SCIENCE FOCUS

Issue 22 | October 2022

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

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.

MS SINENHLANHLA JIMOH

EDITORS NOTE

The latest issue of Science Focus highlights notable research achievements from industry experts at the National Institute for Communicable Diseases (NICD for Q1 2022/2023). Aside from presenting important statistical findings and the volume of peer-reviewed publications produced, the magazine also highlights top published authors and articles with high impact factor scores.

Prof Penny Moore kicks off the edition with a feature in the highly respected New England Journal of Medicine. As co-author, Moore probed the SARS-CoV-2 variant, Omicron, with the objective of decoupling infection from severe disease. The article referenced COVID-19 vaccine coverage in South Africa, stating that immunity is not solely acquired through vaccination, but also through previous infection. The journal makes for a fascinating read.

The fungus, Cryptococcus is the most common cause of meningitis and the second leading cause of death in adults living with HIV. With this in mind, a multi-stakeholder collaborative study was facilitated to determine the effectiveness of flucytosine-based treatment in reducing HIV-associated cryptococcal meningitis deaths. Published in The Lancet Infectious Diseases, the local cross-sectional study concluded that flucytosine-based treatment is associated with a substantial survival benefit when delivered routinely. Funded by the NICD, the study involved various authors, including Ms Rudzani Mashau and Prof Nelesh Govender.

A host of NICD authors, including Profs Cheryl Cohen and Anne von Gottberg, collaborated on a PHIRST-C cohort study related to SARS-CoV-2 incidence, transmission and reinfection in both rural and urban settings. With data on disease burden, transmission and asymptomatic infection in Africa being limited, the objective of the study was to evaluate the burden and spread of SARS-CoV-2 in a rural and urban community in South Africa. Featured in The Lancet Infectious Diseases, 222 households and 1 200 household members partook in the study, which revealed that increased household transmission of the Beta and Delta variants likely contributed to successive waves.

The institute salutes every NICD researcher who continues to pave the way in publishing important public health papers in high-impact publications, including Science, Cell Host & Microbe and the Journal of Medical Virology, to highlight a few. Staff members are encouraged to send their comments to the Communications Unit.

Happy reading!

On behalf of the team,
Sinenhlanhla Jimoh
Senior Communications Manager

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

Top Published Authors for Q1 of 2022/2023

1

PROF CHERYL COHEN

1

PROF ANNE VON GOTTBERG

2

PROF PENNY MOORE

3

DR NICOLE WOLTER

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

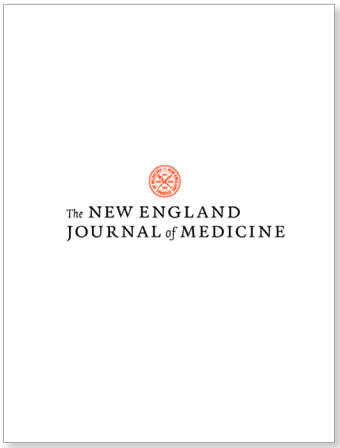
PROF PENNY MOORE

Omicron - Decoupling Infection from Severe Disease

MOORE PL, BADEN LR

The New England Journal of Medicine **IMPACT FACTOR: 176,079**

South Africa, like much of Africa, suffers from relatively low Covid-19 vaccine coverage, with only 43% of South African adults having been fully vaccinated. However, immunity can result from either vaccination or previous infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), so vaccine coverage alone does not capture population immunity. South Africa has faced four waves of the Covid-19 pandemic, each dominated by a different variant of SARS-CoV-2, which suggests the possibility of a high prevalence of underlying seropositivity due to previous infection. Seropositivity could affect the severity of disease caused by new variants.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS 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

MASHAU RC, **MEIRING ST**, **QUAN VC**, NEL J, GREENE GS, GARCIA A, MENEZES C, REDDY DL, VENTER M, STACEY S, MADUA M, BORETTI L, HARRISON TS, MEINTJES G, SHROUFI A, TRIVINO-DURAN L, BLACK J, **GOVENDER NP**; GERMS-SA

The 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

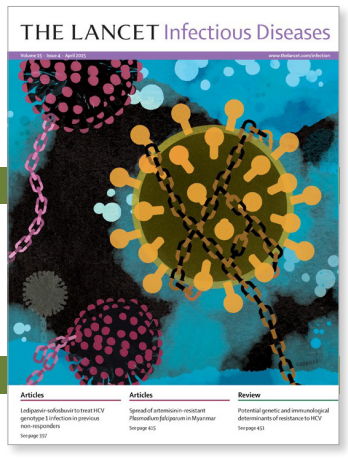
In this cross-sectional study, we compared outcomes of adults aged 18 years and older with incident laboratory-confirmed cryptococcal meningitis treated with or without flucytosine-containing regimens at 19 sentinel hospitals in South Africa. A case of cryptococcosis was defined as illness in an adult 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.



FUNDING

National Institute for Communicable Diseases, a Division of the National Health Laboratory Service.

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PROF CHERYL COHEN

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

CHERYL COHEN, **JACKIE KLEYNHANS**, **ANNE VON GOTTBERG**, MEREDITH L MCMORROW, **NICOLE WOLTER**, **JINAL N BHIMAN**, **JOCELYN MOYES**, **MIGNON DU PLESSIS**, **MAIMUNA CARRIM**, **AMELIA BUYS**, NEIL A MARTINSON, KATHLEEN KAHN, STEPHEN TOLLMAN, LIMAKATSO LEBINA, FLOIDY WAFAWANAKA, JACQUES D DU TOIT, FRANCESC XAVIER GÓMEZ-OLIVÉ, FATIMAH S DAWOOD, **THULISA MKHENCELE**, KAIYUAN SUN, CÉCILE VIBOUD, STEFANO TEMPIA

The Lancet Infectious Diseases **IMPACT FACTOR: 71,421**

BACKGROUND

By August, 2021, South Africa had been affected by three waves of SARS-CoV-2; the second associated with the beta variant and the third with the delta variant. Data on SARS-CoV-2 burden, transmission, and asymptomatic infections from Africa are scarce. We aimed to evaluate SARS-CoV-2 burden and transmission in one rural and one urban community in South Africa.

METHODS

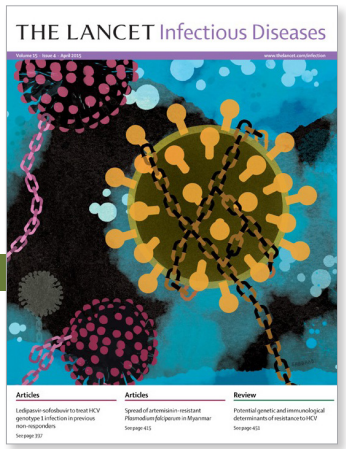
We conducted a prospective cohort study of households in Agincourt, Mpumalanga province (rural site) and Klerksdorp, North West province (urban site) from July, 2020 to August, 2021. We randomly selected households for the rural site from a health and sociodemographic surveillance system and for the urban site using GPS coordinates. Households with more than two members and where at least 75% of members consented to participate were eligible. Midturbinate nasal swabs were collected twice a week from household members irrespective of symptoms and tested for SARS-CoV-2 using real-time RT-PCR (RT-rtPCR). Serum was collected every 2 months and tested for anti-SARS-CoV-2 antibodies. Main outcomes were the cumulative incidence of SARS-CoV-2 infection, frequency of reinfection, symptomatic fraction (percent of infected individuals with ≥1 symptom), the duration of viral RNA shedding (number of days of SARS-CoV-2 RT-rtPCR positivity), and the household cumulative infection risk (HCIR; number of infected household contacts divided by the number of susceptible household members).

FINDINGS

222 households (114 at the rural site and 108 at the urban site), and 1200 household members (643 at the rural site and 557 at the urban site) were included in the analysis. For 115 759 nasal specimens from 1200 household members (follow-up 92·5%), 1976 (1·7%) were SARS-CoV-2-positive on RT-rtPCR. By RT-rtPCR and serology combined, 749 of 1200 individuals (62·4% [95% CI 58·1-66·4]) had at least one SARS-CoV-2 infection episode, and 87 of 749 (11·6% [9·4-14·2]) were reinfected. The mean infection episode duration was 11·6 days (SD 9·0; range 4-137). Of 662 RT-rtPCR-confirmed episodes (>14 days after the start of follow-up) with available data, 97 (14·7% [11·9-17·9]) were symptomatic with at least one symptom (in individuals aged <19 years, 28 [7·5%] of 373 episodes symptomatic; in individuals aged ≥19 years, 69 [23·9%] of 289 episodes symptomatic). Among 222 households, 200 (90·1% [85·3-93·7]) had at least one SARS-CoV-2-positive individual on RT-rtPCR or serology. HCIR overall was 23·9% (195 of 817 susceptible household members infected [95% CI 19·8-28·4]). HCIR was 23·3% (20 of 86) for symptomatic index cases and 23·9% (175 of 731) for asymptomatic index cases (univariate odds ratio [OR] 1·0 [95% CI 0·5-2·0]). On multivariable analysis, accounting for age and sex, low minimum cycle threshold value (≤30 vs >30) of the index case (OR 5·3 [2·3-12·4]) and beta and delta variant infection (vs Wuhan-Hu-1, OR 3·3 [1·4-8·2] and 10·4 [4·1-26·7], respectively) were associated with increased HCIR. People living with HIV who were not virally supressed (≥400 viral load copies per mL) were more likely to develop symptomatic illness when infected with SAR-CoV-2 (OR 3·3 [1·3-8·4]), and shed SARS-CoV-2 for longer (hazard ratio 0·4 [95% CI 0·3-0·6]) compared with HIV-uninfected individuals.

