Issue 17- June 2021

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 National Institute for Communicable Diseases' (NICD) research achievements are highlighted in this edition of Science Focus, which covers the fourth quarter of the previous fiscal year. The Science Focus, which is jam-packed with notable research discoveries, highlights the quantity of peer-reviewed articles, top published authors, and high-impact factor score articles.

This issue features, amongst others, Dr Tendesayi Kufa-Chakezha's 'Trends in RPR seropositivity among children younger than 2 years', a 9-year study that concluded in 2019. Efforts to improve COVID-19 comprehension continues with Dr Kurt Wibmer and Prof Penny Moore unpacking how SARS-CoV-2 501Y.V2 escapes neutralization by COVID-19 donor plasma.

Jackie Kleynhans and Prof Cheryl Cohen join forces in an insightful ecological modelling study that focuses on the estimated impact of the pneumococcal conjugate vaccine on pneumonia mortality in South Africa, a study that spanned from 1999 to 2016. Prof Cohen continues assess the burden of influenza illness, a disease prevalent among young children, older adults and those with underlying conditions. Titled 'Global burden of influenza-associated lower respiratory tract infections and hospitalizations among adults', the review makes for an interesting read.

The publication of important health papers and high-impact publications in, amongst others, the Journal of Tropical Pediatrics, Nature Medicine, PLOS Medicine and Clinical Infectious Diseases, is indicative of the commitment of NICD researchers in achieving scientific excellence through research efforts that will benefit and inform policies. The research achievements in this issue are admirable and the NICD celebrates the successes of these curious, forward-thinking individuals.

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

On behalf of the team,

Sinenhlanhla Jimoh
Senior Communications Manager

Science engagement: no longer just an optional extra

By Dr Shüné Oliver

If you have been applying for funding, whether in the local or international sphere, you may have noticed that a section of application forms that was once small is becoming larger; larger and with more components that require completion: science engagement. This fills many with a light dread and trepidation. This, however, may need to be reconsidered.

One of the mandates of the National Research Foundation (NRF) is 'supporting and promoting public awareness of, and engagement with, science'. Science engagement aims to create a society that is both knowledgeable about science as well as critically engaged with science issues (see: https://www.dst.gov.za/images/Science_Engagement_Strategy_-_SES.pdf and http://www0.sun.ac.za/scicom/wp-content/uploads/2018/06/2017_sci_engagement_strategy_imp.pdf). It is also worth noting that the new CEO of the NRF has made it very clear that in these taxing financial times they are only likely to fund projects that benefit society.

This should not be the only motivation to participate in science engagement. Research does not (or rather, should not) occur in silos. Whether your work is basic science or more applied, funding often comes from the pockets of taxpayers and, as such, publicly funded researchers have an obligation to give back to the community. There are two clear examples of the importance of science engagement. The first is the issue of climate change. This complex and multi-faceted phenomenon is highly controversial. Viewpoints on this matter are typically politically charged (https://link.springer.com/article/10.1007/s10584-020-02791-6) rather than focused on scientific reality. This is an example of an area that requires careful science engagement with the public. Closer to our field of public health, the voices of the vaccine hesitant represent a challenge to not only the COVID-19 vaccine rollout, but vaccination programmes in general (https://theconversation.com/vaccinating-africa-against-covid-19-riding-a-roller-coaster-of-poor-information-159716). This critical public health challenge can only be tackled by strategic and sensitive engagement between scientists, government, and the public.

Communicating with the public is often not a priority or is a source of discomfort to many scientists. It is easy to think that the public is not interested in your field of research. Yet, research shows that many scientists feel this way, so you are not alone. Many scientists also feel that the media may oversimplify their work, or science in general. There is also a surprising hesitancy in many scientists to use social media to promote their work, seeing it as unnecessary or a waste of time. Yet research shows that higher media interest often correlates with higher Hirsch (h)-indices (https://journals.sagepub.com/doi/10.1177/1077699014550092). Science engagement through social media is becoming as much a part of the scientific endeavour as is publishing. This is because the two often go hand in hand, with numerous post-publications efforts required to increase the impact of your published articles.

Science engagement is therefore practically and philosophically important for all scientists. Yet, how do you start your journey into science engagement? This is challenging, as it is not something that is part of the scientist's training. The approach to science engagement is different depending on the stage of your career. An early career scientist is not likely to be contacted for expert commentary, but this does not mean that emerging scientists are exempt from science engagement. In fact, science engagement is arguably more crucial for this demographic, as this is a career-building tool for young scientists. A good starting point is with, The Conversation', an excellent forum to bring your research to the public (https://theconversation.com/how-to-pitch-to-the-conversation-105850). An advantage of this online forum is that you can engage with people who have uploaded comments and you can track the amount of interest shown in your article. It is also common to have your article from 'The Conversation' republished by other news agencies. Furthermore, social media outlets have some of the most potent tools available with which to engage with the public. Many publishers are now including the use of social media to promote their publications. Investigate the options available to you from your publisher. Make sure you understand how Altmetrics work to track the impact of your work (https://www.altmetric.com/audience/researchers/).

