diseases, Emerging Infectious Diseases, and Frontiers in Immunology.

Finally, the NICD would like to congratulate three of its colleagues who have been nominated for National Science and Technology Forum (NTSF) Awards. The awards honour and celebrate outstanding contributions that encourage and reward excellence in the fields off science, engineering, technology and innovation. Dr Givemore Munhenga, Principal Medical Scientist and Senior Researcher at Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD) has been nominated for a 'TW Kambule-NSTF Award: Researcher' award. Senior Scientist at the Centre for HIV and STIs, Dr Simone Richardson, has been nominated for a 'TW Kambule-NSTF Award' in the Emerging Researcher category. And lastly, the Network for Genomics Surveillance in South Africa Team Leader and Co-Founder, Dr Jinal Bhiman, and Scientific Lead for Global Immunology and Immune Sequencing for Epidemic Response South Africa (GIISER-SA) has been nominated for 'Data for Research Award.'

NICD staff members are encouraged to continue to send their comments to the Communications Unit.

Happy reading!

On behalf of the team.

Sinenhlanhla Jimoh
Senior Communications Manager

NSTF Awards Nominees

Dr Givemore Munhenga
TW Kambule-NSTF Award: Researcher

Dr Simone Richardson
TW Kambule-NSTF Award: Emerging Researcher

Dr Jinal Bhiman
Data for Research Award

EXCEPTIONAL RESEARCH STATISTICS

TOP 5

MOST PUBLISHED AUTHORS IN Q3 OF 2021/2022

1

PROF NELESH GOVENDER

2

PROF CHERYL COHEN

2

PROF PENNY MOORE

3

PROF JANUSZ PAWESKA

4

PROF CAROLINE TIEMESSEN

5

DR TENDESAYI KUFA

5

MS JACKIE KLEYNHANS

5

DR NICOLE WOLTER

5

DR WAASILA JASSAT

FEATURED RESEARCH ABSTRACTS FOR THE THIRD QUARTER OF 2021/2022

Dr Shaheed Vally Omar

Dr Harry Moultrie

Dr Farzana Ismail

Assessment of epidemiological and genetic characteristics and clinical outcomes of resistance to bedaquiline in patients treated for rifampicin-resistant tuberculosis: a cross-sectional and longitudinal study

Nazir Ahmed Ismail, **Shaheed Vally Omar*, Harry Moultrie***, Zaheda Bhyat, Francesca Conradie, M Enwerem, Hannetjie Ferreira, Jennifer Hughes, Lavania Joseph, Yulene Kock, Vancy Letsaolo, Gary Maartens, Graeme Meintjes, Dumisani Ngcamu, Nana Okozi, Xavier Padanilam, Anja Reuter, Rodolf Romero, Simon Schaaf, Julian te Riele, Ebrahim Variava, Minty van der Meulen, Farzana Ismail†, Norbert Ndjeka†*

Lancet Infectious Diseases
Impact Factor: 25.071

Background: Bedaquiline improves outcomes of patients with rifampicin-resistant and multidrug-resistant (MDR) tuberculosis; however, emerging resistance threatens this success. We did a cross-sectional and longitudinal analysis evaluating the epidemiology, genetic basis, and treatment outcomes associated with bedaquiline resistance, using data from South Africa (2015–19).

Methods: Patients with drug-resistant tuberculosis starting bedaquiline-based treatment had surveillance samples submitted at baseline, month 2, and month 6, along with demographic information. Culture-positive baseline and post-baseline isolates had phenotypic resistance determined. Eligible patients were aged 12 years or older with a positive culture sample at baseline or, if the sample was invalid or negative, a sample within 30 days of the baseline sample submitted for bedaquiline drug susceptibility testing. For the longitudinal study, the first surveillance sample had to be phenotypically susceptible to bedaquiline for inclusion. Whole-genome sequencing was done on bedaquiline-resistant isolates and a subset of bedaquiline-susceptible isolates. The National Institute for Communicable Diseases tuberculosis reference laboratory, and national tuberculosis surveillance databases were matched to the Electronic Drug-Resistant Tuberculosis Register. We assessed baseline resistance prevalence, mutations, transmission, cumulative resistance incidence, and odds ratios (ORs) associating risk factors for resistance with patient outcomes.

Findings: Between Jan 1, 2015, and July 31, 2019, 8041 patients had surveillance samples submitted, of whom 2023 were included in the cross-sectional analysis and 695 in the longitudinal analysis. Baseline bedaquiline resistance prevalence was 3·8% (76 of 2023 patients; 95% CI 2·9–4·6), and it was associated with previous exposure to bedaquiline or clofazimine (OR 7·1, 95% CI 2·3–21·9) and with rifampicin-resistant or MDR tuberculosis with additional resistance to either fluoroquinolones or injectable drugs (pre-extensively-drug resistant [XDR] tuberculosis: 4·2, 1·7–10·5) or to both (XDR tuberculosis: 4·8, 2·0–11·7). *Rv0678* mutations were the sole genetic basis of phenotypic resistance. Baseline resistance could be attributed to previous bedaquiline or clofazimine exposure in four (5·3%) of 76 patients and to primary transmission in six (7·9%). Odds of successful treatment outcomes were lower in patients with baseline bedaquiline resistance (0·5, 0·3–1). Resistance during treatment developed in 16 (2·3%) of 695 patients, at a median of 90 days (IQR 62–195), with 12 of these 16 having pre-XDR or XDR.

Interpretation: Bedaquiline resistance was associated with poorer treatment outcomes. Rapid assessment of bedaquiline resistance, especially when patients were previously exposed to bedaquiline or clofazimine, should be prioritised at baseline or if patients remain culture-positive after 2 months of treatment. Preventing resistance by use of novel combination therapies, current treatment optimisation, and patient support is essential.

Prof Nelesh Govender

Global guideline for the diagnosis and management of rare yeast infections: an initiative of the ECMM in cooperation with ISHAM and ASM

Chen SC, Perfect J, Colombo AL, Cornely OA, Groll AH, Seidel D, Albus K, de Almedia JN Jr, Garcia-Effron G, Gilroy N, Lass-Flörl C, Ostrosky-Zeichner L, Pagano L, Papp T, Rautemaa-Richardson R, Salmanton-García J, Spec A, Steinmann J, Arikan-Akdagli S, Arenz DE, Sprute R, Duran-Graeff L, Freiberger T, Girmenia C, Harris M, Kanj SS, Roudbary M, Lortholary O, Meletiadis J, Segal E, Tuon FF, Wiederhold N, Bicanic T, Chander J, Chen YC, Hsueh PR, Ip M, Munoz P, Spriet I, Temfack E, Thompson L, Tortorano AM, Velegraki A, ***Govender NP***

