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

SCIENCE FOCUS

A quarterly nexus of scientific insights

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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.

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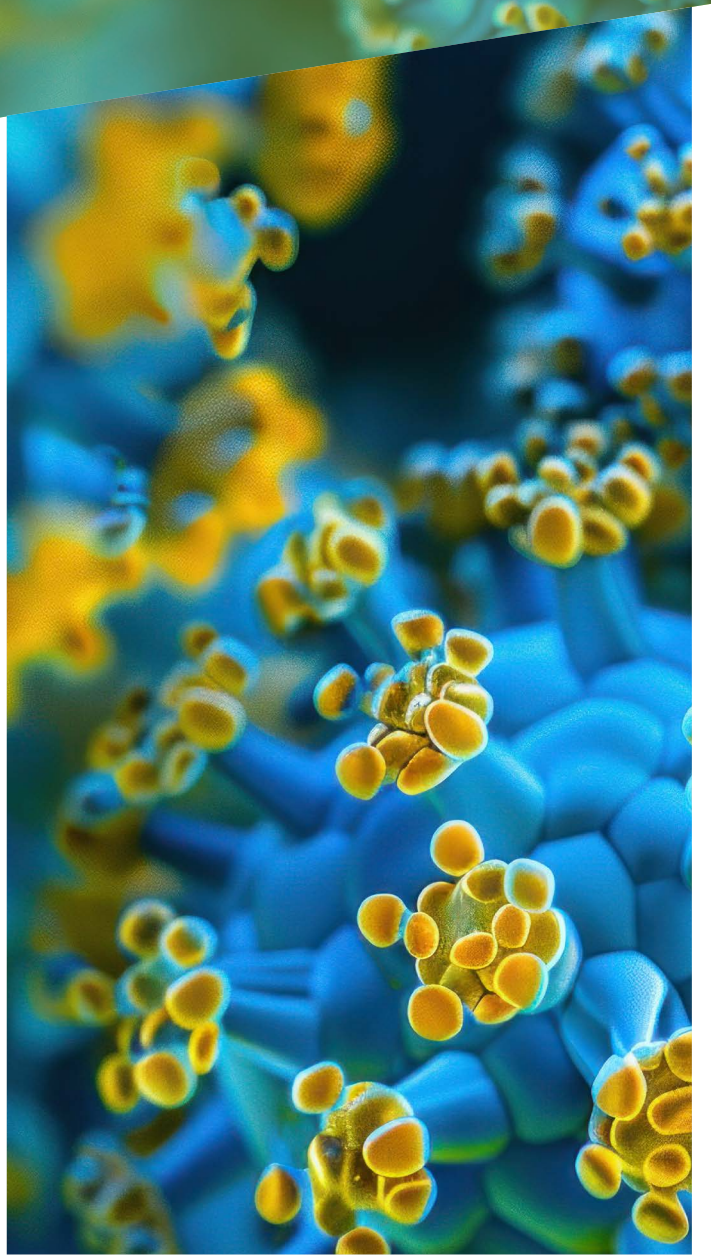
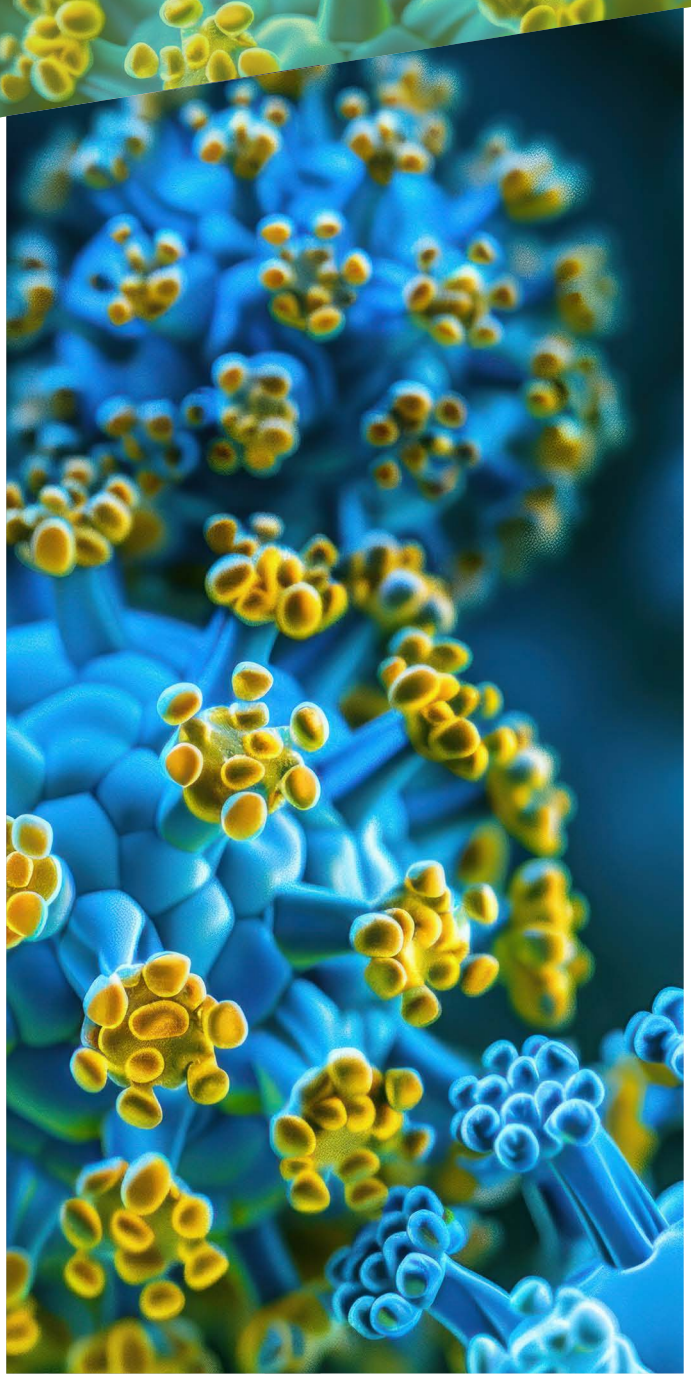




Disclaimer: Impact factor scores contained in this publication were compiled in June /July 2024.

MR VUYO SABANI

SENIOR COMMUNICATIONS MANAGER

NICD research provides valuable insights and deepens our understanding of the world

The Science Focus team is excited to present the latest issue of the National Institute for Communicable Diseases (NICD) quarterly publication, showcasing the Institute's scientific output for Quarter 1 (April-June 2024). This issue provides invaluable insights into the prevention, epidemiology, and treatment of various illnesses. The featured studies cover a wide range of public health and infectious disease topics, enhancing our understanding of these fields.

Mr Phuthi Sekwadi, Dr Linda Erasmus, and their colleagues who compiled the "Enteric Fever Surveillance Report, South Africa 2020-2023," published in the Public Health Bulletin South Africa, recommend that preventing and controlling enteric fever in South Africa should involve raising awareness among healthcare workers for proper identification and treatment of cases.

In the publication "Lived Experience of People with Cryptococcal Meningitis: A Qualitative Study," Mr Neo Legare, Dr Vanessa Quan, and colleagues discovered that individuals with HIV-associated cryptococcal meningitis face significant challenges both before and after diagnosis. They suggest that patients starting or restarting antiretroviral therapy should receive education as part of HIV counselling, emphasising the risks associated with cryptococcal meningitis.

Ms Moshibudi Poncho Phafane, and her team, in study "Factors Associated with Mortality Among Laboratory-Diagnosed Drug-Resistant Tuberculosis Patients on Treatment, KwaZulu-Natal Province, 2017-2019," highlight that early Integration of TB/HIV services, especially HIV testing and provision of antiretroviral treatment for all co-infected patients, may contribute to improving the clinical state of TB patients and reduce mortalities. This is crucial as tuberculosis remains a leading cause of death in South Africa.

We hope you find these and other research publications in this issue engaging and informative.

Thank you for your support!

