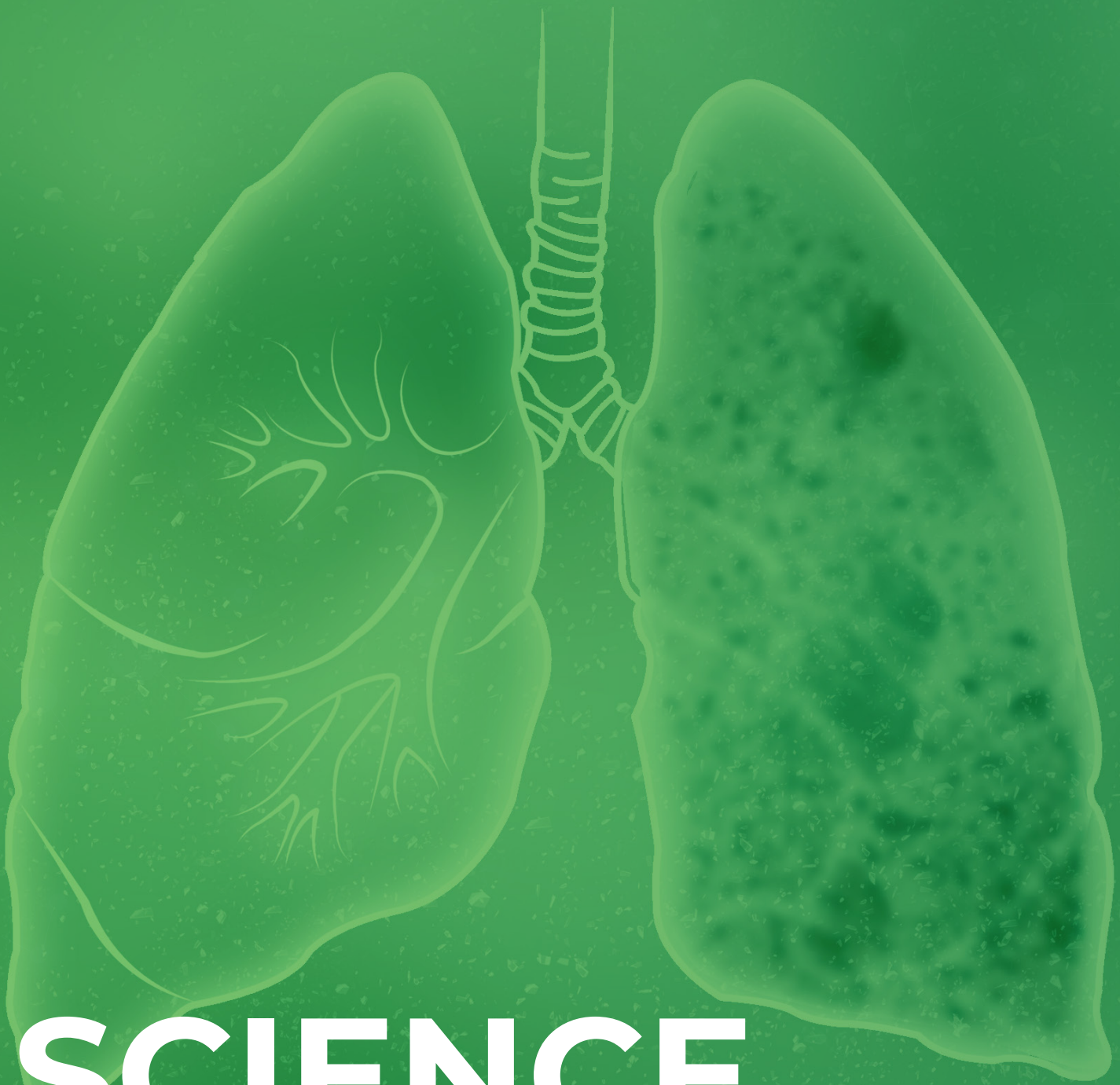
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Issue 21 - August 2022



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

The latest issue of the Science Focus highlights significant research accomplishments from industry experts at the National Institute for Communicable Diseases (NICD). Aside from presenting important statistical results and the proportion of peer-reviewed publications generated, the magazine also highlights top published authors and articles with high impact factor scores.

In ensuring that the Science Focus aligns with the institute's research objectives and aspirations, the NICD Communications Unit is focused on expanding the criteria and scope of features for the publication.

Staff are encouraged to share their thoughts, ideas and suggestions for improvement with sinenhlanhlaj@nicd.ac.za

The edition kicks off with Drs Shaheed Vally Omar and Farzana Ismail from the Centre for Tuberculosis who researched bedaquiline-resistant tuberculosis that is associated with Rv0678 mutations. The use of bedaquiline began in 2015 in South Africa to treat drug-resistant tuberculosis. The authors describe mutations associated with phenotypic resistance to bedaquiline in surveillance isolates identified among patients beginning, or not responding clinically and microbiologically, to a bedaquiline-based regimen. Featured in The New England Journal of Medicine, this makes for a fascinating read.

A host of NICD authors collaborated on a data linkage study that focused on the early assessment of the clinical severity of the SARS-CoV-2 omicron variant using S gene target failure (SGTF). The South African study aimed to assess the clinical severity of infections through data linkages for national, South African COVID-19 case data, SARS-CoV-2 laboratory test data, SARS-CoV-2 genome data, and COVID-19 hospital admissions data. An early analysis suggest a reduced chance of hospitalisation among indiviuals with SGTF, in comparison to non-SGTF infections diagnosed during the same period. Furthermore, SGTF-infected individuals had a significantly reduced chance of developing severe disease, which may be attributed to previous immunity.

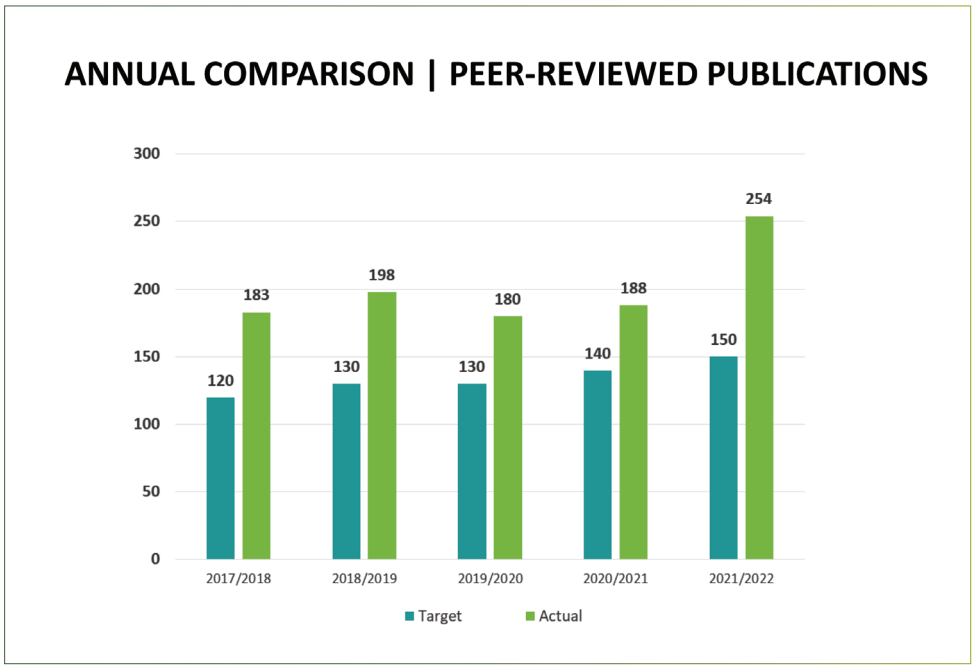
The seroprevalence of SARS-CoV-2, after the second wave in South Africa, in HIV-infected and uninfected persons took centre stage in a cross-sectional household survey that involved Dr Nicole Wolter and Prof Cheryl Cohen, and others. The survey involved nearly 8,000 participants and revealed that persons living with HIV (PLWHIV) with a high viral load were less likely to be seropositive, compared to HIV-uninfected individuals. This finding is likely as a result of inadequate antibody production that highlights the need to prioritise this group for intervention.

In alignment with our strive for excellence we report that the NICD has exceeded its yearly peer-reviewed publications target for the past five years (see Graphic 1). Congratulations to all the NICD researchers who contributed to this historic milestone, as well as those who continue to collaborate and publish research findings in key public health journals.

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



Graphic 1: The annual peer-reviewed publication targets are represented by the blue columns, whereas the actuals are represented by the green columns.

EXCEPTIONAL RESEARCH STATISTICS

TOP 5

MOST PUBLISHED AUTHORS IN Q4 OF 2021/2022

1

Prof Cheryl Cohen

2

Prof Anne von Gottberg

3

Dr Waasila Jassat

4

Prof Penny Moore

5

Dr Nicole Wolter

Dr Shaheed Vally Omar

BEDAQUILINE-RESISTANT TUBERCULOSIS ASSOCIATED WITH RV0678 MUTATIONS

Omar Shaheed V, Ismail Farzana, *Ndjeka Norbert, Kaniga Koné, Ismail Nazir A*

The NEW ENGLAND JOURNAL of MEDICINE

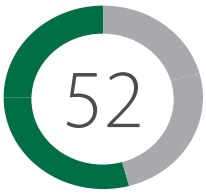
Impact factor: 91,253

Bedaquiline is used to treat drug-resistant tuberculosis. Programmatic use of bedaquiline in South Africa began in 2015 and by March 2020 accounted for just over half of global use. Resistance to bedaquiline was initially reported to be due to target-based mutations in the gene atpE encoding subunit C of the ATP synthase complex. However, non–target-based mutations in the mmpR (Rv0678) gene encoding the MmpS5–MmpL5 efflux pump repressor are increasingly associated with bedaquiline resistance, although some have shown hypersusceptibility.

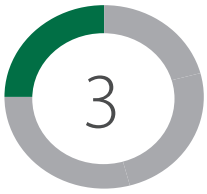
We describe mutations associated with phenotypic resistance to bedaquiline in surveillance isolates identified in South Africa among patients beginning or not responding clinically and microbiologically to a bedaquiline-based regimen. Ethics approval was obtained from the University of Witwatersrand Human Research Ethic Committee. Bedaquiline testing was performed at the World Health Organization supranational tuberculosis reference laboratory in Johannesburg, which is accredited according to the International Organization for Standardization 15189 standards. Bedaquiline phenotypic drug susceptibility was evaluated with the use of previously described methods and criteria for interpretation. Sanger sequencing or whole-genome sequencing, with a mutation-frequency cutoff set at 5%, was used to identify phenotypically resistant isolates as previously described.

The NEW ENGLAND JOURNAL of MEDICINE

SOCIAL MEDIA



TWITTER



FACEBOOK

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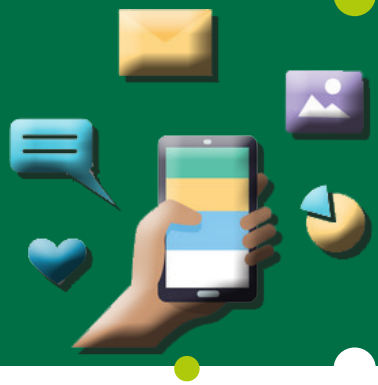
This simple action can reach thousands of individuals, locally and abroad.

Thank you



Dr Nicole Wolter

Prof Cheryl Cohen

EARLY ASSESSMENT OF THE CLINICAL SEVERITY OF THE SARS-COV-2 OMICRON VARIANT IN SOUTH AFRICA: A DATA LINKAGE STUDY

Wolter N, Jassat W, Walaza S, Welch R, Moultrie H, Groome M, Amoako DG, Everatt J, Bhiman JN, Scheepers C, Tebeila N, Chiwandire N, du Plessis M, Govender N, Ismail A, Glass A, *Mlisana K, Stevens W, Treurnicht FK, Makatini Z, Hsiao N yuan, Parboosing R, Wadula J, Hussey H, Davies MA, Boulle A,* ***von Gottberg A, Cohen C***

The Lancet

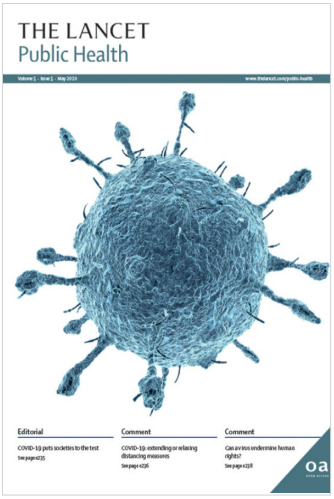
Impact factor: 79,323

Background: The SARS-CoV-2 omicron variant of concern was identified in South Africa in November, 2021, and was associated with an increase in COVID-19 cases. We aimed to assess the clinical severity of infections with the omicron variant using S gene target failure (SGTF) on the Thermo Fisher Scientific TaqPath COVID-19 PCR test as a proxy.