Lancet Infectious Diseases
Impact Factor: 25.071

Uncommon, or rare, yeast infections are on the rise given increasing numbers of patients who are immunocompromised or seriously ill. The major pathogens include those of the genera *Geotrichum, Saprochaete, Magnusiomyces,* and *Trichosporon* (ie, basidiomycetes) and *Kodamaea, Malassezia, Pseudozyma* (ie, now *Moesziomyces* or *Dirkmeia*), *Rhodotorula, Saccharomyces,* and *Sporobolomyces* (ie, ascomycetes). A considered approach to the complex, multidisciplinary management of infections that are caused by these pathogens is essential to optimising patient outcomes; however, management guidelines are either region-specific or require updating. In alignment with the One World–One Guideline initiative to incorporate regional differences, experts from diverse geographical regions analysed publications describing the epidemiology and management of the previously mentioned rare yeasts. This guideline summarises the consensus recommendations with regards to the diagnostic and therapeutic options for patients with these rare yeast infections, with the intent of providing practical assistance in clinical decision making. Because there is less clinical experience of patients with rare yeast infections and studies on these patients were not randomised, nor were groups compared, most recommendations are not robust in their validation but represent insights by use of expert opinions and in-vitro susceptibility results. In this Review, we report the key features of the epidemiology, diagnosis, antifungal susceptibility, and treatment outcomes of patients with *Geotrichum, Saprochaete, Magnusiomyces,* and *Trichosporon* spp infections.

Dr Anthony Smith

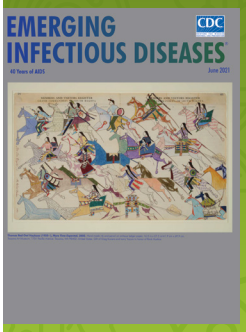
Dr Juno Thomas

Emergence of *Vibrio cholerae* O1 Sequence Type 75, South Africa, 2018 - 2020

Anthony M. Smith, *François-Xavier Weill, Elisabeth Njamkepo, Hlengiwe M. Ngomane, Ntsieni Ramalwa, Phuti Sekwadi,* ***Juno Thomas***

Emerging Infectious Diseases
Impact Factor: 6.883

We describe the molecular epidemiology of cholera in South Africa during 2018–2020. *Vibrio cholerae* O1 sequence type (ST) 75 recently emerged and became more prevalent than the *V. cholerae* O1 biotype El Tor pandemic clone. ST75 isolates were found across large spatial and temporal distances, suggesting local ST75 spread.



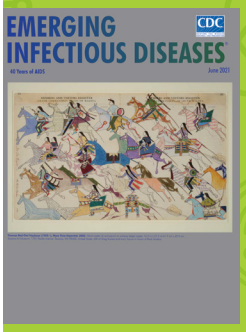
Mrs Antoinette A. Grobbelaar

Mammarenaviruses of Rodents, South Africa and Zimbabwe

Antoinette A. Grobbelaar, *Jocelyn Jardine, Felicity J. Burt, Alasdair J. Shepherd, Susan P. Shepherd, Patricia A. Leman, Alan Kemp, Lawrence E.O. Braack, Jacqueline Weyer, Janusz T. Paweska, Robert Swanepoel*

Emerging Infectious Diseases
Impact Factor: 6.883

We conducted a survey for group-specific indirect immunofluorescence antibody to mammarenaviruses by using Lassa fever and Mopeia virus antigens on serum specimens of 5,363 rodents of 33 species collected in South Africa and Zimbabwe during 1964–1994. Rodents were collected for unrelated purposes or for this study and stored at −70°C. We found antibody to be widely distributed in the 2 countries; antibody was detected in serum specimens of 1.2%–31.8% of 14 species of myomorph rodents, whereas 19 mammarenavirus isolates were obtained from serum specimens and viscera of 4 seropositive species. Phylogenetic analysis on the basis of partial nucleoprotein sequences indicates that 14 isolates from *Mastomys natalensis,* the Natal multimammate mouse, were Mopeia virus, whereas Merino Walk virus was characterized as a novel virus in a separate study. The remaining 4 isolates from 3 rodent species potentially constitute novel viruses pending full characterization.

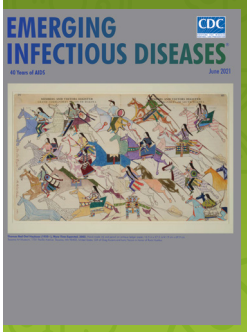


Prof Janusz Paweska

Rift Valley Fever Virus Seroprevalence among Humans, Northern Kwazulu- Natal Province, South Africa, 2018 -2019

Janusz T. Paweska, *Veerle Msimang, Joe Kgaladi, Orienka Hellferscee, Jacqueline Weyer, Petrus Jansen van Vuren*

Emerging Infectious Diseases
Impact Factor: 6.883



We detected Rift Valley fever virus (RVFV) IgM and IgG in human serum samples collected during 2018–2019 in northern KwaZulu-Natal Province, South Africa. Our results show recent RVFV circulation and likely RVFV endemicity in this tropical coastal plain region of South Africa in the absence of apparent clinical disease.

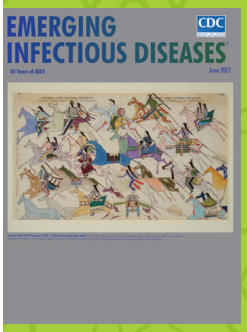
Ms Jackie Kleynhans

Prof Cheryl Cohen

SARS-CoV-2 Seroprevalence in a Rural and Urban Household Cohort during First and Second Waves of Infections, South Africa, July 2020-March 2021

Kleynhans J, *Tempia S, Wolter N, von Gottberg A, Bhiman JN, Buys A, Moyes J, McMorrow ML, Kahn K, Gómez-Olivé FX, Tollman S, Martinson NA, Wafawanaka F, Lebina L, du Toit J, Jassat W, Neti M, Brauer M,* ***Cohen C;*** *PHIRST-C Group*

Emerging Infectious Diseases
Impact Factor: 6.883



Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections may be underestimated because of limited access to testing. We measured SARS-CoV-2 seroprevalence in South Africa every 2 months during July 2020–March 2021 in randomly selected household cohorts in 2 communities. We compared seroprevalence to reported laboratory-confirmed infections, hospitalizations, and deaths to calculate infection–case, infection–hospitalization, and infection–fatality ratios in 2 waves of infection. Post–second wave seroprevalence ranged from 18% in the rural community children <5 years of age, to 59% in urban community adults 35–59 years of age. The second wave saw a shift in age distribution of case-patients in the urban community (from persons 35–59 years of age to persons at the extremes of age), higher attack rates in the rural community, and a higher infection–fatality ratio in the urban community. Approximately 95% of SARS-CoV-2 infections were not reported to national surveillance.

