Issue 19 - February 2022

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

SCIENCE FOCUS

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

Editor's Note

The first Science Focus for 2022 highlights notable research achievements from scientific experts at the National Institute for Communicable Diseases (NICD). In addition to the outstanding statistical findings, the number of peer-reviewed articles produced, the top published authors and high impact factor score articles are also included.

The edition kicks off with the feature, 'Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: a cohort study' makes for a interesting read. With contributions from Dr Waasila Jassat and Prof Cheryl Cohen, data from the DATCOV national active surveillance system for COVID-19 admissions were analysed. The study compared the characteristics of patients with COVID-19 who were hospitalised during waves one and two, and unpacks the risk factors for in-hospital mortality.

Next, Prof Nelesh Govender takes a closer look at rare yeast infections in 'Global guideline for the diagnosis and management of rare yeast infections: an initiative of the European Confederation of Medical Mycology (ECMM) in cooperation with The International Society for Human & Animal Mycology (ISHAM) and American Society for Microbiology (ASM).' The piece explains that uncommon yeast infections are showing an upward trend, given an increase in the number of patients who are immunocompromised or seriously ill. Key features of the epidemiology, diagnosis, antifungal susceptibility, and treatment outcomes of patients suffering these rare infections are reported.

Those at risk of COVID-19 in-hospital mortality would benefit from COVID-19 prevention programmes, for example vaccine prioritisation and early referral. This interpretation is deduced from the research conducted by, among others, Dr Waasila Jassat and Prof Lucille Blumberg. 'Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study' examines the interaction between COVID-19, non-communicable diseases, and chronic infectious diseases. The factors associated with in-hospital mortality among patients with COVID-19 are investigated.

The Science Focus would be incomplete without the contribution from Prof Penny Moore, and the publication, 'In utero human cytomegalovirus infection is associated with increased levels of putatively protective maternal antibodies in non-primary infection: evidence for boosting but not protection' does not disappoint. The study compared 42 mothers of infants, with congenital CMV infections (transmitters), to 75 CMVseropositive mothers, whose infants were CMV-uninfected (non-transmitters). Interestingly, no evidence was found that higher levels of CMV-specific antibodies are associated with reduced risk of congenital CMV infection in non-primary maternal infection.

The NICD salutes the researchers who continue to question the status quo, and in doing so publish important public health papers in high-impact publications, including The Lancet, Clinical Infectious Diseases, and Clinical Microbiology and Infection.

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

Happy reading!

On behalf of the team.

Sinenhlanhla Jimoh
Senior Communications Manager

EXCEPTIONAL RESEARCH STATISTICS

TOP 5

MOST PUBLISHED AUTHORS IN Q2 OF 2021/2022

1

PROF CHERYL COHEN

2

PROF ANNE VON GOTTBERG

2

DR SIBONGILE WALAZA

3

PROF STEFANO TEMPIA

4

PROF LUCILLE BLUMBERG

4

DR ORIENKA HELLFERSCEE

4

DR NICOLE WOLTER

5

PROF PENNY MOORE

5

PROF NELESH GOVENDER

FEATURED RESEARCH ABSTRACTS FOR THE SECOND QUARTER OF 2021/2022

Dr Waasila Jassat

Prof Cheryl Cohen

Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: a cohort study

Jassat W, *Mudara C, Ozougwu L, Tempia S, Blumberg L, Davies MA, Pillay Y, Carter T, Morewane R, Wolmarans M, von Gottberg A, Bhiman JN, Walaza S,* ***Cohen C; DATCOV author group.***

Lancet Global Health
Impact Factor: 26.763

Background: The first wave of COVID-19 in South Africa peaked in July, 2020, and a larger second wave peaked in January, 2021, in which the SARS-CoV-2 501Y.V2 (Beta) lineage predominated. We aimed to compare in-hospital mortality and other patient characteristics between the first and second waves.

Methods: In this prospective cohort study, we analysed data from the DATCOV national active surveillance system for COVID-19 admissions to hospital from March 5, 2020, to March 27, 2021. The system contained data from all hospitals in South Africa that have admitted a patient with COVID-19. We used incidence risk for admission to hospital and determined cutoff dates to define five wave periods: pre-wave 1, wave 1, post-wave 1, wave 2, and post-wave 2. We compared the characteristics of patients with COVID-19 who were admitted to hospital in wave 1 and wave 2, and risk factors for in-hospital mortality accounting for wave period using random-effect multivariable logistic regression.

Findings: Peak rates of COVID-19 cases, admissions, and in-hospital deaths in the second wave exceeded rates in the first wave: COVID-19 cases, 240·4 cases per 100 000 people vs 136·0 cases per 100 000 people; admissions, 27·9 admissions per 100 000 people vs 16·1 admissions per 100 000 people; deaths, 8·3 deaths per 100 000 people vs 3·6 deaths per 100 000 people. The weekly average growth rate in hospital admissions was 20% in wave 1 and 43% in wave 2 (ratio of growth rate in wave 2 compared with wave 1 was 1·19, 95% CI 1·18–1·20). Compared with the first wave, individuals admitted to hospital in the second wave were more likely to be age 40–64 years (adjusted odds ratio [aOR] 1·22, 95% CI 1·14–1·31), and older than 65 years (aOR 1·38, 1·25–1·52), compared with younger than 40 years; of Mixed race (aOR 1·21, 1·06–1·38) compared with White race; and admitted in the public sector (aOR 1·65, 1·41–1·92); and less likely to be Black (aOR 0·53, 0·47–0·60) and Indian (aOR 0·77, 0·66–0·91), compared with White; and have a comorbid condition (aOR 0·60, 0·55–0·67). For multivariable analysis, after adjusting for weekly COVID-19 hospital admissions, there was a 31% increased risk of in-hospital mortality in the second wave (aOR 1·31, 95% CI 1·28–1·35). In-hospital case-fatality risk increased from 17·7% in weeks of low admission (<3500 admissions) to 26·9% in weeks of very high admission (>8000 admissions; aOR 1·24, 1·17–1·32).

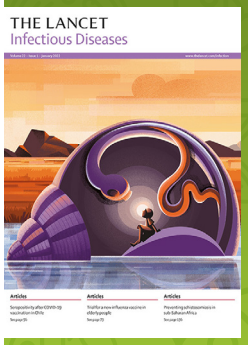
Interpretation: In South Africa, the second wave was associated with higher incidence of COVID-19, more rapid increase in admissions to hospital, and increased in-hospital mortality. Although some of the increased mortality can be explained by admissions in the second wave being more likely in older individuals, in the public sector, and by the increased health system pressure, a residual increase in mortality of patients admitted to hospital could be related to the new Beta lineage.

Prof Nelesh Govender

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

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

Lancet Infectious Diseases
Impact Factor: 25.071



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

Dr Waasila Jassat

Prof Lucille Blumberg

Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study

Jassat W, *Cohen C, Tempia S, Masha M, Goldstein S, Kufa T, Murangandi P, Savulescu D, Walaza S, Bam JL, Davies MA, Prozesky HW, Naude J, Mnguni AT, Lawrence CA, Mathema HT, Zamparini J, Black J, Mehta R, Parker A, Chikobvu P, Dawood H, Muvhango N, Strydom R, Adelekan T, Mdlovu B, Moodley N, Namavhandu EL, Rheeder P, Venturas J, Magula N,* ***Blumberg L; DATCOV author group***

Lancet HIV
Impact Factor: 12.767

Background: The interaction between COVID-19, non-communicable diseases, and chronic infectious diseases such as HIV and tuberculosis is unclear, particularly in low-income and middle-income countries in Africa. South Africa has a national HIV prevalence of 19% among people aged 15–49 years and a tuberculosis prevalence of 0·7% in people of all ages. Using a nationally representative hospital surveillance system in South Africa, we aimed to investigate the factors associated with in-hospital mortality among patients with COVID-19.

Methods: In this cohort study, we used data submitted to DATCOV, a national active hospital surveillance system for COVID-19 hospital admissions, for patients admitted to hospital with laboratory-confirmed SARS-CoV-2 infection between March 5, 2020, and March 27, 2021. Age, sex, race or ethnicity, and comorbidities (hypertension, diabetes, chronic cardiac disease, chronic pulmonary disease and asthma, chronic renal disease, malignancy in the past 5 years, HIV, and past and current tuberculosis) were considered as risk factors for COVID-19-related in-hospital mortality. COVID-19 in-hospital mortality, the main outcome, was defined as a death related to COVID-19 that occurred during the hospital stay and excluded deaths that occurred because of other causes or after discharge from hospital; therefore, only patients with a known in-hospital outcome (died or discharged alive) were included. Chained equation multiple imputation was used to account for missing data and random-effects multivariable logistic regression models were used to assess the role of HIV status and underlying comorbidities on COVID-19 in-hospital mortality.