Methods: We did data linkages for national, South African COVID-19 case data, SARS-CoV-2 laboratory test data, SARS-CoV-2 genome data, and COVID-19 hospital admissions data. For individuals diagnosed with COVID-19 via TaqPath PCR tests, infections were designated as either SGTF or non-SGTF. The delta variant was identified by genome sequencing. Using multivariable logistic regression models, we assessed disease severity and hospitalisations by comparing individuals with SGTF versus non-SGTF infections diagnosed between Oct 1 and Nov 30, 2021, and we further assessed disease severity by comparing SGTF-infected individuals diagnosed between Oct 1 and Nov 30, 2021, with delta variant-infected individuals diagnosed between April 1 and Nov 9, 2021.

Findings: From Oct 1 (week 39), 2021, to Dec 6 (week 49), 2021, 161 328 cases of COVID-19 were reported in South Africa. 38 282 people were diagnosed via TaqPath PCR tests and 29 721 SGTF infections and 1412 non-SGTF infections were identified. The proportion of SGTF infections increased from two (3·2%) of 63 in week 39 to 21 978 (97·9%) of 22 455 in week 48. After controlling for factors associated with hospitalisation, individuals with SGTF infections had significantly lower odds of admission than did those with non-SGTF infections (256 [2·4%] of 10 547 vs 121 [12·8%] of 948; adjusted odds ratio [aOR] 0·2, 95% CI 0·1-0·3). After controlling for factors associated with disease severity, the odds of severe disease were similar between hospitalised individuals with SGTF versus non-SGTF infections (42 [21%] of 204 vs 45 [40%] of 113; aOR 0·7, 95% CI 0·3-1·4). Compared with individuals with earlier delta variant infections, SGTF-infected individuals had a significantly lower odds of severe disease (496 [62·5%] of 793 vs 57 [23·4%] of 244; aOR 0·3, 95% CI 0·2-0·5), after controlling for factors associated with disease severity.

Interpretation: Our early analyses suggest a significantly reduced odds of hospitalisation among individuals with SGTF versus non-SGTF infections diagnosed during the same time period. SGTF-infected individuals had a significantly reduced odds of severe disease compared with individuals infected earlier with the delta variant. Some of this reduced severity is probably a result of previous immunity.



Rudzani C. Mashau

Prof Nelesh Govender

OUTCOMES OF FLUCYTOSINE-CONTAINING COMBINATION TREATMENT FOR CRYPTOCOCCAL MENINGITIS IN A SOUTH AFRICAN NATIONAL ACCESS PROGRAMME: A CROSS-SECTIONAL OBSERVATIONAL STUDY

Rudzani C. Mashau, Susan T. Meiring, Vanessa C. Quan, *Jeremy Nel,* **Greg S. Greene**, *Andrea Garcia, Colin Menezes, Denasha L. Reddy, Michelle Venter, Sarah Stacey, Matamela Madua, Lia Boretti, Thomas S. Harrison, Graeme Meintjes, Amir Shroufi, Laura Trivino Duran, John Black,* ***Nelesh P. Govender,*** *GERMS-SA†*

Lancet Infectious Diseases

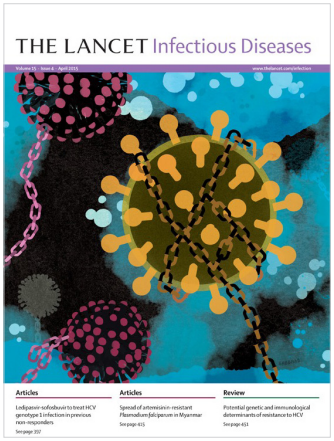
Impact factor: 71,421

Background: Although flucytosine is a key component of WHO-recommended induction treatment for HIV-associated cryptococcal meningitis, this antifungal agent is not widely available in low-income and middle-income countries due to limited production and cost. In 2018, a national flucytosine access programme was initiated in South Africa. We aimed to determine the effectiveness of flucytosine-containing induction regimens in routine care to motivate for the urgent registration of flucytosine and its inclusion in treatment guidelines.

Methods: In this cross-sectional study, we compared outcomes of adults aged 18 years and older with incident laboratory-confirmed cryptococcal meningitis treated with or without flucytosine-containing regimens at 19 sentinel hospitals in South Africa. A case of cryptococcosis was defined as illness in an adult with: (1) positive cerebrospinal fluid (CSF) India ink microscopy; (2) a positive CSF cryptococcal antigen test; or (3) culture of Cryptococcus neoformans or Cryptococcus gattii from CSF or any other specimen. We excluded patients without a case report form, those with an unknown or negative HIV serology result, those with a recurrent episode, and those who did not receive antifungal treatment in hospital. We assessed cumulative in-hospital mortality at 14 days and 30 days and calculated the overall crude in-hospital case-fatality ratio. We used random-effects logistic regression to examine the association between treatment group and in-hospital mortality.

Findings: From July 1, 2018, to March 31, 2020, 10 668 individuals were diagnosed with laboratory-confirmed cryptococcal meningitis, 7787 cases diagnosed at non-enhanced surveillance sites and 567 cases from eight enhanced surveillance sites with no access to flucytosine were excluded. Of 2314 adults with a first episode of cryptococcosis diagnosed at 19 facilities with access to flucytosine, 1996 had a case report form and of these, 1539 received induction antifungal treatment and were confirmed HIV-seropositive first-episode cases. Of 1539 patients who received antifungal therapy, 596 (38·7%) individuals received a flucytosine-containing regimen and 943 (61·3%) received another regimen. The median age was 36 years (IQR 32-43) and 906 (58·9%) participants were male and 633 (41·1%) were female. The crude in-hospital case-fatality ratio was 23·9% (95% CI 20·0-27·0; 143 of 596) in those treated with flucytosine-containing regimens and 37·2% (95% CI 34·0-40·0; 351 of 943) in those treated with other regimens. Patients admitted to non-academic hospitals (adjusted odds ratio [aOR] 1·95 [95% CI 1·53-2·48]; p<0·0001) and those who were antiretroviral treatment-experienced (aOR 1·30 [1·02-1·67]; p=0·033) were more likely to receive flucytosine. After adjusting for relevant confounders, flucytosine treatment was associated with a 53% reduction in mortality (aOR 0·47 [95% CI 0·35-0·64]; p<0·0001). Among survivors, the median length of hospital admission in the flucytosine group was 11 days (IQR 8-15) versus 17 days (13-21) in the comparison group (p=0·0010).

Interpretation: In-hospital mortality among patients treated with a flucytosine-containing regimen was comparable to reduced mortality reported in patients receiving a flucytosine-containing regimen in a recent multicentre African clinical trial. Flucytosine-based treatment can be delivered in routine care in a middle-income country with a substantial survival benefit.



Dr Harry Moultrie

INCREASED RISK OF SARS-COV-2 REINFECTION ASSOCIATED WITH EMERGENCE OF OMICRON IN SOUTH AFRICA

Pulliam JRC, van Schalkwyk C, ***Govender N, von Gottberg A, Cohen C, Groome MJ****, Dushoff J, Mlisana K,* ***Moultrie H***

Science

Impact factor: 47,728

Introduction: Globally, there have been more than 404 million cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with 5.8 million confirmed deaths as of February 2022. South Africa has experienced four waves of SARS-CoV-2 transmission, with the second, third, and fourth waves being driven by the Beta, Delta, and Omicron variants, respectively. A key question with the emergence of new variants is the extent to which they are able to reinfect those who have had a prior natural infection.

Rationale: We developed two approaches to monitor routine epidemiological surveillance data to determine whether SARS-CoV-2 reinfection risk has changed through time in South Africa in the context of the emergence of the Beta (B.1.351), Delta (B.1.617.2), and Omicron (B.1.1.529) variants. We analyzed line-list data on positive tests for SARS-CoV-2 with specimen receipt dates between 4 March 2020 and 31 January 2022 collected through South Africa's National Notifiable Medical Conditions Surveillance System. Individuals having sequential positive tests at least 90 days apart were considered to have suspected reinfections. Our routine monitoring of reinfection risk included comparison of reinfection rates with the expectation under a null model (approach 1) and estimation of the time-varying hazards of infection and reinfection throughout the epidemic (approach 2) based on model-based reconstruction of the susceptible populations eligible for primary and second infections.

Results: A total of 105,323 suspected reinfections were identified among 2,942,248 individuals with laboratory-confirmed SARS-CoV-2 who had a positive test result at least 90 days before 31 January 2022. The number of reinfections observed through the end of the third wave in September 2021 was consistent with the null model of no change in reinfection risk (approach 1). Although increases in the hazard of primary infection were observed after the introduction of both the Beta and Delta variants, no corresponding increase was observed in the reinfection hazard (approach 2). Contrary to expectation, the estimated hazard ratio for reinfection versus primary infection was lower during waves driven by the Beta and Delta variants than for the first wave: the relative hazard ratio for wave 2 versus wave 1 was 0.71 [95% confidence interval (95% CI): 0.60 to 0.85]; the relative hazard ratio for wave 3 versus wave 1 was 0.54 (95% CI: 0.45 to 0.64). By contrast, the recent spread of the Omicron variant has been associated with an increase in reinfection hazard coefficient. The estimated relative hazard ratio for reinfection versus primary infection versus wave 1 was 1.75 (95% CI: 1.48 to 2.10) for the period of Omicron emergence (1 November 2021 to 30 November 2021) and 1.70 (95% CI: 1.44 to 2.04) for wave 4 versus wave 1. Individuals with identified reinfections since 1 November 2021 had experienced primary infections in all three prior waves, and an increase in third infections has been detected since mid-November 2021. Many individuals experiencing third infections had second infections during the third (Delta) wave that ended in September 2021, strongly suggesting that these infections resulted from immune evasion rather than waning immunity.

Conclusion: Population-level evidence suggests that the Omicron variant is associated with a marked ability to evade immunity from prior infection. In contrast, there is no population-wide epidemiological evidence of immune escape associated with the Beta or Delta variants. This finding has important implications for public health planning, particularly in countries such as South Africa with high rates of immunity from prior infection. The further development of methods to track reinfection risk during pathogen emergence, including refinements to assess the impact of waning immunity, account for vaccine-derived protection, and monitor the risk of multiple reinfections, will be important for future pandemic preparedness.

Prof Cheryl Cohen

EFFECTIVE SURVEILLANCE OF VARIANTS

Kucharski AJ, ***Cohen C***

Science

Impact factor: 47,728

As countries move into a third year of the COVID-19 pandemic, they continue to face the threat of novel variants and the challenge of monitoring them. In England, the Real-time Assessment of Community Transmission (REACT-1) study has been tracking community infection levels since May 2020, routinely collecting samples from hundreds of thousands of randomly selected individuals and testing for the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On page 1406 of this issue, Elliott et al. (1) show a rapid increase of the Omicron variant in REACT-1 data during December 2021, estimating that this variant grew from comprising 10% of all infections to 90% in just over a week. By contrast, it took around a month for Delta to reach such prevalence. The REACT-1 program demonstrates the value of community surveillance programs as immunity builds and new variants emerge.

Rudzani C. Mashau

Prof Nelesh Govender

CULTURE-CONFIRMED NEONATAL BLOODSTREAM INFECTIONS AND MENINGITIS IN SOUTH AFRICA, 2014–19: A CROSS-SECTIONAL STUDY

Rudzani C Mashau, Susan T Meiring, *Angela Dramowski,* ***Rindidzani E Magobo, Vanessa C Quan, Olga Perovic, Anne von Gottberg, Cheryl Cohen,*** *Sithembiso Velaphi, Erika van Schalkwyk,* ***Nelesh P Govender****, for Baby GERMS-SA**

Lancet Global Health

Impact factor: 38,927

Background: Few population-level estimates of invasive neonatal infections have been reported from sub-Saharan Africa. We estimated the national incidence risk, aetiology, and pathogen antimicrobial susceptibility for culture-confirmed neonatal bloodstream infections and meningitis in South Africa.

Methods: We conducted a cross-sectional study of neonates (<28 days of life) admitted to neonatal or paediatric wards of 256 public sector health facilities in South Africa during 2014–19. Diagnostic pathology records from Jan 1, 2014, to Dec 31, 2019, were extracted from a national pathology data warehouse. A case was defined as a neonate with at least one positive blood or cerebrospinal fluid culture during a 14-day period. Incidence risk was calculated using annual numbers of registered livebirths. Among the causative pathogens identified, we calculated the proportion of cases attributed to each of them, as well as the rates of antibiotic susceptibility of Gram-positive and Gram-negative bacteria.