Mrs Joy Ebonwu

Prof Caroline Tiemessen

An HIV vaccine protective allele in *FCGR2C* associates with increased odds of perinatal acquisition

Ebonwu J, *Lassauniere R, Paximadis M, Goosen M, Strehlau R, Gray GE, Kuhn L,* ***Tiemessen CT***

Fronteirs in Immunology
Impact Factor: 6.429

In the Thai RV144 HIV-1 vaccine trial, a three-variant haplotype within the Fc gamma receptor 2C gene *(FCGR2C)* reduced the risk of HIV-1 acquisition. A follow-on trial, HVTN702, of a similar vaccine candidate found no efficacy in South Africa, where the predominant population is polymorphic for only a single variant in the haplotype, c.134-96C>T (rs114945036). To investigate a role for this variant in HIV-1 acquisition in South Africans, we used the model of maternal-infant HIV-1 transmission. A nested case-control study was conducted of infants born to mothers living with HIV-1, comparing children with perinatally-acquired HIV-1 (cases, n = 176) to HIV-1-exposed uninfected children (controls, n = 349). All had received nevirapine for prevention of mother-to-child transmission. The *FCGR2C* copy number and expression variants (c.–386G>C, c.–120A>T c.169T>C, and c.798+1A>G) were determined using a multiplex ligation-dependent probe amplification assay and the c.134-96C>T genotype with Sanger sequencing. The copy number, genotype and allele carriage were compared between groups using univariate and multivariate logistic regression. The *FCGR2C* c.134-96C>T genotype distribution and copy number differed significantly between HIV-1 cases and exposed-uninfected controls ($P = 0.002$, $P_{Bonf} = 0.032$ and $P = 0.010$, $P_{Bonf} = > 0.05$, respectively). The FCGR2C c.134-96T allele was overrepresented in the cases compared to the controls (58% vs 42%; P = 0.001, $P_{Bonf} = 0.016$). Adjusting for birthweight and FCGR2C copy number, perinatal HIV-1 acquisition was associated with the c.134-96C>T (AOR = 1.89; 95% CI 1.25-2.87; $P = 0.003$, $P_{Bonf} = 0.048$) and c.169C>T (AOR = 2.39; 95% CI 1.45-3.95; $P = 0.001$, $P_{Bonf} = 0.016$) minor alleles but not the promoter variant at position c.–386G>C. The c.134-96C>T variant was in strong linkage disequilibrium with the c.169C>T variant, but remained significantly associated with perinatal acquisition when adjusted for c.169C>T in multivariate analysis. In contrast to the protective effect observed in the Thai RV144 trial, we found the *FCGR2C* variant c.134-96T-allele associated with increased odds of perinatal HIV-1 acquisition in South African children. These findings, taken together with a similar deleterious association found with HIV-1 disease progression in South African adults, highlight the importance of elucidating the functional relevance of this variant in different populations and vaccination/disease contexts.

Prof Caroline Tiemessen

FcγR genetic variation and HIV-1 vaccine efficacy: Context and considerations

Lassauniere R, and ***Tiemessen CT***

Fronteirs in Immunology
Impact Factor: 6.429

Receptors for the crystallisable fragment (Fc) of immunoglobulin (Ig) G, Fcγ receptors (FcγRs), link the humoral and cellular arms of the immune response, providing a diverse armamentarium of antimicrobial effector functions. Findings from HIV-1 vaccine efficacy trials highlight the need for further study of Fc-FcR interactions in understanding what may constitute vaccine-induced protective immunity. These include host genetic correlates identified within the low affinity Fcγ-receptor locus in three HIV-1 efficacy trials - VAX004, RV144, and HVTN 505. This perspective summarizes our present knowledge of FcγR genetics in the context of findings from HIV-1 efficacy trials, and draws on genetic variation described in other contexts, such as mother-to-child HIV-1 transmission and HIV-1 disease progression, to explore the potential contribution of *FcγR* variability in modulating different HIV-1 vaccine efficacy outcomes. Appreciating the complexity and the importance of the collective contribution of variation within the *FCGR* gene locus is important for understanding the role of FcγRs in protection against HIV-1 acquisition.

Prof Caroline Tiemessen

Reduced CCR5 expression and immune quiescence in black South African controllers

Picton ACP, Paximadis M, Koor G, Bharuthram A, Shalekoff S, Lassauniere R, Ive P, and ***Tiemessen CT***

Fronteirs in Immunology
Impact Factor: 6.429

Unique Individuals who exhibit either suppressive HIV-1 control, or the ability to maintain low viral load set-points and preserve their CD4+ T cell counts for extended time periods in the absence of antiretroviral therapy, are broadly termed HIV-1 controllers. We assessed the extent to which black South African controllers (n=9), differ from uninfected healthy controls (HCs, n=22) in terms of lymphocyte and monocyte CCR5 expression (density and frequency of CCR5-expressing cells), immune activation as well as peripheral blood mononuclear cell (PBMC) mitogen-induced chemokine/cytokine production. In addition, relative CD4+ T cell CCR5 mRNA expression was assessed in a larger group of controllers (n=20) compared to HCs (n=10) and HIV-1 progressors (n=12). Despite controllers having significantly higher frequencies of activated CD4+ and CD8+ T cells (HLA-DR+) compared to HCs, CCR5 density was significantly lower in these T cell populations (*P*=0.039 and *P*=0.064, respectively). This lower CCR5 density was largely attributable to controllers with higher VLs (>400 RNA copies/ml). Significantly lower CD4+ T cell CCR5 density in controllers was maintained (*P*=0.036) when HCs (n=12) and controllers (n=9) were matched for age. CD4+ T cell CCR5 mRNA expression was significantly less in controllers compared to HCs (*P*=0.007) and progressors (*P*=0.002), whereas HCs and progressors were similar (P=0.223). The levels of soluble CD14 in plasma did not differ between controllers and HCs, suggesting no demonstrable monocyte activation. While controllers had lower monocyte CCR5 density compared to the HCs (*P*=0.02), significance was lost when groups were age-matched (*P*=0.804). However, when groups were matched for both CCR5 promoter haplotype and age (n=6 for both) reduced CCR5 density on monocytes in controllers relative to HCs was highly significant (*P*=0.009). Phytohemagglutinin-stimulated PBMCs from the controllers produced significantly less CCL3 (*P*=0.029), CCL4 (*P*=0.008) and IL-10 (*P*=0.028) compared to the HCs, which was largely attributable to the controllers with lower VLs (<400 RNA copies/ml). Our findings support a hypothesis of an inherent (genetic) predisposition to lower CCR5 expression in individuals who naturally control HIV-1, as has been suggested for Caucasian controllers, and thus, likely involves a mechanism shared between ethnically divergent population groups.