On behalf of the team,

Vuyo Sabani
Senior Communications Manager

PROF. CHERYL COHEN

Early life respiratory syncytial virus disease - a preventable burden

Cohen C, Zar HJ

The Lancet Infectious Diseases

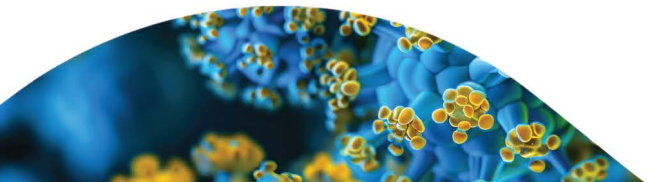
IMPACT FACTOR: 71.42

https://doi.org/10.1016/S1473-3099(24)00261-5

ABSTRACT

Respiratory syncytial virus (RSV) is a major cause of severe lower respiratory tract infection (LRTI), and mortality in infants, predominantly in those younger than 6 months. The predominant burden of severe illness occurs in full-term infants, although children born premature or those with underlying conditions such as cardiac or chronic lung disease are vulnerable to developing more severe disease. The burden is highly skewed to low-income and middle-income countries (LMICs), in which RSV-associated infant mortality rates are much higher than in high-income countries, in part due to a lack of access to care, with an estimated 70% of RSV-associated deaths occurring outside a health facility.

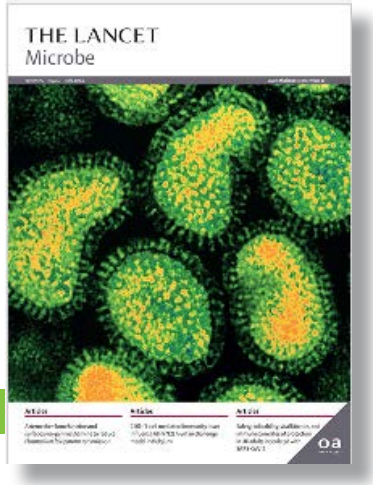
Nirsevimab has now been licensed and implemented in several high income countries, but is not yet available in any LMIC setting, despite more than 95% of RSV-associated LRTI and more than 97% of RSV-attributable deaths occurring in LMICs. A key obstacle to implementation is approval of the product in these settings, which usually depends on WHO pre-qualification, access to sufficient doses and affordability. Tiered pricing, consideration for funding by GAVI and other means of reducing pricing such as voluntary licensing to generic manufactures (as has been effectively done for HIV drugs) are needed. The experience through COVID has shown that fast tracking of immunization is possible. RSV is now a preventable disease in infants – widespread implementation of such an effective intervention is urgently needed in LMICs, to achieve protection for the most vulnerable children and reduce global inequity.



DR SHAHEED V. OMAR

MmpR5 protein truncation and bedaquiline resistance in *Mycobacterium tuberculosis* isolates from South Africa: a genomic analysis

Leah W Roberts, Kerri M Malone, Martin Hunt, **Lavania Joseph**, Penelope Wintringer, Jeff Knaggs, Derrick Crook, Maha R Farhat, Zamin Iqbal, **Shaheed V Omar**



The Lancet Microbe

IMPACT FACTOR: 20.9

https://doi.org/10.1016/S2666-5247(24)00053-3

Background: The antibiotic bedaquiline is a key component of new WHO regimens for drug-resistant tuberculosis; however, predicting bedaquiline resistance from bacterial genotypes remains challenging. We aimed to understand the genetic mechanisms of bedaquiline resistance by analysing *Mycobacterium tuberculosis* isolates from South Africa.

Method: For this genomic analysis, we conducted whole-genome sequencing of *Mycobacterium tuberculosis* samples collected at two referral laboratories in Cape Town and Johannesburg, covering regions of South Africa with a high prevalence of tuberculosis. We used the tool ARIBA to measure the status of predefined genes that are associated with bedaquiline resistance. To produce a broad genetic landscape of *M tuberculosis* in South Africa, we extended our analysis to include all publicly available isolates from the European Nucleotide Archive, including isolates obtained by the CRyPTIC consortium, for which minimum inhibitory concentrations of bedaquiline were available.

Findings: Between Jan 10, 2019, and July, 22, 2020, we sequenced 505 *M tuberculosis* isolates from 461 patients. Of the 64 isolates with mutations within the mmpR5 regulatory gene, we found 53 (83%) had independent acquisition of 31 different mutations, with a particular enrichment of truncated MmpR5 in bedaquiline-resistant isolates resulting from either frameshift mutations or the introduction of an insertion element. Truncation occurred across three *M tuberculosis* lineages, and were present in 66% of bedaquiline-resistant isolates. Although the distributions overlapped, the median minimum inhibitory concentration of bedaquiline was 0·25 mg/L (IQR 0·12-0·25) in mmpR5-disrupted isolates, compared with 0·06 mg/L (0·03-0·06) in wild-type *M tuberculosis*.

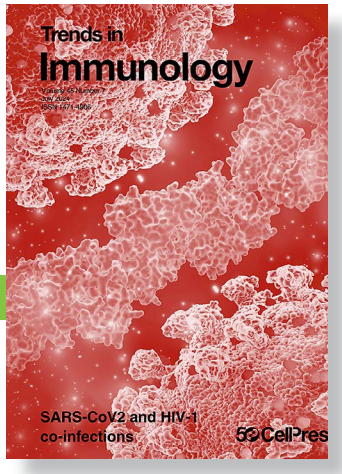
Interpretation: Reduction in the susceptibility of *M tuberculosis* to bedaquiline has evolved repeatedly across the phylogeny. In our data, we see no evidence that this reduction has led to the spread of a successful strain in South Africa. Binary phenotyping based on the bedaquiline breakpoint might be inappropriate to monitor resistance to this drug. We recommend the use of minimum inhibitory concentrations in addition to MmpR5 truncation screening to identify moderate increases in resistance to bedaquiline.

DR BOITUMELO MOTSOENENG

PROF. PENNY MOORE

SARS-CoV-2 humoral immunity in people living with HIV-1

Motsoeneng B, Bhiman JN, Richardson SI, Moore Penny L



Trends in Immunology

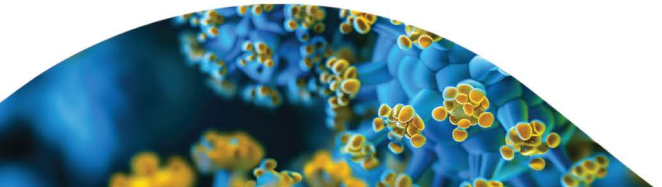
IMPACT FACTOR: 13.1

https://doi.org/10.1016/j.it.2024.05.005

ABSTRACT

The effect of COVID-19 on the high number of immunocompromised people living with HIV-1 (PLWH), particularly in Africa, remains a critical concern. Here, we identify key areas that still require further investigation, by examining COVID-19 vaccine effectiveness, and understanding antibody responses in SARS-CoV-2 infection and vaccination in comparison with people without HIV-1 (PWOH).

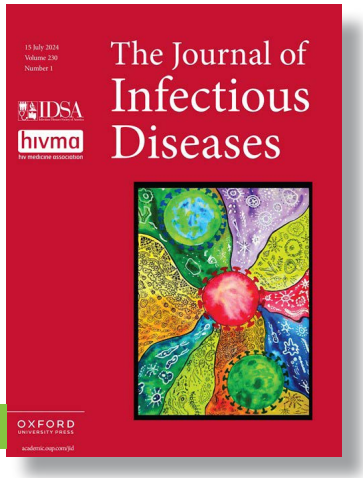
We also assess the potential impact of pre-existing immunity against endemic human coronaviruses on SARS-CoV-2 responses in these individuals. Lastly, we discuss the consequences of persistent infection in PLWH (or other immunocompromised individuals), including prolonged shedding, increased viral diversity within the host, and the implications on SARS-CoV-2 evolution in Africa.