Findings: Among 43 438 records of positive cultures, there were 37 631 incident cases of neonatal infection with at least one pathogen isolated. The overall incidence risk of culture-confirmed infections was 6·0 per 1000 livebirths (95% CI 6·0–6·1). The incidence risk of late-onset sepsis (days 3–27 of life) was 4·9 per 1000 livebirths (4·9–5·0) and that of early-onset sepsis (days 0–2 of life) was 1·1 per 1000 livebirths (1·1–1·1); risk ratio 4·4 (95% CI 4·3–4·5). The cause of infection differed by syndrome, timing of infection onset, facility, and province, although Klebsiella pneumoniae (26%), Acinetobacter baumannii (13%), and Staphylococcus aureus (12%) were the dominant pathogens overall. Gram-negative bacteria had declining susceptibility to most antibiotics over the study period.

Interpretation: We found a high incidence risk of late-onset sepsis with provincial variations, predominance of K pneumoniae, and declining antibiotic susceptibility among Gram-negative bacteria. This national surveillance in an upper-middle-income country provides a baseline burden of neonatal infections against which the impact of future clinical and public health interventions can be measured.

Prof Cheryl Cohen

DEATHS FROM RSV IN YOUNG INFANTS-THE HIDDEN COMMUNITY BURDEN

Cohen C, *Zar HJ*

The Lancet Global Health

Impact factor: 26,763

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection (LRTI) in children. In 2015, the global burden in children under 5 years was estimated to be 33·1 million RSV-associated LRTI episodes, 3·2 million hospitalisations, and around 60 000 in-hospital deaths, but there were up to 118 200 estimated deaths when accounting for community-based mortality. The Global Burden of Diseases, Injuries, and Risk Factors Study reported that in 2016, RSV accounted for 10·7 million LRTI episodes and more than 41 000 deaths in children younger than 5 years. A more recent analysis of RSV-associated hospitalisations in 58 countries estimated that there were 2·5–4·1 million hospitalisations in children in 2019. However, studies of the burden of RSV in infants have largely been done in health-care facilities, with a paucity of data from community settings, in part because of the difficulties of capturing community deaths and confirming RSV. Estimates of the overall burden of RSV-associated mortality have therefore mainly relied on modelling studies.

Dr Nicole Wolter

Prof Cheryl Cohen

SEROPREVALENCE OF SARS-COV-2 AFTER THE SECOND WAVE IN SOUTH AFRICA IN HIV-INFECTED AND UNINFECTED PERSONS: A CROSS-SECTIONAL HOUSEHOLD SURVEY

Wolter N, *Tempia S,* ***von Gottberg A, Bhiman JN, Walaza S, Kleynhans J, Moyes J, Buys A,*** *McMorrow ML, Aitken S, Magni S, Yun J, Fellows T, Maakamedi T, Weiner R, Cawood C, Martinson N, Lebina L,* ***Jassat W,*** *Brauer M,* ***Cohen C***

Clinical Infectious Diseases

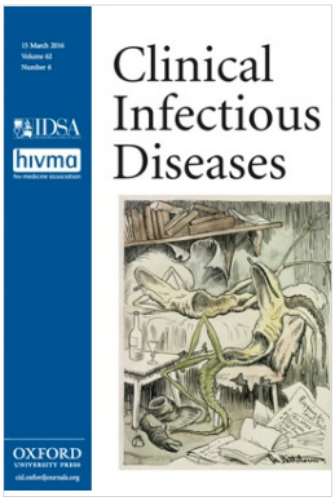
Impact factor: 9,079

Background: Seroprevalence studies are important for quantifying the burden of SARS-CoV-2 infections in resource-constrained countries.

Methods: We conducted a cross-sectional household survey spanning the second pandemic wave (November 2020 - April 2021) in three communities. Blood was collected for SARS-CoV-2 antibody (two ELISA assays targeting spike and nucleocapsid) and HIV testing. An individual was considered seropositive if testing positive on ≥1 assay. Factors associated with infection, and the age-standardised infection to case detection rate (ICR), infection hospitalisation rate (IHR) and infection fatality rate (IFR) were calculated.

Results: Overall 7959 participants were enrolled, with a median age of 34 years and HIV prevalence of 22.7%. SARS-CoV-2 seroprevalence was 45.2% (95% confidence interval 43.7% - 46.7%), and increased from 26.9% among individuals enrolled in December 2020 to 47.1% among individuals in April 2021. On multivariable analysis, seropositivity was associated with age, sex, race, being overweight/obese, having respiratory symptoms, and low socioeconomic status. Persons living with HIV (PLWHIV) with high viral load were less likely to be seropositive compared to HIV-uninfected individuals. The site-specific ICR, IHR and IFR ranged across sites from 4.4% to 8.2%, 1.2% to 2.5% and 0.3% to 0.6%, respectively.

Conclusions: South Africa has experienced a large burden of SARS-CoV-2 infections, with <10% of infections diagnosed. Lower seroprevalence among non-virally suppressed PLWHIV, likely as a result of inadequate antibody production, highlights the need to prioritise this group for intervention.



Dr Susan Meiring

Prof Cheryl Cohen

PROLONGED SHEDDING OF SARS-COV-2 AT HIGH VIRAL LOADS AMONGST HOSPITALISED IMMUNOCOMPROMISED PERSONS LIVING WITH HIV, SOUTH AFRICA

Meiring S, *Tempia S,* ***Bhiman JN, Buys A, Kleynhans J, Makhasi M,*** *McMorrow M,* ***Moyes J, Quan V, Walaza S, Du Plessis M, Wolter N, von Gottberg A, Cohen C,***
COVID-19 shedding study group

Clinical Infectious Diseases

Impact factor: 9,079

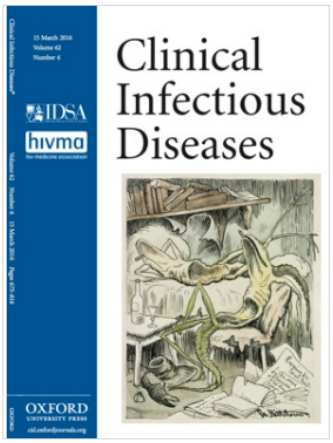
Background: We assessed SARS-CoV-2 RNA shedding duration and magnitude amongst persons living with HIV (PLHIV).

Methods: From May through December 2020, we conducted a prospective cohort study at 20 hospitals in South Africa. Adults hospitalised with symptomatic COVID-19 were enrolled and followed every two days with nasopharyngeal/oropharyngeal (NP/OP) swabs until documentation of cessation of SARS-CoV-2 shedding (two consecutive negative NP/OP swabs). Real-time reverse transcription-polymerase chain reaction testing for SARS-CoV-2 was performed and Cycle-threshold (Ct) values <30 were considered a proxy for high SARS-CoV-2 viral load. Factors associated with prolonged shedding were assessed using accelerated time-failure Weibull regression models.

Results: Of 2,175 COVID-19 patients screened, 300 were enrolled and 257 individuals (155 HIV-uninfected and 102 PLHIV) had >1 swabbing visit (median 5 visits (range2-21)). Median time to cessation of shedding was 13 days (inter-quartile range (IQR)6-25) and did not differ significantly by HIV-infection.

Discussion: Amongst a subset of 94 patients (41 PLHIV and 53 HIV-uninfected) with initial respiratory sample Ct-value <30, median time of shedding at high SARS-CoV-2 viral load was 8 days (IQR4-17). This was significantly longer in PLHIV with CD4 count<200cells/µl, compared to HIV-uninfected persons (median 27 days (IQR8-43) versus 7 days (IQR 4-13); aHR 0.14, 95%CI 0.07-0.28, p<0.001), with similar results in unsuppressed-HIV versus HIV-uninfected persons.

Conclusion: Although SARS-CoV-2 shedding duration did not differ significantly by HIV-infection, amongst a subset with high initial SARS-CoV-2 viral loads, immunocompromised PLHIV shed SARS-CoV-2 at high viral loads for longer than HIV-uninfected persons. Better HIV control may potentially decrease transmission time of SARS-CoV-2.



Prof Caroline Tiemessen

PREDICTORS OF CELL-ASSOCIATED HIV-1 DNA OVER 1 YEAR IN VERY EARLY TREATED INFANTS

*Kuhn L, **Paximadis M, Da Costa Dias B**, Shen Y, Mncube S, Strehlau R, Shiau S, Patel F, Burke M, Technau K-G, **Sherman GG, Loubser S**, Abrams EJ, **Tiemessen CT,** for the LEOPARD study team*

Clinical Infectious Diseases

Impact factor: 9,079

Background: Younger age of antiretroviral therapy (ART) initiation is associated with smaller viral reservoirs in perinatally acquired HIV-1 infection, but there is wide variability among early-treated infants. Predictors of this variability are not fully described.

Methods: Sixty-three neonates diagnosed with HIV-1 <48 hours after birth in Johannesburg, South Africa, were started on ART as soon as possible. Fifty-nine (94%) infants received nevirapine prophylaxis from birth until ART start. Viably preserved peripheral blood mononuclear cells (PBMCs) collected at regular intervals to 48 weeks, and from mothers at enrollment, were tested using integrase-targeted, semi-nested, real-time quantitative hydrolysis probe (TaqMan) PCR assays to quantify total HIV-1 subtype C viral DNA (vDNA). Predictors were investigated using generalized estimating equation regression.

Results: Thirty-one (49.2%) infants initiated ART <48 hours, 24 (38.1%) <14 days, and 8 (12.7%) >14 days of birth. Three-quarters were infected despite maternal antenatal ART (however, only 9.5% of women had undetectable viral load closest to delivery) and 86% were breastfed. Higher infant CD4+ T-cell percentage and viral load <100 000 copies/mL pre-ART were associated with lower vDNA in the first 48 weeks after ART start. No antenatal maternal ART and breastfeeding were also associated with lower vDNA. Older age at ART initiation had a discernible negative impact when initiated >14 days.

Conclusions: Among very early treated infants, higher CD4+ T-cell percentage and viral load <100 000 copies/mL pre-ART, infection occurring in the absence of maternal antenatal ART, and breastfeeding were associated with lower levels of HIV-1 DNA in the first 48 weeks of treatment. Clinical Trials Registration. clinicaltrials.gov (NCT02431975).

Dr Melinda Suchard

ALLOIMMUNITY TO CLASS 2 HUMAN LEUCOCYTE ANTIGENS MAY REDUCE HIV-1 ACQUISITION-A NESTED CASE-CONTROL STUDY IN HIV-1 SERODISCORDANT COUPLES.

Melinda S. Suchard, *Neil Martinson,* **Susan Malfeld**, *Debbie de Assis Rosa,Romel D. Mackelprang, Jairam Lingappa, Xuanlin Hou, Helen Rees,Sinead Delany-Moretlwe, Hadassa Goldfein, Heena Ranchod, David Coetzee, Kennedy Otwombe3,11, Lynn Morris,* ***Caroline T. Tiemessen,*** *and Dana M. Savulescu*

Frontiers in Immunology

Impact factor: 7,561

Enveloped viruses, including the Human Immunodeficiency Virus-1 (HIV), incorporate host proteins such as human leucocyte antigens (HLA) into their envelope. Pre-existing antibodies against HLA, termed HLA antibodies, may bind to these surface proteins and reduce viral infectivity. Related evidence includes macaque studies which suggest that xenoimmunization with HLA antigens may protect against simian immunodeficiency virus infection. Since HIV gp120 shows homology with class 2 HLA, including shared affinity for binding to CD4, class 2 HLA antibodies may influence HIV acquisition via binding to gp120 on the viral envelope. We conducted a nested case-control study on HIV serodiscordant couples, comparing the frequency of HLA antibodies among highly exposed persistently seronegative controls with those who went on to acquire HIV (HIV-seroconverters). We first performed low resolution HLA typing on 143 individuals who were HIV-infected at enrollment (index partners) and their corresponding sexual partners (115 highly exposed persistently seronegative individuals and 28 HIV-seroconverters). We then measured HLA class 1 and 2 antibodies in the highly exposed persistently seronegative individuals and HIV-seroconverters at early and late timepoints. We analyzed whether such antibodies were directed at HLA specificities of their HIV-infected index partners, and whether autoantibodies or complement-fixing class 2 HLA antibodies were present. Seventy-nine percent of highly exposed persistently seronegative individuals had HLA antibodies; 56% against class 1 and 50% against class 2 alleles. Half of the group of highly exposed persistently seronegative individuals, prior to seroconversion, expressed class 2 HLA antibodies, compared with only 29% of controls (p=0.05). HIV infection was a sensitizing event leading to de novo development of antibodies against HLA-A and HLA-B loci, but not against class 2 loci. HLA autoantibodies were present in 27% of highly exposed persistently seronegative individuals. Complement-fixing class 2 HLA antibodies did not differ significantly between highly exposed persistently seronegative individuals and seroconverters. In multivariable regression, presence of class 2 HLA antibodies at early timepoints was associated with reduced odds of HIV acquisition (odds ratio 0.330, confidence interval 0.112-0.976, p=0.045). These epidemiological data suggest that pre-existing class 2 HLA antibodies were associated with reduced odds of HIV acquisition.