If you would like some food for thought about science engagement and some useful resources, please visit the links below. Science engagement is no longer an optional extra, but something that all active researchers should be involved in. How are you going to get involved?

- https://www.mdpi.com/2071-1050/12/19/7854/pdf
- https://www.nature.com/articles/npjscilearn201610
- https://secure.wiley.com/commsciencepromo?utm_source=uberflip&utm_medium=display&utm_term=linkcta&utm_content=wespromo&utm_campaign=w26kn-wesnurture
- https://senseaboutscience.org/activities/public-engagement-guide/

EXCEPTIONAL RESEARCH STATISTICS

NUMBER OF PEER-REVIEWED ARTICLES PRODUCED

QUARTER 1	53
QUARTER 2	44
QUARTER 3	51
QUARTER 4	47

TOP 3

MOST PUBLISHED AUTHORS IN Q4 OF 2020/2021

1

PROF CHERYL COHEN

2

PROF PENNY MOORE

2

PROF STEFANO TEMPIA

2

PROF GAYLE SHERMAN

2

PROF ANNE VON GOTTBERG

3

DR SIBONGILE WALAZA

3

PROF ADRIAN PUREN

3

DR JAISHREE RAMAN

FEATURED RESEARCH ABSTRACTS FOR THE FOURTH QUARTER OF 2020/2021

Dr Kurt Wibmer

Prof Penny Moore

SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

Wibmer CK, Ayres F, Hermanus T, Madzivhandila M, Kgagudi P, Lambson BE, Marion Vermeulen M, van den Berg K, Rossouw T, Boswell M, Ueckermann V, Meiring S, von Gottberg A, Cohen C, Morris L, Bhiman JL, ***Moore PL.***

Nature Medicine
Impact Factor: 36.30

SARS-CoV-2 501Y.V2, a novel lineage of the coronavirus causing COVID-19, contains multiple mutations within two immunodominant domains of the spike protein. Here we show that this lineage exhibits complete escape from three classes of therapeutically relevant monoclonal antibodies. Furthermore 501Y.V2 shows substantial or complete escape from neutralizing antibodies in COVID-19 convalescent plasma. These data highlight the prospect of reinfection with antigenically distinct variants and may foreshadow reduced efficacy of current spike-based vaccines.

Ms Jackie Kleynhans

Prof Cheryl Cohen

Estimated impact of the pneumococcal conjugate vaccine on pneumonia mortality in South Africa, 1999 through 2016: An ecological modelling study

Kleynhans J, *Tempia S, Shioda K, von Gottberg A, Weinberger DM,* ***Cohen C***

PLoS Medicine
Impact Factor: 10.500

Background: Data on the national-level impact of pneumococcal conjugate vaccine (PCV) introduction on mortality are lacking from Africa. PCV was introduced in South Africa in 2009. We estimated the impact of PCV introduction on all-cause pneumonia mortality in South Africa, while controlling for changes in mortality due to other interventions.

Methods and findings: We used national death registration data in South Africa from 1999 to 2016 to assess the impact of PCV introduction on all-cause pneumonia mortality in all ages, with the exclusion of infants aged <1 month. We created a composite (synthetic) control using Bayesian variable selection of nondiarrheal, nonpneumonia, and nonpneumococcal deaths to estimate the number of expected all-cause pneumonia deaths in the absence of PCV introduction post-2009. We compared all-cause pneumonia deaths from the death registry to the expected deaths in 2012 to 2016. We also estimated the number of prevented deaths during 2009 to 2016. Of the 9,324,638 deaths reported in South Africa from 1999 to 2016, 12·6% were pneumonia-related. Compared to number of deaths expected, we estimated a 33% (95% credible interval (CrI) 26% to 43%), 23% (95%CrI 17% to 29%), 25% (95%CrI 19% to 32%), and 23% (95%CrI 11% to 32%) reduction in pneumonia mortality in children aged 1 to 11 months, 1 to 4 years, 5 to 7 years, and 8 to 18 years in 2012 to 2016, respectively. In total, an estimated 18,422 (95%CrI 12,388 to 26,978) pneumonia-related deaths were prevented from 2009 to 2016 in children aged <19 years. No declines were estimated among adults following PCV introduction. This study was mainly limited by coding errors in original data that could have led to a lower impact estimate, and unmeasured factors could also have confounded estimates.