Dr Shaheed Vally Omar

Bedaquiline Drug Resistance Emergence Assessment in MDR-TB (DREAM): a 5-Year Prospective In-Vitro Surveillance Study of Bedaquiline and Other Second-Line Drug-Susceptibility Testing in MDR-TB Isolates

Kaniga K, Hasan R, Jou R, Vasiliauskienė E, Chuchottaworn C, Ismail N, Metchock B, Miliauskas S, Viet Nhung N, Rodrigues C, Shin S, Simsek H, Smithtikarn S, Ngoc ALT, Boonyasopun J, Kazi M, Kim S, Kamolwat P, Musteikiene G, Sacopon CA, Tahseen S, Vasiliauskaitė L, Wu MH, ***Vally Omar S***

Journal of Clinical Microbiology
Impact Factor: 5.948

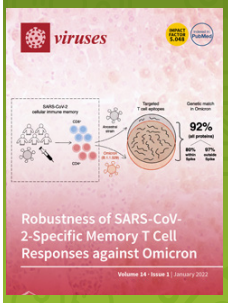
Bedaquiline Drug Resistance Emergence Assessment in Multidrug-resistant-tuberculosis (MDR-TB) (DREAM) was a 5-year (2015–2019) phenotypic drug-resistance surveillance study across 11 countries. DREAM assessed the susceptibility of 5036 MDR-TB isolates of bedaquiline-treatment-naïve patients to bedaquiline and other anti-tuberculosis drugs by the 7H9 broth microdilution (BMD) and 7H10/7H11 agar dilution (AD) minimal inhibitory concentration (MIC) methods. Bedaquiline AD MIC quality control (QC) range for the H37Rv reference strain was unchanged, but the BMD MIC QC range (0.015–0.12 µg/ml) was adjusted compared with ranges from a multilaboratory, multicountry reproducibility study conforming to Clinical and Laboratory Standards Institute Tier-2 criteria. Epidemiological cut-off values of 0.12 µg/ml by BMD and 0.25 µg/ml by AD were consistent with previous bedaquiline breakpoints. An area of technical uncertainty or Intermediate category was set at 0.25 µg/ml and 0.5 µg/ml for BMD and AD, respectively. When applied to the 5036 MDR-TB isolates, bedaquiline-susceptible, intermediate and bedaquiline-resistant rates were 97.9%, 1.5% and 0.6%, respectively, for BMD, and 98.8%, 0.8% and 0.4% for AD. Resistance rates were: ofloxacin 35.1%, levofloxacin 34.2%, moxifloxacin 33.3%, 1.5% linezolid and 2% clofazimine. Phenotypic cross resistance between bedaquiline and clofazimine was 0.4% in MDR-TB and 1% in pre-extensively drug-resistant (pre-XDR-TB)/XDR-TB populations. Co-resistance to bedaquiline and linezolid, and clofazimine and linezolid, were 0.1% and 0.3%, respectively, in MDR-TB, and 0.2% and 0.4% in pre-XDR-TB/XDR-TB populations. Resistance rates to bedaquiline appear to be low in the bedaquiline-treatment-naïve population. No treatment-limiting patterns for cross-resistance and co-resistance have been identified with key TB drugs to date.

Prof Janusz Paweska

Vector Competence of Eucampsipoda africana (Diptera: Nycteribiidae) (Chiroptera:Pteropodidae)

Janusz T. Paweska, *Petrus Jansen van Vuren, Nadia Storm, Wanda Markotter and Alan Kemp*

Viruses
Impact Factor: 5.048



This study aimed to determine the vector competence of bat-associated nycteribiid flies *(Eucamsipoda africana)* for Marburg virus (MARV) in the Egyptian Rousette Bat (ERB), *Rousettus aegyptiacus.* In flies fed on subcutaneously infected ERBs and tested from 3 to 43 days post infection (dpi), MARV was detected only in those that took blood during the peak of viremia, 5–7 dpi. Seroconversion did not occur in control bats in contact with MARV-infected bats infested with bat flies up to 43 days post exposure. In flies inoculated intra-coelomically with MARV and tested on days 0–29 post inoculation, only those assayed on day 0 and day 7 after inoculation were positive by q-RT-PCR, but the virus concentration was consistent with that of the inoculum. Bats remained MARV-seronegative up to 38 days after infestation and exposure to inoculated flies. The first filial generation pupae and flies collected at different times during the experiments were all negative by q-RT-PCR. Of 1693 nycteribiid flies collected from a wild ERB colony in Mahune Cave, South Africa where the enzootic transmission of MARV occurs, only one (0.06%) tested positive for the presence of MARV RNA. Our findings seem to demonstrate that bat flies do not play a significant role in the transmission and enzootic maintenance of MARV. However, ERBs eat nycteribiid flies; thus, the mechanical transmission of the virus through the exposure of damaged mucous membranes and/or skin to flies engorged with contaminated blood cannot be ruled out.

Dr Tendesayi Kufa-Chakezha

Epidemiology of SARS-CoV-2 infection and SARS-CoV-2 positive hospital admissions among children in South Africa

Kufa T, *Jassat W, Cohen C, Tempia S, Masha M, Wolter N, Walaza S, von Gottberg A, Govender NP, Hunt G, Shonhiwa AM, Ebonwu J, Ntshoe G, Maruma W, Bapela P, Ndhlovu N, Mathema H, Modise M, Shuping L, Manana PN, Moore D, Dangor Z, Verwey C, Madhi SA, Saloojee H, Zar HJ, Blumberg L*

Influenza and Other Respiratory Viruses
Impact Factor: 4.38

Introduction: We describe epidemiology and outcomes of confirmed SARS-CoV-2 infection and positive admissions among children <18 years in South Africa, an upper-middle income setting with high inequality.

Methods: Laboratory and hospital COVID-19 surveillance data, 28 January - 19 September 2020 was used. Testing rates were calculated as number of tested for SARS-CoV-2 divided by population at risk; test positivity rates were calculated as positive tests divided by total number of tests. In-hospital case fatality ratio (CFR) was calculated based on hospitalized positive admissions with outcome data who died in-hospital and whose death was judged SARS-CoV-2 related by attending physician.

Findings: 315 570 children aged <18 years were tested for SARS-CoV-2; representing 8.9% of all 3 548 738 tests and 1.6% of all children in the country. Of children tested, 46 137 (14.6%) were positive. Children made up 2.9% (n = 2007) of all SARS-CoV-2 positive admissions to sentinel hospitals. Among children, 47 died (2.6% case-fatality). In-hospital deaths were associated with male sex [adjusted odds ratio (aOR) 2.18 (95% confidence intervals [CI] 1.08–4.40)] vs female; age <1 year [aOR 4.11 (95% CI 1.08–15.54)], age 10–14 years [aOR 4.20 (95% CI1.07–16.44)], age 15–17 years [aOR 4.86 (95% 1.28–18.51)] vs age 1–4 years; admission to a public hospital [aOR 5.07(95% 2.01–12.76)] vs private hospital and ≥1 underlying conditions [aOR 12.09 (95% CI 4.19–34.89)] vs none.