Dr Tsidiso Maphanga

Prof Nelesh Govender

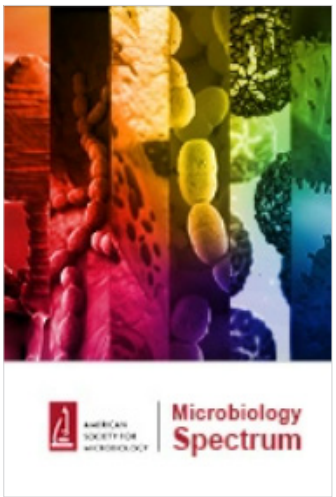
IN VITRO ANTIFUNGAL ACTIVITY OF MANOGEPIX AND OTHER ANTIFUNGAL AGENTS AGAINST SOUTH AFRICAN CANDIDA AURIS ISOLATES FROM BLOODSTREAM INFECTIONS

Maphanga TG, Mpembe RS, Naicker SD, Govender NP; *for GERMS-SA*

Microbiology Spectrum

Impact factor: 7,171

We determined the susceptibility of South African Candida auris bloodstream surveillance isolates to manogepix, a novel antifungal, and several registered antifungal agents. C. auris isolates were submitted to a reference laboratory between 2016 and 2017. Species identification was confirmed by phenotypic methods. We determined MICs for amphotericin B, anidulafungin, caspofungin, micafungin, itraconazole, posaconazole, voriconazole, fluconazole, and flucytosine using Sensititre YeastOne and manogepix using a modified Clinical and Laboratory Standards Institute broth microdilution method. Clade distribution was determined for a subset of isolates using whole-genome sequencing. Of 394 tested isolates, 357 were resistant to at least 1 antifungal class. The manogepix MIC range was 0.002 to 0.06 µg/mL for 335 isolates with fluconazole monoresistance. Nineteen isolates were resistant to both fluconazole and amphotericin B yet still had low manogepix MICs (range, 0.004 to 0.03 µg/mL). Two isolates from the same patient were panresistant but had manogepix MICs of 0.004 µg/mL and 0.008 µg/mL. Comparing MIC50 values, manogepix was >3-fold more potent than azoles, 4-fold more potent than echinocandins, and 9-fold more potent than amphotericin B. Of 84 sequenced isolates, the manogepix MIC range for 70 clade III isolates was 0.002 to 0.031 µg/mL, for 13 clade I isolates was 0.008 to 0.031 µg/mL, and for one clade IV isolate, 0.016 µg/mL. Manogepix exhibited potent activity against all isolates, including those resistant to more than one antifungal agent and in three different clades. These data support manogepix as a promising candidate for treatment of C. auris infections. Since C. auris was first detected in South Africa in 2012, health care-associated transmission events and large outbreaks have led to this pathogen accounting for more than 1 in 10 cases of candidemia. A large proportion of South African C. auris isolates are highly resistant to fluconazole but variably resistant to amphotericin B and echinocandins. There is also an emergence of pandrug-resistant C. auris isolates, limiting treatment options. Therefore, the development of new antifungal agents such as fosmanogepix or the use of new combinations of antifungal agents is imperative to the continued effective treatment of C. auris infections. Manogepix, the active moiety of fosmanogepix, has shown excellent activity against C. auris isolates. With the emergence of C. auris isolates that are pandrug-resistant in South Africa, our in vitro susceptibility data support manogepix as a promising new drug candidate for treatment of C. auris and difficult-to-treat C. auris infections.



Ms Jackie Kleynhans

Prof Cheryl Cohen

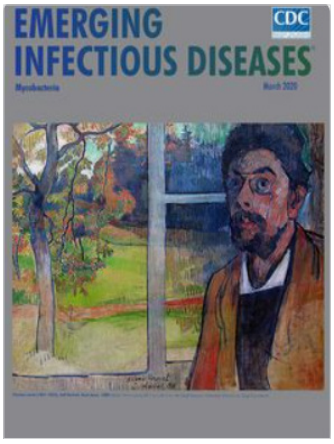
SARS-COV-2 SEROPREVALENCE AFTER THIRD WAVE OF INFECTIONS, SOUTH AFRICA

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 JD,* ***Jassat W, Neti M,*** *Brauer M,* ***Cohen C;*** *PHIRST-C Group1*

Emerging Infectious Diseases

Impact factor: 6,883

By November 2021, after the third wave of severe acute respiratory syndrome coronavirus 2 infections in South Africa, seroprevalence was 60% in a rural community and 70% in an urban community. High seroprevalence before the Omicron variant emerged may have contributed to reduced illness severity observed in the fourth wave.



Dr Naazneen Moolla

Dr Jacqueline Weyer

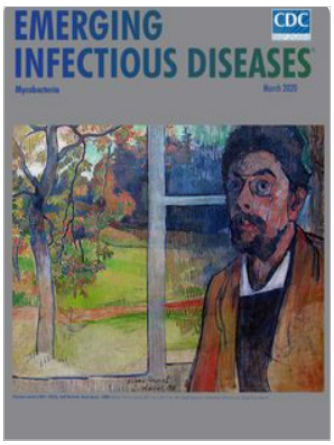
NEAR-COMPLETE GENOME SEQUENCE OF NDUMU VIRUS FROM GARISSA, KENYA, 1997

Naazneen Moolla, *Natalie Viljoen,* ***Venessa Patharoo, Antoinette Grobbelaar, Arshad Ismail, Jacqueline Weyer***

Emerging Infectious Diseases

Impact factor: 6,883

We report a nearly complete genome sequence of Ndumu virus (NDUV) identified using a metagenomics approach. The sequence was derived from a viral isolate obtained from a bovine calf following a diagnostic investigation of the 1997 to 1998 Rift Valley fever (RVF) outbreak in the Garissa District of northeastern Kenya.



Prof Anne von Gottberg

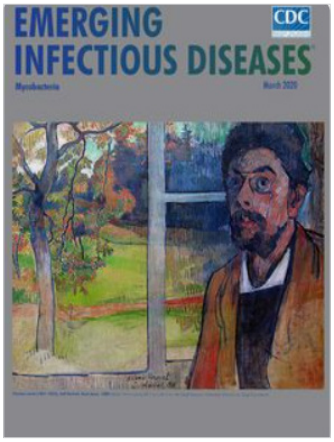
STREPTOCOCCUS PNEUMONIAE SEROTYPES ASSOCIATED WITH DEATH, SOUTH AFRICA, 2012-2018

Müller A, ***Kleynhans J, de Gouveia L, Meiring S, Cohen C,*** *Hathaway LJ,* ***von Gottberg A***

Emerging Infectious Diseases

Impact factor: 6,883

The Streptococcus pneumoniae polysaccharide capsule plays a role in disease severity. We assessed the association of serotype with case-fatality ratio (CFR) in invasive pneumococcal disease (IPD) and meningitis in South Africa, 2012-2018 (vaccine era), using multivariable logistic regression by manual backward elimination. The most common serotypes causing IPD were 8 and 19A. In patients <15 years of age, serotypes associated with increased CFR in IPD, compared with serotype 8 and controlling for confounding factors, were 11A, 13, 19F, 15A, and 6A. None of these serotypes were associated with increased CFR in meningitis. Among IPD patients >15 years of age, serotype 15B/C was associated with increased CFR. Among meningitis patients of all ages, serotype 1 was associated with increased CFR. PCV13 serotypes 1, 3, 6A, 19A, and 19F should be monitored, and serotypes 8, 12F, 15A, and 15B/C should be considered for inclusion in vaccines to reduce deaths caused by S. pneumoniae.



Mr Etienne Muller

Dr Ranmini Kularatne

PHENOTYPIC AND GENOTYPIC ACYCLOVIR RESISTANCE SURVEILLANCE OF GENITAL HERPES SIMPLEX VIRUS 2 IN SOUTH AFRICA

Etienne E. Muller, Dumisile V. Maseko, Ranmini S. Kularatne

Antiviral Research

Impact factor: 5,97

Acyclovir (ACV) is currently included in the syndromic management algorithm for genital ulcer disease in South Africa, and is the recommended first-line treatment for herpes simplex virus 2 (HSV-2). In the majority of cases, HSV-2 resistance to ACV is due to amino acid changes within the viral thymidine kinase (TK). Phenotypic and genotypic ACV resistance surveillance of HSV-2 derived from genital ulcer disease swab specimens was conducted at a primary healthcare facility in Johannesburg between 2018 and 2020. The objectives of this surveillance were to identify ACV resistance-associated mutations and polymorphisms in HSV-2 TK, and to determine the phenotypic ACV resistance profiles of the corresponding clinical HSV-2 isolates. Genotypic analysis of TK from 67 HSV-2 positive genital ulcer swabs revealed 48 specimens with TK mutations, conferring 113 nucleotide changes. No resistance-associated mutations were found, however, we identified nine known natural polymorphisms (R26H, A27T, S29A, G39E, N78D, L140F, T159I, R220K and R284S) and five amino acid changes of unknown significance (R18C, G39K, M70R, P75S and L263P). Phenotypic susceptibility testing of 52 cultivable HSV-2 isolates revealed all to be susceptible to ACV with IC50 values of <2 µg/ml. The five amino acid changes of unknown significance identified by genotypic testing were not correlated to phenotypic ACV resistance, and therefore grouped as natural polymorphisms. We did not detect any unknown or resistance-associated mutations in specimens that could not be phenotypically tested for ACV resistance. Our findings will supplement existing databases of HSV antiviral resistance-associated mutations and polymorphisms that could be used for genotypic ACV resistance screening.

Prof Penny Moore

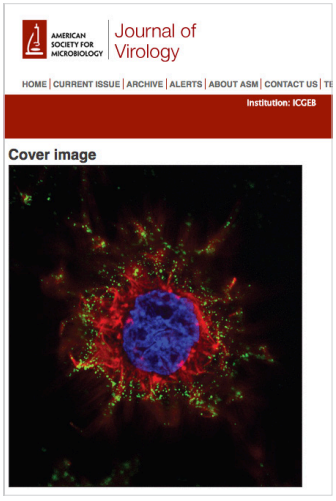
SINGLE-CHAIN VARIABLE FRAGMENTS OF BROADLY NEUTRALIZING ANTIBODIES PREVENT HIV CELL-CELL TRANSMISSION

van Dorsten RT, Reh L, Trkola A, Morris L, ***Moore PL***

Journal of Virology

Impact factor: 5,103

Broadly neutralizing antibodies (bNAbs) are able to prevent HIV infection following passive administration. Single-chain variable fragments (scFv) may have advantages over IgG as their smaller size permits improved diffusion into mucosal tissues. We have previously shown that scFv of bNAbs retain significant breadth and potency against cell-free viral transmission in a TZM-bl assay. However, scFv have not been tested for their ability to block cell-cell transmission, a model in which full-sized bNAbs lose potency. We tested four scFv (CAP256.25, PGT121, 3BNC117, and 10E8v4) compared to IgG, in free-virus and cell-cell neutralization assays in A3.01 cells, against a panel of seven heterologous viruses. We show that free-virus neutralization titers in the TZM-bl and A3.01 assays were not significantly different and confirm that scFv show a 1- to 32-fold reduction in activity in the cell-free model, compared to IgG. However, whereas IgG shows 3.4- to 19-fold geometric mean potency loss in cell-cell neutralization compared to free-virus transmission, scFv had more comparable activity in the two assays, with only a 1.3- to 2.3-fold reduction. Geometric mean 50% inhibitory concentration (IC50) of scFv for cell-cell transmission ranged from 0.65 µg/mL (10E8v4) to 2.3 µg/mL (3BNC117), with IgG and scFv neutralization showing similar potency against cell-associated transmission. Therefore, despite the reduced activity of scFv in cell-free assays, their retention of activity in the cell-cell format may make scFv useful for the prevention of both modes of transmission in HIV prevention studies. IMPORTANCE Broadly neutralizing antibodies (bNAbs) are a major focus for passive immunization against HIV, with the recently concluded HVTN Antibody Mediated Protection trial providing proof of concept. Most studies focus on cell-free HIV; however, cell-associated virus may play a significant role in HIV infection, pathogenesis, and latency. Single-chain variable fragments (scFv) of antibodies may have increased tissue penetration and reduced immunogenicity. We previously demonstrated that scFv of four HIV-directed bNAbs (CAP256.25, PGT121, 3BNC117, and 10E8v4) retain significant potency and breadth against cell-free HIV. As some bNAbs have been shown to lose potency against cell-associated virus, we investigated the ability of bNAb scFv to neutralize this mode of transmission. We demonstrate that unlike IgG, scFv of bNAbs are able to neutralize cell-free and cell-associated virus with similar potency. These scFv, which show functional activity in the therapeutic range, may therefore be suitable for further development as passive immunity for HIV prevention.