INTERPRETATION

In this study, 565 (85·3%) SARS-CoV-2 infections were asymptomatic and index case symptom status did not affect HCIR, suggesting a limited role for control measures targeting symptomatic individuals. Increased household transmission of beta and delta variants was likely to have contributed to successive waves of SARS-CoV-2 infection, with more than 60% of individuals infected by the end of follow-up.



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DR HARRY MOULTRIE

Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa

JULIET R. C. PULLIAM, CARI VAN SCHALKWYK, **NEVASHAN GOVENDER**, **ANNE VON GOTTBERG**, **CHERYL COHEN**, **MICHELLE J. GROOME**, JONATHAN DUSHOFF, KOLEKA MLISANA, AND **HARRY MOULTRIE**

Science **IMPACT FACTOR: 63,798**

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.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

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: 71,798**

ABSTRACT

We provide two methods for monitoring reinfection trends in routine surveillance data to identify signatures of changes in reinfection risk and apply these approaches to data from South Africa's severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic to date. Although we found no evidence of increased reinfection risk associated with circulation of the Beta (B.1.351) or Delta (B.1.617.2) variants, we did find clear, population-level evidence to suggest immune evasion by the Omicron (B.1.1.529) variant in previously infected individuals in South Africa. Reinfections occurring between 1 November 2021 and 31 January 2022 were detected in individuals infected in all three previous waves, and there has been an increase in the risk of having a third infection since mid-November 2021.

DR SIMONE RICHARDSON

SARS-CoV-2 Omicron triggers cross-reactive neutralization and Fc effector functions in previously vaccinated, but not unvaccinated individuals

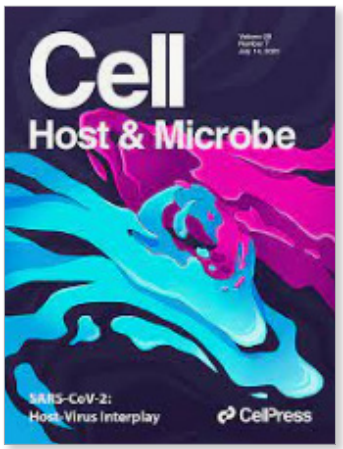
RICHARDSON SI, **MADZORERA VS**, **SPENCER H**, **MANAMELA NP**, VAN DER MESCHT M, **LAMBSON B**, **OOSTHUYSEN B**, **AYRES F**, **MOLAUDZI Z**, **MOYO-GWETE T**, **MZINDLE N**, **MOTLOU T**, MENDES A, TEGALLY H, VENTER M, DE OLIVEIRA T, UECKERMANN V, ROSSOUW TM, BOSWELL MT, **MOORE, PL**

Cell Host and Microbe **IMPACT FACTOR: 31,316**

PROF PENNY MOORE

ABSTRACT

The SARS-CoV-2 Omicron variant escapes neutralizing antibodies elicited by vaccines or infection. However, whether Omicron triggers cross-reactive humoral responses to other variants of concern (VOCs) remains unknown. We used plasma from 20 unvaccinated and 7 vaccinated individuals infected by Omicron BA.1 to test binding, Fc effector function, and neutralization against VOCs. In unvaccinated individuals, Fc effector function and binding antibodies targeted Omicron and other VOCs at comparable levels. However, Omicron BA.1-triggered neutralization was not extensively cross-reactive for VOCs (14- to 31-fold titer reduction), and we observed 4-fold decreased titers against Omicron BA.2. In contrast, vaccination followed by breakthrough Omicron infection associated with improved cross-neutralization of VOCs with titers exceeding 1:2,100. This has important implications for the vulnerability of unvaccinated Omicron-infected individuals to reinfection by circulating and emerging VOCs. Although Omicron-based immunogens might be adequate boosters, they are unlikely to be superior to existing vaccines for priming in SARS-CoV-2-naive individuals.



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DR NICOLE WOLTER

PROF CHERYL COHEN

Clinical severity of Omicron sub-lineage BA.2 compared to BA.1 in South Africa

WOLTER N, JASSAT W, DATCOV GEN AUTHOR GROUP (**SCHEEPERS C. BHIMAN JN**), **VON GOTTBERG A, COHEN C**

Science **IMPACT FACTOR: 21,81**

The omicron SARS-CoV-2 variant of concern (B.1.1.529) was first reported in South Africa in mid-November, 2021. Early data indicated that infection with omicron (around 99% BA.1 lineage during this period) was associated with a lower risk of hospitalisation and lower risk of severe illness, once hospitalised, compared with delta (B.1.617.2) variant infection.1 Recently, the BA.2 lineage has increased in many areas globally, including South Africa, associated with increases in case numbers in some settings. In South Africa, the BA.2 lineage was first detected on Nov 17, 2021. From week 49 of 2021 (starting Dec 5, 2021), the proportion of BA.2 lineage began to increase, making up 84% (27 of 32) of all sequenced samples by week 5 of 2022 (week ending Feb 5, 2022).2 Replacement of BA.1 by BA.2 occurred in a period when SARS-CoV-2 case numbers were declining from the fourth wave peak in South Africa and was associated with a brief increase in case numbers in children of school-going age and slowing of the rate of decline compared with previous waves. The BA.1 lineage contains a 69–70 amino acid deletion in the spike protein, which is associated with S-gene target failure (SGTF) when tested using the TaqPath COVID-19 PCR test (Thermo Fisher Scientific, Waltham, MA, USA). At the time of this study, BA.2 lacks this deletion, hence infections with BA.2 are S-gene positive on this assay.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MR MWIZA SINGINI

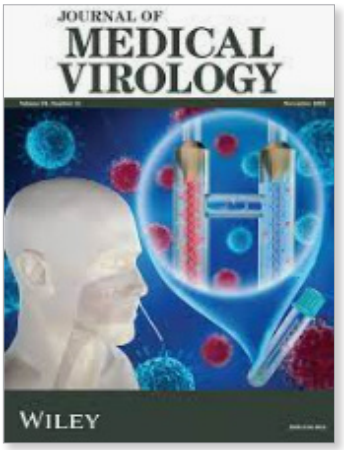
Usefulness of high-risk HPV early oncoprotein (E6 and E7) serological markers in the detection of Cervical Cancer: A systemic review and meta analysis

SINGINI MG, **SINGH E**, BRADSHAW D, **CHEN WC**, **MOTLHALE M**, DE VILLIERS CB, **MUCHENGETI M**, MATHEW CG, NEWTON R, BENDER N, WATERBOER T, SITAS F

Journal of Medical Virology **IMPACT FACTOR: 20,693**

ABSTRACT

We reviewed the literature on the importance of selected anti-high-risk human papillomavirus (HR-HPV) antibodies (namely, 16/18 and early oncoproteins E6 and E7) as potential serological markers for early detection of individuals at high risk of cervical cancer. We searched for studies in PubMed and Embase databases published from 2010 to 2020 on antibodies against HR-HPV E6 and E7 early proteins and cervical cancer. Pooled sensitivity and specificity for HPV16 and HPV18 antibodies were calculated using a bivariate hierarchical random-effects model. A total of 69 articles were identified; we included three studies with 1550 participants. For the three HPV16/18 E6 and E7 antibody tests, enzyme-linked immunosorbent assay-based assays had a sensitivity of 18% for detecting CIN2+ (95% confidence interval [CI]: 15-21) and a specificity of 96% (95% CI: 92-98), for slot-blot, sensitivity was 28.9% (95% CI: 23.3-35.1) and specificity was 72% (95% CI: 66.6-77.0) for detecting CIN2+, and for multiplex HPV serology assay based on a glutathione S-transferase, sensitivity was 16% (95% CI: 8.45-28.6) and specificity was 98% (95% CI: 97-99) for detecting invasive cervical cancer. HR-HPV16/18 E6 and E7 serological markers showed high specificity, but sensitivity was suboptimal for the detection of cervical cancer in either population screening settings or as point-of-care screening tests."