DR BOITUMELO MOTSOENENG

DR SIMONE I. RICHARDSON

Hemagglutinin stalk-specific Fc-mediated functions are associated with protection against influenza-illness after seasonal influenza vaccination



Motsoeneng Boitumelo M, Dhar N, Nunes MC, Krammer F, Madhi SA, **Moore Penny L, Richardson SI**

The Journal of Infectious Diseases

IMPACT FACTOR: 5.226

https://doi.org/10.1093/infdis/jiae241

Background: Future vaccine candidates aim to elicit antibodies against the conserved hemagglutinin stalk domain. Understanding the protective mechanism of these antibodies, which mediate broad neutralization and Fc-mediated functions, following seasonal vaccination is critical.

Methods: Plasma samples were obtained from pregnant women with or without HIV-1 enrolled in a randomised trial (138 trivalent inactivated vaccine [TIV] and 145 placebo recipients). Twenty-three influenza cases were confirmed within 6 months postpartum. We measured H1 stalk-specific antibody-dependent cellular phagocytosis (ADCP), complement deposition (ADCD) and cellular cytotoxicity (ADCC) at enrolment and 1-month postvaccination.

Results: Lower H1 stalk-specific ADCP and ADCD activity was detected for participants with confirmed influenza compared with individuals without illness 1-month postvaccination. Pre-existing ADCP scores ≥250 reduced the odds of A/H1N1 infection (odds ratio [OR], 0.11; P = .01) with an 83% likelihood of risk reduction. Following TIV, ADCD scores of ≥25 and ≥15 significantly reduced the odds against A/H1N1 (OR, 0.10; P = .01) and non-group 1 (OR, 0.06; P = .0004) influenza virus infections, respectively. These ADCD scores were associated with >84% likelihood of risk reduction.

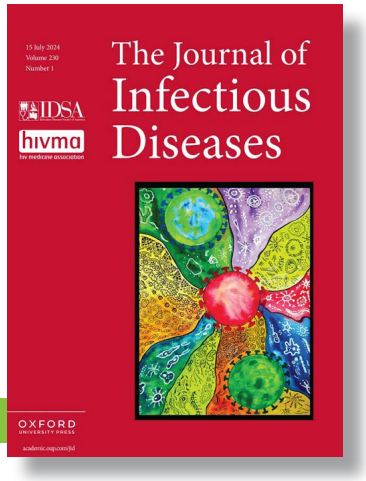
Conclusions: Overall, H1 stalk-specific Fc effector function correlates with protection against influenza illness following influenza vaccination during pregnancy. These findings provide insight into the protective mechanisms of hemagglutinin stalk antibodies.

MS RITO MKHARI

DR MIGNON DU PLESSIS

Genomic diversity and antimicrobial susceptibility of invasive *Neisseria meningitidis* in South Africa, 2016-2021

Rito L Mkhari, Susan Meiring, Linda de Gouveia, Wai Yin Chan, Keith A Jolley, Daria Van Tyne, Lee H Harrison, Henju Marjuki, **Arshad Ismail, Vanessa Quan, Cheryl Cohen, Sibongile Walaza, Anne von Gottberg, Mignon du Plessis**



The Journal Infectious Diseases

IMPACT FACTOR: 5.0

https://doi.org/10.1093/infdis/jiae225

Background: Invasive meningococcal isolates in South Africa have in previous years (<2008) been characterized by serogroup B, C, W, and Y lineages over time, with penicillin intermediate resistance (peni) at 6%. We describe the population structure and genomic markers of peni among invasive meningococcal isolates in South Africa, 2016–2021.

Method: Meningococcal isolates were collected through national, laboratory-based invasive meningococcal disease (IMD) surveillance. Phenotypic antimicrobial susceptibility testing and whole-genome sequencing were performed, and the mechanism of reduced penicillin susceptibility was assessed in silico.

Results: Of 585 IMD cases reported during the study period, culture and PCR-based capsular group was determined for 477/585 (82%); and 241/477 (51%) were sequenced. Predominant serogroups included NmB (210/477; 44%), NmW (116/477; 24%), NmY (96/477; 20%), and NmC (48/477; 10%). Predominant clonal complexes (CC) were CC41/44 in NmB (27/113; 24%), CC11 in NmW (46/56; 82%), CC167 in NmY (23/44; 53%), and CC865 in NmC (9/24; 38%). Peni was detected in 16% (42/262) of isolates, and was due to the presence of a *pen*A mosaic, with the majority harboring *pen*A7, *pen*A9, or *pen*A14.

Conclusions: IMD lineages circulating in South Africa were consistent with those circulating prior to 2008; however, peni was higher than previously reported, and occurred in a variety of lineages.

MS WILHELMINA STRASHEIM

PROF. OLGA PEROVIC

Whole-Genome Sequencing of Human and Porcine *Escherichia coli* Isolates on a Commercial Pig Farm in South Africa

Wilhelmina Strasheim, **Michelle Lowe**, **Anthony M. Smith** , Eric M. C. Etter and **Olga Perovic**

Antibiotics 2024, 13, 543

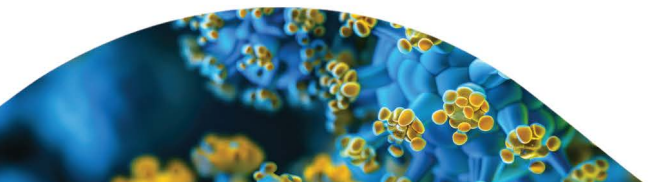
IMPACT FACTOR: 4.8

https://doi.org/10.3390/antibiotics13060543

ABSTRACT

Escherichia coli is an indicator micro-organism in One Health antibiotic resistance surveillance programs. The purpose of the study was to describe and compare *E. coli* isolates obtained from pigs and human contacts from a commercial farm in South Africa using conventional methods and whole-genome sequencing (WGS). Porcine *E. coli* isolates were proportionally more resistant phenotypically and harbored a richer diversity of antibiotic resistance genes as compared to human *E. coli* isolates. Different pathovars, namely ExPEC (12.43%, 21/169), ETEC (4.14%, 7/169), EPEC (2.96%, 5/169), EAEC (2.96%, 5/169) and STEC (1.18%, 2/169), were detected at low frequencies. Sequence type complex (STc) 10 was the most prevalent (85.51%, 59/169) among human and porcine isolates. Six STcs (STc10, STc86, STc168, STc206, STc278 and STc469) were shared at the human–livestock interface according to multilocus sequence typing (MLST). Core-genome MLST and hierarchical clustering (HC) showed that human and porcine isolates were overall genetically diverse, but some clustering at HC2–HC200 was observed. In conclusion, even though the isolates shared a spatiotemporal relationship, there were still differences in the virulence potential, antibiotic resistance profiles and cgMLST and HC according to the source of isolation.

Keywords: *Escherichia coli*; pigs; close human contacts; One Health; antibiotic resistance; whole-genome sequencing; virulence factors; core-genome MLST and hierarchical clustering; sequence type complex 10; South Africa.

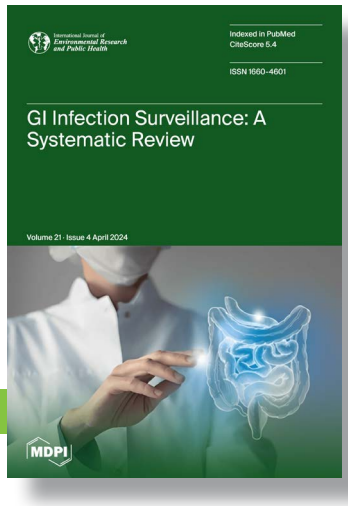


MS THERESA TAONA MAZARIRE

DR GIVEMORE MUNHENGA

The impact of climatic factors on temporal mosquito distribution and population dynamics in an area targeted for sterile insect technique pilot trials

Theresa Taona Mazarire, Leanne Lobb, Solomon Wakshom Newete, and **Givemore Munhenga**