Dr Veerle Msimang

FACTORS AFFECTING THE USE OF BIOSECURITY MEASURES FOR THE PROTECTION OF RUMINANT LIVESTOCK AND FARM WORKERS AGAINST INFECTIOUS DISEASES IN CENTRAL SOUTH AFRICA

Veerle Msimang, *Melinda K. Rostal, Claudia Cordel, Catherine Machalaba, Stefano Tempia, Whitney Bagge, Felicity J. Burt, William B. Karesh,* ***Janusz T. Paweska****, Peter T. N. Thompson*

Transboundary and Emerging Diseases

Impact factor: 5,005

Biosecurity measures have been introduced to limit economic losses and zoonotic exposures to humans by preventing and controlling animal diseases. However, they are implemented on individual farms with varying frequency. The goal of this study was to evaluate which biosecurity measures were used by farmers to prevent infectious diseases in ruminant livestock and to identify factors that influenced these decisions. We conducted a survey in 264 ruminant livestock farmers in a 40,000 km2 area in the Free State and Northern Cape provinces of South Africa. We used descriptive statistics, to characterize biosecurity measures and farm attributes, then multivariable binomial regression to assess the strength of the association between the attributes and the implementation of biosecurity measures including property fencing, separate equipment use on different species, separate rearing of species, isolation of sick animals, isolation of pregnant animals, quarantine of new animals, animal transport cleaning, vaccination, tick control and insect control. Ninety-nine percent of farmers reported using at least one of the 10 biosecurity measures investigated (median [M]: 6; range: 0–10). The most frequently used biosecurity measures were tick control (81%, 214 out of 264), vaccination (80%, 211 out of 264) and isolation of sick animals (72%, 190 out of 264). More biosecurity measures were used on farms with 65–282 animals (M: 6; odds ratio [OR]: 1.52) or farms with 283–12,030 animals (M: 7; OR: 1.87) than on farms with fewer than 65 animals (M: 4). Furthermore, farmers who kept two animal species (M: 7; OR: 1.41) or three or more species (M: 7) used more biosecurity measures than single-species operations (M: 4). Farmers with privately owned land used more biosecurity measures (M: 6; OR: 1.51) than those grazing their animals on communal land (M: 3.5). Farms that reported previous Rift Valley fever (RVF) outbreaks used more biosecurity measures (M: 7; OR: 1.25) compared with farms without RVF reports (M: 6) and those that purchased animals in the 12 months prior to the survey (M: 7; OR: 1.19) compared with those that did not (M: 6). When introducing new animals into their herds (n = 122), most farmers used fewer biosecurity measures than they did for their existing herd: 34% (41 out of 122) used multiple biosecurity measures like those of vaccination, tick control, quarantine or antibiotic use, whereas 36% (44 out of 122) used only one and 30% (37 out of 122) used none. Certain farm features, primarily those related to size and commercialization, were associated with more frequent use of biosecurity measures. Given the variation in the application of biosecurity measures, more awareness and technical assistance are needed to support the implementation of a biosecurity management plan appropriate for the type of farm operation and available resources.

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: 9,079

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.

Dr Shune Oliver

Prof Basil Brooke

THE EFFECT OF BLOOD FEEDING ON INSECTICIDE RESISTANCE INTENSITY AND ADULT LONGEVITY IN THE MAJOR MALARIA VECTOR ANOPHELES FUNESTUS (DIPTERA: CULICIDE)

Shune V. Oliver, *Candice L. Lyons,* ***Basil D. Brooke***

Scientific Reports

Impact factor: 4,38

Insecticide-based vector control is key to the reduction and elimination of malaria. Although insecticide resistance is common in malaria vector populations, the operational implications are often unclear. High intensity pyrethroid resistance in the major malaria vector Anopheles funestus has been linked to control failure in Southern Africa. The aim of this study was to assess linkages between mosquito age, blood feeding and the intensity of pyrethroid resistance in two An. funestus laboratory strains that originate from southern Mozambique, namely the moderately pyrethroid resistant FUMOZ and the highly resistant FUMOZ-R. Resistance tended to decline with age. This effect was significantly mitigated by blood feeding and was most apparent in cohorts that received multiple blood meals. In the absence of insecticide exposure, blood feeding tended to increase longevity of An. funestus females and, following insecticide exposure, enhanced their levels of deltamethrin resistance, even in older age groups. These effects were more marked in FUMOZ-R compared to FUMOZ. In terms of programmatic decision-making, these data suggest that it would be useful to assess the level and intensity of resistance in older female cohorts wherever possible, notwithstanding the standard protocols for resistance testing using age-standardised samples.

Ms Ashmika Singh

Dr Shune Oliver

THE DYNAMIC GUT MICROBIOTA OF ZOOPHILIC MEMBERS OF THE ANOPHELES GAMBIAE COMPLEX (DIPTERA: CULICIDAE)

Ashimika Singh, *Mushal Allam,* ***Stanford Kwenda,*** *Zamantungwa T.H. Khumalo,* ***Arshad Ismail, Shune V. Oliver***

Scientific Reports

Impact factor: 4,38

The gut microbiota of mosquitoes plays a critical role in the life history of the animal. There is a growing body of research characterising the gut microbiota of a range of mosquito species, but there is still a paucity of information on some members of the Anopheles gambiae complex. In this study, the gut microbiota of four laboratory strains were characterised. SENN (Anopheles arabiensis—insecticide susceptible major vector), SENN DDT (Anopheles arabiensis—insecticide resistant major vector), MAFUS (Anopheles merus—minor vector) and SANGWE (Anopheles quadriannulatus—non-vector) were used in this study. The microbiota of fourth instar larvae, 3-day old, 15-day old non-blood fed and 15-day old blood fed females were characterised by MALDI-TOF mass spectroscopy and 16 s rRNA gene sequencing by next generation sequencing. The four strains differed in species richness but not diversity. The major vectors differ in β-diversity from that of the minor and non-vectors. There was no difference in α- or β-diversity in 15 non-blood fed females and 15-day old females that had 3 blood meals before day 15. These differences may be related to a mixture of the effect of insecticide resistance phenotype as well as a potential relationship to vector competence to a limited extent. Bacterial diversity is affected by species and age. There is also a potential relationship between the differences in gut microbiota and capacity to transmit parasites. This genetic background of the mosquitoes, however, play a major role, and must be considered in this relationship.

Dr Nicole Wolter

INTERNATIONAL LINKS BETWEEN STREPTOCOCCUS PNEUMONIAE VACCINE SEROTYPE 4 SEQUENCE TYPE (ST) 801 IN NORTHERN EUROPEAN SHIPYARD OUTBREAKS OF INVASIVE PNEUMOCOCCAL DISEASE

Gladstone RA, Siira L, Brynildsrud OB, Vestrheim DF, Turner P, Clarke SC, Srifuengfung S, Ford R, Lehmann D, Egorova E, Voropaeva E, Haraldsson G, Kristinsson KG, McGee L, Breiman RF, Bentley SD, Sheppard CL, Fry NK, Corander J, Toropainen M, Steens A, Akpaka PE, Ampofo K, Antonio M, Balaji V, Beall BW, Belabbès H, Benisty R, Bigogo G, Brooks AW, Carter PE, Cornick JE, Corso A, Cristina de Cunto Brandileone M, Cristine Grassi Almeida S, Croucher NJ, Dagan R, Davydov A, Diawara I, Doiphode S, ***du Plessis M****, Elmdaghri N, Köseoglu Eser Ö, Everett DB, Faccone D, Gagetti P, Givon-Lavi N, Hasanuzzaman M, Hawkins PA, Hryniewicz W, Hulten KG, Ip M, Kapusta A, Kandasamy R, Kastrin T, Keenan J, Klugman KP, Kwambana-Adams B, Law PY, Lees JA, Leung Ho P, Li Y, Lo SW, Ochoa TJ, Madhi SA, Metcalf BJ, Moïsi J, Mucavele Fundação Manhiça H,* ***Ndlangisa KM****, Nurse-Lucas M, Nzenze SA, Obaro SK, Paragi M, Pollard AJ, Ravikumar KL, Sadowy E, Saha SK, Sampane-Donkor E, Devi Sekaran S, Shakoor S, Shrestha S, Sigauque B, Skoczynska A, Soo ko K, Tientcheu PE, Titov L, Urban Y, Verani J, van Tonder AJ,* ***von Gottberg A****,* **Wolter N**

Vaccine

Impact factor: 3,641

Background: Pneumococcal disease outbreaks of vaccine preventable serotype 4 sequence type (ST)801 in shipyards have been reported in several countries. We aimed to use genomics to establish any international links between them.

Methods: Sequence data from ST801-related outbreak isolates from Norway (n = 17), Finland (n = 11) and Northern Ireland (n = 2) were combined with invasive pneumococcal disease surveillance from the respective countries, and ST801-related genomes from an international collection (n = 41 of > 40,000), totalling 106 genomes. Raw data were mapped and recombination excluded before phylogenetic dating.

Results: Outbreak isolates were relatively diverse, with up to 100 SNPs (single nucleotide polymorphisms) and a common ancestor estimated around the year 2000. However, 19 Norwegian and Finnish isolates were nearly indistinguishable (0–2 SNPs) with the common ancestor dated around 2017.

Conclusion: The total diversity of ST801 within the outbreaks could not be explained by recent transmission alone, suggesting that harsh environmental and associated living conditions reported in the shipyards may facilitate invasion of colonising pneumococci. However, near identical strains in the Norwegian and Finnish outbreaks does suggest that transmission between international shipyards also contributed to those outbreaks. This indicates the need for improved preventative measures in this working population including pneumococcal vaccination.

Dr Waasila Jassat

DECREASED SEVERITY OF DISEASE DURING THE FIRST GLOBAL OMICRON VARIANT COVID-19 OUTBREAK IN A LARGE HOSPITAL IN TSHWANE, SOUTH AFRICA

Abdullah F, Myers J, Basu D, Tintinger G, Ueckermann V, Mathebula M, Ramlall R, Spoor S, de Villiers T, Van der Walt Z, Cloete J, Soma-Pillay P, Rheeder P, Paruk F, Engelbrecht A, Lalloo V, Myburg M, Kistan J, van Hougenhouck-Tulleken W, Boswell MT, Gray G, ***Welch R,*** *Blumberg L,* ***Jassat W***

International Journal of Infectious Diseases

Impact factor: 3,623

Introduction: The coronavirus disease 2019 (COVID-19) first reported in Wuhan, China in December 2019 is a global pandemic that is threatening the health and wellbeing of people worldwide. To date there have been more than 274 million reported cases and 5.3 million deaths. The Omicron variant first documented in the City of Tshwane, Gauteng Province, South Africa on 9 November 2021 led to exponential increases in cases and a sharp rise in hospital admissions. The clinical profile of patients admitted at a large hospital in Tshwane is compared with previous waves.

Methods: 466 hospital COVID-19 admissions since 14 November 2021 were compared to 3962 admissions since 4 May 2020, prior to the Omicron outbreak. Ninety-eight patient records at peak bed occupancy during the outbreak were reviewed for primary indication for admission, clinical severity, oxygen supplementation level, vaccination and prior COVID-19 infection. Provincial and city-wide daily cases and reported deaths, hospital admissions and excess deaths data were sourced from the National Institute for Communicable Diseases, the National Department of Health and the South African Medical Research Council.

Results: For the Omicron and previous waves, deaths and ICU admissions were 4.5% vs 21.3% (p<0.00001), and 1% vs 4.3% (p<0.00001) respectively; length of stay was 4.0 days vs 8.8 days; and mean age was 39 years vs 49,8 years. Admissions in the Omicron wave peaked and declined rapidly with peak bed occupancy at 51% of the highest previous peak during the Delta wave. Sixty two (63%) patients in COVID-19 wards had incidental COVID-19 following a positive SARS-CoV-2 PCR test. Only one third (36) had COVID-19 pneumonia, of which 72% had mild to moderate disease. The remaining 28% required high care or ICU admission. Fewer than half (45%) of patients in COVID-19 wards required oxygen supplementation compared to 99.5% in the first wave. The death rate in the face of an exponential increase in cases during the Omicron wave at the city and provincial levels shows a decoupling of cases and deaths compared to previous waves, corroborating the clinical findings of decreased severity of disease seen in patients admitted to the Steve Biko Academic Hospital.

Conclusion: There was decreased severity of COVID-19 disease in the Omicron-driven fourth wave in the City of Tshwane, its first global epicentre.