Findings: Among the 219 265 individuals admitted to hospital with laboratory-confirmed SARS-CoV-2 infection and known in-hospital outcome data, 51 037 (23·3%) died. Most commonly observed comorbidities among individuals with available data were hypertension in 61 098 (37·4%) of 163 350, diabetes in 43 885 (27·4%) of 159 932, and HIV in 13 793 (9·1%) of 151 779. Tuberculosis was reported in 5282 (3·6%) of 146 381 individuals. Increasing age was the strongest predictor of COVID-19 in-hospital mortality. Other factors associated were HIV infection (adjusted odds ratio 1·34, 95% CI 1·27–1·43), past tuberculosis (1·26, 1·15–1·38), current tuberculosis (1·42, 1·22–1·64), and both past and current tuberculosis (1·48, 1·32–1·67) compared with never tuberculosis, as well as other described risk factors for COVID-19, such as male sex; non-White race; underlying hypertension, diabetes, chronic cardiac disease, chronic renal disease, and malignancy in the past 5 years; and treatment in the public health sector. After adjusting for other factors, people with HIV not on antiretroviral therapy (ART; adjusted odds ratio 1·45, 95% CI 1·22–1·72) were more likely to die in hospital than were people with HIV on ART. Among people with HIV, the prevalence of other comorbidities was 29·2% compared with 30·8% among HIV-uninfected individuals. Increasing number of comorbidities was associated with increased COVID-19 in-hospital mortality risk in both people with HIV and HIV-uninfected individuals.

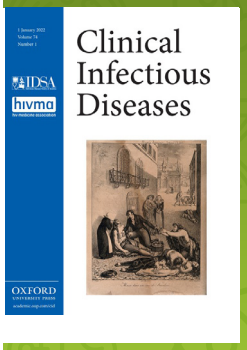
Interpretation: Individuals identified as being at high risk of COVID-19 in-hospital mortality (older individuals and those with chronic comorbidities and people with HIV, particularly those not on ART) would benefit from COVID-19 prevention programmes such as vaccine prioritisation as well as early referral and treatment.

Prof Penny Moore

In utero human cytomegalovirus infection is associated with increased levels of putatively protective maternal antibodies in nonprimary infection: evidence for boosting but not protection

Dorfman JR, Balla SR, Pathirana J, Groome MK, Madhi SA, ***Moore PL***

Clinical Infectious Diseases
Impact Factor: 9.079



Background: Although primary maternal cytomegalovirus infections are associated with higher risk of in utero transmission, most fetal infections worldwide result from nonprimary maternal infections. Antibodies directed at glycoprotein B (gB) and the gH/gL/pUL128-130-131 pentamer can neutralize virus, and higher levels of antibody directed at several particular pentamer epitopes defined by monoclonal antibodies (mAbs) are associated with reduced risk of fetal cytomegalovirus (CMV) transmission during primary maternal infection. This had not been explored in maternal nonprimary infection.

Methods: In a setting where most maternal CMV infections are nonprimary, 42 mothers of infants with congenital CMV infections (transmitters) were compared to 75 CMV-seropositive mothers whose infants were CMV-uninfected (nontransmitters). Control infants were matched by sex, maternal human immunodeficiency virus (HIV) status, and gestational age. We measured the ability of maternal antibodies to block 3 key pentameric epitopes: one in the gH subunit, another straddling UL130/UL131, and the third straddling gH/gL/UL128/UL130. We tested if levels of antibodies directed at these epitopes were higher in nontransmitters compared to transmitters.

Results: Levels of all 3 putatively protective pentamer-directed antibodies were significantly higher in transmitters compared to nontransmitters. In contrast, antibodies targeting an epitope on gB were not different. Total antibody specific for pentamer and for gB were also higher in transmitters.

Conclusions: We found no evidence that higher levels of any CMV-specific antibodies were associated with reduced risk of congenital CMV infection in nonprimary maternal infection. Instead, we found higher maternal antibody targeting epitopes on CMV pentamer in transmitters than nontransmitters, providing evidence for antibody boosting but not protection.

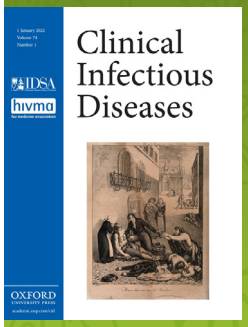
Dr Nicole Wolter

Prof Anne von Gottberg

Epidemiology of Pertussis in Individuals of All Ages Hospitalized With Respiratory Illness in South Africa, January 2013—December 2018

Wolter N, *Cohen C, Tempia S, Walaza S, Moosa F, du Plessis M, McMorrow ML, Treurnicht FK, Hellferscee O, Dawood H, Variava E,* ***von Gottberg A***

Clinical Infectious Diseases
Impact Factor: 9.079



Background: Policy recommendations on pertussis vaccination need to be guided by data, which are limited from low- and middle-income countries. We aimed to describe the epidemiology of pertussis in South Africa, a country with high human immunodeficiency virus (HIV) prevalence and routine pertussis vaccination for 6 decades including the acellular vaccine since 2009.

Methods: Hospitalized patients of all ages were enrolled at 5 sentinel sites as part of a pneumonia surveillance program from January 2013 through December 2018. Nasopharyngeal specimens and induced sputum were tested by polymerase chain reaction (PCR) for Bordetella pertussis. In addition, demographic and clinical information were collected. Incidence rates were calculated for 2013-2016, and multivariable logistic regression performed to identify factors associated with pertussis.

Results: Over the 6-year period 19 429 individuals were enrolled, of which 239 (1.2%) tested positive for B. pertussis. Detection rate was highest in infants aged <6 months (2.8%, 155/5524). Mean annual incidence was 17 cases per 100 000 population, with the highest incidence in children <1 year of age (228 per 100 000). Age-adjusted incidence was 65.9 per 100 000 in HIV-infected individuals compared to 8.5 per 100 000 in HIV-uninfected individuals (risk ratio 30.4, 95% confidence interval: 23.0-40.2). Ten individuals (4.2%) with pertussis died; of which 7 were infants aged <6 months and 3 were immunocompromised adults.

Conclusions: Pertussis continues to be a significant cause of illness and hospitalization in South Africa, despite routine vaccination. The highest burden of disease and death occurred in infants; however, HIV-infected adults were also identified as an important group at risk of B. pertussis infection.

Dr Susan Meiring

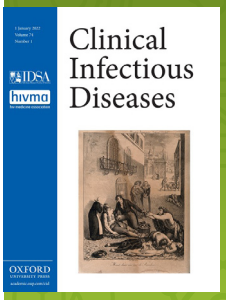
Prof Anne von Gottberg

Human Immunodeficiency Virus Infection Is Associated With Increased Meningococcal Carriage Acquisition Among First-year Students in 2 South African Universities

Meiring S, *Cohen C, de Gouveia L, du Plessis M, Ganesh K, Kleynhans J, Quan V, Tempia S,* ***von Gottberg A***

Clinical Infectious Diseases
Impact Factor: 9.079

Background: Invasive meningococcal disease clusters occur amongst university students and may reflect higher carriage prevalence amongst this population. We aimed to measure meningococcal carriage prevalence, acquisition and risk factors amongst first-year university students in South Africa, a middle-income country. Methods: In summer to autumn 2017, after consenting to participate, we collected oropharyngeal swabs and questionnaires on carriage risk factors and tested students for HIV infection at two universities, during registration week (survey one) and 6-8 weeks later (survey two). Meningococci were detected by culture and polymerase chain reaction. Results: We enrolled 2120 students at registration. Mean age was 18.5 years, 59% (1252/2120) were female and 0.8% (16/1984) were HIV-infected. Seventy-eight percent of students returned for survey two (1655/2120).Amongst the cohort, carriage prevalence was 4.7% (77/1655) at registration; increasing to 7.9% (130/1655) at survey two: 5.0% (83) acquired new carriage, 2.8% (47) had persistent carriage, 1.8% (30) cleared the initial carriage and 90.3% (1495) remained carriage-free. At both surveys, non-genogroupable meningococci predominated, followed by genogroups Y, B, W and C. On multinomial analysis risk factors for carriage acquisition included attending nightclubs (adjusted relative risk ratio (aRRR) 2.1 (95%CI=1.1-4.0)), having intimate kissing partners (aRRR 1.8 (95%CI=1.1-2.9)) and being HIV-infected (aRRR 5.0 (95%CI=1.1-24.4)). Conclusion: Meningococcal carriage amongst first-year university students increased after two months. Social-behavioural risk factors were associated with increased carriage for all analyses. HIV-infection was associated with carriage acquisition. Until vaccination programmes become mandatory in South African universities, data suggest that HIV-infected students could benefit most from meningococcal vaccination.

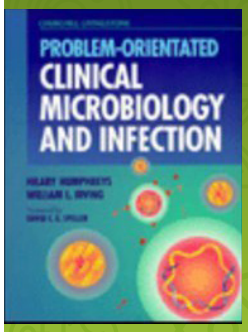


Prof Gayle Sherman

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

Radebe L, Mazanderani AH, ***Sherman GG***

Clinical Microbiology and Infection
Impact Factor: 3.918



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.