International Journal of Environmental Research and Public Health

IMPACT FACTOR: 4.614

https://doi.org/10.3390/ijerph21050558

ABSTRACT

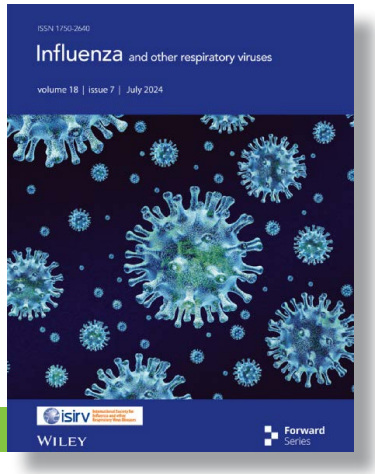
It is widely accepted that climate affects the mosquito life history traits; however, its precise role in determining mosquito distribution and population dynamics is not fully understood. This study aimed to investigate the influence of various climatic factors on the temporal distribution of *Anopheles arabiensis* populations in Mamfene, South Africa between 2014 and 2019. Time series analysis, wavelet analysis, cross-correlation analysis, and regression model combined with the autoregressive integrated moving average (ARIMA) model were utilized to assess the relationship between climatic factors and *An. arabiensis* population density. In total 3826 adult *An. arabiensis* collected was used for the analysis. ARIMA (0, 1, 2) (0, 0, 1)12 models closely described the trends observed in *An. arabiensis* population density and distribution. The wavelet coherence and time-lagged correlation analysis showed positive correlations between *An. arabiensis* population density and temperature (r = 0.537), humidity (r = 0.495) and rainfall (r = 0.298) whilst wind showed negative correlations (r = −0.466). The regression model showed that temperature (p = 0.00119), rainfall (p = 0.0436), and humidity (p = 0.0441) as significant predictors for forecasting *An. arabiensis* abundance. The extended ARIMA model (AIC = 102.08) was a better fit for predicting *An. arabiensis* abundance compared to the basic model. *Anopheles arabiensis* still remains the predominant malaria vector in the study area and climate variables were found to have varying effects on the distribution and abundance of *An. arabiensis*. This necessitates other complementary vector control strategies such as the Sterile Insect Technique (SIT) which involves releasing sterile males into the environment to reduce mosquito populations. This requires timely mosquito and climate information to precisely target releases and enhance the effectiveness of the program, consequently reducing the malaria risk.

MS KATE BISHOP

DR SIBONGILE WALAZA

Risk factors for severe COVID-19 among children and adolescents enrolled in acute respiratory infection sentinel surveillance in South Africa, 2020-2022

Kate Bishop, Susan Meiring, Stefano Tempia, **Anne von Gottberg, Nicole Wolter, Jackie Kleynhans, Fahima Moosa, Mignon du Plessis, Jocelyn Moyes, Mvuyo Makhasi, Boitumelo Chuene,** Aaron M Samuels, Halima Dawood, Gary Reubenson, Heather J Zar, **Vanessa Quan, Cheryl Cohen, Sibongile Walaza**



Influenza and other Respiratory viruses

IMPACT FACTOR: 4.4

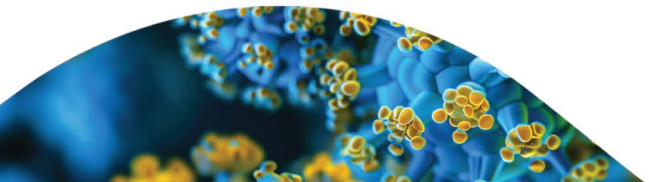
https://doi.org/10.1111/irv.13300

Background: Identifying children at risk for severe COVID-19 disease from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may guide future mitigation interventions. Using sentinel surveillance data, we aimed to identify risk factors for SARS-CoV-2-associated hospitalisation among patients aged ≤ 18 years with respiratory illness.

Method: From April 2020 to March 2022, patients meeting study case definitions were enrolled at four outpatient influenza-like illness (ILI) and five inpatient severe respiratory infection (SRI) surveillance sites and tested for SARS-CoV-2 infection using polymerase chain reaction (PCR). Each ILI clinic shared a catchment area with its corresponding SRI hospital. Potential risk factors for SARS-CoV-2-associated hospitalisation were analysed using multivariable logistic regression by comparing inpatient versus outpatient SARS-CoV-2 cases.

Results: Of 4688 participants aged ≤ 18 years, 4556 (97%) with complete PCR and HIV data were included in the analysis. Among patients with ILI and SRI, 92/1145 (8%) and 154/3411 (5%) tested SARS-CoV-2 positive, respectively. Compared to outpatients, hospitalised SARS-CoV-2 cases were associated with age < 6 months ([adjusted odds ratio (aOR) 8.0, 95% confidence interval (CI) 2.7-24.0] versus 1-4 years); underlying medical condition other than HIV [aOR 5.8, 95% CI 2.3-14.6]; laboratory-confirmed Omicron BA.1/BA.2 or Delta variant ([aOR 4.9, 95% CI 1.7-14.2] or [aOR 2.8, 95% CI 1.1-7.3] compared to ancestral SARS-CoV-2); and respiratory syncytial virus coinfection [aOR 6.2, 95% CI 1.0-38

Conclusion: Aligning with previous research, we identified age < 6 months or having an underlying condition as risk factors for SARS-CoV-2-associated SRI hospitalisation and demonstrated the potential of sentinel surveillance to monitor COVID-19 in children.



DR THANDEKA MOYO-GWETE

PROF. PENNY MOORE

Evaluating the antibody response elicited by diverse HIV envelope immunogens in the African green monkey (Vervet) model

Moyo-Gwete T, Ayres F, Mzindle NB, Makhado Z, Manamela NP, Richardson SI, Kitchin D, van Graan S, van Heerden J, Parbhoo N, Chege GK, **Moore Penny L**

Scientific Reports

IMPACT FACTOR: 3.8

https://doi.org/10.1038/s41598-024-63703-7

ABSTRACT

African Green (Vervet) monkeys have been extensively studied to understand the pathogenesis of infectious diseases. Using vervet monkeys as pre-clinical models may be an attractive option for low-resourced areas as they are found abundantly and their maintenance is more cost-effective than bigger primates such as rhesus macaques. We assessed the feasibility of using vervet monkeys as animal models to examine the immunogenicity of HIV envelope trimer immunogens in pre-clinical testing. Three groups of vervet monkeys were subcutaneously immunized with either the BG505 SOSIP.664 trimer, a novel subtype C SOSIP.664 trimer, CAP255, or a combination of BG505, CAP255 and CAP256. SU SOSIP.664 trimers.

All groups of vervet monkeys developed robust binding antibodies by the second immunization with the peak antibody response occurring after the third immunization. Similar to binding, antibody dependent cellular phagocytosis was also observed in all the monkeys. While all animals developed potent, heterologous Tier 1 neutralizing antibody responses, autologous neutralization was limited with only half of the animals in each group developing responses to their vaccine-matched pseudovirus. These data suggest that the vervet monkey model may yield distinct antibody responses compared to other models. Further study is required to further determine the utility of this model in HIV immunization studies.

MS LILIWE SHUPING

The impact of colistin-based regimens on mortality compared to other antimicrobials in patients with carbapenem-resistant *Enterobacterales bacteremia* in South African hospitals: a cross-sectional study

Nqobile Ngoma, **Olga Perovic,** Alex de Voux, Alfred Musekiwa, **Liliwe Shuping for GERMS-SA**

BMC Infectious Diseases

IMPACT FACTOR: 3.7

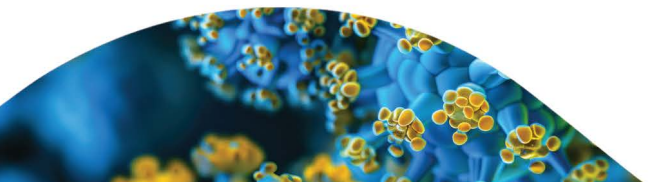
https://doi.org/10.1186/s12879-024-09459-x

Background: Treatment of carbapenem-resistant Enterobacterales (CRE) infections in low-resource settings is challenging particularly due to limited treatment options. Colistin is the mainstay drug for treatment; however, nephrotoxicity and neurotoxicity make this drug less desirable. Thus, mortality may be higher among patients treated with alternative antimicrobials that are potentially less efficacious than colistin. We assessed mortality in patients with CRE bacteremia treated with colistin-based therapy compared to colistin-sparing therapy.