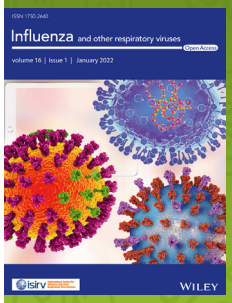
Conclusions: Children with underlying conditions were at greater risk of severe SARS-CoV-2 outcomes. Children > 10 years, those in certain provinces and those with underlying conditions should be considered for increased testing and vaccination.

Prof Cheryl Cohen

Cohort profile: A Prospective Household cohort study of Influenza, Respiratory syncytial virus and other respiratory pathogens community burden and Transmission dynamics in South Africa, 2016–2018

Cohen C, *McMorrow ML, Martinson NA, Kahn K, Treurnicht FK, Moyes J, Mkhencele T, Hellferscee O, Lebina L, Moroe M, Motlhaoleng K, Gómez-Olivé FX, Wagner R, Tollman S, Wafawanaka F, Ngobeni S, Kleynhans J, Mathunjwa A, Buys A, Maake L, Wolter N, Carrim M, Piketh S, Language B, Mathee A, von Gottberg A, Tempia S; PHIRST group*

Influenza and Other Respiratory Viruses
Impact Factor: 4.380



Purpose: The PHIRST study (Prospective Household cohort study of Influenza, Respiratory Syncytial virus, and other respiratory pathogens community burden and Transmission dynamics in South Africa) aimed to estimate the community burden of influenza and respiratory syncytial virus (RSV) including the incidence of infection, symptomatic fraction, and to assess household transmission.

Participants: We enrolled 1684 individuals in 327 randomly selected households in a rural and an urban site over three consecutive influenza and two RSV seasons. A new cohort of households was enrolled each year. Participants were sampled with nasopharyngeal swabs twice-weekly during the RSV and influenza seasons of the year of enrolment. Serology samples were collected at enrolment and before and after the influenza season annually.

Findings to date: There were 122 113 potential individual follow-up visits over the 3 years, and participants were interviewed for 105 783 (87%) of these. Out of 105 683 nasopharyngeal swabs, 1258 (1%) and 1026 (1%) tested positive on polymerase chain reaction (PCR) for influenza viruses and RSV, respectively. Over one third of individuals had PCR-confirmed influenza each year. Overall, there was influenza transmission to 10% of household contacts of an index case.

Future plans: Future planned analyses include analysis of influenza serology results and RSV burden and transmission. Households enrolled in the PHIRST study during 2016-2018 were eligible for inclusion in a study of SARS-CoV-2 transmission initiated in July 2020. This study uses similar testing frequency to assess the community burden of SARS-CoV-2 infection and the role of asymptomatic infection in virus transmission.

Dr Selamawit Woldesenbet

Prof Adrian Puren

The prevalence of unintended pregnancy and its association with HIV status among pregnant women in South Africa, a national antenatal survey, 2019

Selamawit Woldesenbet, *Tendesayi Kufa, Carl Lombard Samuel Manda, Diane Morof, Mireille Cheyip, Kassahun Ayalew,* ***Adrian Puren***

Scientific reports
Impact Factor: 4.379

To describe the prevalence of unintended pregnancy and its association with HIV status among pregnant women in South Africa. A cross-sectional survey was conducted between October and mid-November 2019 among pregnant women aged 15–49 years in 1589 selected public antenatal care facilities. Pregnancy intention was assessed using two questions from the London Measure of Unplanned Pregnancy. Survey logistic regression examined factors associated with unintended pregnancy. Among 34,946 participants, 51.6% had an unintended pregnancy. On multivariable analysis, the odds of unintended pregnancy was higher among women who knew their HIV-positive status before pregnancy but initiated treatment after the first antenatal visit (adjusted odds ratio [aOR], 1.5 [95% confidence interval (CI):1.2–1.8]), women who initiated treatment before pregnancy (aOR, 1.3 [95% CI:1.2–1.3]), and women with a new HIV diagnosis during pregnancy (aOR, 1.2 [95% CI:1.1–1.3]) compared to HIV-negative women. Women who were single, in a non-cohabiting or a cohabiting relationship, and young women (15–24 years) had significantly higher risk of unintended pregnancy compared to married women and women aged 30–49 years, respectively. A comprehensive approach, including regular assessment of HIV clients' pregnancy intention, and adolescent and youth-friendly reproductive health services could help prevent unintended pregnancy.

Prof Penny Moore

Coordinated Fc-effector and neutralization functions in HIV-infected children define a window of opportunity for HIV vaccination

Nduati EW, Gorman MJ, Sein Y, Hermanus T, Oyaro I, Muema DM, Ndung'u T, Alter G, ***Moore PL***

AIDS
Impact Factor: 4.177

Objectives: Antibody function has been extensively studied in HIV-infected adults but is relatively understudied in children. Emerging data suggests enhanced development of broadly neutralizing antibodies (bNAbs) in children but Fc effector functions in this group are less well defined. Here, we profiled overall antibody function in HIV-infected children.

Design: Plasma samples from a cross-sectional study of 50 antiretroviral therapy-naive children (aged 1–11 years) vertically infected with HIV-1 clade A were screened for HIV-specific binding antibody levels and neutralizing and Fc-mediated functions.

Methods: Neutralization breadth was determined against a globally representative panel of 12 viruses. HIV-specific antibody levels were determined using a multiplex assay. Fc-mediated antibody functions measured were antibody-dependent: cellular phagocytosis (ADCP); neutrophil phagocytosis (ADNP); complement deposition (ADCD) and natural killer function (ADNK).

Results: All children had HIV gp120-specific antibodies, largely of the IgG1 subtype. Fifty-four percent of the children exhibited more than 50% neutralization breadth, with older children showing significantly broader neutralization activity. Apart from ADCC, observed only in 16% children, other Fc-mediated functions were common (>58% children). Neutralization breadth correlated with Fc-mediated functions suggesting shared determinants of enhanced antibody function exist.

Conclusions: These results are consistent with previous observations that children may develop high levels of neutralization breadth. Furthermore, the striking association between neutralization breadth and Fc effector function suggests that HIV vaccination in children could yield multifunctional antibodies. Paediatric populations may therefore provide an ideal window of opportunity for HIV vaccination strategies.