Mrs Rebecca van Dorsten

Combinations of single chain variable fragments from HIV broadly 1 neutralizing antibodies demonstrate high potency and breadth

Van Dorsten RT, *Wagh K, Moore PL, Morris L*

Frontiers in Immonology
Impact Factor: 7.561

Broadly neutralizing antibodies (bNAbs) are currently being assessed in clinical trials for their ability to prevent HIV infection. Single chain variable fragments (scFv) of bNAbs have advantages over full antibodies as their smaller size permits improved diffusion into mucosal tissues and facilitates vector-driven gene expression. We have previously shown that scFv of bNAbs individually retain significant breadth and potency. Here we tested combinations of five scFv derived from bNAbs CAP256-VRC26.25 (V2-apex), PGT121 (N332-supersite), 3BNC117 (CD4bs), 8ANC195 (gp120-gp41 interface) and 10E8v4 (MPER). Either two or three scFv were combined in equimolar amounts and tested in the TZM-bl neutralization assay against a multiclade panel of 17 viruses. Experimental IC50 and IC80 data were compared to predicted neutralization titers based on single scFv titers using the Loewe additive and the Bliss-Hill model. Like full-sized antibodies, combinations of scFv showed significantly improved potency and breadth compared to single scFv. Combinations of two or three scFv generally followed an independent action model for breadth and potency with no significant synergy or antagonism observed overall although some exceptions were noted. The Loewe model underestimated potency for some dual and triple combinations while the Bliss-Hill model was better at predicting IC80 titers of triple combinations. Given this, we used the Bliss-Hill model to predict the coverage of scFv against a 45-virus panel at concentrations that correlated with protection in the AMP trials. Using IC80 titers and concentrations of 1µg/mL, there was 93% coverage for one dual scFv combination (3BNC117+10E8v4), and 96% coverage for two of the triple combinations (CAP256.25+3BNC117+10E8v4 and PGT121+3BNC117+10E8v4). Combinations of scFv, therefore, show significantly improved breadth and potency over individual scFv and given their size advantage, have potential for use in passive immunization.

Dr Simone Richardson

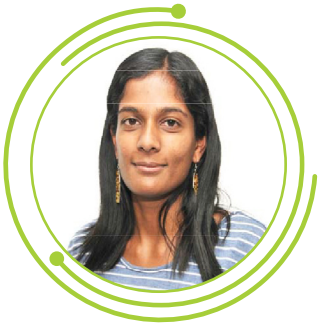
Prof Penny Moore

HIV broadly neutralizing antibodies expressed as IgG3 preserve neutralization potency and show improved Fc effector function.

Richardson SI, *Ayres F, Manamela NP, Oosthuysen B, Makhado Z, Lambson BE, Morris L,* ***Moore PL.***

Frontiers in Immonology
Impact Factor: 7.561

The ability of several broadly neutralizing antibodies (bNAbs) to protect against HIV infection is enhanced through Fc receptor binding. Antibody isotype modulates this effect, with IgG3 associated with improved HIV control and vaccine efficacy. We recently showed that an IgG3 variant of bNAb CAP256-VRC26.25 exhibited more potent neutralization and phagocytosis than its IgG1 counterpart. Here, we expanded this analysis to include additional bNAbs targeting all major epitopes. A total of 15 bNAbs were expressed as IgG1 or IgG3, and pairs were assessed for neutralization potency against the multi-subtype global panel of 11 HIV strains. Binding to the neonatal Fc receptor (FcRn) and Fcγ receptors were measured using ELISA and antibody-dependent cellular cytotoxicity (ADCC) and phagocytosis were measured using infectious viruses and global panel Env SOSIP trimers, respectively. IgG3 bNAbs generally showed similar or increased (up to 60 fold) neutralization potency than IgG1 versions, though the effect was virus-specific. This improvement was statistically significant for CAP256-VRC26.25, 35022, PGT135 and CAP255. G3. IgG3 bNAbs also showed significantly improved binding to FcγRIIa which correlated with enhanced phagocytosis of all trimeric Env antigens. Differences in ADCC were epitope-specific, with IgG3 bNAbs to the MPER, CD4 binding site and gp120-gp41 interface showing increased ADCC. We also explored the pH dependence of IgG1 and IgG3 variants for FcRn binding, as this determines the half-life of antibodies. We observed reduced pH dependence, associated with shorter half-lives for IgG3 bNAbs, with κ-light chains. However, IgG3 bNAbs that use λ-light chains showed similar pH dependence to their IgG1 counterparts. This study supports the manipulation of the constant region to improve both the neutralizing and Fc effector activity of bNAbs, and suggests that IgG3 versions of bNAbs may be preferable for passive immunity given their polyfunctionality.



Ms Serisha Naicker

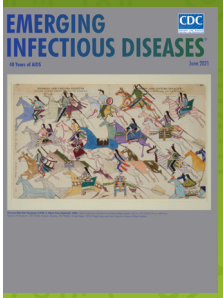
Prof Nelesh Govender

Clade distribution of *Candida auris* in South Africa using whole genome sequencing of clinical and environmental isolates

Naicker SD, *Maphanga TG, Chow NA, Allam M, Kwenda S, Ismail A,* ***Govender NP***

Emerging microbes and infections
Impact Factor: 7.163

In South Africa, *Candida auris* was the third most common cause of candidemia in 2016–2017. We performed single nucleotide polymorphism (SNP) genome-wide analysis of 115 *C. auris* isolates collected between 2009 and 2018 from national laboratory-based surveillance, an environmental survey at four hospitals and a colonization study during a neonatal unit outbreak. The first known South African *C. auris* strain from 2009 clustered in clade IV. Overall, 98 strains clustered within clade III (85%), 14 within clade I (12%) and three within clade IV (3%). All environmental and colonizing strains clustered in clade III. We also identified known clade-specific resistance mutations in the *ERG11* and *FKS1* genes. Identification of clade I strains between 2016 and 2018 suggests introductions from South Asia followed by local transmission. SNP analysis characterized most *C. auris* strains into clade III, the clade first reported from South Africa, but the presence of clades I and IV strains also suggest early introductions from other regions.



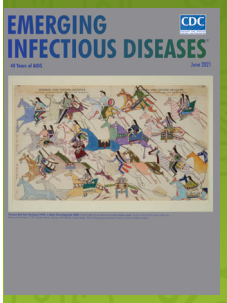
Prof John Frean

Anthemosoma garnhami in an HIV-Infected Man from Zimbabwe Living in South Africa

Daviv Stead, Desiree du Plessis, Lisa Ming Sun, ***John Frean***

Emerging infectious diseases
Impact Factor: 6.883

An HIV-positive man from Zimbabwe living in South Africa sought treatment for multiple clinical signs, including fever, weight loss, anemia, and splenomegaly. We identified in his blood an African rodent piroplasm, Anthemosoma garnhami, related to Babesia species. This finding extends the known geographic and host range of A. garnhami.



Prof Cheryl Cohen

Decline of influenza and respiratory syncytial virus detection in facility-based surveillance during the COVID-19 pandemic, South Africa, January to October 2020

Stefano Tempia, Sibongle Walaza, Jinal N Bhiman, Meredith L. McMorrow, Jocelyn Moyes, Thulisa Mkhencele, Susan Meiring, Vanessa Quan, Kate Bishop, Johanna M. McAnerney, Anne von Gottberg, Nicole Wolter, Mignon Du Plessis, Florette K. Treurnicht, Orienka Hellferscee, Halima Dawood, Fathima Naby, Ebrahim Variava, Comfort Siwele, Neydis Baute, Jeremy Nel, Gary Reubenson, Heather J. Zar, ***Cheryl Cohen***

Eurosurveillance
Impact Factor: 6.307

Background: In South Africa, COVID-19 control measures to prevent SARS-CoV-2 spread were initiated on 16 March 2020. Such measures may also impact the spread of other pathogens, including influenza virus and respiratory syncytial virus (RSV) with implications for future annual epidemics and expectations for the subsequent northern hemisphere winter.

Methods: We assessed the detection of influenza and RSV through facility-based syndromic surveillance of adults and children with mild or severe respiratory illness in South Africa from January to October 2020, and compared this with surveillance data from 2013 to 2019.

Results

Facility-based surveillance revealed a decline in influenza virus detection during the regular season compared with previous years. This was observed throughout the implementation of COVID-19 control measures. RSV detection decreased soon after the most stringent COVID-19 control measures commenced; however, an increase in RSV detection was observed after the typical season, following the re-opening of schools and the easing of measures.