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DR CATHRINE SCHEEPERS

Emergence and phenotypic characterization of the global SARS-CoV-2 C.1.2 lineage

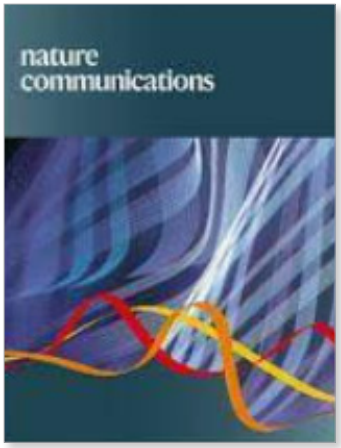
CATHRINE SCHEEPERS, **JOSIE EVERATT**, **DANIEL G. AMOAKO**, HOURIIYAH TEGALLY, **CONSTANTINOS KURT WIBMER**, **ANELE MNGUNI**, **ARSHAD ISMAIL**, **BOITSHOKO MAHLANGU**, **BRONWEN E. LAMBSON, DARREN P. MARTIN**, EDUAN WILKINSON, JAMES EMMANUEL SAN, JENNIFER GIANDHARI, NELIA MANAMELA, **NOXOLO NTULI**, PRUDENCE KGAGUDI, SANDILE CELE, **SIMONE I. RICHARDSON**, SURESHNEE PILLAY,THABO MOHALE, UPASANA RAMPHAL, YESHNEE NAIDOO, ZAMANTUNGWA T. KHUMALO, GAURAV KWATRA, GLENDA GRAY, LINDA-GAIL BEKKER, SHABIR A. MADHI, VICKY BAILLIE, WESLEY C. VAN VOORHIS, FLORETTE K. TREURNICHT, MARIETJIE VENTER, KOLEKA MLISANA, **NICOLE WOLTER**, ALEX SIGAL, CAROLYN WILLIAMSON, NEI-YUAN HSIAO, NOKUKHANYA MSOMI, TONGAI MAPONGA, WOLFGANG PREISER, ZINHLE MAKATINI, RICHARD LESSELLS, **PENNY L. MOORE**, TULIO DE OLIVEIRA, **ANNE VON GOTTBERG**, AND **JINAL N. BHIMAN**

DR JINAL BHIMAN

Nature Communications **IMPACT FACTOR: 17,694**

ABSTRACT

Global genomic surveillance of SARS-CoV-2 has identified variants associated with increased transmissibility, neutralization resistance and disease severity. Here we report the emergence of the PANGO lineage C.1.2, detected at low prevalence in South Africa and eleven other countries. The initial C.1.2 detection is associated with a high substitution rate, and includes changes within the spike protein that have been associated with increased transmissibility or reduced neutralization sensitivity in SARS-CoV-2 variants of concern or variants of interest. Like Beta and Delta, C.1.2 shows significantly reduced neutralization sensitivity to plasma from vaccinees and individuals infected with the ancestral D614G virus. In contrast, convalescent donors infected with either Beta or Delta show high plasma neutralization against C.1.2. These functional data suggest that vaccine efficacy against C.1.2 will be equivalent to Beta and Delta, and that prior infection with either Beta or Delta will likely offer protection against C.1.2."



MS JACKIE KLEYNHANS

SARS-CoV-2 Seroprevalence after Third Wave of Infections, South Africa

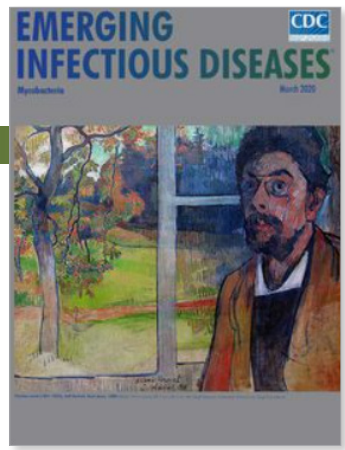
JACKIE KLEYNHANS, STEFANO TEMPIA, **NICOLE WOLTER**, **ANNE VON GOTTBERG**, **JINAL N BHIMAN**, **AMELIA BUYS**, **JOCELYN MOYES**, MEREDITH L MCMORROW, KATHLEEN KAHN, F XAVIER GÓMEZ-OLIVÉ, STEPHEN TOLLMAN, NEIL A MARTINSON, FLOIDY WAFAWANAKA, LIMAKATSO LEBINA, JACQUES D DU TOIT, **WAASILA JASSAT**, **MZIMASI NETI**, MARIEKE BRAUER, **CHERYL COHEN**, **PHIRST-C GROUP**

Emerging Infectious Diseases **IMPACT FACTOR: 16,126**

PROF CHERYL COHEN

ABSTRACT

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."



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF GAYLE G. SHERMAN

Indeterminate HIV PCR results within South Africa's early infant diagnosis programme, 2010-2019

LEBOHANG RADEBE, **AHMAD HAERI MAZANDERANI**, **GAYLE G. SHERMAN**

Clinical Microbiology and Infection IMPACT FACTOR: 13,31

OBJECTIVES

We describe the extent of, and variables associated with, indeterminate HIV-PCR results and final HIV status within South Africa's early infant diagnosis (EID) programme between 2010 and 2019.

METHODS

Retrospective analysis of routine paediatric HIV-PCR laboratory data from South Africa's National Health Laboratory Service Data Warehouse between 2010 and 2019. Final HIV status was determined by linking patient results (including HIV-PCR, HIV viral load, HIV serology and CD4 counts) using a probabilistic matching algorithm. Multivariate logistic regression was performed to determine variables associated with final HIV status among patients with an indeterminate HIV-PCR result.

RESULTS

Among 4 429 742 specimens registered for HIV-PCR testing from 3 816 166 patients, 113 209 (2.97%) tested positive and 22 899 (0.6%) tested indeterminate. As a proportion of HIV-detected results, 15.7% (23 896/151 832) of total and 31.5% (4900/15 566), 18.8% (11 400/60 794) and 10.1% (7596/75 472) among patients aged <7 days, 7 days–3 months and ≥3 months, respectively, were reported as indeterminate. Overall, 39.7% of patients with an indeterminate result had a linked HIV test to determine HIV status, of which 53.6% were positive with a median time to repeat testing of 30 days (interquartile range 15–69). Among patients who tested indeterminate, variables associated with a significantly higher odds of having a positive HIV status included testing indeterminate at birth (adjusted odds ratio (AOR) 0.63 (0.48–0.83) and 0.52 (0.39–0.69) for testing indeterminate at 7 days–3 months and ≥3 months respectively compared with birth), within a hospital (AOR 2.45 (1.99–3.03)), and in districts with an intra-uterine transmission rate ≥1.1% (AOR 3.14 (1.84–5.35)) ($p < 0.001$).

DISCUSSION

Indeterminate HIV-PCR results represent a considerable burden of missed diagnostic opportunities, diagnostic dilemmas and delays in making a definite diagnosis among HIV-infected infants within South Africa's EID programme. Alternative EID verification practices are urgently needed.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR NICOLE WOLTER

Pathogens detected using a syndromic molecular diagnostic platform in patients hospitalized with severe respiratory illness in South Africa in 2017.9

MALEFU MOLELEKI, **MIGNON DU PLESSIS**, KEDIBONE NDLANGISA, CAYLA REDDY, **ORIENKA HELLFERSCEE**, OMPHE MEKGOE, MEREDITH MCMORROW, **SIBONGILE WALAZA**, **CHERYL COHEN**, STEFANO TEMPIA, **ANNE VON GOTTBERG**, **NICOLE WOLTER**

International Journal of Infectious Diseases **IMPACT FACTOR: 12,074**

ABSTRACT

Objectives

We describe the use of a multipathogen platform, TaqMan array card (TAC) real-time polymerase chain reaction, for the detection of pathogens in patients hospitalized with severe respiratory illness (SRI

METHODS

Prospective hospital-based syndromic surveillance for acute and chronic SRI was carried out at two sentinel sites in South Africa between January and December 2017. We tested respiratory specimens for 21 respiratory pathogens and blood samples for nine bacteria using TAC. Pathogen detection was compared by age group and HIV status using the chi-square test.

RESULTS

During 2017, 956 patients of all ages were enrolled in the SRI surveillance, and of these, 637 (67%) patients were included in this study (637 blood, 487 naso- and oro-pharyngeal swabs, and 411 sputum specimens tested). At least one pathogen was detected in 83% (527/637) of patients. Common pathogens detected included Haemophilus influenzae (225/637; 35%), Streptococcus pneumoniae (224/637; 35%), rhinovirus (144/637; 23%), Staphylococcus aureus (129/637; 20%), Klebseilla pneumoniae (85/637; 13%), Mycobacterium tuberculosis (75/637; 12%), and respiratory syncytial virus (57/637; 9%). Multiple pathogens (≥2) were codetected in 57% (364/637) of patients.

CONCLUSION

Although the use of a multi-pathogen platform improved pathogen yield, pathogen co-detections were common and would need clinical assessment for usefulness in individual-level treatment and management decisions."

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR JINAL BHIMAN

PROF PENNY MOORE

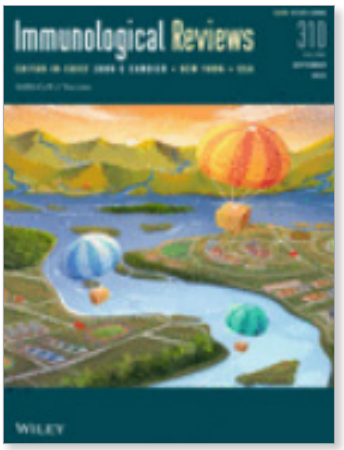
Leveraging South African HIV research to define SARS-CoV-2 immunity triggered by sequential variants of concern

BHIMAN JN, MOORE PL

Immunological Reviews **IMPACT FACTOR: 10,983**

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), has shifted our paradigms about B cell immunity and the goals of vaccination for respiratory viruses. The development of population immunity, through responses directed to highly immunogenic regions of this virus, has been a strong driving force in the emergence of progressively mutated variants. This review highlights how the strength of the existing global virology and immunology networks built for HIV vaccine research enabled rapid adaptation of techniques, assays, and skill sets, to expeditiously respond to the SARS-CoV-2 pandemic. Allying real-time genomic surveillance to immunological platforms enabled the characterization of immune responses elicited by infection with distinct variants, in sequential epidemic waves, as well as studies of vaccination and hybrid immunity (combination of infection- and vaccination-induced immunity). These studies have shown that consecutive variants of concern have steadily diminished the ability of vaccines to prevent infection, but that increasing levels of hybrid immunity result in higher frequencies of cross-reactive responses. Ultimately, this rapid pivot from HIV to SARS-CoV-2 enabled a depth of understanding of the SARS-CoV-2 antigenic vulnerabilities as population immunity expanded and diversified, providing key insights for future responses to the SARS-CoV-2 pandemic."