Dr Kerrigan McCarthy

Dr Melinda Suchard

THE SHOW IS NOT OVER–WILD-TYPE POLIO IN MALAWI IS A WAKE UP CALL AND AN OPPORTUNITY FOR ELIMINATION EFFORTS

McCarthy K, Howard W, Yousif M, Moonsamy S, Suchard M

International Journal of Infectious Diseases

Impact factor: 3,623

With the world on the cusp of poliovirus eradication, the finding of a case of wild-type poliovirus 1 (WPV1) in a 4-year old child from Lilongwe, Malawi in November 2021 and reported in February (WHO-AFRO 2022) has come as a blow and in some respects, as an opportunity. In a statement released on February 17, 2022, the Malawian Ministry of Health confirmed the case and declared a public health emergency (WHO-AFRO 2022). Immediate investigations have been initiated, and no evidence of community transmission is presently discernible. In a statement also released on February 17, 2020, the Global Polio Eradication Initiative (GPEI) indicated that the virus is genetically related to a 2019 Pakistani isolate from Sindh Province, as evidenced by sequencing done at the National Institute for Communicable Diseases, with sequencing and phylogenetic analysis confirmed by the Centers for Disease Control, Atlanta, USA (Global Polio Eradication Initiative 2022).

Ms Andronica Moipone Shonhiwa

COVID-19 CLUSTER AMONG 2020 MATRIC RAGE FESTIVAL ATTENDEES, KWAZULU-NATAL PROVINCE, SOUTH AFRICA, NOVEMBER–DECEMBER 2020

Shonhiwa AM, *Tshabane C, Born K, Ngoma N, Pillay S, Thabane E, Matiea I, Mdose H,* ***Nevashan G, Ntshoe G,*** *Vivien E*

International Journal of Infectious Diseases

Impact factor: 3,623

South Africa moved to lockdown alert Level-1 on 20 September 2020 midnight, lockdown regulations were relaxed, gatherings were permitted with the number of people not exceeding 50% of normal venue capacity. The National Institute for Communicable Diseases was alerted by a clinician of a number of COVID-19 cases amongst young people who reportedly have attended the 2020 Matric Rage Festival, KwaZulu-Natal Province. This prompted an investigation to ascertain the existence of a COVID-19 cluster related to attendance of Rage Festival (Rage) and provide epidemiological characteristics of the cluster.

Prof Janusz Paweska

CLIMATE CONDITIONS DURING A RIFT VALLEY FEVER POST-EPIZOOTIC PERIOD IN FREE STATE, SOUTH AFRICA, 2014-2019

Assaf Anyamba, Richard Damoah, Alan Kemp, Jennifer L. Small, Melinda K. Rostal, Whitney Bagge, Claudia Cordel, Robert Brand, William B. Karesh, ***Janusz T. Paweska***

Frontiers in Veterinary Science

Impact factor: 3,412

Rift Valley fever virus (RVFV) activity in Southern Africa tends to occur during periods of sustained elevated rainfall, cooler than normal conditions, and abundant vegetation cover creating ideal conditions for the increase and propagation of populations of RVFV mosquito vectors. These climatic and ecological conditions are modulated by large-scale tropical-wide El Niño–Southern Oscillation (ENSO) phenomena. The aim of this 5-year study was to investigate climatic conditions during Rift Valley fever "post-epizootic" period in Free State province of the Republic of South Africa, which historically experienced the largest RVF outbreaks in this country. We collected satellite-derived rainfall, land surface temperature (LST), and normalized difference vegetation index (NDVI) data since 2014 to understand broad environmental conditions in the years following a period of sustained and widespread large RVF outbreaks (2008–2011) in the region. We found this post-epizootic/interepizootic period to be characterized by below-normal rainfall (~-500 mm), above LSTs (~+12°C), depressed NDVI (60% below normal), and severe drought as manifested particularly during the 2015–2016 growing season. Such conditions reduce the patchwork of appropriate habitats available for emergence of RVFV vectors and diminish chances of RVFV activity. However, the 2016–2017 growing season saw a marked return to somewhat wetter conditions without any reported RVFV transmission. In general, the aggregate vector collections during this 5-year period follow patterns observed in climate measurements. During the 2017–2018 growing season, late and seasonally above average rainfall resulted in a focal RVF outbreak in one location in the study region. This unanticipated event is an indicator of cryptic RVF activity during post-epizootic period and may be a harbinger of RVFV activity in the coming years.

Ms Shelina Moonsamy

Dr Nishi Prabdial-Sing

PREVALENCE AND INCIDENCE RATES OF LABORATORY-CONFIRMED HEPATITIS B INFECTION IN SOUTH AFRICA, 2015 TO 2019

Moonsamy S., Suchard M., Pillay P., Prabdial-Sing N

BMC Public Health

Impact factor: 3,295

Background: Hepatitis B virus (HBV), a global public health threat, is targeted for elimination by 2030. As national HBV prevalence and incidence is lacking for South Africa, our study aimed to provide such data in the public health sector.

Methods: We analysed laboratory-confirmed HBV data from 2015 to 2019 to determine annual prevalence and incidence rates of HBV infection per 100,000 population, HBsAg and anti-HBc IgM test positivity rates, and HBsAg and anti-HBc IgM testing rates per 100,000 population. Time trend and statistical analyses were performed on HBsAg and anti-HBc IgM test positivity rates.

Results: The national prevalence rate of HBV infection per 100,000 population increased from 56.14 in 2015 to 67.76 in 2019. Over the five years, the prevalence rate was higher in males than females, highest amongst individuals 25 to 49 years old and highest in Gauteng province. The HBsAg test positivity rate dropped from 9.77% in 2015 to 8.09% in 2019. Over the five years, the HBsAg test positivity rate was higher in males than females, amongst individuals 25 to 49 years old and amongst individuals of Limpopo province. Amongst HBsAg positive children under 5 years old, the majority (65.7%) were less than a year old. HBsAg testing rates per 100,000 population were higher in females under 45 years of age and in males 45 years and above. The national incidence rate of acute HBV infection per 100,000 population dropped from 3.17 in 2015 to 1.69 in 2019. Over the five-year period, incidence rates were similar between males and females, highest amongst individuals 20 to 39 years old and highest in Mpumalanga province. Amongst individuals 20 to 24 years old, there was a substantial decline in the incidence and anti-HBc IgM test positivity rates over time. Anti-HBc IgM testing rates per 100,000 population were higher in females under 40 years of age and in males 40 years and above.

Conclusion: Critical to hepatitis B elimination is strengthened infant vaccination coverage and interruption of vertical transmission. Transmission of HBV infection in adults may be reduced through heightened awareness of transmission routes and prevention measures.

Ms Judith Mwansa-Kambafwile

TREATMENT INITIATION AMONG TUBERCULOSIS PATIENTS: THE ROLE OF SHORT MESSAGE SERVICE (SMS) TECHNOLOGY AND WARD-BASED OUTREACH TEAMS (WBOTS)

Mwansa-Kambafwile, *J., Chasela, C., Levin, J., Ismail, N., and Menezes, C*

BMC Public Health

Impact factor: 3,295

In South Africa, tuberculosis (TB) is a public health problem with treatment initiation failure rates varying between 14.9 and 25%. Lack of proper provider/patient communication on next steps after testing, not being aware that results are ready; and other competing priorities are some of the reasons for this failure. We aimed to assess the effectiveness of Short Message Service (SMS) technology and ward-based outreach teams (WBOTs) in improving TB treatment initiation. A 3-arm randomized controlled trial (Standard of care-SOC, SMS technology or WBOTs) was conducted between September 2018 and April 2020. Newly diagnosed TB patients randomly allocated to SMS and WBOTs groups were sent reminder messages (text message or paper slip respectively) that results were ready. Due to unforeseen challenges (financial and impact of the COVID 19 pandemic), implementation was only in two of the eight clinics planned.

Dr Selamawit Woldesenbet

Prof Adrian Puren

ASSOCIATION BETWEEN VIRAL SUPPRESSION DURING THE THIRD TRIMESTER OF PREGNANCY AND UNINTENDED PREGNANCY AMONG WOMEN ON ANTIRETROVIRAL THERAPY: RESULTS FROM THE 2019 ANTENATAL HIV SENTINEL SURVEY, SOUTH AFRICA

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

PLOS

Impact factor: 3,24

About half of the pregnancies among women living with HIV (WLWH) receiving antiretroviral therapy (ART) in sub-Saharan African countries are reported to be unintended. Unintended pregnancy is associated with late initiation of antenatal care (ANC), and may delay provision of viral load monitoring services, antenatal adherence counselling and support, and other services that promote sustained viral suppression throughout pregnancy. This study examines the association between unsuppressed viral load during the third trimester of pregnancy and unintended pregnancy among women who initiated ART before pregnancy.

Dr Shune Oliver

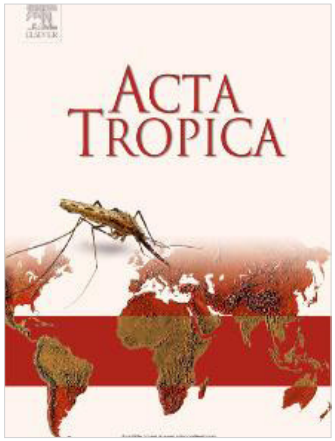
CHARACTERISATION OF THE EPIGENETIC ARCHITECTURE OF THE MAJOR MALARIA VECTOR ANOPHELES ARABIENSIS (DIPTERA: CULICIDAE) AFTER TREATMENT WITH EPIGENETIC MODULATORS AND HEAVY METALS

Alexander C.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 Mahlape P. Mahlangu

Dr Ranmini Kularatne

MOLECULAR CHARACTERISATION AND DETECTION OF MACROLIDE AND FLUORO-QUINOLONE RESISTANCE DETERMINANTS IN MYCOPLASMA GENITALIUM IN SOUTH AFRICA, 2015-2018

Mahlape P. Mahlangu, Etienne E. Müller, Bianca Da Costa Dias, Johanna M.E. Venter, Ranmini S. Kularatne

Sexually Transmitted Diseases

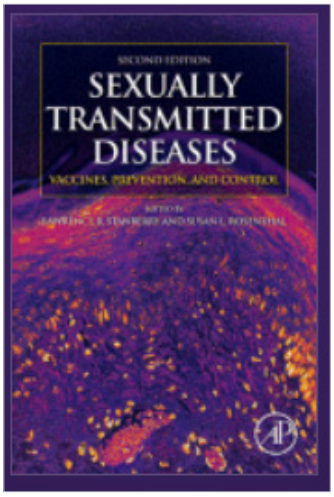
Impact factor: 2,83

Introduction: Antimicrobial resistance in Mycoplasma genitalium is a global concern, as therapeutic options are limited. We aimed to determine the prevalence of macrolide and fluoroquinolone resistance-associated genetic determinants and strain diversity in M. genitalium-positive surveillance specimens from symptomatic primary healthcare centre (PHC) attendees in South Africa (2015-2018). A secondary objective was to investigate for an association between M. genitalium strain type, HIV serostatus and antimicrobial resistance.

Methods: A total of 196 M. genitalium-positive specimens from adult males and females presenting with genital discharge to PHCs were tested for resistance-associated mutations in 23S rRNA, parC and gyrA. A dual-locus sequence type (DLST) was assigned to M. genitalium strains based on the detection of single nucleotide polymorphisms (SNPs) in the semi-conserved 5′ region of the mgpB gene (MG191-sequence typing) as well as the enumeration of short tandem repeats (STRs) within the lipoprotein (LP) gene (MG309 STR typing).

Results: The A2059G mutation in 23S rRNA, associated with macrolide resistance, was detected in 3/182 (1.7%; 95% CI 0.3 - 4.7) specimens. We did not detect gyrA or parC mutations associated with fluoroquinolone resistance in specimens that could be sequenced. Molecular typing with DLST revealed genetic heterogeneity, with DLST 4-11 being the most common M. genitalium strain type detected. There were no associations between DLST and macrolide resistance or HIV-infection.

Conclusion: We found a low prevalence of M. genitalium strains with macrolide resistance-associated mutations over a four-year surveillance period. Ongoing antimicrobial resistance surveillance is essential for informing genital discharge syndromic treatment guidelines.



Dr Susan Meiring

Prof Nelesh Govender

STUDY PROTOCOL FOR A POPULATION-BASED OBSERVATIONAL SURVEILLANCE STUDY OF CULTURE-CONFIRMED NEONATAL BLOODSTREAM INFECTIONS AND MENINGITIS IN SOUTH AFRICA: BABY GERMS-SA

Meiring S, Mashau R, Magobo R, Perovic O, Quan V, Cohen C, de Gouveia L, von Gottberg A, *Mackay C, Mailula MT, Phayane R, Dramowski A,* ***Govender NP***

BMJ Open

Impact factor: 2,692

Worldwide, neonatal mortality remains high accounting for 47% of childhood deaths in 2019 and including an estimated 500 000 deaths from neonatal infections. While 42% of global neonatal deaths occur in sub-Saharan Africa, there is limited understanding of population-level burden and aetiology of neonatal infections outside tertiary-level institutions.