Conclusion: COVID-19 non-pharmaceutical interventions led to reduced circulation of influenza and RSV in South Africa. This has limited the country's ability to provide influenza virus strains for the selection of the annual influenza vaccine. Delayed increases in RSV case numbers may reflect the easing of COVID-19 control measures. An increase in influenza virus detection was not observed, suggesting that the measures may have impacted the two pathogens differently. The impact that lowered and/or delayed influenza and RSV circulation in 2020 will have on the intensity and severity of subsequent annual epidemics is unknown and warrants close monitoring

Ms Johanna Venter

Dr Ranmini Kularatne

Treponema pallidum Macrolide Resistance and Molecular Epidemiology in Southern Africa, 2008 to 2018

Johanna M E Venter, Etienne E Müller, Mahlape P Mahlangu, Ranmini S Kularatne

Journal of Clinical Microbiology
Impact Factor: 5.948

Treponema pallidum macrolide resistance and clinical treatment failure have emerged rapidly within communities where macrolides have been used as convenient, oral therapeutic alternatives to benzathine penicillin G for syphilis or for other clinical indications. Macrolides are not included in the South African syndromic management guidelines for genital ulcer disease; however, in 2015, a 1-g dose of azithromycin was incorporated into treatment algorithms for genital discharge. We determined the prevalence of 23S rRNA macrolide resistance-associated point mutations in 135 T. pallidum-positive surveillance specimens from Botswana, Zimbabwe, and South Africa between 2008 and 2018. Additionally, we investigated the association between macrolide resistance, T. pallidum strain type, and HIV coinfection. A significant increase in the prevalence of the A2058G macrolide resistance-associated point mutation was observed in specimens collected after 2015. There was a high level of molecular heterogeneity among T. pallidum strains circulating in the study communities, with strain type 14d/f being the most predominant in South Africa. Fourteen novel strain types, derived from three new *tpr* gene restriction fragment length polymorphism patterns and seven new *tp0548* gene sequence types, were identified. There was an association between A2058G-associated macrolide resistance and T. pallidum strain types 14d/f and 14d/g but no association between T. pallidum macrolide resistance and HIV coinfection. The majority of T. pallidum strains, as well as strains containing the A2058G mutation, belonged to the SS14-like clade. This is the first study to extensively detail the molecular epidemiology and emergence of macrolide resistance in T. pallidum in southern Africa.

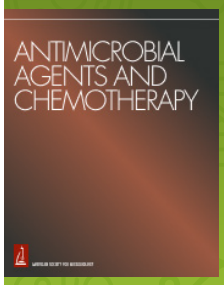
Dr Tsidiso Maphanga

Prof Nelesh Govender

In Vitro Antifungal Resistance of *Candida auris* Isolates from Bloodstream Infections, South Africa.

Maphanga TG, *Naicker SD, Kwenda S, Muñoz JF, van Schalkwyk E, Wadula J, Nana T, Ismail A, Coetzee J, Govind C, Mtshali PS, Mpembe RS,* ***Govender NP***

ASM Journals - Antimicrobial Agents and Chemotherapy
Impact Factor: 5.79



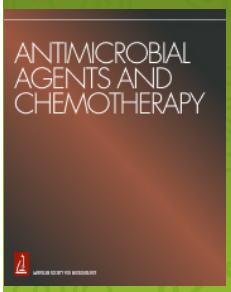
Candida auris is a multidrug-resistant fungal pathogen that is endemic in South African hospitals. We tested bloodstream *C. auris* isolates that were submitted to a reference laboratory for national laboratory-based surveillance for candidemia in 2016 and 2017. We confirmed the species identification by phenotypic/molecular methods. We tested susceptibility to amphotericin B, anidulafungin, caspofungin, micafungin, itraconazole, posaconazole, voriconazole, fluconazole, and flucytosine using broth microdilution and Etest methods. We interpreted MICs using tentative breakpoints. We sequenced the genomes of a subset of isolates and compared them to the *C. auris* B8441 reference strain. Of 400 *C. auris* isolates, 361 (90%) were resistant to at least one antifungal agent, 339 (94%) to fluconazole alone (MICs of ≥32 µg/ml), 19 (6%) to fluconazole and amphotericin B (MICs of ≥2 µg/ml), and 1 (0.3%) to amphotericin B alone. Two (0.5%) isolates from a single patient were pan-resistant (resistant to fluconazole, amphotericin B, and echinocandins). Of 92 isolates selected for whole-genome sequencing, 77 clustered in clade III, including the pan-resistant isolates, 13 in clade I, and 2 in clade IV. Eighty-four of the isolates (91%) were resistant to at least one antifungal agent; both resistant and susceptible isolates had mutations. The common substitutions identified across the different clades were VF125AL, Y132F, K177R, N335S, and E343D in *ERG11;* N647T in *MRR1;* A651P, A657V, and S195G in *TAC1b;* S639P in *FKS1HP1;* and S58T in *ERG3*. Most South African *C. auris* isolates were resistant to azoles, although resistance to polyenes and echinocandins was less common. We observed mutations in resistance genes even in phenotypically susceptible isolates.

Dr Ranmini Kularatne

Demographic and Behavioral Risk Factors Associated with Reduced Susceptibility of *Neisseria gonorrhoeae* to First-Line Antimicrobials in South African Men with Gonococcal Urethral Discharge

Ranmini S. Kularatne, *Tendesayi Kufa, Lindy Gumede, Dumisile V. Maseko, David A. Lewis*

ASM Journals - Antimicrobial Agents and Chemotherapy
Impact Factor: 5.79



Neisseria gonorrhoeae is the predominant cause of male urethral discharge in South Africa, and escalating prevalence of gonococcal antimicrobial resistance (AMR) is a major health concern both in-country and globally. We analyzed the demographic, behavioral, and clinical characteristics of 685 men presenting with gonococcal urethral discharge to sentinel surveillance clinics over a 3-year period (2017 to 2019) to determine the burden of factors that are known to be associated with *N. gonorrhoeae* AMR to first-line therapy (defined as group 1 isolates exhibiting resistance or reduced susceptibility to extended-spectrum cephalosporins or azithromycin). Among 685 men with gonococcal urethral discharge, median age was 28 years (interquartile range [IQR], 24 to 32). Only two men (2/632; 0.3%) self-identified as homosexual; however, on further enquiry, another 16 (2%) confirmed that they had sex with men only. Almost 30% practiced oral sex and were at risk for pharyngeal gonococcal infection. In univariate analysis, male circumcision (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.49 to 0.99) and recent sex outside the country (OR, 1.83; 95% CI, 1.21 to 2.76) were significantly associated with having a category 1 N. gonorrhoeae isolate. In a multivariable model, only sex outside South Africa increased the odds of being infected with a decreased susceptible/resistant *N. gonorrhoeae* isolate (adjusted odds ratio [aOR], 1.64; 95% CI, 1.05 to 2.55). These findings warrant the intensification of *N. gonorrhoeae* AMR surveillance among recently arrived migrant and overseas traveler populations, as well as the inclusion of extragenital specimens for *N. gonorrhoeae* AMR surveillance purposes.

Dr Mignon du Plessis

Prof Anne von Gottberg

The Role of Molecular Testing in Pediatric Meningitis Surveillance in Southern and East African Countries, 2008-2017

du Plessis M, *de Gouveia L, Freitas C, Abera NA, Lula BS, Raboba JL, Nhantumbo AA, Jantjies E, Uwimana J, Phungwayo N, Maphalala G, Masona G, Muyombe J, Mugisha D, Nalumansi E, Odongkara M, Lukwesa-Musyani C, Nakazwe R, Dondo V, Macharaga J, Weldegebriel GG, Mwenda JM, Serhan F, Cohen AL, Lessa FC,* ***von Gottberg A***

Journal of Infectious Diseases
Impact Factor: 5.226

Background: As part of the global Invasive Bacterial Vaccine-Preventable Diseases Surveillance Network, 12 African countries referred cerebrospinal fluid (CSF) samples to South Africa's regional reference laboratory. We evaluated the utility of real-time polymerase chain reaction (PCR) in detecting and serotyping/grouping *Haemophilus influenzae, Neisseria meningitidis*, and *Streptococcus pneumoniae* (HNS).

Methods: From 2008 to 2017, CSF samples collected from children <5 years old with suspected meningitis underwent routine microbiology testing in-country, and 11 680 samples were submitted for HNS PCR at the regional reference laboratory. Unconditional logistic regression, with adjustment for geographic location, was performed to identify factors associated with PCR positivity.

Results: The overall HNS PCR positivity rate for all countries was 10% (1195 of 11 626 samples). In samples with both PCR and culture results, HNS PCR positivity was 11% (744 of 6747 samples), and HNS culture positivity was 3% (207 of 6747). Molecular serotype/serogroup was assigned in 75% of PCR-positive specimens (762 of 1016). Compared with PCR-negative CSF samples, PCR-positive samples were more often turbid (adjusted odds ratio, 6.80; 95% confidence interval, 5.67-8.17) and xanthochromic (1.72; 1.29-2.28), had elevated white blood cell counts (6.13; 4.71-7.99) and high protein concentrations (5.80; 4.34-7.75), and were more often HNS culture positive (32.70; 23.18-46.12).

Conclusion: PCR increased detection of vaccine-preventable bacterial meningitis in countries where confirmation of suspected meningitis cases is impeded by limited culture capacity.