Method: We conducted a cross-sectional study using secondary data from a South African national laboratory-based CRE bacteremia surveillance system from January 2015 to December 2020. Patients hospitalized at surveillance sentinel sites with CRE isolated from blood cultures were included. Multivariable logistic regression modeling, with multiple imputations to account for missing data, was conducted to determine the association between in-hospital mortality and colistin-based therapy versus colistin-sparing therapy.

Results: We included 1 607 case-patients with a median age of 29 years (interquartile range [IQR], 0–52 years) and 53% (857/1 607) male. Klebsiella pneumoniae caused most of the infections (82%, n=1 247), and the most common carbapenemase genes detected were blaOXA-48-like (61%, n=551), and blaNDM (37%, n=333). The overall in-hospital mortality was 31% (504/1 607). Patients treated with colistin-based combination therapy had a lower case fatality ratio (29% [152/521]) compared to those treated with colistin-sparing therapy 32% [352/1 086]) (p=0.18). In our imputed model, compared to colistin-sparing therapy, colistin-based therapy was associated with similar odds of mortality (adjusted odds ratio [aOR] 1.02; 95% confidence interval [CI] 0.78-1.33, p=0.873).

Conclusion: In our resource-limited setting, the mortality risk in patients treated with colistin-based therapy was comparable to that of patients treated with colistin-sparing therapy. Given the challenges with colistin treatment and the increasing resistance to alternative agents, further investigations into the benefit of newer antimicrobials for managing CRE infections are needed.



DR AHMAD MAZANDERANI

DR GAYLE G. SHERMAN

Attrition rates in HIV viral load monitoring and factors associated with overdue testing among children within South Africa's antiretroviral treatment program: retrospective descriptive analysis

Ahmad Haeri Mazanderani, Lebohang Radebe, Gayle G Sherman

JMIR PUBLIC HEALTH AND SURVEILLANCE

IMPACT FACTOR: 3.5

https://doi.org/10.2196/40796

Introduction: Numerous studies in South Africa have reported low HIV viral load (VL) suppression and high attrition rates within the pediatric HIV treatment program.

Objectives: Using routine laboratory data, we evaluated HIV VL monitoring, including mobility and overdue VL (OVL) testing, within 5 priority districts in South Africa.

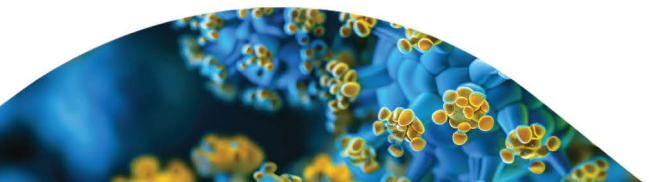
Method: We performed a retrospective descriptive analysis of National Health Laboratory Service (NHLS) data for children and adolescents aged 1-15 years having undergone HIV VL testing between May 1, 2019, and April 30, 2020, from 152 facilities within the City of Johannesburg, City of Tshwane, eThekwini, uMgungundlovu, and Zululand. HIV VL test–level data were deduplicated to patient-level data using the NHLS CDW (Corporate Data Warehouse) probabilistic record-linking algorithm and then further manually deduplicated. An OVL was defined as no subsequent VL determined within 18 months of the last test.

Variables associated with the last VL test, including age, sex, VL findings, district type, and facility type, are described. A multivariate logistic regression analysis was performed to identify variables associated with an OVL test.

Results: Among 21,338 children and adolescents aged 1-15 years who had an HIV VL test, 72.70% (n=15,512) had a follow-up VL test within 18 months. Furthermore, 13.33% (n=2194) of them were followed up at a different facility, of whom 3.79% (n=624) were in a different district and 1.71% (n=281) were in a different province. Among patients with a VL of ≥1000 RNA copies/mL of plasma, the median time to subsequent testing was 6 (IQR 4-10) months. The younger the age of the patient, the greater the proportion with an OVL, ranging from a peak of 52% among 1-year-olds to a trough of 21% among 14-year-olds.

On multivariate analysis, 2 consecutive HIV VL findings of ≥1000 RNA copies/mL of plasma were associated with an increased adjusted odds ratio (AOR) of having an OVL (AOR 2.07, 95% CI 1.71-2.51). Conversely, patients examined at a hospital (AOR 0.86, 95% CI 0.77-0.96), those with ≥2 previous tests (AOR 0.78, 95% CI 0.70-0.86), those examined in a rural district (AOR 0.63, 95% CI 0.54-0.73), and older age groups of 5-9 years (AOR 0.56, 95% CI 0.47-0.65) and 10-14 years (AOR 0.51, 95% CI 0.44-0.59) compared to 1-4 years were associated with a significantly decreased odds of having an OVL test.

Conclusion: Considerable attrition occurs within South Africa's pediatric HIV treatment program, with over one-fourth of children having an OVL test 18 months subsequent to their previous test. In particular, younger children and those with virological failure were found to be at increased risk of having an OVL test. Improved HIV VL monitoring is essential for improving outcomes within South Africa's pediatric antiretroviral treatment program.



DR MAZVITA SENGAYI-MUCHENGETI

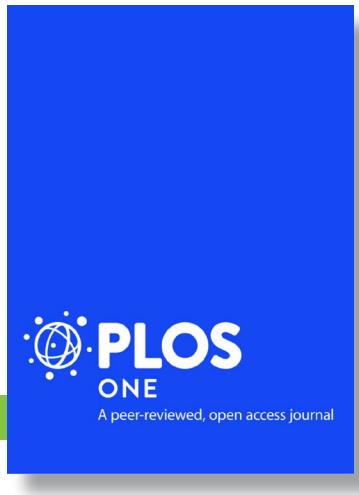
Cancer diagnostic service use in people living with HIV in South Africa: A cross-sectional study

Olago V, Nimako G, Bartels L, Bohlius J, Dhokotera T, Egger M, Singh E,
Sengayi-Muchengeti M

PLOS One

IMPACT FACTOR: 2.9

https://doi.org/10.1371/journal.pone.0291897



Objective: The objective of this study was to map place of cancer diagnosis in relation to Human Immunodeficiency Virus (HIV) care centre among people living with HIV (PLHIV) within South Africa (SA) using national laboratory database.

Design: We linked HIV and cancer laboratory data from 2004-2014 using supervised machine-learning algorithms. We performed a cross-sectional analysis comparing province where individuals accessed their HIV care versus where they had their cancer diagnosis.

Setting: We used laboratory test records related to HIV diagnostics and care, such as CD4 cell counts and percentages, rapid tests, qualitative Polymerase Chain Reaction (PCR), antibody and antigen tests for HIV data that was documented as HIV positive and laboratory diagnosed cancer records from SA.

Study population: Our study population consisted of HIV records from the National Health Laboratory Service (NHLS) that linked to cancer record at the National Cancer Registry (NCR) between 2004-2014.

Primary and secondary outcomes: We linked HIV records from NHLS to cancer records at NCR in order to study the inherent characteristics of the population with both HIV and cancer.

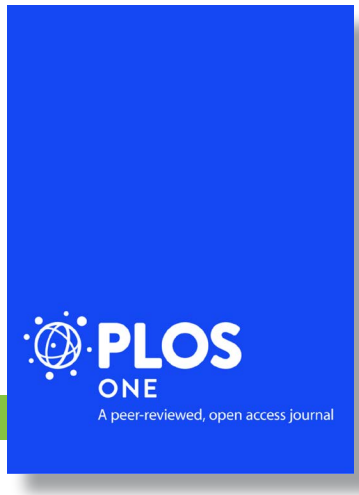
Results: The study population was 68,284 individuals with cancer and documented HIV related laboratory test. The median age at cancer diagnosis was 40 [IQR, 33-48] years for the study population with most cancers in PLHIV diagnosed in females 70.9% [n = 46,313]. Of all the PLHIV and cancer, 25% (n = 16,364 $p < 0.001$) sought treatment outside their province of residence with 60.7% (n = 10,235) travelling to Gauteng. KZN had 46.6% (n = 4,107) of its PLHIV getting cancer diagnosis in Gauteng. Western Cape had 95% (n = 6,200) of PLHIV getting cancer diagnosis within the province.