Ms Nozuko P. Blasich

Prof Nelesh Govender

Association of semi-quantitative cryptococcal antigen results in plasma with subclinical cryptococcal meningitis and mortality among patients with advanced HIV disease

Blasich NP, *Wake RM, Rukasha I, Prince Y,* ***Govender NP***

Medical Mycology
Impact Factor: 4.076

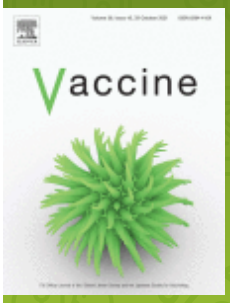
Blood cryptococcal antigen (CrAg) titers >160 are associated with concurrent subclinical cryptococcal meningitis (CM). When lumbar puncture (LP) is not immediately available in a CrAg screening program, semi-quantitative CrAg assays may provide risk stratification for CM. Two semi-quantitative assays (SQ [Immuno-Mycologics, Norman, OK, USA] and CryptoPS [Biosynex, Strasbourg, France]) were evaluated against a qualitative lateral flow assay (LFA) using 194 plasma samples from a cohort of HIV-seropositive individuals with CD4 counts <100 cells/µl. We compared SQ and CryptoPS results to titers for LFA-positive samples. Among patients with LP, we examined the association between semi-quantitative CrAg results and CM. We used a Cox proportional hazards model to determine the association between SQ score and mortality. Of 194 participants, 60 (31%) had positive LFA results, of whom 41 (68%) had a titer of ≤160 and 19 (32%) a titer >160. Fifty individuals with antigenemia had an LP; a clinically useful SQ score that identified all ten cases of subclinical CM was ≥3 (100% sensitivity, 55% specificity). Patients with an SQ score of 3 or 4 also had a 2.2-fold increased adjusted hazards of 6-month mortality (95% CI: 0.79–6.34; p = 0.13) versus those with score of <3. Nine of ten patients with subclinical CM had a strong-positive CryptoPS result versus 10/40 without subclinical CM (p < 0.001). Semi-quantitative assays offered a sensitive though not specific means of gauging the risk of concurrent CM in this patient population.

Prof Cheryl Cohen

A Research and Development (R&D) roadmap for influenza vaccines: Looking toward the future

Moore KA, Ostrowsky JT, Kraigsley AM, Mehr AJ, Bresee JS, Friede MH, Gellin BG, Golding JP, Hart PJ, Moen A, Weller CL, Osterholm MT; ***Influenza Vaccines R&D Roadmap Taskforce (Cheryl Cohen contributed to manuscript)***

Vaccine
Impact Factor: 3.641



Improved influenza vaccines are urgently needed to reduce the burden of seasonal influenza and to ensure a rapid and effective public-health response to future influenza pandemics. The Influenza Vaccines Research and Development (R&D) Roadmap (IVR) was created, through an extensive international stakeholder engagement process, to promote influenza vaccine R&D. The roadmap covers a 10-year timeframe and is organized into six sections: virology; immunology; vaccinology for seasonal influenza vaccines; vaccinology for universal influenza vaccines; animal and human influenza virus infection models; and policy, finance, and regulation. Each section identifies barriers, gaps, strategic goals, milestones, and additional R&D priorities germane to that area. The roadmap includes 113 specific R&D milestones, 37 of which have been designated high priority by the IVR expert taskforce. This report summarizes the major issues and priority areas of research outlined in the IVR. By identifying the key issues and steps to address them, the roadmap not only encourages research aimed at new solutions, but also provides guidance on the use of innovative tools to drive breakthroughs in influenza vaccine R&D.

Ms Genevie Ntshoe

Prof Nicola Page

A systematic review on mobile health applications for foodborne disease outbreak management

Ntshoe G, *Shonhiwa AM, Govender N,* ***Page N***

BMC Public Health
Impact Factor: 3.295

Background: Foodborne disease outbreaks are common and notifiable in South Africa; however, they are rarely reported and poorly investigated. Surveillance data from the notification system is suboptimal and limited, and does not provide adequate information to guide public health action and inform policy. We performed a systematic review of published literature to identify mobile application-based outbreak response systems for managing foodborne disease outbreaks and to determine the elements that the system requires to generate foodborne disease data needed for public action.

Methods: Studies were identified through literature searches using online databases on PubMed/Medline, CINAHL, Academic Search Complete, Greenfile, Library, Information Science & Technology. Search was limited to studies published in English during the period January 1990 to November 2020. Search strategy included various terms in varying combinations with Boolean phrases "OR" and "AND". Data were collected following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement. A standardised data collection tool was used to extract and summarise information from identified studies. We assessed qualities of mobile applications by looking at the operating system, system type, basic features and functionalities they offer for foodborne disease outbreak management.

Results: Five hundred and twenty-eight (528) publications were identified, of which 48 were duplicates. Of the remaining 480 studies, 2.9% (14/480) were assessed for eligibility. Only one of the 14 studies met the inclusion criteria and reported on one mobile health application named MyMAFI (My Mobile Apps for Field Investigation). There was lack of detailed information on the application characteristics. However, based on minimal information available, MyMAFI demonstrated the ability to generate line lists, reports and offered functionalities for outbreak verification and epidemiological investigation. Availability of other key components such as environmental and laboratory investigations were unknown.

Conclusions: There is limited use of mobile applications on management of foodborne disease outbreaks. Efforts should be made to set up systems and develop applications that can improve data collection and quality of foodborne disease outbreak investigations.

Prof Gayle Sherman

Data protection, data management, and data sharing: stakeholder perspectives on the protection of personal health information in South Africa

Ciara Staunton, Kathrina Tschigg, ***Gayle Sherman***

PLOS ONE
Impact Factor: 3.24

The Protection of Personal Information Act (POPIA) 2013 came into force in South Africa on 1 July 2020. It seeks to strengthen the processing of personal information, including health information. While POPIA is to be welcomed, there are concerns about the impact it will have on the processing of health information. To ensure that the National Health Laboratory Service [NHLS] is compliant with these new strict processing requirements and that compliance does not negatively impact upon its current screening, treatment, surveillance and research mandate, it was decided to consider the development of a NHLS POPIA Code of Conduct for Personal Health. As part of the process of developing such a Code and better understand the challenges faced in the processing of personal health information in South Africa, 19 semi-structured interviews with stakeholders were conducted between June and September 2020. Overall, respondents welcomed the introduction of POPIA. However, they felt that there are tensions between the strengthening of data protection and the use of personal information for individual patient care, treatment programmes, and research. Respondents reported a need to rethink the management of personal health information in South Africa and identified 5 issues needing to be addressed at a national and an institutional level: an understanding of the importance of personal information; an understanding of POPIA and data protection; improve data quality; improve transparency in data use; and improve accountability in data use. The application of POPIA to the processing of personal health information is challenging, complex, and likely costly. However, personal health information must be appropriately managed to ensure the privacy of the data subject is protected, but equally that it is used as a resource in the individual's and wider public interest.

Dr Elvira Singh

Ranking lifestyle risk factors for cervical cancer among Black women: A case-control study from Johannesburg, South Africa

Mwiza Gideon SinginiID1,2, Freddy SitasID3,4,5, Debbie Bradshaw3 , Wenlong Carl Chen1,6, Melitah MotlhaleID1,2, Abram Bunya Kamiza6 , Chantal Babb de Villiers7 , Cathryn M. Lewis8,9, Christopher G. MathewID6,9, Tim Waterboer10, Robert Newton11,12, Mazvita Muchengeti1,2,13, ***Elvira Singh***

PLOS ONE
Impact Factor: 3.24

Background: Aside from human papillomavirus (HPV), the role of other risk factors in cervical cancer such as age, education, parity, sexual partners, smoking and human immunodeficiency virus (HIV) have been described but never ranked in order of priority. We evaluated the contribution of several known lifestyle co-risk factors for cervical cancer among black South African women.