Ms Babongile C. Ndlovu

Dr Elvira Singh

SKIN CANCER RISK FACTORS AMONG BLACK SOUTH AFRICANS - THE JOHANNESBURG CANCER STUDY, 1995 – 2016

Babongile C. Ndlovu, Mazvita Sengayi-Muchengeti, *Caradee Y. Wright,* ***Wenlong C. Chen, Lazarus Kuonza, Elvira Singh***

Immunity, Inflammation and Disease

Impact factor: 2,493

Background: The Black population has lower skin cancer incidence compared to White, Indian/Asian, and Mixed-race populations in South Africa; however, skin cancer still exists in the Black population. The aim of this study is to identify risk factors associated with skin cancer among Black South Africans.

Materials and Methods: A case-control study was conducted. Cases were patients with keratinocyte cancers (KCs) and/or melanoma skin cancers (MSCs) and controls were cardiovascular patients. Sociodemographic exposures, environmental health variables, smoking, and HIV status were assessed. Stepwise logistic regression was used to identify risk factors associated with KCs and MSCs.

Results: The KCs histological subtypes showed that there were more squamous cell carcinomas (SCCs) (78/160 in females, and 72/160 in males) than basal cell carcinomas (BCCs). The SCC lesions were mostly found on the skin of the head and neck in males (51%, 38/72) and on the trunk in females (46%, 36/78). MSC was shown to affect the skin of the lower limbs in both males (68%, 27/40) and females (59%, 36/61). Using females as a reference group, when age, current place of residency, type of cooking fuel used, smoking, and HIV status were adjusted for, males had an odds ratio (OR) of 2.04 for developing KCs (confidence interval [CI]: 1.08–3.84, p = .028). Similarly, when age, current place of residency, and place of cooking (indoors or outdoors) were adjusted for, males had an OR of 2.26 for developing MSC (CI: 1.19–4.29, p = .012).

Conclusions: Differences in the anatomical distribution of KCs by sex suggest different risk factors between sexes. There is a positive association between being male, smoking, rural dwelling, and a positive HIV status with KCs and being male and rural dwelling with MSC. The rural dwelling was a newly found association with skin cancer and warrants further investigation.

Dr Givemore Munhenga

Prof Basil Brooke

MALARIA RISK AND RECEPTIVITY: CONTINUING DEVELOPMENT OF INSECTICIDE RESISTANCE IN THE MAJOR MALARIA VECTOR ANOPHELES ARABIENSIS IN NORTHERN KWAZULU-NATAL, SOUTH AFRICA

Givemore Munhenga, Shune V. Oliver, Leanne N. Lobb, *Theresa T. Mazarire, Windy Sekgele, Thabo Mashatola, Nondumiso Mabaso, Dumsani M. Dlamini, Malibongwe Zulu, Fortunate Moletsane,* ***Blazenka D. Letinic,*** *Jacek Zawada,* ***Ashley Burke, Yael Dahan-Moss, Avhatakali Matamba, Maria Kaiser, Basil Brooke***

South African Journal of Science

Impact factor: 2,197

Malaria incidence in South Africa is highest in the three endemic provinces: KwaZulu-Natal, Mpumalanga and Limpopo. The contribution to malaria transmission by several mosquito species, variation in their resting behaviours and low levels of insecticide resistance makes it necessary to periodically monitor Anopheles species assemblages and resistance phenotypes in vector populations. The aim of this study was therefore to assess Anopheles species assemblage in northern KwaZulu-Natal and to collect insecticide susceptibility data for An. arabiensis, the primary vector of malaria in that province. Anopheles specimens were collected from Mamfene, Jozini, northern KwaZulu-Natal from November 2019 to April 2021. Progeny of wild-collected An. arabiensis females were used for standard insecticide susceptibility tests and synergist bioassays. Anopheles arabiensis contributed 85.6% (n=11 062) of the total catches. Samples for subsequent insecticide susceptibility bioassays were selected from 212 An. arabiensis families. These showed low-level resistance to DDT, permethrin, deltamethrin, and bendiocarb, as well as full susceptibility to pirimiphos-methyl. Synergist bioassays using piperonyl butoxide and triphenyl phosphate suggest oxygenase-based pyrethroid and esterase-mediated sequestration of bendiocarb. These low levels of resistance are unlikely to be operationally significant at present. It is concluded that northern KwaZulu-Natal Province remains receptive to malaria transmission despite ongoing control and elimination interventions. This is due to the perennial presence of the major vector An. arabiensis and other secondary vector species. The continued detection of low-frequency insecticide resistance phenotypes in An. arabiensis is cause for concern and requires periodic monitoring for changes in resistance frequency and intensity.

Prof Gayle Sherman

MOTIVATIONAL INTERVIEWING RETENTION COUNSELING AND ADHERENCE TO EARLY INFANT DIAGNOSTIC HIV TESTING SCHEDULE IN SOUTH AFRICA: THE PAEDLINK RANDOMIZED TRIAL

Onoya D, Jinga N, Nattey C, Mongwenyana C, Mngadi S, MacLeod WB, ***Sherman G***

Medicine

Impact factor: 1,889

Introduction: We report the PAEDLINK randomized trial results on the effect of motivational interviewing (MI) retention counseling on the adherence of postpartum women to the early infant diagnostic human immunodeficiency virus (HIV) testing schedule.

Methods: HIV positive women and their babies were enrolled 3 to 6 days after delivery at 4 midwife obstetric units in the Gauteng province of South Africa and randomized into (A) MI retention counseling and telephonic tracing, (B) biannual telephonic tracing, and (C) standard care. Mother–baby pairs were followed up for 18 months via medical records. The uptake of child HIV tests and maternal retention in the 0 to 6 and 7 to 18 month periods were modeled using Log-binomial regression.

Results: Overall, 501/711 enrolled mother–baby pairs received a second HIV polymerase chain reaction test by 6 months (70.0%, 70.5%, and 70.0% in groups A, B, and C, respectively). A higher proportion of intervention children (60.9%) were tested at 7 to 90 days than group B (68.3%, adjusted risk ratio [aRR] 0.8 for B vs A, 95% confidence interval [CI]: 0.7–0.9) and group C children (75.3%, aRR 0.9 for C vs A, 95% CI: 0.9–1.0). Child testing between 7 and 18-months was also higher in group A than C (10.7% A, vs 5.5% C, RR 2.0, 95% CI: 1.0–3.7). However, maternal retention was similar across groups, with 41.6% and 16.3% retained during the 0 to 6 and the 7 to 18-months periods, respectively.

Prof John Frean

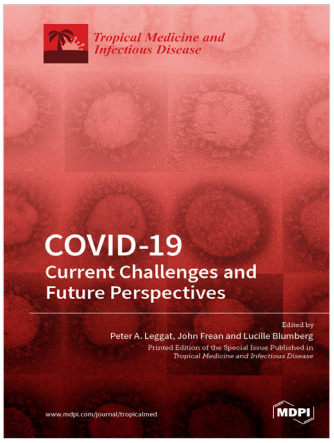
CLINICAL IMPROVEMENT OF DISSEMINATED ACANTHAMOEBA INFECTION IN A PATIENT WITH ADVANCED HIV USING A NON-MILTERFOSINE-BASED TREATMENT REGIMEN IN A LOW-RESOURCE SETTING

Denasha L. Reddy, Eunice van den Berg, Wayne Grayson, Matilda Mphahlele, ***John Frean***

Tropical Medicine and Infectious Disease

Impact factor: 0,6

Disseminated Acanthamoeba species infection is likely an underrecognized and underdiagnosed opportunistic infection in patients with advanced human immunodeficiency virus (HIV) disease in South Africa. It presents a unique clinical challenge in that the diagnosis can be difficult to establish and management options are limited in low-resource settings. To our knowledge, there is a paucity of literature to date on the successful use of combination treatment options for patients in low-resource settings without access to miltefosine. We present a case describing the clinical improvement of disseminated Acanthamoeba infection in a patient with advanced HIV using a non-miltefosine-based treatment regimen. The case serves to highlight that Acanthamoeba sp. infection should be considered as a differential diagnosis for nodular and ulcerative cutaneous lesions in patients with advanced HIV in South Africa, and that although there are alternative options for combination treatment in countries without access to miltefosine, efforts should be made to advocate for better access to miltefosine for the treatment of acanthamoebiasis in South Africa.



Prof John Frean

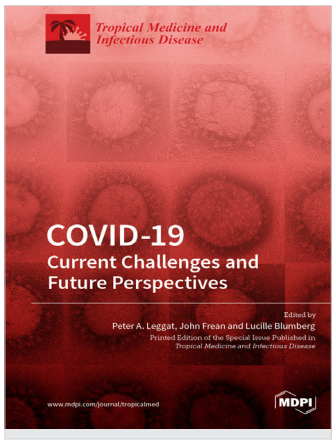
EXPOSURE OF SOUTH AFRICAN ABATTOIR WORKERS TO COXIELLA BURNETTI

Liesl De Boni, Sumaya Mall, ***Veerle Msimang****, Alex de Voux,* ***Jennifer Rossouw, John Frean***

Tropical Medicine and Infectious Disease

Impact factor: 0,6

Abattoir workers may contract Q fever by inhalation of Coxiella burnetii bacteria in aerosols generated by slaughtering livestock, or in contaminated dust. We estimated the seroprevalence of C. burnetii and examined the associated factors in a survey of South African abattoir workers. Coxiella burnetii seropositivity was determined by detection of IgG antibodies against C. burnetii phase II antigen. Logistic regression, adjusted for clustering and sampling fraction, was employed to analyze risk factors associated with C. burnetii seropositivity. Among 382 workers from 16 facilities, the overall seroprevalence was 33% (95% confidence interval (CI): 28-38%) and ranged from 8% to 62% at the facility level. Prolonged contact with carcasses or meat products (odds ratio (OR): 4.6, 95% CI: 1.51-14.41) and prior abattoir or butchery work experience (OR: 1.9, 95% CI: 1.13-3.17) were associated with C. burnetii seropositivity. In contrast, increasing age and livestock ownership were inversely associated. Precautions to protect abattoir personnel from Q fever are discussed.



Dr Tendesayi Kufa-Chakezha

Prof Adrian Puren

RECENCY OF HIV INFECTION, ANTIRETROVIRAL THERAPY USE AND VIRAL LOADS AMONG SYMPTOMATIC SEXUALLY TRANSMITTED INFECTION SERVICE ATTENDEES IN SOUTH AFRICA

T Kufa, F Radebe, E Cutler, M Goosen, L Wiesner, D Greyling, V Maseko, R Kularatne, A Puren

South African Medical Journal

Impact factor: 0,556

Background: Better integration of HIV and sexually transmitted infection (STI) prevention and treatment services is needed to accelerate progress towards the goal of zero new HIV infections.

Objectives: To describe HIV positivity, antiretroviral therapy (ART) use, viral suppression and recency of HIV infection among symptomatic STI service attendees at two primary care clinics in South Africa.

Methods: In a cross-sectional study, male and female STI service attendees presenting with symptoms consistent with STI syndromes were enrolled following informed consent. An interviewer-administered questionnaire was completed and appropriate genital and blood specimens were collected for STI testing and HIV biomarker measurements including recency of infection and antiretroviral (ARV) drug levels. Descriptive statistics were used to describe enrolled attendees, and to determine the proportion of attendees who were HIV-positive, recently infected, taking ART and virally suppressed. HIV-positive attendees with detectable ARVs were considered to be on ART, while those with viral loads (VLs) ≤200 copies/mL were considered virally suppressed.

Results: Of 451 symptomatic attendees whose data were analysed, 93 (20.6%) were HIV-positive, with 15/93 (16.1%) being recently infected. Recent infection was independently associated with genital ulcer disease at presentation, especially ulcers with no detectable STI pathogens. Among the 78 (83.9%) with long-term infection, only 30 (38.5%) were on ART, with 23/30 (76.7%) virally suppressed.

Conclusions: In a population at risk of HIV transmission, there was a high burden of recent infection and unsuppressed VLs. Incorporating pre-exposure prophylaxis, ART initiation and adherence support into STI services will be necessary for progress towards eliminating HIV transmission.

Ms Faith Moyo

Dr Tendesayi Kufa-Chakezha

POPULATION-LEVEL RISK FACTORS FOR VERTICAL TRANSMISSION OF HIV IN THE NATIONAL PREVENTION OF MOTHER-TO-CHILD TRANSMISSION PROGRAMME IN SOUTH AFRICA: AN ECOLOGICAL ANALYSIS

Moyo F, Haeri Mazanderani AH, Sherman GG, Kufa T

South African Medical Journal

Impact factor: 0,556

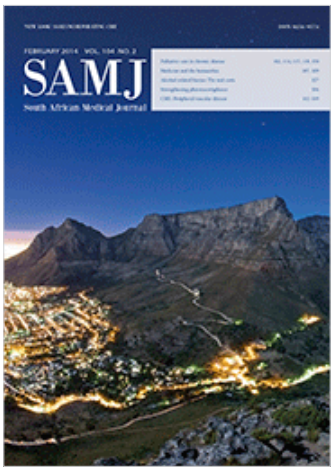
Background: Although South Africa has an overall mother-to-child transmission (MTCT) of HIV rate <5%, case rates remain high.