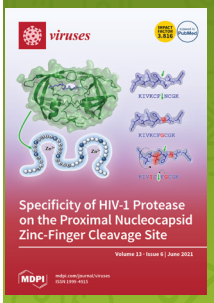
Prof Janusz Paweska

A 1958 Isolate of Kedougou Virus (KEDV) from Ndumu, South Africa, Expanda the Geographic and Temporal Range of KEDV in Africa

Petrus Jansen van Vuren, Rhys parry, Alexander A. Khromykh, ***Janusz T. Paweska***

Viruses
Impact Factor: 5.048

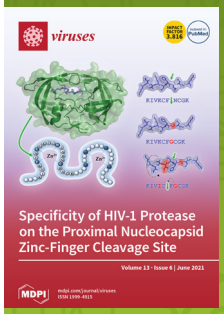
The mosquito-borne flavivirus, Kedougou virus (KEDV), first isolated in Senegal in 1972, is genetically related to dengue, Zika (ZIKV) and Spondweni viruses (SPOV). Serological surveillance studies in Senegal and isolation of KEDV in the Central African Republic indicate occurrence of KEDV infections in humans, but to date, no disease has been reported. Here, we assembled the coding-complete genome of a 1958 isolate of KEDV from a pool of *Aedes circumluteolus* mosquitoes collected in Ndumu, KwaZulu-Natal, South Africa. The AR1071 Ndumu KEDV isolate bears 80.51% pairwise nucleotide identity and 93.34% amino acid identity with the prototype DakAar-D1470 strain and was co-isolated with SPOV through intracerebral inoculation of suckling mice and passage on VeroE6 cells. This historical isolate expands the known geographic and temporal range of this relatively unknown flavivirus, aiding future temporal phylogenetic calibration and diagnostic assay refinement.



Prof Janusz Paweska

Large- Scale International Validation of an Indirect ELISA Based on Recombinant Nucleocapsid Protein of Rift Valley Fever Virus for the Detection of IgG Antibody in Domestic Ruminants

Janusz T. Pweska, *Petrus Jansen van Vuren, Veerle Msimang, Modu Moustapha Lo, Yaya Thiongane, Leopold K. Mulumba-Mfumu, Alqadasi Mansor, Jose M. Fatetine, Joseph W. Magona, Hiver Boussini, Barbara Bazanow, William C. Wilson, Michel Pepin, Hernann Unger, Gerrit Viljoe*



Viruses
Impact Factor: 5.048

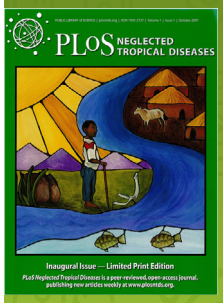
Diagnostic performance of an indirect enzyme-linked immunosorbent assay (I-ELISA) based on a recombinant nucleocapsid protein (rNP) of the Rift Valley fever virus (RVFV) was validated for the detection of the IgG antibody in sheep (n = 3367), goat (n = 2632), and cattle (n = 3819) sera. Validation data sets were dichotomized according to the results of a virus neutralization test in sera obtained from RVF-endemic (Burkina Faso, Democratic Republic of Congo, Mozambique, Senegal, Uganda, and Yemen) and RVF-free countries (France, Poland, and the USA). Cut-off values were defined using the two-graph receiver operating characteristic analysis. Estimates of the diagnostic specificity of the RVFV rNP I-ELISA in animals from RVF-endemic countries ranged from 98.6% (cattle) to 99.5% (sheep) while in those originating from RVF-free countries, they ranged from 97.7% (sheep) to 98.1% (goats). Estimates of the diagnostic sensitivity in ruminants from RVF-endemic countries ranged from 90.7% (cattle) to 100% (goats). The results of this large-scale international validation study demonstrate the high diagnostic accuracy of the RVFV rNP I-ELISA. Standard incubation and inactivation procedures evaluated did not have an adverse effect on the detectable levels of the anti-RVFV IgG in ruminant sera and thus, together with recombinant antigen-based I-ELISA, provide a simple, safe, and robust diagnostic platform that can be automated and carried out outside expensive bio-containment facilities. These advantages are particularly important for less-resourced countries where there is a need to accelerate and improve RVF surveillance and research on epidemiology as well as to advance disease control measures.postpartum. These results emphasise the need for closer monitoring of and rapid reaction to high maternal VLs during pregnancy, at delivery and postpartum for attainment of eMTCT.

Prof John Frean

Trends in the prevalence of microscopically confirmed schistosomiasis in the South African public health sector, 2011–2018

De Boni L, Msimang V, De Voux A, ***Frean J***

PLOS Tropical Diseases
Impact Factor: 4.411



Background: Schistosomiasis, also known as bilharzia, is a chronic parasitic blood fluke infection acquired through contact with contaminated surface water. The illness may be mild or can cause significant morbidity with potentially serious complications. Children and those living in rural areas with limited access to piped water and services for healthcare are the most commonly infected. To address the prevalence of the disease in parts of South Africa (SA) effective national control measures are planned, but have not yet been implemented. This study aimed to estimate the prevalence and trends of public sector laboratory-confirmed schistosomiasis cases in SA over an eight-year (2011–2018) period, to inform future control measures.

Methodology & principal findings: This is a descriptive analysis of secondary data from the National Health Laboratory Service (NHLS). The study included all records of patients for whom microscopic examination detected *Schistosoma* species eggs in urine or stool specimens from January 2011 to December 2018. Crude estimates of the prevalence were calculated using national census mid-year provincial population estimates as denominators, and simple linear regression was used to analyse prevalence trends. A test rate ratio was developed to describe variations in testing volumes among different groups and to adjust prevalence estimates for testing variations.

A total number of 135 627 schistosomiasis cases was analysed with the highest prevalence observed among males and individuals aged 5–19 years. We describe ongoing endemicity in the Eastern Cape Province, and indicate important differences in the testing between population groups.

Conclusion: While there was no overall change in the prevalence of schistosomiasis during the analysis period, an average of 36 people per 100 000 was infected annually. As such, this represents an opportunity to control the disease and improve quality of life of affected people. Laboratory-based surveillance is a useful method for reporting occurrence and evaluating future intervention programs where resources to implement active surveillance are limited.

Prof Cheryl Cohen

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

Cheryl Cohen, *Meredith L. McMorrow, Neil A. Martinson, Kathleen Kahn, Florette K. Treurnicht, Jocelyn Moyes, Orienka Hellferscee, Thulisa Mkhencele, Limakatso Lebina, Matebejane Moroe, Katlego Motlhaoleng, Francesc Xavier Gomez-Olive, Ryan Wagner, Stephen Tollman, Floidy Wafawanaka, Sizzy Ngobeni, Jackie Kleynhans, Azwifari Mathunwa, Amelia Buys, Lorens Maake, Nicole Wolter, Maimuna Carrim, Stuart Piketh, Brigitte Language, Angela Mathee, Anne von Gottberg, Stefano Tempia*

NCBI
Impact Factor: 4.38

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

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

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

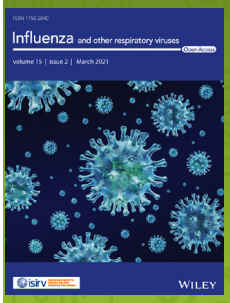
Future plans: Future planned analyses include analysis of influenza serology results and RSV burden and transmission. Households enrolled in the PHIRST study during 2016-2018 were eligible for inclusion in a study of SARS-CoV-2 transmission initiated in July 2020. This study uses similar testing frequency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

Prof Cheryl Cohen

A Retrospective observational cohort study of the effect of antenatal influenza vaccination on birth outcomes in Cape Town, South Africa, 2015-2016

McMorrow ML, Rossi L, Meiring S, Bishop K, Itzikowitz R, Isaacs W, Stellenboom F, Walaza S, Hellferscee O, Treurnicht FK, Zar HJ, Tempia S, ***Cohen C***

Influenza Other Respiratory Viruses
Impact Factor: 4.38



Background: There are conflicting data concerning the impact of antenatal influenza vaccination on birth outcomes including low birthweight (LBW), preterm birth, small for gestational age (SGA), and stillbirth.

Methods: We conducted a retrospective observational cohort study of infants born to women residing in Mitchells Plain, Cape Town. Infants were born at 4 health facilities during May 28 - December 31, 2015 and April 15 - December 31, 2016. We performed crude and multivariable logistic regression, propensity score (PS) matching logistic regression, and inverse probability of treatment weighted (IPTW) regression to assess vaccine effectiveness (VE) against LBW, preterm birth, SGA, and stillbirth adjusting for measured confounders.

Results: Maternal vaccination status, antenatal history, and ≥1 birth outcome(s) were available for 4084/5333 (76.6%) pregnancies, 2109 (51.6%) vaccinated, and 1975 (48.4%) unvaccinated. The proportion LBW was lower in vaccinated (6.9%) vs. unvaccinated (12.5%) in multivariable [VE 0.27 (95% CI 0.07-0.42)], PS [VE 0.30 (95% CI 0.09-0.51)], and IPTW [VE 0.24 (95% CI 0.04-0.45)]. Preterm birth was less frequent in vaccinated (8.6%) than unvaccinated (16.4%) in multivariable [VE 0.26 (0.09-0.40)], PS [VE 0.25 (95% CI 0.09-0.41)], and IPTW [VE 0.34 (95% CI 0.18-0.51)]. The proportion SGA was lower in vaccinated (6.0%) than unvaccinated (8.8%) but not in adjusted models. There were few stillbirths in our study population, 30/4084 (0.7%).