Conclusion: Our results showed health systems inequalities across provinces in SA with respect to cancer diagnosis. KZN for example had nearly half of the PLHIV getting cancer diagnosis outside the province while Western Cape is able to offer cancer diagnostic services to most of the PLHIV in the province. Gauteng is getting over burdened with referral for cancer diagnosis from other provinces. More effort is required to ensure equitable access to cancer diagnostic services within the country.

DR MAZVITA SENGAYI-MUCHENGETI

Breast cancer in women by HIV status: A report from the South African National Cancer Registry

Davidović M, Dhokotera T, Dos-Santos-Silva I, Bohlius J, **Sengayi-Muchengeti M**



PLOS One

IMPACT FACTOR: 2.9

https://doi.org/10.1371/journal.pone.0305274

Background: Breast cancer (BC) is the leading cause of cancer-related morbidity and mortality in women living in South Africa, a country with a high HIV burden. However, characteristics of the double burden of HIV and BC in South Africa have not been properly investigated. We described characteristics of BC cases by HIV status in South Africa.

Method: In this nationwide South African study, we obtained BC records for women aged ≥15 years diagnosed in the public health sector between January 2004 and December 2014. We included records from the National Cancer Registry that had been linked to HIV-related laboratory records from the National Health Laboratory Service. We assessed the odds of being HIV positive versus HIV negative in relation to patient-, cancer-, and municipality-related characteristics.

Results: From 2004-2014, 40 520 BC cases were diagnosed in women aged ≥15 years. Of these, 73.5% had unknown HIV status, 18.7% were HIV negative, and 7.7% were HIV positive. The median age at BC diagnosis was 43 years (interquartile range [IQR]: 37-52) in HIV positive and 57 years (IQR: 46-68) in HIV negative women, respectively. The odds of being HIV positive was higher for women who were aged 30-34 years compared to women aged 35-39 years at cancer diagnosis (odds ratio [OR] 1.38, 95% confidence interval [CI] 1.10-1.71), Black versus non-Black (OR 6.41, 95% CI 5.68-7.23), diagnosed with cancer in rural versus urban areas (OR 1.59, 95% CI 1.40-1.82) and diagnosed in municipalities with low and middle (OR 3.46, 95% CI 2.48-4.82) versus high socioeconomic position (OR 2.69, 95% CI 2.11-3.42).

Conclusion: HIV status was unknown for the majority of BC patients. Among those with known HIV status, being HIV positive was associated with a younger age at cancer diagnosis, being Black and receiving care in municipalities of poor socioeconomic position. Future studies should examine opportunities to integrate HIV and BC control programs.

DR CHIA-YU CHEN

DR SHÜNÉ V. OLIVER

Characterization of the tissue and strain-specific microbiota of *Anopheles funestus Giles* (diptera: culicidae)

Chia-Yu Chen, Wai -Yin Chan, **Arshad Ismail**, and **Shüné V. Oliver**

Tropical Medicines and Infectious Disease

IMPACT FACTOR: 2.9

https://doi.org/10.3390/tropicalmed9040084

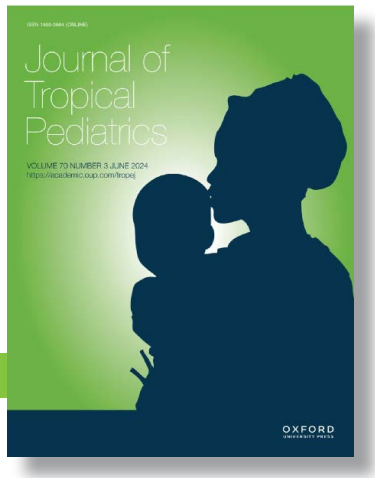
ABSTRACT

The mosquito microbiota is a critical determinant of mosquito life history. It is therefore a target for novel vector control strategies like paratransgenesis. However, the microbiota in *Anopheles funestus*, a major African malaria vector, is poorly characterized. Thus, the study aimed to investigate the overall bacterial landscape in the salivary glands, ovaries and midguts of three laboratory strains of *An. funestus* differing in insecticide-resistant phenotype by sequencing the V3-V4 hypervariable region of bacterial 16S rRNA genes. When examining alpha diversity, the salivary glands harbored significantly more bacteria in terms of species richness and evenness compared to ovaries and midguts. On the strain level, the insecticide-susceptible FANG strain had significantly lower bacterial diversity than the insecticide-resistant FUMOZ and FUMOZ-R strains. When looking at beta diversity, the compositions of microbiota between the three tissues as well as between the strains were statistically different. While there were common bacteria across all three tissues and strains of interest, each tissue and strain did exhibit differentially abundant bacterial genera. However, overall, the top five most abundant genera across all tissues and strains were *Elizabethkingia, Acinetobacter, Aeromanas, Cedecea and Yersinia*. The presence of shared microbiota suggests a core microbiota that could be exploited for paratransgenesis efforts.

DR TENDESAYI KUFA-CHAKEZHA

Gaps in the prevention of mother-to-child transmission of syphilis: a review of reported cases, South Africa, January 2020-June 2022

de Voux Alex, **Maruma Wellington**, Morifi Mabore, **Maduma Modiehi, Ebonwu Joy, Sheik Khadeejah**, Dlamini-Nqeketo S, **Kufa Tendesayi**



Journal of Tropical Pediatrics

IMPACT FACTOR: 1.8

https://doi.org/10.1093/tropej/fmae010

Introduction: Congenital syphilis (CS) is preventable through timely antenatal care (ANC), syphilis screening and treatment among pregnant women. Robust CS surveillance can identify gaps in this prevention cascade. We reviewed CS cases reported to the South African Notifiable Medical Conditions Surveillance System (NMCSS) from January 2020 to June 2022.

Method: CS cases are reported using a case notification form (CNF) containing limited infant demographic and clinical characteristics. During January 2020-June 2022, healthcare workers supplemented CNFs with a case investigation form (CIF) containing maternal and infant testing and treatment information. We describe CS cases with/without a matching CIF and gaps in the CS prevention cascade among those with clinical information.

Findings: During January 2020-June 2022, 938 CS cases were reported to the NMCSS with a median age of 1 day (interquartile range: 0-5). Nine percent were diagnosed based on clinical signs and symptoms only. During January 2020-June 2022, 667 CIFs were reported with 51% (343) successfully matched to a CNF. Only 57% of mothers of infants with a matching CIF had an ANC booking visit (entry into ANC). Overall, 87% of mothers were tested for syphilis increasing to 98% among mothers with an ANC booking visit. Median time between first syphilis test and delivery was 16 days overall increasing to 82 days among mothers with an ANC booking visit.

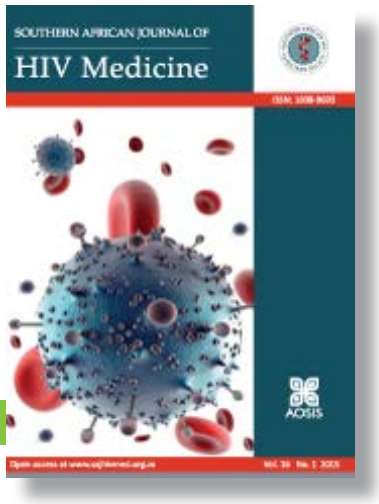
Discussion: Only 37% of CS cases had accompanying clinical information to support evaluation of the prevention cascade. Mothers with an ANC booking visit had increased syphilis screening and time before delivery to allow for adequate treatment.

Keywords: congenital syphilis; notifiable medical condition; surveillance.