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MS BOITUMELO MOTSOENENG

DR SIMONE RICHARDSON

Influenza vaccination results in differential hemagglutinin stalk-directed Fc-mediated functions in individuals living with and without HIV

MOTSOENENG BM, DHAR N, NUNES MC, KRAMMER F, MADHI SA, **MOORE PL**, **RICHARDSON SI**

Frontiers in Immunology IMPACT FACTOR: 8,786

ABSTRACT

Influenza virus hemagglutinin (HA) stalk-specific antibodies have been shown to potently induce Fc-mediated effector functions which are important in protection from disease. In placebo-controlled maternal influenza (MatFlu) vaccination trials of pregnant women living with or without HIV, reduced risk of influenza illness was associated with high HA stalk antibody titers following trivalent inactivated vaccination (TIV). However, the mechanisms of immunity conferred by the HA stalk antibodies were not well understood. Here, we investigated HA stalk-specific Fc effector functions including antibody-dependent cellular phagocytosis (ADCP), antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent complement deposition (ADCD), and FcγRIIa and FcγRIIIa binding in response to seasonal influenza vaccination. These were measured pre- and 1-month post-vaccination in 141 HIV-uninfected women (67 TIV and 74 placebo recipients) and 119 women living with HIV (WLWH; 66 TIV and 53 placebo recipients). In contrast to HIV-uninfected women, where HA stalk-specific ADCP and FcγRIIa binding were significantly boosted, WLWH showed no increase in response to vaccination. HA stalk-specific ADCC potential and FcγRIIIa binding were not boosted regardless of HIV status but were higher in WLWH compared with HIV-uninfected women prior to vaccination. HA stalk-specific ADCD was significantly increased by vaccination in all women, but was significantly lower in the WLWH both pre- and post- vaccination. Co-ordination between HA stalk-specific ADCP and ADCD in WLWH was improved by vaccination. Fc polyfunctionality was enhanced by vaccination in HIV-uninfected women and driven by the HA stalk antibody titers. However, in the WLWH, higher pre-vaccination Fc polyfunctionality was maintained post-vaccination but was decoupled from titer. Overall, we showed differential regulation of Fc effector HA stalk responses, suggesting that HIV infection results in unique humoral immunity in response to influenza vaccination, with relevance for future strategies that aim to target the HA stalk in this population.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF PENNY MOORE

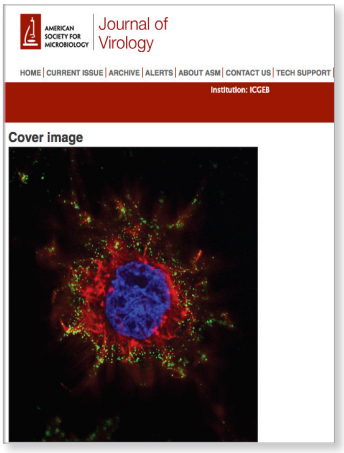
Complementary roles of antibody heavy and light chain somatic hypermutation in conferring breadth and potency to the HIV-1 specific CAP256-VRC26 bNAb lineage

SACKS D, WIEHE K, MORRIS L, **MOORE PL**

Journal of Virology **IMPACT FACTOR: 6,549**

ABSTRACT

Some HIV-infected people develop broadly neutralizing antibodies (bNAbs) that block many diverse, unrelated strains of HIV from infecting target cells and, through passive immunization, protect animals and humans from infection. Therefore, understanding the development of bNAbs and their neutralization can inform the design of an HIV vaccine. Here, we extend our previous studies of the ontogeny of the CAP256-VRC26 V2-targeting bNAb lineage by defining the mutations that confer neutralization to the unmutated common ancestor (CAP256.UCA). Analysis of the sequence of the CAP256.UCA showed that many improbable mutations were located in the third complementarity-determining region of the heavy chain (CDRH3) and the heavy chain framework 3 (FR3). Transferring the CDRH3 from bNAb CAP256.25 (63% breadth and 0.003 µg/mL potency) into the CAP256.UCA introduced breadth and the ability to neutralize emerging viral variants. In addition, we showed that the framework and light chain contributed to potency and that the second CDR of the light chain forms part of the paratope of CAP256.25. Notably, a minimally mutated CAP256 antibody, with 41% of the mutations compared to bNAb CAP256.25, was broader (64% breadth) and more potent (0.39 µg/mL geometric potency) than many unrelated bNAbs. Together, we have identified key regions and mutations that confer breadth and potency in a V2-specific bNAb lineage. These data indicate that immunogens that target affinity maturation to key sites in CAP256-VRC26-like precursors, including the CDRHs and light chain, could rapidly elicit breadth through vaccination. IMPORTANCE A major focus in the search for an HIV vaccine is elucidating the ontogeny of broadly neutralizing antibodies (bNAbs), which prevent HIV infection in vitro and in vivo. The unmutated common ancestors (UCAs) of bNAbs are generally strain specific and acquire breadth through extensive, and sometimes redundant, somatic hypermutation during affinity maturation. We investigated which mutations in the CAP256-VRC26 bNAb lineage conferred neutralization capacity to the UCA. We found that mutations in the antibody heavy and light chains had complementary roles in neutralization breadth and potency, respectively. The heavy chain, particularly the third complementarity-determining region, was responsible for conferring breadth. In addition, previously uninvestigated mutations in the framework also contributed to breadth. Together, approximately half of the mutations in CAP256.25 were necessary for broader and more potent neutralization than many unrelated neutralizing antibodies. Vaccine approaches that promote affinity maturation at key sites could therefore more rapidly produce antibodies with neutralization breadth."



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MS KEDIBONE M NDLANGISA

PROF ANNE VON GOTTBERG

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

KEDIBONE M NDLANGISA , **MIGNON DU PLESSIS** , STEPHANIE LO , **LINDA DE GOUVEIA** , CHRISPIN CHAGUZA , MARTIN ANTONIO , BRENDA KWAMBANA-ADAMS , JENNIFER CORNICK , DEAN B EVERETT , RON DAGAN , PAULINA A HAWKINS , BERNARD BEALL , ALEJANDRA CORSO , SAMANTA CRISTINE GRASSI ALMEIDA , THERESA J OCHOA , STEPHEN OBARO, SADIA SHAKOOR , ERIC S DONKOR, REBECCA A GLADSTONE , PAK LEUNG HO , METKA PARAGI , SANJAY DOIPHODE , SOMPORN SRIFUENGFUNG , REBECCA FORD , JENNIFER MOÏSI, SAMIR K SAHA , GODFREY BIGOGO , BETUEL SIGAUQUE , ÖZGEN KÖSEOGLU ESER , NAIMA ELMDAGHRI , LEONID TITOV , PAUL TURNER , K L RAVI KUMAR , RAMA KANDASAMY , EKATERINA EGOROVA , MARGARET IP , ROBERT F BREIMAN , KEITH P KLUGMAN , LESLEY MCGEE , STEPHEN D BENTLEY, **ANNE VON GOTTBERG** , THE GLOBAL PNEUMOCOCCAL SEQUENCING CONSORTIUM

Microbial Genomics **IMPACT FACTOR: 4,781**

As is the case globally, *Cryptococcus* gattii is a less frequent cause of *cryptococcosis* than Cryptococcus neoformans in South Africa. We performed multilocus sequence typing (MLST) and fluconazole susceptibility testing of 146 isolates randomly selected from 750 South African patients with *C. gattii* disease identified through enhanced laboratory surveillance, 2005 to 2013. The dominant molecular type was VGIV (101/146, 70%), followed by VGI (40/146, 27%), VGII (3/146, 2%) and VGIII (2/146, 1%). Among the 146 C. gattii isolates, 99 different sequence types (STs) were identified, with ST294 (14/146, 10%) and ST155 (10/146, 7%) being most commonly observed. The fluconazole MIC50 and MIC90 values of 105 (of 146) randomly selected *C. gattii* isolates were 4 µg/ml and 16 µg/ml, respectively. VGIV isolates had a lower MIC50 value compared to non-VGIV isolates, but these values were within one double-dilution of each other. HIV-seropositive patients had a ten-fold increased adjusted odds of a VGIV infection compared to HIV-seronegative patients, though with small numbers (99/136; 73% vs. 2/10; 20%), the confidence interval (CI) was wide (95% CI: 1.93–55.31, p = 0.006). Whole genome phylogeny of 98 isolates of South Africa's most prevalent molecular type, VGIV, identified that this molecular type is highly diverse, with two interesting clusters of ten and six closely related isolates being identified, respectively. One of these clusters consisted only of patients from the Mpumalanga Province in South Africa, suggesting a similar environmental source. This study contributed new insights into the global population structure of this important human pathogen.