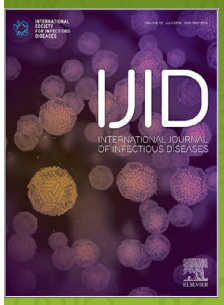
Conclusions: Using multiple analytic approaches, we found that influenza vaccination was associated with lower prevalence of LBW (24-30%) and preterm birth (25-34%) in Cape Town during 2015-2016.

Dr Monica Birkhead

Ultrastructural evidence for vertical transmission of SARS-CoV -2

Monica Birkhead, *Allison J. Glass, Heather Allan-Gould, Carice Goossens, Colleen A. Wright*

International Journal of Infectious Diseases
Impact Factor: 3.623



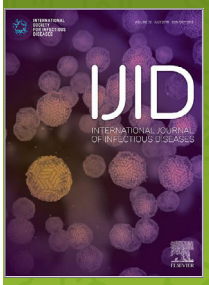
This correspondence briefly describes both the widespread difficulty in identifying virions at the ultrastructural level, and what light microscopy has contributed to our understanding of vertical transmission of SARS-CoV2. It provides the first, published transmission electron micrograph illustrating this phenomenon.

Dr Shira Amar

An outbreak of African swine fever in small-scale pigs, Gauteng, South Africa, July 2020

Amar S, *De Boni L, de Voux A, Heath L, Geertsma P*

International Journal of Infectious Diseases
Impact Factor: 3.623



Objectives: Since 2012, outbreaks of African swine fever (ASF) in domestic pigs have increased outside of South Africa's ASF control zone. This study describes the epidemiological investigation and findings of an ASF outbreak in a small-scale pig unit in Gauteng Province and makes recommendations to prevent future outbreaks.

Methods: PCR testing and molecular analysis were performed on pig tissue samples. Veterinary services conducted epidemiological investigations, forward and backward tracing, and surveillance. Farm management and biosecurity practices were assessed. Quarantine, culling, carcass disposal, and disinfection were implemented.

Results: ASF virus genotype I was detected. A concurrent ASF outbreak in neighbouring Mpumalanga Province was identified as a possible source. Inadequate biosecurity measures probably facilitated viral transmission. Potential mechanisms for the introduction of the ASF virus include swill feeding practices, free roaming of pigs, scavenging, illegal slaughter, and trade of pig products within the community.

Conclusions: Molecular typing of the ASF virus linked the outbreak to an ongoing ASF outbreak in Mpumalanga Province. Pig enterprises with poor biosecurity practices may face greater risk of ASF introduction. Small-scale pig keepers should be targeted for ASF awareness and education campaigns. Innovative and cost-effective biosecurity solutions are needed in this resource-poor setting.

Dr Michelle Groome

Diarrhoeal diseases in Soweto, South Africa, 2020: a cross-sectional community survey

Johnstone SL, Page NA, Thomas J, Madhi SA, Mutevedzi P, Myburgh N, Herrera C, ***Groome MJ***

BMC Public Health
Impact Factor: 3.295

Background: In South Africa, there are limited data on the burden of diarrhoea at a community level, specifically in older children and adults. This community survey estimated rates of and factors associated with diarrhoea across all ages and determined the proportion of cases presenting to healthcare facilities.

Methods: Households were enrolled from an existing urban health and demographic surveillance site. A household representative was interviewed to determine associated factors and occurrence of diarrhoea in the household, for all household members, in the past 2 weeks (including symptoms and health seeking behaviour). Diarrhoeal rate of any severity was calculated for < 5 years, 5–15 years and > 15 years age groups. Factors associated with diarrhoea and health seeking behaviour were investigated using binomial logistic regression.

Results: Diarrhoeal rate among respondents (2.5 episodes/person-year (95% CI, 1.8–3.5)) was significantly higher than for other household members (1.0 episodes/person-year (95% CI, 0.8–1.4); IRR = 2.4 (95% CI, 1.5–3.7) $p < 0.001$). Diarrhoeal rates were similar between age groups, however younger children (< 5 years) were more likely to present to healthcare facilities than adults (OR = 5.9 (95% CI, 1.1–31.4), $p = 0.039$). Oral rehydration solution was used in 44.8% of cases. Having a child between 5 and 15 years in the household was associated with diarrhoea (OR = 2.3 (95% CI, 1.3–3.9), $p = 0.003$) and, while 26.4% of cases sought healthcare, only 4.6% were hospitalised and only 3.4% of cases had a stool specimen collected. While the majority of cases were mild, 13.8% of cases felt they required healthcare but were unable to access it.

Conclusion: Diarrhoeal rate was high across all age groups in this community; however, older children and adults were less likely to present to healthcare, and are therefore underrepresented through facility-based clinical surveillance. Current diarrhoeal surveillance represents a fraction of the overall cases occurring in the community.

Prof Cheryl Cohen

Mortality in children aged <5 years with severe acute respiratory illness in a high HIV-prevalence urban and rural areas of South Africa, 2009–2013

Ayeni OA, Walaza S, Tempia S, Groome M, Kahn K, Madhi SA, Cohen AL, Moyes J, Venter M, Pretorius M, Treurnicht F, Hellferscee O, Von Gottberg A, Wolter N, ***Cohen C***

PLoS One
Impact Factor: 3.24

Background: Severe acute respiratory illness (SARI) is an important cause of mortality in young children, especially in children living with HIV infection. Disparities in SARI death in children aged <5 years exist in urban and rural areas.

Objective: To compare the factors associated with in-hospital death among children aged <5 years hospitalized with SARI in an urban vs. a rural setting in South Africa from 2009–2013.

Methods: Data were collected from hospitalized children with SARI in one urban and two rural sentinel surveillance hospitals. Nasopharyngeal aspirates were tested for ten respiratory viruses and blood for pneumococcal DNA using polymerase chain reaction. We used multivariable logistic regression to identify patient and clinical characteristics associated with in-hospital death.

Results: From 2009 through 2013, 5,297 children aged <5 years with SARI-associated hospital admission were enrolled; 3,811 (72%) in the urban and 1,486 (28%) in the rural hospitals. In-hospital case-fatality proportion (CFP) was higher in the rural hospitals (6.9%) than the urban hospital (1.3%, p<0.001), and among HIV-infected than the HIV-uninfected children (9.6% vs. 1.6%, p<0.001). In the urban hospital, HIV infection (odds ratio (OR):11.4, 95% confidence interval (CI):5.4–24.1) and presence of any other underlying illness (OR: 3.0, 95% CI: 1.0–9.2) were the only factors independently associated with death. In the rural hospitals, HIV infection (OR: 4.1, 95% CI: 2.3–7.1) and age <1 year (OR: 3.7, 95% CI: 1.9–7.2) were independently associated with death, whereas duration of hospitalization ≥5 days (OR: 0.5, 95% CI: 0.3–0.8) and any respiratory virus detection (OR: 0.4, 95% CI: 0.3–0.8) were negatively associated with death.

Conclusion: We found that the case-fatality proportion was substantially higher among children admitted to rural hospitals and HIV infected children with SARI in South Africa. While efforts to prevent and treat HIV infections in children may reduce SARI deaths, further efforts to address health care inequality in rural populations are needed.

Dr Selamawit Woldesenbet

Prof Adrian Puren

Coverage of maternal viral load monitoring during pregnancy in South Africa: Results from the 2019 national Antenatal HIV Sentinel Survey

Woldesenbet S, *Kufa-Chakezha T, Lombard C, Manda S, Cheyip M, Ayalew K,* ***Puren, A***

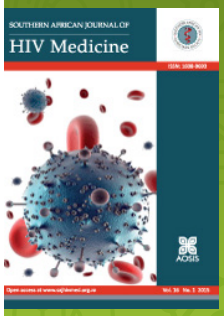
HIV Medicine
Impact Factor: 3.18

Objectives: South Africa has made remarkable progress in increasing the coverage of antiretroviral therapy (ART) among pregnant women; however, viral suppression among pregnant women receiving ART is reported to be low. Access to routine viral load testing is crucial to identify women with unsuppressed viral load early in pregnancy and to provide timely intervention to improve viral suppression. This study aimed to determine the coverage of maternal viral load monitoring nationally, focusing on viral load testing, documentation of viral load test results, and viral suppression (viral load < 50 copies/mL). At the time of this study, the first-line regimen for women initiating ART during pregnancy was non-nucleoside reverse transcriptase (NNRTI)-based regimen.

Methods: Between 1 October and 15 November 2019, a cross-sectional survey was conducted among 15- to 49-year-old pregnant women attending antenatal care in 1589 nationally representative public health facilities. Data on ART status, viral load testing and viral load test results were extracted from medical records. Logistic regression was used to examine factors associated with coverage of viral load testing.