Methods: We used participant data from the Johannesburg Cancer Study, a case-control study of women recruited mainly at Charlotte Maxeke Johannesburg Academic Hospital between 1995 and 2016. A total of 3,450 women in the study had invasive cervical cancers, 95% of which were squamous cell carcinoma. Controls were 5,709 women with cancers unrelated to exposures of interest. Unconditional logistic regression models were used to calculate adjusted odds ratios (ORadj) and 95% confidence intervals (CI). We ranked these risk factors by their population attributable fractions (PAF), which take the local prevalence of exposure among the cases and risk into account.

Results: Cervical cancer in decreasing order of priority was associated with (1) being HIV positive (OR_{adj} = 2.83, 95% CI = 2.53–3.14, PAF = 17.6%), (2) lower educational attainment (OR_{adj} = 1.60, 95% CI = 1.44–1.77, PAF = 16.2%), (3) higher parity (3+ children vs 2–1 children (OR_{adj} = 1.25, 95% CI = 1.07–1.46, PAF = 12.6%), (4) hormonal contraceptive use (ORadj = 1.48, 95% CI = 1.24–1.77, PAF = 8.9%), (5) heavy alcohol consumption (OR_{adj} = 1.44, 95% CI = 1.15–1.81, PAF = 5.6%), (6) current smoking (OR_{adj} = 1.64, 95% CI = 1.41–1.91, PAF = 5.1%), and (7) rural residence (OR_{adj} = 1.60, 95% CI = 1.44–1.77, PAF = 4.4%).

Conclusion: This rank order of risks could be used to target educational messaging and appropriate interventions for cervical cancer prevention in South African women.

Dr Shune Oliver

Characterisation of the epigenetic architecture of the major malaria vector *Anopheles arabiensis* (Diptera: Culicidae) after treatment with epigenetic modulators and heavy metals

Alender G.S.N. Jeanrenaud, Basil D. Brooke, ***Shune V. Oliver***

Acta Tropica
Impact Factor: 3.112

Anopheles arabiensis (a member of the *An. gambiae* species complex) is a major vector of malaria in sub-Saharan Africa. Despite its disease vector status, there is currently a paucity of epigenetic information for this species. The aim this study was therefore to analyse global epigenetic markers and their response to metal exposure in insecticide susceptible and resistant laboratory strains of *An. arabiensis*. This was done using commercially available epigenetic marker quantification kits. In order to validate the efficacy of the kits, several kits were assessed to determine whether changes induced by known epigenetic modulators were detectable using these platforms. The efficacy of the dosages used were determined by examining the effect of the dosages used on insecticide resistant phenotypes. Upon confirmation that the dosages used were sufficient to induce a phenotypic change, the effect on epigenetic markers was assessed. Commercial kits were used to quantify 5-methylcysteine (5-mC) and 5-hydroxymethylcysteine (5-hmC) methylation in DNA, m6A methylation in mRNA as well as Histone Acetyl Transferase (HAT) activity. There was a marked difference in the phenotypic response in adult mosquitoes of the insecticide susceptible strain compared to that of its' resistant counterpart. For males and females of the resistant strain, exposure to nucleic acid modifying drugs typically increased their tolerance to insecticides. The patterns of changes in 5-mC methylation by epigenetic modulators was congruent with previous studies which quantified by mass spectrometry. The two strains differed in methylation patterns under control conditions and responded differentially to larval metal exposure. In the resistant strain, which previously was demonstrated to show increased detoxification enzyme activity and insecticide tolerance after the same treatment, the potential increase in transcriptional activity appeared to be modulated by reduced methylation and increased HAT activity. This study suggests that the commercial epigenetic quantification kits can be used to characterise phenotypic changes in *An. arabiensis,* and also shows that epigenetic regulation of the response to metal exposure is regulated at the DNA as opposed to the RNA level.

Ms Dumisile Maseko

Dr Ranmini Kularatne

Development and trial of a dried tube specimen (DTS) proficiency testing panel for dual HIV/syphilis rapid diagnostic tests

Maseko DV, *Valashiya D,* ***Kularatne RS***

Diagnostic Microbiology and Infectious Disease
Impact Factor: 2.803

Purpose: To develop and trial a dried tube specimen (DTS) panel for proficiency testing of dual HIV/syphilis rapid diagnostic tests (RDTs) at clinical sites.

Results: DTS panels were prepared using plasma samples with known HIV and syphilis results, to give varying reactivity for syphilis and HIV test lines on RDTs. Laboratory DTS panels were stable for a minimum 4-week period at ambient temperatures with no inter-reader variability of results. Field testing of panels with Standard Diagnostics Bioline HIV/Syphilis duo showed 100% correlation with laboratory results, and excellent mean pair agreement between the two clinical sites (k = 1.0). With Chembio Dual Path Platform HIV-Syphilis, there were two false negative results for HIV and syphilis, respectively, at one site; and good mean pair agreement between the two sites (k = 0.9).

Conclusion: It is feasible and practicable to incorporate DTS panels into a field proficiency testing scheme for dual HIV/syphilis RDTs.

Dr Ahmad Mazanderani

Evaluation of the Aptima HIV-1 Quant Dx assay for HIV diagnosis at birth in South Africa

Aurélie Mukendi, Tendesayi Kufa, Gayle G Sherman, Karl-Günter Technau, Caroline T Tiemessen, ***Ahmad Haeri Mazanderani***

Diagnostic Microbiology and Infectious Disease
Impact Factor: 2.803

The increased coverage of antiretroviral therapy has resulted in a decrease in the positive predictive value (PPV) and diagnostic sensitivity of early infant diagnosis assays. To evaluate the diagnostic performance of the Aptima HIV-1 Quant DX assay (Aptima) in detecting HIV infection at birth. The study was a cross-sectional laboratory based evaluation using whole blood DBS specimens. Samples were collected from HIV-exposed neonates at birth at two paediatric facilities in Gauteng between 1st March 2018 – 31st January 2020. Performance of the Aptima compared to the Cobas® AmpliPrep/Cobas® TaqMan HIV-1 Qualitative Test v2.0 was calculated using a two-by-two table and reported as proportions with 95% confidence intervals. A total of 363 infants met the inclusion criteria of which 4 (1.1%) had an Aptima result discordant with CAP/CTM HIV status: two (50%) negative and two (50%) positive. The Aptima assay had a sensitivity of 93.75% (95% CI: 79.19%-99.23%), specificity of 99.4% (95% CI: 97.83%-99.93%), PPV of 93.75% (95% CI: 78.98%-98.36%), negative predictive value of 99.4% (95% CI: 97.73%-99.84%), and overall accuracy of 98.9% (95% CI: 97.2%-99.7%). The Aptima yielded an error code on 37 (10.19%) results, of which 35 (94.59%) were resolved on repeat testing. Of the 32 HIV-detected specimens, 20 had a plasma VL result available (18 on Abbott and 2 on Cobas). The absolute median difference was 0.66 log10 (IQR: 0.36-1.71). The Aptima demonstrated good EID performance and can be considered as a qualitative EID assay.