MICROBIAL GENOMICS

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF NELESH GOVENDER

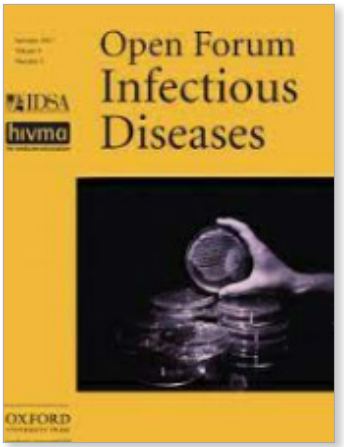
Prior Pulmonary Tuberculosis Is a Risk Factor for Asymptomatic Cryptococcal Antigenemia in a Cohort of Adults With Advanced Human Immunodeficiency Virus Disease

RACHEL M WAKE, NAZIR A ISMAIL, **SHAHEED V OMAR**, **FARZANA ISMAIL**, **CAROLINE T TIEMESSEN**, THOMAS S HARRISON, JOSEPH N JARVIS, **NELESH P GOVENDER**

Open Forum Infectious Diseases **IMPACT FACTOR: 4,427**

ABSTRACT

The greater mortality risk among people with advanced human immunodeficiency virus disease and cryptococcal antigenemia, despite treatment, indicates an increased susceptibility to other infections. We found that prior tuberculosis was an independent risk factor for cryptococcal antigenemia (adjusted odds ratio, 2.72; 95% confidence interval, 1.13-6.52; P = .03) among patients with CD4 counts <100 cells/µL.



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DR TENDESAYI KUFA

Etiological surveillance of Genital Ulcer Syndrome in South Africa: 2019-2020

RANMINI KULARATNE, **JOHANNA ME VENTER, VENESSA MASEKO, ETIENNE MULLER, TENDESAYI KUFA**

Sexually Transmitted Diseases IMPACT FACTOR: 3,868

BACKGROUND

Herpes simplex virus (HSV) has been the leading cause of genital ulcer syndrome (GUS) in South Africa for more than a decade, and acyclovir therapy is incorporated into syndromic management guidelines. We conducted surveillance at 3 sentinel sites to define the common sexually transmitted etiologies of GUS and to determine whether current syndromic management is appropriate. Secondary objectives of surveillance were to determine the seroprevalence of coinfections (HIV, syphilis, HSV-2) in persons presenting with GUS.

METHODS

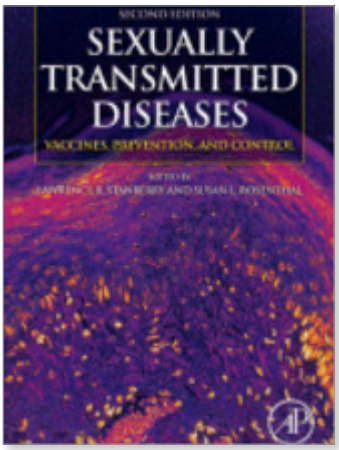
Consecutive, consenting adult men and women presenting with visible genital ulceration were enrolled between January 1, 2019, and December 31, 2020. Genital ulcer swab and blood specimens were collected and transported to a central sexually transmitted infection reference laboratory in Johannesburg.

RESULTS

Among 190 participants with GUS, HSV-2 was the most frequently detected ulcer pathogen (49.0%; 95% confidence interval [CI], 41.9%-56.1%). The relative prevalence of the second most common ulcer-derived pathogen, Treponema pallidum, was 26.3% (95% CI, 20.5%-33.1%), with 90% of primary syphilis cases having a positive rapid plasma reagin (RPR) titer. Male sex was independently associated with primary syphilis compared with herpetic ulcers, after adjusting for the effect of casual sex partners and other exposures (adjusted odds ratio, 3.53; 95% CI, 1.35-9.21; P = 0.010). The overall HIV prevalence among participants was 41.3% (78 of 189; 95% CI, 34.2%-48.6%).

CONCLUSIONS

Herpes simplex virus 2 remains the predominant cause of GUS, justifying the continued use of acyclovir in syndromic guidelines. Adequate supplies of benzathine penicillin G for syphilis treatment are essential at primary health care level, in addition to the provision of syphilis and HIV risk reduction services.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR TENDESAYI KUFA

Etiological surveillance of Male Urethritis Syndrome in South Africa: 2019-2020

RANMINI KULARATNE, **JOHANNA ME VENTER**, **VENESSA MASEKO**, **ETIENNE MULLER**, **TENDESAYI KUFA**

Sexually Transmitted Diseases **IMPACT FACTOR: 3,868**

BACKGROUND

In South Africa, male urethritis syndrome (MUS) is the most common sexually transmitted infection (STI) syndrome in men. We determined the distribution of STI etiologies and the susceptibility profiles of Neisseria gonorrhoeae isolates from men presenting with MUS to 3 sentinel surveillance health care facilities. Secondary objectives were to determine the seroprevalence of co-infections (HIV, syphilis, herpes simplex virus 2).

METHODS

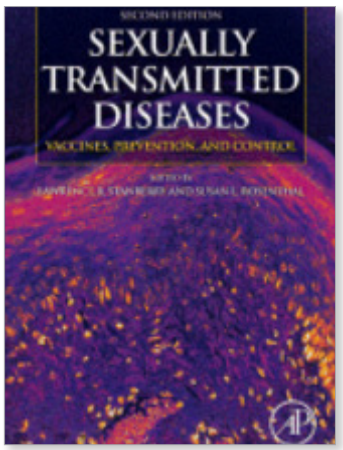
Consecutive, consenting men with symptomatic urethral discharge were enrolled between January 1, 2019, and December 31, 2020. Genital discharge swab and blood specimens were collected and transported to a central STI reference laboratory in Johannesburg, South Africa.

RESULTS

Among 769 men enrolled, N. gonorrhoeae was the commonest cause of MUS (674 [87.8%]; 95% confidence interval [CI], 85.2%-89.9%), followed by Chlamydia trachomatis (161 [21.0%]; 95% CI, 18.2%-24.0%). Of 542 cultivable N. gonorrhoeae isolates, all were susceptible to ceftriaxone (modal minimum inhibitory concentration, 0.004 mg/L) and azithromycin (modal minimum inhibitory concentration, 0.128 mg/L). Seroprevalence rates of HIV, syphilis, and HSV-2 were 21.4% (95% CI, 18.5%-24.5%), 2.3%, and 50.1%, respectively. Condom use at last sexual encounter was reported by only 7%, less than 50% had been medically circumcised, and only 66.7% (58 of 87) who self-reported an HIV-positive status were adherent on antiretroviral drugs.

CONCLUSIONS

Neisseria gonorrhoeae and C.trachomatis were the predominant causes of MUS. Currently recommended dual ceftriaxone and azithromycin therapy are appropriate for MUS syndromic management; however, surveillance must be maintained to timeously detect emerging and increasing gonococcal resistance. Clinic-based interventions must be intensified in men seeing sexual health care to reduce the community transmission and burden of STI and HIV.



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DR TENDESAYI KUFA

Etiological surveillance of Vaginal Discharge Syndrome in South Africa: 2019-2020

RANMINI KULARATNE, **JOHANNA ME VENTER, VENESSA MASEKO, ETIENNE MULLER, TENDESAYI KUFA**

Sexually Transmitted Diseases **IMPACT FACTOR: 3,868**

BACKGROUND

The syndromic management of vaginal discharge syndrome (VDS) is challenging because of the prevalence of mixed infection with sexually transmitted infection (STI) pathogens and non-STI causes, such as bacterial vaginosis and candidiasis (CA). We aimed to determine the relative prevalence of VDS etiologies in women presenting to sentinel primary health care clinics in South Africa. Secondary objectives were to ascertain the predictive value of speculum findings for the presence of STI pathogens and the proportion of women presenting with clinical features of CA who had identifiable yeast on vaginal smear microscopy.

METHODS

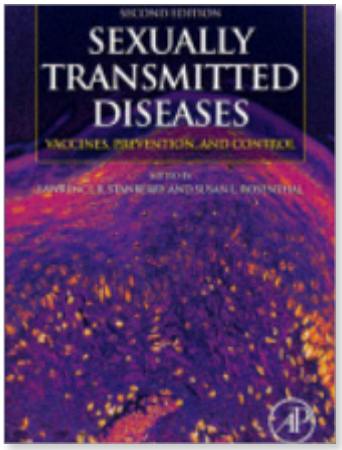
Consecutive, consenting women with complaints of abnormal vaginal discharge were enrolled between January 1, 2019, and December 31, 2020. Genital discharge swab and blood specimens were collected and transported to a central STI reference laboratory in Johannesburg.

RESULTS

A total of 364 women were enrolled at 3 sentinel sites. Bacterial vaginosis was the most common cause of VDS (163 of 361 [45.2%]; 95% confidence interval [CI], 40.1%-50.3%); however, a significant proportion had STI coinfection (71 of 163 [43.6%]; 95% CI, 35.8%-51.5%). The predominant STI etiology was Chlamydia trachomatis (73 [20.2%]; 95% CI, 16.4%-24.7%). An abnormal speculum finding had poor predictive value for STIs, and Gram stain microscopy showed yeast in only 37.2% of vaginal smears from women with CA symptoms.