MR NEO LEGARE

Lived experience of people with cryptococcal meningitis: A qualitative study

Legare Neo A, Quan Vanessa C, Govender Nelesh P, Muchiri JW



Southern African Journal of HIV Medicine

IMPACT FACTOR: 1.6

https://doi.org/10.4102%2Fsajhivmed.v25i1.1560

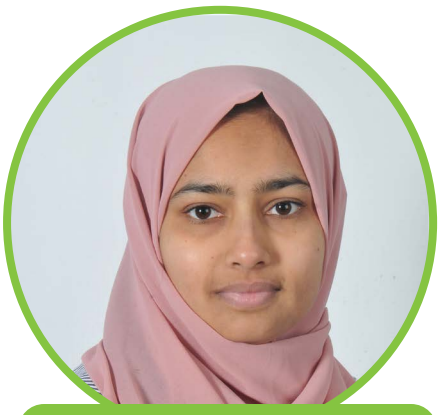
Background: The high burden of cryptococcal meningitis (CM) among people living with HIV persists despite widespread access to antiretroviral therapy. Efforts to prevent CM among people living with HIV could be hindered by a limited understanding of their lived experiences of CM and its diagnosis.

Objectives: To explore and describe the experiences of people diagnosed with HIV-associated CM in routine care. Two public healthcare facilities in Johannesburg, South Africa.

Methods: This was a qualitative-methods exploratory, descriptive, phenomenological study. We conducted semi-structured, individual in-depth interviews with nine purposively sampled participants (comprising 5 men and 4 women). Data were analysed using the Moustakas phenomenological approach.

Results: Five themes and several sub-themes emerged from the data. Participants described their experiences of being diagnosed, which were marked by intense headaches. Diagnosis of CM led to reduced quality of life, fear of death, and loss of income. Participants described their CM treatment experience and health-seeking behaviour including self-medication, seeking help from traditional healers and general practitioners and utilising public health facilities as a last resort. Barriers to care included negative healthcare workers' attitudes, unhealthy lifestyles, and poor knowledge of CM.

Conclusion: People with HIV-associated CM face negative impacts prior to and after diagnosis. These patients struggled to access timely quality healthcare. Patients starting or restarting antiretroviral therapy, and thus at risk for CM, should receive CM education as part of HIV counselling.

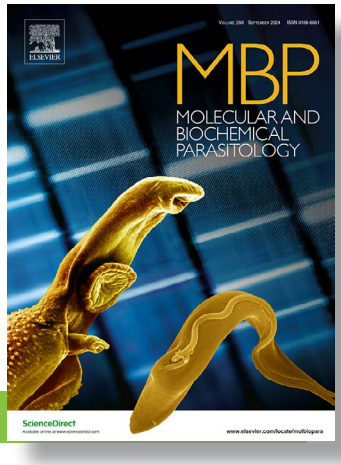


MS NASHRIN F. PATEL

DR SHÜNÉ V. OLIVER

Comparison of the effect of bacterial stimulation on the global epigenetic landscape and transcription of immune genes in primarily zoophilic members of the *Anopheles gambiae* complex (Diptera: Culicidae)

Nashrin F. Patel, Blazenka D. Letinic, Leanne Lobb, Jacek Zawada, Dumsani M. Dlamini, Nondumiso Mabaso, **Givemore Munhenga, Shüné V. Oliver**



Molecular and Biochemical Parasitology

IMPACT FACTOR: 1.4

https://doi.org/10.1016/j.molbiopara.2024.111631

ABSTRACT

Members of the *Anopheles gambiae* complex vary in their vector competence, and this is often attributed to behavioural differences. Similarly, there are differences in transmission capabilities of the zoophilic members of this complex despite exhibiting similar behaviours. Therefore, behavioural differences alone cannot fully explain vector competence variation within members of the *An. gambiae* complex. The immune system of mosquitoes plays a key role in determining susceptibility to parasite infection and consequently transmission capacity. This study aimed to examine variations in the immune response of *An. arabiensis*, *An. merus* and *An. quadriannulatus*, a major, minor, and non-vector respectively. The global epigenetic landscape was characterised and the expression of *Defensin-1* and *Gambicin* was assessed in response to Gram-positive (Streptococcus pyogenes) and Gram-negative (*Escherichia coli*) bacterial infections. The effect of insecticide resistance in *An. arabiensis* on these aspects was also assessed. The immune system was stimulated by a blood-borne bacterial supplementation.

The 5mC, 5hmC, m6A methylation levels and Histone Acetyl Transferase activity were assessed with commercial ELISA kits. The transcript levels of *Defensin-1* and *Gambicin* were assessed by quantitative Real-Time Polymerase Chain Reaction. Species-specific differences in 5mC and m6A methylation existed both constitutively as well as post immune stimulation. The epigenetic patterns observed in the laboratory strains were largely conserved in F1 offspring of wild-caught adults. The methylation patterns in the major vector typically differed from that of the minor/non-vectors. The differences between insecticide susceptible and resistant *An. arabiensis* were more reflected in the expression of *Defensin-1* and *Gambicin*. The expression of these peptides differed in the strains only after bacterial stimulation. *Anopheles merus* and *An. quadriannulatus* expressed significantly higher levels of antimicrobial peptides, both constitutively and after immune stimulation. These findings suggest molecular variations in the immune response of members of the *An. gambiae* complex.

MS LEIGH C. JOHNSTON

Determinants of sub-optimal glycemic control among patients enrolled in a medicine dispensing programme in KwaZulu-Natal: A cohort study, 2018–2021

Leigh C. Johnston, Patrick Ngassa Piotie, Innocent Maposa, Sandhya Singh, **Lazarus Kuonza,** Alex De Voux

African Journal of Primary Health Care & Family Medicine

IMPACT FACTOR: 1.2

https://doi.org/10.4102/phcfm.v16i1.4336

Background: The Central Chronic Medicines Dispensing and Distribution (CCMDD) programme facilitates clinically stable patients to collect their chronic medication from community-based pick-up points.

Aim: We determined baseline glycaemic control and rates and predictors of becoming sub-optimally controlled for type 2 diabetes mellitus (T2DM) CCMDD-enrolled patients.

Setting: The setting of the study was eThekwini, KwaZulu-Natal, South Africa.

Methods: We performed a cohort study (April 2018- December 2021). We linked T2DM CCMDD-enrolled patients to glycated haemoglobin (HbA1c) data from the National Health Laboratory Service. We selected patients optimally controlled at their baseline HbA1c, with ≥ 1 repeat-test available. We used Kaplan–Meier analysis to assess survival rates and extended Cox regression to determine associations between time to sub-optimal control (HbA1c > 7%) and predictors. Adjusted hazard ratios (aHRs), 95% confidence interval (CI), and p-values are reported.

Results: Of the 41145 T2DM patients enrolled in the CCMDD programme, 7960 (19%) had a HbA1c result available. Twenty-seven percent (2147/7960) were optimally controlled at their baseline HbA1c. Of those controlled at baseline, 695 (32%) patients had a repeat test available, with 35% (242/695) changing to sub-optimal status. The HbA1c testing frequency as per national guidelines was associated with a lower hazard of sub-optimal glycaemic control (aHR: 0.46; 95% CI: 0.24–0.91; p-value = 0.024). Patients prescribed dual-therapy had a higher hazard of sub-optimal glycaemic control (aHR: 1.50; 95% CI: 1.16–1.95; p-value = 0.002) versus monotherapy.

Conclusion: The HbA1c monitoring, in-line with testing frequency guidelines, is needed to alert the CCMDD programme of patients who become ineligible for enrolment. Patients receiving dual-therapy require special consideration.

MR PHUTI SEKWADI

DR LINDA ERASMUS

Enteric Fever Surveillance Report, South Africa 2020-2023

Phuti Sekwadi, Hlengiwe Mimmy Ngomane, Bolele Disenyengi, Nomsa Tau, Shannon Smouse, Anthony M. Smith, Juno Thomas, Nicola Page, Linda Erasmus

Public Health Bulletin South Africa

IMPACT FACTOR: N/A

https://www.phbsa.ac.za/wp-content/uploads/2024/06/Enteric-Fever-Surveillance-Report-South-Africa-2020-2023.pdf

ABSTRACT

South Africa is endemic to enteric fever caused by Salmonella Typhi. Sporadic cases occur in most or all provinces annually. Clusters and larger outbreaks occasionally occur. Enteric fever is a category 1 notifiable medical condition in South Africa. Following the last large outbreak in Delmas in 2005, the number of laboratory-confirmed enteric fever cases in South Africa remained stable at less than 150 cases per year until 2022, when 205 cases occurred nationally.