Ms Tafadzwa Dhokotera

Dr Mazvita Muchengeti

Cancer in HIV- positive and HIV-negative adolescents and young adults in South Africa:a cross-sectional study

Dhokotera Tafadzwa, *Bohlius Julia, Egger, Matthias Spoerri, Adrian Ncayiyana Jabulani Ronnie Naidu, Gita, Olago Victor, Zwahlen Marcel, Singh Elvira,* ***Muchengeti Mazvita***

BMJ Open
Impact Factor: 2.69

Objective: To determine the spectrum of cancers in adolescents and young adults (AYAs) living with and without HIV in South Africa.

Design: Cross-sectional study with cancer records provided by the National Cancer Registry (NCR) and HIV records from the National Health Laboratory Service (NHLS).

Setting and participants :The NHLS is the largest provider of pathology services in the South African public sector. The NCR is a division of the NHLS. We included AYAs (aged 10–24 years) diagnosed with cancer by public health sector laboratories between 2004 and 2014 (n=8479). HIV status was obtained through record linkages and text mining.

Primary and secondary outcomes: We determined the spectrum of cancers by HIV status in AYAs. We used multivariable logistic regression to describe the association of cancer in AYAs with HIV, adjusting for age, sex, ethnicity and calendar period. We imputed (post hoc) the HIV status for AYA with unknown HIV status.

Results: 8479 AYAs were diagnosed with cancer, HIV status was known for 45% (n=3812). Of those whose status was known, about half were HIV positive (n=1853). AYAs living with HIV were more likely to have Kaposi's sarcoma (adjusted OR (aOR) 218, 95% CI 89.9 to 530), cervical cancer (aOR 2.18, 95% CI 1.23 to 3.89), non-Hodgkin's lymphoma (aOR 2.12, 95% CI 1.69 to 2.66) and anogenital cancers other than cervix (aOR 2.73, 95% CI 1.27 to 5.86) than AYAs without HIV. About 44% (n=1062) of AYAs with HIV-related cancers had not been tested for HIV.

Conclusions: Targeted HIV testing for AYAs diagnosed with cancer, followed by immediate start of antiretroviral therapy, screening for cervical precancer and vaccination against human papilloma virus is needed to decrease cancer burden in AYAs living with HIV in South Africa.

Mr Wayne Howard

Dr Melinda Suchard

Sensitivity of the acute flaccid paralysis surveillance system for poliovirus in South Africa, 2016–2019

Wayne Howard, *Shelina Moonsamy, Lerato Seakamela, Sabelle Jallow, Faith Modiko, Heleen du Plessis, Rosina Sibiya, Mercy Kamupira, Elizabeth Masethi,* ***Melinda Suchard***

Journal of Medical Microbiology
Impact Factor: 2.472

Introduction: Global poliovirus eradication is a public health emergency of international concern. The acute flaccid paralysis (AFP) surveillance programme in South Africa has been instrumental in eliminating polioviruses and keeping the country poliovirus free.

Gap statement: The sensitivity of surveillance for polioviruses by every African country is of global interest in the effort to ensure global health security from poliovirus re-emergence.

Aim: To describe the epidemiology of polioviruses from AFP cases and environmental samples in South Africa and to report the performance of the AFP surveillance system for the years 2016–2019 against targets established by the World Health Organization (WHO).

Methods: Stool specimens from AFP or suspected AFP cases were received and tested as per WHO guidelines. Environmental samples were gathered from sites across the Gauteng province using the grab collection method. Concentration was effected by the two-phase polyethylene glycol method approved by the WHO. Suspected polioviruses were isolated in RD and/or L20B cell cultures through identification of typical cytopathic effects. The presence of polioviruses was confirmed by intratypic differentiation PCR. All polioviruses were sequenced using the Sanger method, and their VP1 gene analysed for mutations.

Results: Data from 4597 samples (2385 cases) were analysed from the years 2016–2019. Two cases of immunodeficiency-associated vaccine-derived poliovirus (iVDPV) type 3 were detected in 2017 and 2018. A further 24 Sabin type 1 or type 3 polioviruses were detected for the 4 years. The national surveillance programme detected an average of 3.1 cases of AFP/100000 individuals under 15 years old (2.8/100000–3.5/100000). The stool adequacy of the samples received was 53.0% (47.0–55.0%), well below the WHO target of 80% adequacy. More than 90% of results were released from the laboratory within the turnaround time (96.6%) and non-polio enteroviruses were detected in 11.6% of all samples. Environmental surveillance detected non-polio enterovirus in 87.5% of sewage samples and Sabin polioviruses in 12.5% of samples.

Conclusion: The AFP surveillance programme in South Africa is sensitive to detect polioviruses in South Africa and provided no evidence of wild poliovirus or VDPV circulation in the country.

Dr Nishi Prabdial-Sing

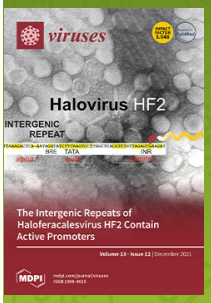
Dr Melinda Suchard

Establishment of outlook thresholds for Hepatatis A in South Africa using laboratory surveillance 2017-2020

Nishi Prabdial-Sing, *Villyen Motaze, Jack Manamela, Kerrigan McCarthy and* ***Melinda Suchard***

MPDI
Impact Factor: n/a

As South Africa transitions from endemic to intermediate endemicity, hepatitis A surveillance needs strengthening to monitor trends in disease incidence and to identify outbreaks. We used passive laboratory-based surveillance data from the National Health Laboratory Services to calculate national hepatitis A incidence and to establish thresholds for outbreaks. Incidence was calculated by age and geographic location. The static threshold used two or three standard deviations (SDs) above the mean hepatitis A incidence in 2017–2019, and a cumulative summation (CuSum2) threshold used three SDs above the mean of the preceding seven months. These thresholds were applied to hepatitis A data for 2020. From 2017 to 2020, the mean incidence of hepatitis A IgM was 4.06/100,000 and ranged from 4.23 to 4.85/100,000 per year. Hepatitis A incidence was highest in the Western Cape province (WCP) (7.00–10.92/100,000 per year). The highest incidence was in the 1–9-year-olds. The incidence of hepatitis A in 2020 exceeded the static threshold in two districts of the WCP: Cape Winelands in January and Overberg district in August. The provincial incidence did not exceed the static and CuSum2 thresholds. District-level analysis using either threshold was sensitive enough to monitor trends and to alert district health authorities, allowing early outbreak responses.



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