CONCLUSIONS

Bacterial vaginosis is the predominant cause of VDS in South Africa; however, STI coinfection is common. Clinical findings are poorly predictive of STI etiologies or candidiasis; therefore, a rapid and accurate STI point-of-care test would be useful in optimizing VDS management.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS MELITAH MOTLHALE

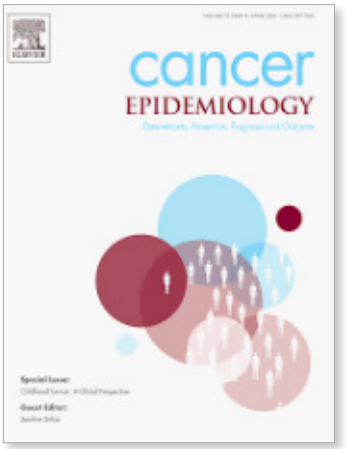
Epidemiology of Kaposi Sarcoma in Subharan Africa

MOTLHALE M, SITAS F, BRADSHAW D, **CHEN WC**, DE VILLIERS CB, LEWIS CM, **MUCHENGETI M**, WATERBOER T, MATHEW CG, NEWTON R, **SINGH E**

Cancer Epidemiology **IMPACT FACTOR: 2,89**

ABSTACT

Kaposi's sarcoma (KS) has become a common AIDS-defining cancer in sub-Saharan Africa. Kaposi's sarcoma-associated human herpesvirus strongly modulated by HIV-related immune suppression are the principal causes of this cancer. No other risk factors have been identified as playing a strong role. HIV prevention programs and good coverage of antiretroviral therapy (ART) in developed countries resulted in a remarkable decline in HIV-KS incidence and better KS prognosis. By contrast, in sub-Saharan Africa, population ART rollout has lagged, but clinical studies have shown positive results in reduction of KS incidence and better KS prognosis. However, the effect of ART rollout in relation to population KS incidence is unclear. We describe the incidence of KS in sub-Saharan Africa, in four time-periods, (1) before 1980 (before HIV/AIDS era); (2) 1981–2000 (early HIV/AIDS era, limited or no ART coverage); (3) 2001–2010 (early ART coverage period); and (4) 2011–2016 (fair to good ART coverage period). We used KS incidence data available from WHO-International Agency for Research on Cancer (IARC) publications and the Africa Cancer Registry Network. National HIV prevalence and ART coverage data were derived from UNAIDS/WHO. A rapid increase in KS incidence was observed throughout sub-Saharan Africa as the HIV epidemic progressed, reaching peak incidences in Period 2 (pre-ART rollout) of 50.8 in males and 20.3 per 100 000 in females (Zimbabwe, Harare). The overall unweighted average decline in KS incidence between 2000 and 2010 and 2011–2016 was 27%, but this decline was not statistically significant across the region. ART rollout coincides with a decline in KS incidence across several regions in sub-Saharan Africa. The importance of other risk factors such as reductions in HIV incidence could not be ascertained.



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MS MELITAH MOTLHALE

Lifestyle Factors Associated with Sex Differences in Kaposi Sarcoma incidence among adults Black South Africans : A case control study

MOTLHALE M, SITAS F, BRADSHAW D, **CHEN WC**, DE VILLIERS CB, LEWIS CM, **MUCHENGETI M**, WATERBOER T, MATHEW CG, NEWTON R, **SINGH E**

Cancer Epidemiology **IMPACT FACTOR: 2,89**

ABSTRACT

Kaposi Sarcoma (KS) is endemic in several countries in Southern and Eastern Africa, relatively rare worldwide but a leading cancer among people living with HIV. KS has always been more common in adult males than females. We assessed the prevalence of known cancer modifying factors (parity, hormonal contraceptive use in females, sex-partners, smoking and alcohol consumption in both sexes), and their relationship to KS, and whether any of these could account for the unequal KS sex ratios. We calculated logistic regression case-control adjusted odds ratios (ORadj), and 95% confidence intervals (95%CI), between KS and each of the modifying factors, using appropriate comparison controls. Controls were cancer types that had no known relationship to exposures of interest (infection or alcohol or smoking or contraceptive use). The majority of the 1275 KS cases were HIV positive (97%), vs. 15.7% in 10,309 controls. The risk of KS among those with HIV was high in males (ORadj=116.70;95%CI=71.35-190.88) and females (ORadj=93.91;95%CI=54.22-162.40). Among controls, the prevalence of smoking and alcohol consumption was five and three times higher in males vs. females. We found a positive association between KS and heavy vs. non-drinking (ORadj=1.31;95%CI=1.03-1.67), and in current heavy vs. never smokers (ORadj=1.82;95%CI=1.07-3.10). These associations remained positive for alcohol consumption (but with wider CIs) after stratification by sex, and restriction to HIV positive participants. We found no evidence of interactions of smoking and alcohol by sex. Smoking and alcohol consumption may provide a possible explanation for the KS sex differences, given both exposures are more common in men, but confounding and bias cannot be fully ruled out. The role smoking and alcohol play in relation to viral loads of HIV/KSHV, differences in immunological responses or other genetic differences between males and females warrant further studies.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF JOHN FREAN

Q fever - an underappreciated occupational disease in South Africa

JOHN FREAN

Occupational Health **IMPACT FACTOR: 2,57**

Q fever is an infectious illness of zoonotic origin and protean clinical features. Q (for 'query') fever was first described in 1935 during an outbreak of febrile illness in abattoir workers in Brisbane, Australia.1 The agent, originally thought to be a type of rickettsia, was later isolated in Australia and the United States, and named Coxiella burnetii in 1948. It is an unusual aerobic Gram-negative obligate intracellular bacterium. C. burnetii is a pathogen or coloniser of a wide variety of animals, wild and domestic; the traditional reservoirs of human disease are farmed livestock, namely cattle, sheep, and goats. Birthing domestic cats and dogs have also been sources of outbreaks.2 Organisms localise to placenta and mammary glands and, while infections in animals are usually clinically silent, they can cause outbreaks of abortion. Organisms are excreted via birth products, milk, faeces, and urine. C. burnetii differs in several ways from rickettsiae in being highly environmentally resistant, because of a spore-like stage; it shows antigenic phase variation; it produces granulomatous, rather than vasculitic pathology; and it can cause chronic infection.3 Most importantly, humans acquire it predominantly by the airborne route, especially when exposed to animal birth products or slaughtered animals; also by inhalation of dust residue contaminated by infected birth fluids, blood, faeces, or urine. Windborne spread can disperse contaminated dust over long distances. The organism is highly infectious, but person-to-person spread is uncommon. Transmission via unpasteurised milk or by crushing ticks has been described rarely; tick bites are not important for human infections, but accidental inhalation of tick faeces is a likely mode of infection.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS BABONGILE NDLOVU

Skin Cancer Risk factors among Black South Africans: The Johannesburg Cancer Study, 1995 - 2016

NDLOVU B, **SENGAYI- MUCHENGETI M**, WRIGHT CV, **CHEN WC**, **KUONZA L**, **SINGH E**

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

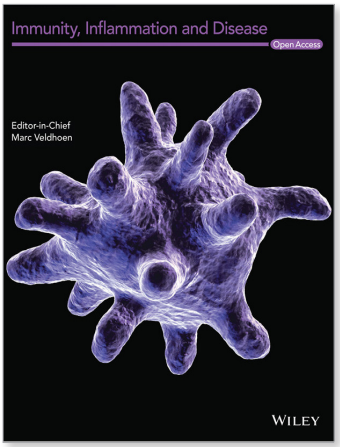
A case-control study was conducted. Cases were patients with keratinocyte cancers (KCs) and/or melanoma skin cancers (MSCs) and controls were cardiovascular patients. So-ciodemographic exposures, environmental health variables, smoking, and HIV status were assessed. Stepwise logistic regression was used 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.



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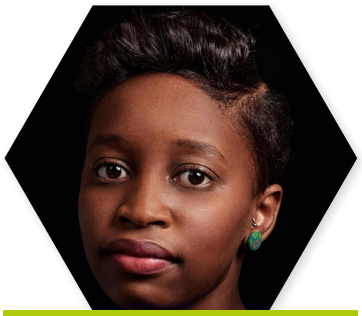
PROF LIZETTE LEONIE KOEKEMOER

Effect of larval density and additional anchring surface on the life-history traits of a laboratory colonized Anopheles funestus strain

MUNYARADZI PRINCE ZENGENENE, **GIVEMORE MUNHENGA**, FREDROS OKUMU, **LIZETTE LEONIE KOEKEMOER**

Medical and Veterinary Entomology IMPACT FACTOR: 2,479

Optimal rearing conditions, inclusive of larval rearing density, are critical for sustained mosquito productivity. There is limited information on favourable conditions for the larval rearing of Anopheles funestus, the dominant malaria vector in east and southern Africa. This work investigated the effects of larval rearing densities and additional anchoring surface on An. funestus development using a life table approach. Larval cohorts were reared at four different larval densities using the same rearing surface area, larval food concentrations and temperature conditions. Rearing larvae at high densities extended the larval developmental time and reduced adult productivity. Adding an extra larval anchoring surface when rearing larvae at high density resulted in extended larval developmental time, increased larval survivorship and produced bigger adults. These findings improve our understanding of the relationship between larval density and developmental traits in An. funestus and provides baseline information for An. funestus rearing under laboratory conditions.