In 2023, national case numbers returned to below 150 cases (141 cases). At provincial level, an increased number of cases occurred in the Western Cape and North West provinces in 2021, with a concurrent decrease in the number of cases reported from Gauteng Province. However, in 2022, the number of cases identified in Gauteng Province increased notably. Core-genome multilocus sequence typing (cgMLST) analysis of whole genome sequencing (WGS) data from Salmonella Typhi isolates submitted to the National Institute for Communicable Diseases (NICD) showed that the increased number of cases in the Western Cape and North West provinces was driven by specific clusters (outbreaks) as defined by the genetic relatedness of isolates. Similarly, several enteric fever clusters were identified in Gauteng Province using core-genome multilocus sequence typing (cgMLST) analysis.

Cases of enteric fever caused by the strain identified in North West Province were subsequently also identified in other provinces. The ongoing challenge of identifying the source(s) of infection in some provinces attests to the complex epidemiology and range of transmission pathways for this pathogen. Recommendations for the prevention and control of enteric fever in South Africa include raising healthcare worker awareness for identification and appropriate treatment of cases; follow-up and management of chronic carriers to reduce transmission; and community health education on general preventative measures such as hand hygiene, water treatment, and food safety practices.

MS MOSHIBUDI P. PHAFANE

Factors associated with mortality among laboratory-diagnosed drug-resistant tuberculosis patients on treatment, KwaZulu-Natal Province, 2017-2019

Moshibudi Poncho Phafane, Jacqueline Ngozo, Zanele Radebe, Elizabeth Lutge, Joy Ebonwu

Pan African Medical Journal

IMPACT FACTOR: N/A

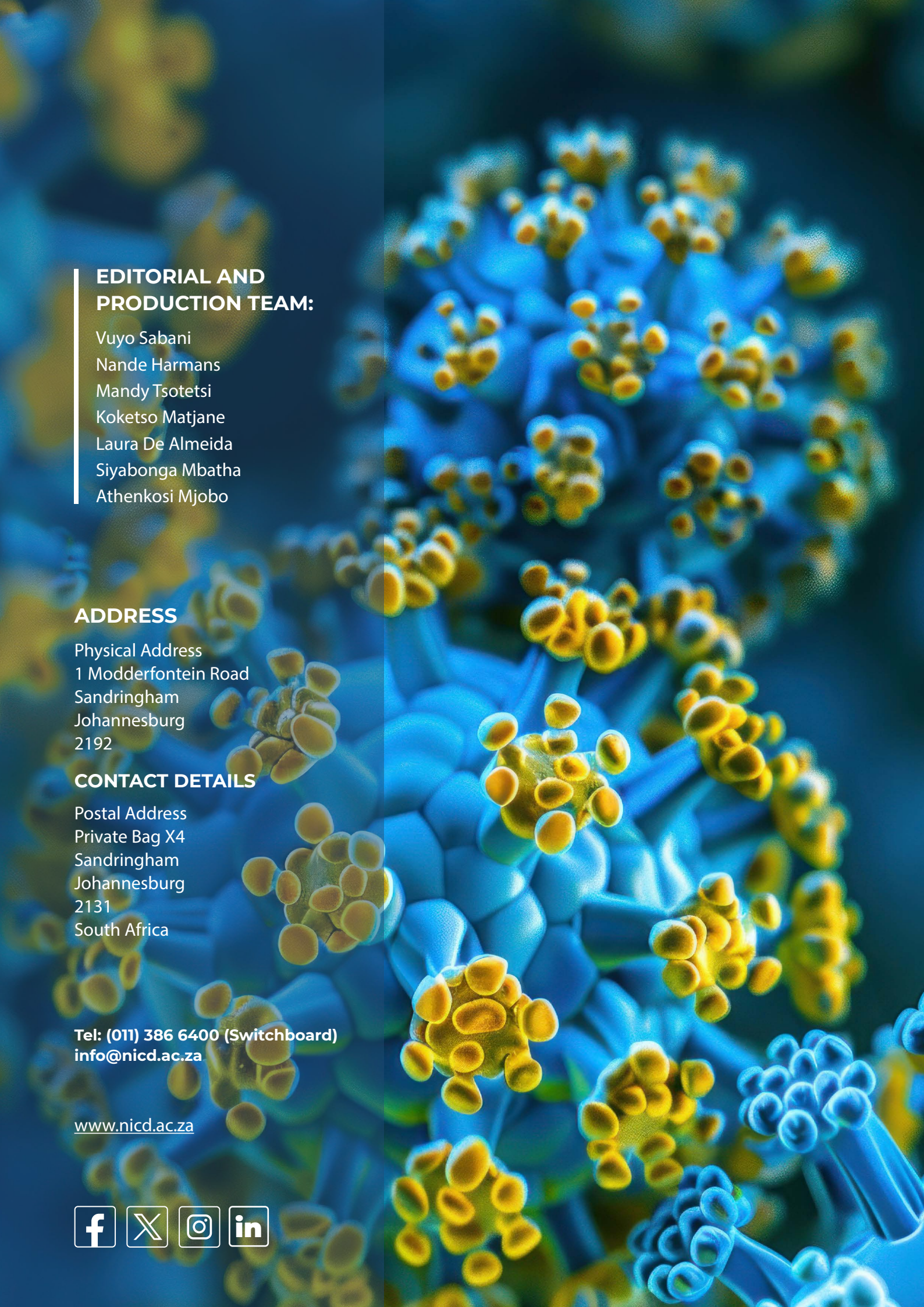
https://www.panafrican-med-journal.com//content/article/47/181/full

Introduction: Tuberculosis (TB) remains a leading cause of death in South Africa. KwaZulu-Natal (KZN) is one of the provinces with a high burden of TB/drug-resistant TB cases and deaths. We determined predictors for mortality among drug-resistant TB patients on treatment in KZN province.

Method: We conducted a retrospective cohort study using secondary data from the Electronic Drug-Resistant Tuberculosis Register. We used a modified Poisson regression model with robust standard errors to determine predictors for drug-resistant TB mortality.

Results: Of the 7,692 eligible patients, 1,234 (16.0%) died. Males predominated (707, 57.3%) and the median age was 36 years (Interquartlile Range: 29-45 years). The majority (978, 79.2%) were HIV-TB co-infected with 911 (93%) on antiretroviral treatment (ART). The predictors included HIV-TB co-infection without ART (aIRR 3.4; 95% CI: 2.3-5.1), unknown ART status (aIRR: 1.8; 95% CI: 1.4-2.3), aged ≥60 years (aIRR: 2.1; 95% CI: 1.6-2.7), previous drug-resistant TB (aIRR: 1.5; 95% CI: 1.2-1.8) and exposure to second-line drugs (aIRR: 1.7; 95% CI: 1.4-2.0). Other predictors were hospitalization during treatment initiation (aIRR 2.5; 95% CI 2.0-3.1), initiation in other treatment facilities (aIRR: 2.2; 95% CI: 1.6-2.9) and rifampicin-resistant (aIRR: 1.2; 95% CI: 1.1-1.4). Bedaquiline fumarate was a significant protective factor against death (aIRR: 0.5; 95% CI: 0.4-0.5).

Conclusion: Older age, HIV co-infection without ART, hospitalization for treatment initiation, exposure to second-line drugs and a previous episode of drug-resistant TB were predictors for DR-TB mortality. Early treatment initiation and provision of antiretroviral treatment for all co-infected patients may reduce DR-TB mortality in the Province.



EDITORIAL AND PRODUCTION TEAM:

Vuyo Sabani
Nande Harmans
Mandy Tsotetsi
Koketso Matjane
Laura De Almeida
Siyabonga Mbatha
Athenkosi Mjobo

ADDRESS

Physical Address
1 Modderfontein Road
Sandringham
Johannesburg
2192

CONTACT DETAILS

Postal Address
Private Bag X4
Sandringham
Johannesburg
2131
South Africa

Tel: (011) 386 6400 (Switchboard)
info@nicd.ac.za

www.nicd.ac.za