Objectives. To identify population-level predictors of MTCT to inform targeted interventions to further reduce paediatric HIV incidence.

Methods: The study was an ecological analysis of routine laboratory HIV-related test data from a synthetic cohort of women of reproductive age living with HIV (WRLHIV), identified from the National Health Laboratory Service's Corporate Data Warehouse between 2016 and 2017. Criteria based on syphilis screening and timing of HIV-related tests were used to identify pregnant and non-pregnant WRLHIV. Pregnant WRLHIV were followed from cohort entry at the first antenatal care (fANC) visit, through delivery to exit at the latest viral load (VL) or 15 months post delivery. Follow-up for non-pregnant WRLHIV started at cohort entry on 1 January 2016 to exit at the latest VL or 31 December 2018. HIV VL tests performed at cohort entry, delivery and cohort exit described viraemia (VL ≥50 copies/mL) at subdistrict level. A negative binomial regression model determined the association between MTCT cases and the number of viraemic WRLHIV at different time points, controlling for number of WRLHIV aged <25 years at cohort entry and other routine HIV-related indicators at subdistrict level.

Results: Of 3 386 507 WRLHIV identified, 178 319 (5.3%) met criteria for pregnancy. Median (interquartile range (IQR)) proportions of women with fANC booking <20 weeks' gestation, maternal HIV seroprevalence during antenatal care (ANC) and antiretroviral therapy (ART) coverage during ANC were 68.2% (62.9 - 72.8), 31.5% (23.4 - 35.7) and 94.8% (89.7 - 97.8), respectively. Viraemia was consistently higher in pregnant v. non-pregnant WRLHIV at median proportions of 42.9% (38.3 - 59.3) v. 35.0% (25.9 - 49.0) at cohort entry (p<0.001) and 36.3% (25.0 - 48.4) v. 29.6% (21.0 - 42.6) at cohort exit (p<0.001). In total, 4 535 children aged <24 months tested HIV polymerase chain reaction-positive, representing a median subdistrict-level case rate of 1 372 (914 - 2 077) per 100 000 live births. Maternal viraemia postpartum, maternal HIV seroprevalence and ART coverage during ANC positively correlated with cases of MTCT, while higher proportions of women with fANC booking <20 weeks' gestation were associated with a decline in MTCT cases.

Conclusions: Findings suggest that maternal viraemia postpartum, geographical areas with a higher burden of maternal HIV, women initiating ART late in pregnancy and/or incident maternal HIV during pregnancy are significant population-level predictors of MTCT in the national prevention of MTCT programme. Scale-up of HIV prevention services is required to lower maternal HIV prevalence, while expanded access to HIV testing will fast-track ART initiation among WRLHIV. Increased VL monitoring is critical to improve VL suppression rates for elimination of MTCT.



Ms Tafadzwa Dhokotera

Dr Mazvita Sengayi-Muchengeti

CERVICAL CANCER IN WOMEN LIVING IN SOUTH AFRICA: A RECORD LINKAGE STUDY OF THE NATIONAL HEALTH LABORATORY SERVICE AND THE NATIONAL CANCER REGISTRY

Dhokotera Tafadzwa, *Asangbeh, Serra, Bohlius Julia,* ***Singh Elvira,*** *Egger Matthias, Rohner Eliane, Ncayiyana Jabulani, Clifford Gary M,* ***Olago Victor, Segayi-Muchengeti, Mazvita***

ecancermedicalscience

Impact factor: 0,43

Introduction: In countries with high HIV prevalence, it is important to understand the cervical cancer (CC) patterns by HIV status to ensure targeted prevention measures. We aimed to determine the factors associated with CC compared to non-infection related cancer in women living in South Africa.

Methods: This was a cross-sectional study of women aged 15 years and older diagnosed with CC and non-infection related cancer in the South African public health sector from 2004 to 2014. The National Cancer Registry provided data on cancer, whilst HIV status was determined from routinely collected HIV related data from the National Health Laboratory Service. We explored the association of HIV infection, age, ethnicity and calendar period with CC compared to non-infection related cancer.

Results: From 2004 to 2014, 49,599 women were diagnosed with CC, whilst 78,687 women had non-infection related cancer. About 40% (n = 20,063) of those with CC and 28% (n = 5,667) of those with non-infection related cancer had a known HIV status. The median age at CC diagnosis was 44 years (interquartile range (IQR): 37-52) and 54 years (IQR: 46-64) for HIV positive and negative women, respectively, and for non-infection related cancer, 45 years (IQR: 47-55) and 56 years (IQR: 47-66) for HIV negative and positive women, respectively. Diagnosis of CC was associated with HIV positivity, Black ethnicity, earlier calendar period (2004-2006) and the ages 30-49 years. In comparison with Black women, the odds of CC were 44% less in Coloured women, 50% less in Asian women and 51% less in White women.

Conclusions: HIV positive women presented a decade earlier with CC compared to HIV negative women. A large proportion of women with CC were unaware of their HIV status with a disproportionate burden of CC in Black women. We recommend women attending CC screening facilities to be offered HIV testing so that recommendations for their follow-up visits are given according to their HIV status.

Dr Simone Richardson

Prof Penny Moore

SARS-COV-2 BETA AND DELTA VARIANTS TRIGGER FC EFFECTOR FUNCTION WITH INCREASED CROSS-REACTIVITY

Richardson SI, Manamela NP, Motsoeneng BM, Kaldine H, Ayres F, Makhado Z, *Mennen M, Skelem S, Williams N, Sullivan NJ, Misasi J, Gray GG, Bekker L, Ueckermann V, Rossouw TM, Boswell MT, Ntusi NAB, Burgers WA,* ***Moore PL***

Cell Reports Medicine

Impact factor: n/a

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) variants of concern (VOCs) exhibit escape from neutralizing antibodies, causing concern about vaccine effectiveness. However, while non-neutralizing cytotoxic functions of antibodies are associated with improved disease outcome and vaccine protection, Fc effector function escape from VOCs is poorly defined. Furthermore, whether VOCs trigger Fc functions with altered specificity, as has been reported for neutralization, is unknown. Here, we demonstrate that the Beta VOC partially evades Fc effector activity in individuals infected with the original (D614G) variant. However, not all functions are equivalently affected, suggesting differential targeting by antibodies mediating distinct Fc functions. Furthermore, Beta and Delta infection trigger responses with significantly improved Fc cross-reactivity against global VOCs compared with D614G-infected or Ad26.COV2.S-vaccinated individuals. This suggests that, as for neutralization, the infecting spike sequence affects Fc effector function. These data have important implications for vaccine strategies that incorporate VOCs, suggesting these may induce broader Fc effector responses.

Dr Dale Kitchin

Prof Penny Moore

AD26.COV2.S BREAKTHROUGH INFECTIONS INDUCE HIGH TITERS OF ANTIBODIES CAPABLE OF NEUTRALIZING VARIANTS OF CONCERN

Kitchin D*, Richardson SI*, van der Mescht, ***Motlou T, Mzindle N, Moyo-Gwete T, Makhado Z, Ayres F, Manamela NP, Spencer H, Lambson BE, Oosthuysen B,*** *Mennen M, Skelem S, Williams N, Ntusi NAB, Burgers WA, Gray GG, Bekker L, Boswell MT, Rossouw TM, Ueckermann V,* ***Moore PL*** *(*Equal contribution)*

Cell Reports Medicine

Impact factor: n/a

The Janssen (Johnson & Johnson) Ad26.COV2.S non-replicating viral vector vaccine has been widely deployed for COVID-19 vaccination programs in resource-limited settings. Here we confirm that neutralizing and binding antibody responses to Ad26.COV2.S vaccination are stable for 6 months post-vaccination, when tested against multiple SARS-CoV-2 variants. Secondly, using longitudinal samples from individuals who experienced clinically mild breakthrough infections 4 to 5 months after vaccination, we show dramatically boosted binding antibodies, Fc effector function, and neutralization. These high titer responses are of similar magnitude to humoral immune responses measured in convalescent donors who had been hospitalised with severe illness, and are cross-reactive against diverse SARS-CoV-2 variants, including the neutralization-resistant Omicron (B.1.1.529) variant that currently dominates global infections, as well as SARS-CoV-1. These data have implications for population immunity in areas where the Ad26.COV2.S vaccine has been widely deployed, but where ongoing infections continue to occur at high levels.

Prof Nelesh Govender

INFECTIOUS DISEASES AS 'A COLOURFUL UNIVERSE OF POSSIBILITIES'

Govender NP

Southern African Journal of Infectious Diseases

Impact factor: n/a

In the aftermath of the second coronavirus disease 2019 (COVID-19) wave in South Africa, during which members of the Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) had been drawn into every aspect of the response from front-line clinical care to epidemic control and cutting-edge vaccinology and science research, I proposed the Wisdom series to the FIDSSA Council. The pandemic was an acute reminder that healthcare professionals trained in infectious diseases are essential to the integrity of South Africa's health system. Despite this, a very few people choose to pursue a medical, nursing or scientific career focussed on infectious diseases. Simultaneously, many specialists in the field have chosen to leave, seeking greener pastures. Even before the pandemic, we had recognised that the infectious diseases medical speciality was in crisis.

Ms Siobhan L Johnstone

Dr Juno Thomas

IDENTIFYING GAPS IN HAND HYGIENE PRACTISE TO SUPPORT TAILORED TARGET AUDIENCE MESSAGING IN SOWETO: A CROSS SECTIONAL COMMUNITY SURVEY

Siobhan L Johnstone, Nicola Page, Michelle Groome**, Shabir A. Madhi, Portia Mutevedzi, **Juno Thomas

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Effective risk communication is essential for outbreak mitigation, as recently highlighted during the coronavirus disease 2019 (COVID-19) pandemic. Hand hygiene is one of the proposed public health interventions to protect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) acquisition and transmission along with social distancing, improved ventilation, environmental cleaning, and wearing of masks. Improving hand hygiene practices in the community requires an understanding of the socio-behavioural context. This cross-sectional community survey in Soweto identified gaps in hand hygiene, which can inform appropriate messaging at the community level. Only 42% of survey respondents practiced adequate hand hygiene. Tailored educational messaging should be targeted at young adults in particular, and the importance of soap for hand hygiene must be emphasised for all age groups. Risk communication should expand to focus on preventing multiple infectious diseases during and beyond the COVID-19 pandemic.

Mr Phuti Sekwadi

Mr Nevashan Govender

A DESCRIPTIVE STUDY OF A SARS-COV-2 SUPER SPREADER EVENT: A FUNERAL AND A HOUSE-PARTY IN A DISTRICT MUNICIPALITY OF THE EASTERN CAPE PROVINCE, SOUTH AFRICA, 2020

Phuti Sekwadi, *Nomlindo Makubalo, Ntathu Mini, Lifukazi Ngcwangu,* ***Mzimasi Neti, Ahmad Haeri Mazanderani, Nevashan Govender***

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Introduction: Coronavirus Disease 2019 (COVID-19) is a respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to the World Health Organisation, modes of transmission for SARS-CoV-2 include contact, droplet and airborne transmission has also been reported. On 16 March 2020, Nelson Mandela Bay District in the Eastern Cape Province recorded its first case of SARS-CoV-2, which was travel related. On 21 March 2020, over 1000 people attended a funeral of a healthcare worker in one of the townships within the district. This study aims to quantify the incident infections associated with a single funeral and describe the chain of transmission.

Methods: This is a retrospective descriptive study that uses COVID-19 data collected between March and April 2020 in Nelson Mandela Bay district. Interviews were conducted with newly reported COVID-19 cases by healthcare professionals through telephonic platforms and face-to-face. Data obtained through the interviews included possible exposures, risk factors, and demographics. Data analysis was done using Microsoft Excel.

Results: Four-hundred-and-twelve cases of COVID-19 were reported within the district during the study period. Of the first 100 cases reported within the district, 42% (42/100) were linked to the funeral; these included people who attended the funeral and those who had contact with the funeral attendees.

Conclusion: While funerals cannot be avoided, adherence to COVID-19 guidelines on funerals can help reduce infection transmission rates. Platforms such as virtual funeral services and virtual memorial services can help reduce the risk of COVID-19 transmission associated with these types of events.

Editorial and production team:

Sinenhlanhla Jimoh
Nileen Gale
Lesego Sibilanga
Puseletso Kobedi
Carina Kriel

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