THANDEKA MOYO-GWETE

PROF PENNY MOORE

Leveraging on past investment in understanding the immunology of COVID-19 – the South African experience

THANDEKA MOYO-GWETE, MOORE PL

South African Journal of Science IMPACT FACTOR: 2,134

ABSTRACT

The COVID-19 pandemic, and in particular the emergence of viral variants, resulted in an enormous global public health crisis. South African scientists, with a long history of studying viral evolution and antibody responses, were well positioned to pivot their research to focus on SARS-CoV-2. Using the expertise and infrastructure developed over decades for HIV vaccine research, South Africa took a leadership role in studying the antibody response elicited by SARS-CoV-2 infection and vaccination. We describe key scientific outcomes of those studies, and the drivers of a successful national response.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR MAZVITA SENGAYI-MUCHENGETI

Cohort Profile : The South HIVCancer Match (SAM) - Study a national population based cohort

MUCHENGETI M, BARTELS L, **OLAGO V**, **DHOKOTERA T**, **CHEN WC**, SPOERRIE A, ROHNER E, BUTIKOFER L, **RUFFIEUX Y**, **SINGH E**, EGGER M, BOHLIUS J

BMJ Open **IMPACT FACTOR: 0,73**

Purpose The South African HIV Cancer Match (SAM) Study is a national cohort of people living with HIV (PLWH). It was created using probabilistic record linkages of routine laboratory records of PLWH retrieved by National Health Laboratory Services (NHLS) and cancer data from the National Cancer Registry. The SAM Study aims to assess the spectrum and risk of cancer in PLWH in the context of the evolving South African HIV epidemic. The SAM Study's overarching goal is to inform cancer prevention and control programmes in PLWH in the era of antiretroviral treatment in South Africa.

Participants PLWH (both adults and children) who accessed HIV care in public sector facilities and had HIV diagnostic or monitoring laboratory tests from NHLS.

Findings to date The SAM cohort currently includes 5 248 648 PLWH for the period 2004 to 2014; 69% of these are women. The median age at cohort entry was 33.0 years (IQR: 26.2–40.9). The overall cancer incidence in males and females was 235.9 (95% CI: 231.5 to 240.5) and 183.7 (181.2–186.2) per 100 000 person-years, respectively.

Using data from the SAM Study, we examined national cancer incidence in PLWH and the association of different cancers with immunodeficiency. Cancers with the highest incidence rates were Kaposi sarcoma, cervix, breast, non-Hodgkin's lymphoma and eye cancer.

Future plans The SAM Study is a unique, evolving resource for research and surveillance of malignancies in PLWH. The SAM Study will be regularly updated. We plan to enrich the SAM Study through record linkages with other laboratory data within the NHLS (eg, tuberculosis, diabetes and lipid profile data), mortality data and socioeconomic data to facilitate comprehensive epidemiological research of comorbidities among PLWH.

BMJ Open

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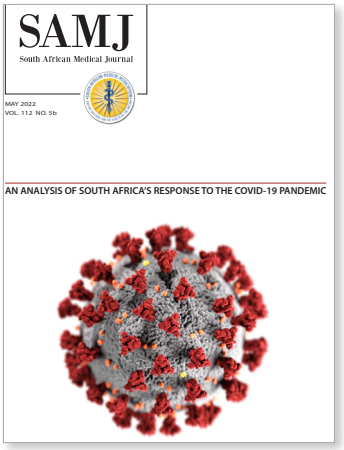
DR NATALIE MAYET

Governing a pandemic: A case study of South Africa's coordination and management structures used to respond to the COVID-19 pandemic

D MOONASAR, E LEONARD, R NAIDOO, Y PILLAY, **N GOVENDER**, R MOREWANE, W RAMKRISHNA, T FURUMELE, O P RAMADAN, A PILLAY, **N MAYET**

South African Medical Journal **IMPACT FACTOR: 0,566**

"During a public health emergency, coordination and management are essential for ensuring timeous, decisive, and harmonised leadership. In this paper, the governance structures utilised in South Africa (SA) during the COVID-19 pandemic are recorded and the key strengths and weaknesses of response in the country are discussed. A qualitative methodology is used for the case study and comprises insights from stakeholders who were at the forefront of SA's response as well as from documentation that was used to guide the response. Structured, transparent, science-based and agile coordination and management systems are necessary to gain the public's trust during a public health emergency. This case study contributes to the literature on governing a pandemic and shares lessons learned from the COVID-19 response. The lessons learned by the stakeholders within the SA governance structures can be leveraged in future public health emergencies within SA and other low- and middle-income countries



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MS SINENHLANHLA JIMOH

DR NATALIE MAYET

Risk communication and community engagement–unlocking the key to South Africa's response to SARS-CoV-2

LEBURU N, SHILUMANI C, BHENGU C, MATLALA N, MAJA P, **JIMOH S, MAYET N**

South African Medical Journal **IMPACT FACTOR: 0,566**

BACKGROUND

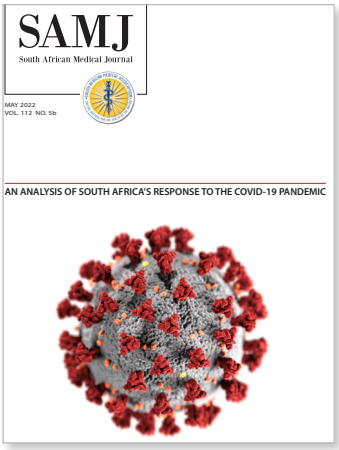
COVID-19 has changed the way that governments communicate and engage with citizens. In emergencies, effective communication must be immediate, grounded in science, transparent, easy to understand and in language-appropriate messaging delivered through multiple and varied platforms. For the South African (SA) COVID-19 response, the intent was to design an agile, locally relevant Risk Communication and Community Engagement (RCCE) strategy as the pandemic was unfolding and to constantly evaluate its implementation. Early involvement of communities in the formulation and direction of a risk communication plan is essential to its success. Objective. To outline the significance of the RCCE's robust communication strategy during the COVID-19 response and the lessons learnt in executing the strategy.

METHODS

This is a qualitative review of documents and reports generated and utilised by the RCCE Technical Working Group (TWG) and reflects the lessons learnt from discussions and multiple engagements at district, provincial and national levels. The review incorporates lessons learnt from international practice, resource documents from the World Health Organization (WHO), RCCE readiness and response to coronavirus disease, feedback from the Behavioural Science Ministerial Advisory Committee, input from the call centre, website and various established social media platforms.

RESULTS

Communication and building trust with multiple stakeholders begin before an outbreak and is a prerequisite to facilitate the timeous flow of information, particularly in the context of a rapidly evolving outbreak of a new disease, where the scientific community does not immediately have all the answers. Initial COVID-19 messages were therefore filled with challenges that ranged from the lack of scientific and epidemiological information to rumours, conspiracy theories and misinformation. The findings validate that empowering communities to act, strengthening public trust and community participation using multiple channels as well as timely responses to rumours and misinformation are important drivers of COVID-19 communication efforts in SA. Communication efforts must be accelerated to translate science into locally relevant languages and the impact of interventions must be measured to appropriately direct limited resources. Conclusion. The risk communication strategy incorporated several key lessons that could be used to improve communication and inform future emergency response communication that is immediate, science-based, transparent, inclusive and encourages community participation.



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DR SIBONGILE WALAZA

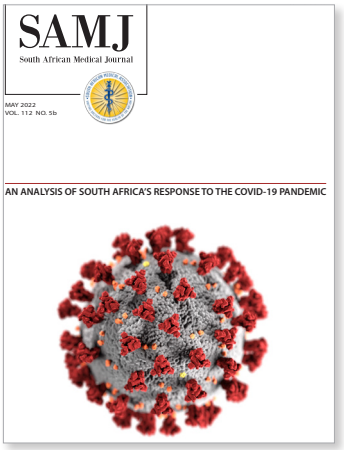
Leveraging epidemiology as a decision support tool during the COVID-19 epidemic in South Africa

SILAL SP, **GROOME MJ**, **GOVENDER N**, PULLIAM JRC, RAMADAN OP, **PUREN A**, **JASSAT W**, LEONARD E, MOULTRIE H, MEYER-RATH KG, RAMKRISHNA W, LANGA T, FURUMELE T, MOONASAR D, **COHEN C**, **WALAZA S**

South African Medical Journal **IMPACT FACTOR: 0,566**

ABSTRACT

By May 2021, South Africa (SA) had experienced two 'waves' of COVID-19 infections, with an initial peak of infections reached in July 2020, followed by a larger peak of infections in January 2021. Public health decisions rely on accurate and timely disease surveillance and epidemiological analyses, and accessibility of data at all levels of government is critical to inform stakeholders to respond effectively. In this paper, we describe the adaptation, development and operation of epidemiological surveillance and modelling systems in SA in response to the COVID-19 epidemic, including data systems for monitoring laboratory-confirmed COVID-19 cases, hospitalisations, mortality and recoveries at a national and provincial level, and how these systems were used to inform modelling projections and public health decisions. Detailed descriptions on the characteristics and completeness of individual datasets are not provided in this paper. Rapid development of robust data systems was necessary to support the response to the SA COVID-19 epidemic. These systems produced data streams that were used in decision-making at all levels of government. While much progress was made in producing epidemiological data, challenges remain to be overcome to address gaps to better prepare for future waves of COVID-19 and other health emergencies.