Results: Of 8112 participants eligible for viral load testing, 81.7% received viral load testing, and 94.1% of the viral load test results were documented in the medical records. Of those who had viral load test results documented, 74.1% were virally suppressed. Women initiated on ART during pregnancy and who received ART for three months had lower coverage of viral load testing (73%) and viral suppression (56.8%) compared with women initiated on ART before pregnancy (82.8% and 76.1%, respectively). Initiating ART during pregnancy rather than before pregnancy was associated with a lower likelihood of receiving a viral load test during pregnancy (adjusted odds ratio = 1.6, 95% confidence interval: 1.4–1.8).

Conclusions: Viral load result documentation was high; viral load testing could be improved especially among women initiating ART during pregnancy. The low viral suppression among women who initiated ART during pregnancy despite receiving ART for three months highlights the importance of enhanced adherence counselling during pregnancy. Our finding supports the WHO recommendation that a Dolutegravir-containing regimen be the preferred regimen for women who are newly initiating ART during pregnancy for more rapid viral suppression.



Mrs Bhavani Moodley

Prof John Frean

Improving the quality of malaria diagnosis in southern Africa through the development of a regional malaria slide bank

Bhavani Moodley, *Anderson Chinorumba, Cheryl Hamman, Avhatakali Matamba, Chadwick H. Sikaala, Immo Kleinschmidt,* ***John Frean***

Malaria Journal
Impact Factor: 2.979

Background: A malaria slide bank (MSB) is a useful asset for any malaria microscopy testing laboratory to have access to. However, it is not feasible for every country to have its own MSB. If countries are able to pool their resources, a regional MSB is a viable solution. This paper describes the methodology, costing and lessons learnt of establishing and maintaining an MSB over a 3-year period, for a Southern Africa Development Community region.

Methods: A national reference laboratory in South Africa was granted funding for setting up the MSB; it possessed experienced staff and suitable resources. Two additional full-time personnel were employed to carry out the activities of this project. Strict protocols for donor/patient blood sample screening, smear preparation, mass staining, quality control and slide validation were followed. Slides from the MSB were used for training and proficiency testing purposes. The initial and recurrent yearly costs to set up and maintain the MSB were calculated.

Results: Over 35 months, 154 batches (26,623 slides) were prepared; the majority were *Plasmodium falciparum*. Ninety-two percent (141/154) of batches passed internal quality control, and 89% (93/104) passed external validation. From these slides, two training slide sets and six proficiency testing slide sets were sent out. The initial year's cost to establish an MSB was calculated at approximately $165,000, and the recurrent year-on-year cost was $130,000.

Conclusions: The key components for maintaining a high-quality MSB are consistent funding, competent staff and adherence to standardized protocols. Travel to malaria-endemic areas for access to non-falciparum malaria species, and dilution of *P. falciparum* blood to desired parasite densities, are extremely useful to ensure variety. The MSB created here supported multiple laboratories in eight countries, and has the potential to expand.

Mrs Kate Bishop

Prof Cheryl Cohen

An evaluation of an influenza vaccination campaign targeting pregnant women in 27 clinics in two provinces of South Africa, 2015 – 2018

Bishop K, *McMorrow M, Meiring S, Walaza S, Rossi L, Mhlanga S, Tempia S, Mathunjwa A, Kleynhans J, Appiah GD, J McAnerney JM, Zar HJ,* ***Cohen C***

BMC health services research
Impact Factor: 2.655

Introduction: Despite prioritization, routine antenatal influenza vaccine coverage is < 16% in South Africa. We aimed to describe maternal influenza vaccine coverage in 27 antenatal clinics (ANCs) in Gauteng and Western Cape (WC) Provinces, where in collaboration with the Department of Health (DoH), we augmented the annual influenza vaccination programme among pregnant women.

Methods: From 2015 through 2018, 40,230 additional doses of influenza vaccine were added to the available stock and administered as part of routine antenatal care. Educational talks were given daily and data were collected on women attending ANCs. We compared characteristics of vaccinated and unvaccinated women using multivariable logistic regression.

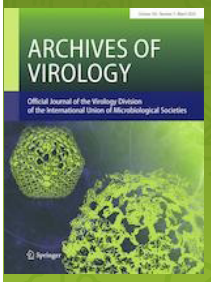
Results: We screened 62,979 pregnant women during the period when Southern Hemisphere influenza vaccines were available (27,068 in Gauteng and 35,911 in WC). Vaccine coverage at the targeted clinics was 78.7% (49,355/62682), although pregnant women in WC were more likely to be vaccinated compared to those in the Gauteng (Odds ratio (OR) =3.7 p < 0.001). Women aged 25—29 and > 35 years were less likely to be vaccinated than women aged 18—24 years (OR = 0.9 $p = 0.053$; OR = 0.9 $p < 0.001$). HIV positive status was not associated with vaccination (OR = 1.0 $p = 0.266$). Reasons for not vaccinating included: vaccine stock-outs where ANCs depleted available stock of vaccines and/or were awaiting delivery of vaccines (54.6%, 6949/12723), refusal/indecision (25.8%, 3285), and current illness that contraindicated vaccination (19.6%, 2489).

Conclusion: Antenatal vaccination uptake was likely improved by the increased vaccine supply and vaccine education offered during our campaign.

Prof Janusz Paweska

2021 Taxonomic update of phylum Negarnaviricota (Riboviria: Orthornavirae), including the large orders Bunyavirales and Mononegavirales

Jens H. Kuhn, Scot Adkins, Bernard R. Agwanda, Rim Al Kubrusli, Sergey V. Alkhovsky, Gaya K. Amarasinghe, Tatjana Avsic-Zupanc, Maria A. Ayllon, Justin Bahl, Anne Balkema-Buschmann, Matthew J. Ballinger, Christopher F. Basher, Eric Bergeron, Brian H. Bird, Carol D. Blair, Kim R. Blasdell, Dennis A. Bente, Dag-Ragnar Blystad, Jamie Bojko, Wayne B. Borth, Steven Bradfute, Rachel Breyta, Thomas Briese, Paul A. Brown, Judith K. Brown, Ursula J.Buchholz, Michael J. Buchmeier, Alender Burkreyev, Felicity Burt, Carmen Buttner, Charles H. Calisher, Mengji Cao,Inmaculada Casas, Kartik Chandran, Remi N. Charrel, Qi Cheng, Yuya Chaik, ***Janusz T. Paweska***



Archives of Virology
Impact Factor: 2.574

In March 2021, following the annual International Committee on Taxonomy of Viruses (ICTV) ratification vote on newly proposed taxa, the phylum *Negarnaviricota* was amended and emended. The phylum was expanded by four families (*Aliusviridae, Crepuscuviridae, Myriaviridae*, and *Natareviridae*), three subfamilies (Alpharhabdovirinae, Betarhabdovirinae, and Gammarhabdovirinae), 42 genera, and 200 species. Thirty-nine species were renamed and/or moved and seven species were abolished. This article presents the updated taxonomy of *Negarnaviricota* as now accepted by the ICTV.

Dr Ahmad Mazanderani

Evaluating the performance of the GeneXpert HIV-1 qualitative assay as a consecutive test for a new early infant diagnosis algorithm in South Africa

Mukendi A, Kufa T, Murray T, Burke M, Strehlau R, Technau KG, Tiemessen CT, Sherman GG, ***Mazanderani AH***

South African Medical Journal
Impact Factor: 1.614

Background: The proportion of HIV-exposed infants and young children infected with HIV in South Africa (SA) has declined markedly over the past decade as a result of the country's comprehensive prevention of mother-to-child transmission programme. This decrease has in turn reduced the positive predictive value (PPV) of diagnostic assays, necessitating review of early infant diagnosis (EID) algorithms to ensure improved accuracy.

Objectives: To evaluate the performance of the GeneXpert HIV-1 qualitative assay (Xpert EID) as a consecutive test for infants with an 'HIV-detected' polymerase chain reaction screening test at birth.

Methods: We retrospectively analysed a longitudinal cohort of HIV-exposed infants on whom birth testing was performed, using whole-blood ethylenediaminetetra-acetic acid samples, from four tertiary sites in Gauteng Province between June 2014 and December 2019. Birth samples from all infants with a Cobas AmpliPrep/Cobas TaqMan HIV-1 Qualitative Test v2.0 (CAP/CTM v2.0) HIV-detected screening test, a concurrent Xpert EID test and a subsequent confirmatory CAP/CTM v2.0 test on a separate specimen were included. Performance of the Xpert EID in predicting final HIV status was determined as proportions with 95% confidence intervals (CIs). A comparison of indeterminate CAP/CTM v2.0 results, as per National Health Laboratory Service resulting practice, with discordant CAP/CTM v2.0 v. Xpert EID results was performed.