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MS NOZUKO P. BLASICH

PROF NELESH GOVENDER

Retrospective Assessment of a National Reflex Cryptococcal Antigen Screening Program in South Africa Through Interlaboratory Comparison of Lateral Flow Assay Results

MS NOZUKO P. BLASICH, COETZEE LM, SRIRUTTAN C, DESANTO D, GREENE GS, GLENCROSS DK, **GOVENDER NP**

Laboratory Medicine **IMPACT FACTOR: 0,49**

Abstract

OBJECTIVE

Reflex cryptococcal antigen (CrAg) screening of blood specimens with a CD4 count of <100 cells/µL was performed at 45 South African CD4 laboratories using a lateral flow assay (LFA). Our objective was to evaluate the reliability of routine LFA results through comparative interlaboratory testing.

METHODS

All CrAg-positive and a selected number of CrAg-negative samples from the CD4 laboratories were retested at paired microbiology laboratories using the same LFA. Samples with discordant results were tested at a reference laboratory, using the LFA (with CrAg titers).

RESULTS

During interlaboratory testing, 12,502 samples were retested, with 93 (0.7%) discordant results and a between-laboratory agreement of 99.3% (Cohen's kappa, 0.98). The proportion of retested samples with discordant results ranged from 0.17% to 5.31% per laboratory pair (median 0.28%), with 3 reporting >3% of results as discordant.

CONCLUSION

Routine CrAg screening results were reliable, with <1% of samples having discordant results, mainly due to interpretation and transcription errors.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS MAIMUMA CARRIM

DR NICOLE WOLTER

Unmasking pneumococcal carriage in a high HIV prevalence population in two community cohorts with a high prevalence of HIV in South Africa, 2016-2018: the PHIRST study

MAIMUNA CARRIM, STEFANO TEMPIA, DEUS THINDWA, NEIL A. MARTINSON, KATHLEEN KAHN, STEFAN FLASCHE, **ORIENKA HELLFERSCEE**, FLORETTE K. TREURNICHT, MEREDITH L. MCMORROW, JOCELYN MOYES, **THULISA MKHENCELE**, **AZWIFARWI MATHUNJWA**, **JACKIE KLEYNHANS**, LIMAKATSO LEBINA, KATLEGO MOTHLAOLENG, FLOIDY WAFAWANAKA, FRANCESC XAVIER GMEZ-OLIVE, CHERYL COHEN, **ANNE VON GOTTBERG**, **NICOLE WOLTER**

Clinical Infectious Diseases

IMPACT FACTOR: n/a

BACKGROUND

Longitudinal pneumococcus colonization data in high human immunodeficiency virus (HIV) prevalence settings following pneumococcal conjugate vaccine introduction are limited.

METHODS

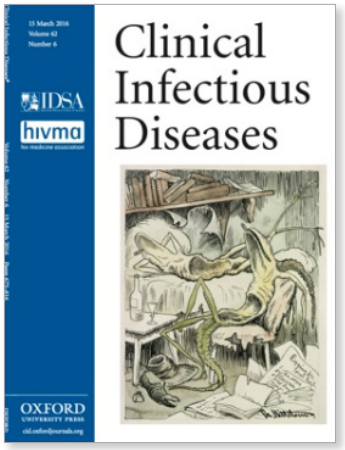
In 327 randomly selected households, 1684 individuals were enrolled and followed-up for 6 to 10 months during 2016 through 2018 from 2 communities. Nasopharyngeal swabs were collected twice weekly and tested for pneumococcus using quantitative lytA real-time polymerase chain reaction. A Markov model was fitted to the data to define the start and end of an episode of colonization. We assessed factors associated with colonization using logistic regression.

RESULTS

During the study period, 98% (1655/1684) of participants were colonized with pneumococcus at least once. Younger age (<5 years: adjusted odds ratio [aOR], 14.1; 95% confidence [CI], 1.8–111.3, and 5–24 years: aOR, 4.8, 95% CI, 1.9–11.9, compared with 25–44 years) and HIV infection (aOR, 10.1; 95% CI, 1.3–77.1) were associated with increased odds of colonization. Children aged <5 years had fewer colonization episodes (median, 9) than individuals ≥5 years (median, 18; P < .001) but had a longer episode duration (<5 years: 35.5 days; interquartile range, 17–88) vs. ≥5 years: 5.5 days (4–12). High pneumococcal loads were associated with age (<1 year: aOR 25.4; 95% CI, 7.4–87.6; 1–4 years: aOR 13.5, 95% CI 8.3–22.9; 5–14 years: aOR 3.1, 95% CI, 2.1–4.4 vs. 45–65 year old patients) and HIV infection (aOR 1.7; 95% CI 1.2–2.4).

CONCLUSIONS

We observed high levels of pneumococcus colonization across all age groups. Children and people living with HIV were more likely to be colonized and had higher pneumococcal loads. Carriage duration decreased with age highlighting that children remain important in pneumococcal transmission.



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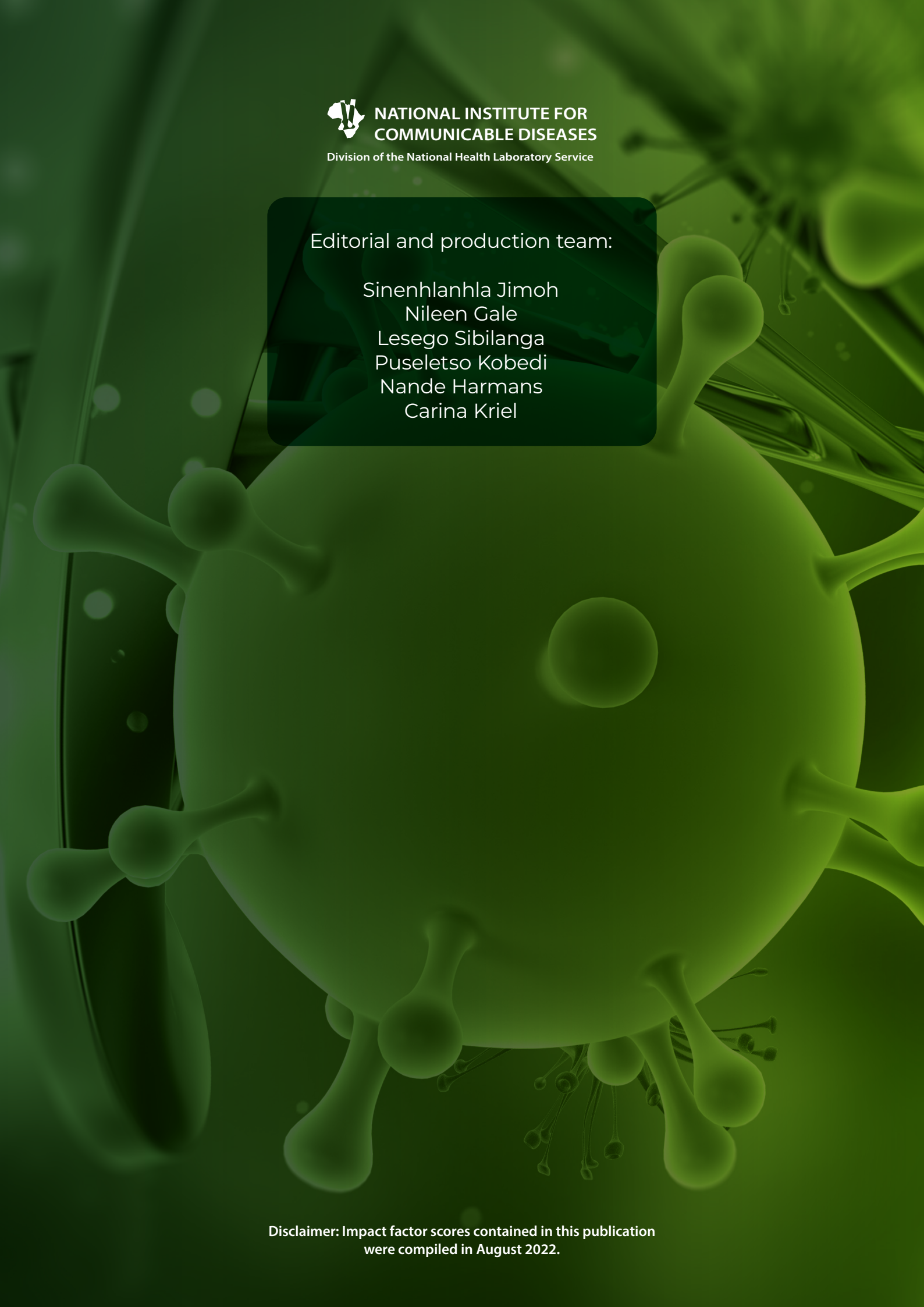

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