Results: Of 150 infants who met the inclusion criteria, 6 (3.9%) had an Xpert EID result discordant with final HIV status: 5 (3.3%) were false negatives and 1 (0.7%) was false positive. As a consecutive test, the Xpert EID yielded a sensitivity of 96.5% (95% CI 92 - 98.9), specificity of 85.7% (95% CI 42.1 - 99.6), PPV of 99.3% (95% CI 95.7 - 99.9), negative predictive value of 54.5% (95% CI 32.5 - 74.9) and overall accuracy of 96.1% (95% CI 91.5 - 98.5). Using discordant CAP/CTM v2.0/Xpert EID results as criteria to verify indeterminate results instead of current practice would have reduced the number of indeterminate screening results by 42.1%, from 18 (12.6%) to 11 (7.2%), without increasing the false-positive rate.

Conclusions: Addition of the Xpert EID as a consecutive test for specimens with an HIV-detected PCR screening result has the potential to improve the PPV and reduce the indeterminate rate, thereby reducing diagnostic challenges and time to final status, in SA's EID programme.

Ms Mabore Morifi

Dr Tendesayi Kufa

Congenital Syphilis Case Surveillance in South Africa 2017-19: Experience, Challenges and Opportunities

Morifi M, *Malevu N, Odayan S, McCarthy K,* ***Kufa T***

Journal of tropical pediatrics
Impact Factor: 1.165

Background: Untreated or inadequately treated maternal syphilis infection may be transmitted from mother to child resulting in congenital syphilis (CS) infection. In South Africa (SA), CS is a notifiable medical condition (NMC). The NMC surveillance system (NMCSS) was improved by introducing an electronic notification application, a new case notification form and training resources in July 2017. We describe CS surveillance in SA and report on experiences from implementing an improved NMCSS from August 2017 to December 2019.

Methods: We present the CS case definition, data collected by the CS case investigation and notification forms and data flow through the NMCSS. Descriptive statistics were used to analyse CS notifications received from August 2017 to December 2019. Qualitative inductive analysis of the stakeholder communications diary was conducted to identify CS surveillance challenges.

Results: There were 418 CS notifications submitted from 80 facilities in 35 out of 52 districts. Of the notified cases, 194 (46.8%) were male and the median age at notification was 7 days (interquartile range: 3–16 days). The majority were diagnosed in hospital (98.6%). KwaZulu–Natal Province notified the most cases (52.9%) followed by Gauteng (28.0%). Challenges in CS surveillance included the lack of awareness of the CS case definition, completed paper-based notifications not reaching the NMCSS and the limited ability of the system to distinguish improved notifications from increase in disease burden.

Conclusion: Improved CS surveillance through NMCSS was implemented in SA. Training, support and mentoring on CS and the notification system will be needed to inform elimination efforts.

Dr Naazneen Moolla

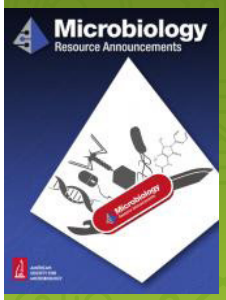
Dr Jacqueline Weyer

Near-Complete Genome Sequence of Ndumu Virus from Garissa, Kenya, 1997

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

ASM Journals - Microbiology resource announcements
Impact Factor: 0.19

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



Dr Orienka Hellferscee

Prof Cheryl Cohen

Detection of Victoria lineage influenza B viruses with K162 and N163 deletions in the hemagglutinin gene, South Africa, 2018

Orienka Hellferscee, *Florette Treurnicht, Lucinda Gaelejwe, Alexandra Moerdyk, Gary Reubenson, Meredith McMorrow, Stefano Tempia, Johanna McAnerney, Sibongile Walaza, Nicole Wolter, Anne von Gotteberg,* ***Cheryl Cohen***

Health Science Reports
Impact Factor: n/a

Background: A group of Victoria lineage influenza B viruses with a two amino acid deletion in the hemagglutinin (HA) at residues K162 and N163, was detected during the 2016 to 2017 Northern Hemisphere influenza season and continues to spread geographically. We describe the first identification of viruses with these deletions from South Africa in 2018.

Methods: Nasopharyngeal samples were obtained from the syndromic surveillance programs. Real-time reverse transcription-polymerase chain reaction was used for virus detection and lineage determination. Influenza genetic characterization was done using next-generation sequencing on the MiSeq platform. The duration of virus circulation was determined using thresholds calculated using the Moving Epidemic Method; duration was used as an indicator of disease transmissibility and impact.

Results: In 2018, 42% (426/1015) of influenza-positive specimens were influenza B viruses. Of 426 influenza B-positive samples, 376 (88%) had the lineage determined of which 75% (283/376) were Victoria lineage. The transmissibility of the 2018 South African influenza season was high for a few weeks, although the severity remained moderate through most of the season. The sequenced 2018 South African Victoria lineage influenza B viruses clustered in sub-clade V1A.1 with the 162-163 deletions.

Conclusions: We report the first detection of the 162-163 deletion variant of influenza B/Victoria viruses from South Africa in 2018, and suggest that this deletion variant replaced the previous circulating influenza B/Victoria viruses. These deletions putatively affect the antigenic properties of the viruses because they border an immune-dominant region at the tip of the HA. Therefore, close monitoring of these newly emerging viruses is essential.

Ms Babongile Ndlovu

Mr Wenlong Chen

Completeness of Reporting for Breast Cancer Data in the National Pathology-Based Cancer Registry in South Africa

Ndlovu BC, *Sengayi-Muchengeti M, Kellett P, Kuonza L, Cubasch H, Singh E,* ***Chen WC***

Journal of Registry Management
Impact Factor: n/a

Background: It is important for a cancer registry to have adequate coverage of the catchment area to accurately estimate the cancer burden. This study aimed to determine the pathology-based South African National Cancer Registry's (NCR's) catchment rate of breast cancer cases using a hospital-based cancer registry as reference.

Methods: Using 2 record linkage approaches, a combination of deterministic record linkage (DRL) and probabilistic record linkage (PRL), we linked a breast cancer hospital registry (n = 398) from 2015 with breast cancer registry data from the NCR (n = 16,642). Firstly, using DRL, we matched and linked records using the unique laboratory report number. Records that were not matched using DRL were linked using PRL. Manual reviews of both data sources were then performed to evaluate records that did not match using either DRL or PRL. The NCR's catchment rate was calculated using the total number of matched records from the hospital registry to the NCR breast cancer registry.

Results: Of 398 records from the hospital registry, 397 were matched to the NCR breast cancer registry, giving the NCR a catchment rate of 99.75%. A total of 291 records were matched with NCR records by DRL; 95, by PRL; and 11, by manual review. Only 1 record did not match.

Conclusion: Nearly all hospital breast cancer cases were found in the NCR database. This suggests that the workflow used by the NCR for the identification, collection, and registration of breast cancer cases diagnosed histologically is adequate for this hospital.

In honour and remembrance of respected public health medicine specialist, the late **Dr Elvira Singh.**

Dr Kerrigan McCarthy

Prof Nelesh Govender

The importation and establishment of community transmission of SARS-CoV-2 during the first eight weeks of the South African COVID-19 epidemic

McCarthy KM, *Tempia S, Kufa T, Kleynhans J, Wolter N, Jassat W, Ebonwu J, von Gottberg A, Erasmus L, Muchengeti M, Walaza S, Ntshoe G, Shonhiwa AM, Manana PN, Pillay Y, Moonasar D, Muthivhi T, Mngemane S, Mlisana K, Chetty K, Blumberg LH, Cohen C,* ***Govender NP***

The Lancet - Eclinical Medicine
Impact Factor: n/a

Background: We describe the epidemiology of COVID-19 in South Africa following importation and during implementation of stringent lockdown measures.

Methods: Using national surveillance data including demographics, laboratory test data, clinical presentation, risk exposures (travel history, contacts and occupation) and outcomes of persons undergoing COVID-19 testing or hospitalised with COVID-19 at sentinel surveillance sites, we generated and interpreted descriptive statistics, epidemic curves, and initial reproductive numbers (Rt).

Findings: From 4 March to 30 April 2020, 271,670 SARS-CoV-2 PCR tests were performed (462 tests/100,000 persons). Of these, 7,892 (2.9%) persons tested positive (median age 37 years (interquartile range 28–49 years), 4,568 (58%) male, cumulative incidence of 13.4 cases/100,000 persons). Hospitalization records were found for 1,271 patients (692 females (54%)) of whom 186 (14.6%) died. Amongst 2,819 cases with data, 489/2819 (17.3%) travelled internationally within 14 days prior to diagnosis, mostly during March 2020 (466 (95%)). Cases diagnosed in April compared with March were younger (median age, 37 vs. 40 years), less likely female (38% vs. 53%) and resident in a more populous province (98% vs. 91%). The national initial R_t was 2.08 (95% confidence interval (CI): 1.71–2.51).

Interpretation: The first eight weeks following COVID-19 importation were characterised by early predominance of imported cases and relatively low mortality and transmission rates. Despite stringent lockdown measures, the second month following importation was characterised by community transmission and increasing disease burden in more populous provinces.

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