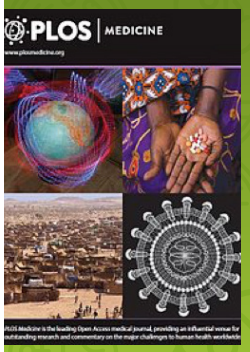
Conclusions: This study found that the introduction of PCV was associated with substantial reduction in all-cause pneumonia deaths in children aged 1 month to <19 years. The model predicted an effect of PCV in age groups who were eligible for vaccination (1 months to 4 years), and an indirect effect in those too old (8 to 18 years) to be vaccinated. These findings support sustaining pneumococcal vaccination to reduce pneumonia-related mortality in children.

Prof Cheryl Cohen

Global burden of influenza-associated lower respiratory tract infections and hospitalizations among adults: A systematic review and meta-analysis

Lafond KE, Porter RM, Whaley MJ, Suizan Z, Ran Z, Aleem MA, Thapa B, Sar B, Proschle VS, Peng Z, Feng L, Coulibaly D, Nkwembe E, Olmedo A, Ampofo W, Saha S, Chadha M, Mangiri A, Setiawaty V, Ali SS, Chaves SS, Otorbaeva D, Keosavanh O, Saleh M, Ho A, Alexander B, Oumzil H, Baral KP, Huang QS, ***Cohen C, et al***

PloS Med
Impact Factor: 10.500



Background: Influenza illness burden is substantial, particularly among young children, older adults, and those with underlying conditions. Initiatives are underway to develop better global estimates for influenza-associated hospitalizations and deaths. Knowledge gaps remain regarding the role of influenza viruses in severe respiratory disease and hospitalizations among adults, particularly in lower-income settings.

Methods and findings: We aggregated published data from a systematic review and unpublished data from surveillance platforms to generate global meta-analytic estimates for the proportion of acute respiratory hospitalizations associated with influenza viruses among adults. We searched 9 online databases (Medline, Embase, CINAHL, Cochrane Library, Scopus, Global Health, LILACS, WHOLIS, and CNKI; 1 January 1996-31 December 2016) to identify observational studies of influenza-associated hospitalizations in adults, and assessed eligible papers for bias using a simplified Newcastle-Ottawa scale for observational data. We applied meta-analytic proportions to global estimates of lower respiratory infections (LRIs) and hospitalizations from the Global Burden of Disease study in adults ≥20 years and by age groups (20-64 years and ≥65 years) to obtain the number of influenza-associated LRI episodes and hospitalizations for 2016. Data from 63 sources showed that influenza was associated with 14.1% (95% CI 12.1%-16.5%) of acute respiratory hospitalizations among all adults, with no significant differences by age group. The 63 data sources represent published observational studies (n = 28) and unpublished surveillance data (n = 35), from all World Health Organization regions (Africa, n = 8; Americas, n = 11; Eastern Mediterranean, n = 7; Europe, n = 8; Southeast Asia, n = 11; Western Pacific, n = 18). Data quality for published data sources was predominantly moderate or high (75%, n = 56/75). We estimate 32,126,000 (95% CI 20,484,000-46,129,000) influenza-associated LRI episodes and 5,678,000 (95% CI 3,205,000-9,432,000) LRI hospitalizations occur each year among adults. While adults <65 years contribute most influenza-associated LRI hospitalizations and episodes (3,464,000 [95% CI 1,885,000-5,978,000] LRI hospitalizations and 31,087,000 [95% CI 19,987,000-44,444,000] LRI episodes), hospitalization rates were highest in those ≥65 years (437/100,000 person-years [95% CI 265-612/100,000 person-years]). For this analysis, published articles were limited in their inclusion of stratified testing data by year and age group. Lack of information regarding influenza vaccination of the study population was also a limitation across both types of data sources.

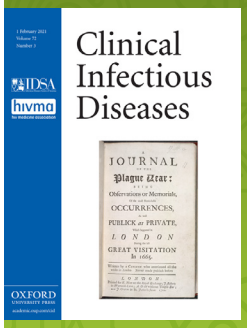
Conclusions: In this meta-analysis, we estimated that influenza viruses are associated with over 5 million hospitalizations worldwide per year. Inclusion of both published and unpublished findings allowed for increased power to generate stratified estimates, and improved representation from lower-income countries. Together, the available data demonstrate the importance of influenza viruses as a cause of severe disease and hospitalizations in younger and older adults worldwide.

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 Disease
Impact Factor: 8.313



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 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 transmission during primary maternal infection. This had not been explored in maternal nonprimary infection.

Methods: In a setting where most maternal cytomegalovirus infections are nonprimary, 42 mothers of infants with congenital CMV infections (transmitters) were compared to 75 cytomegalovirus-seropositive mothers whose infants were cytomegalovirus-uninfected (nontransmitters). Control infants were matched by sex, maternal HIV status and gestational age. We measured the ability of maternal antibodies to block three 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 three putatively protective pentamer-directed antibodies were significantly higher in transmitters compared to nontransmitters. In contrast, antibodies targeting an epitope on glycoprotein B 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 Clement Adu-Gyamfi

Dr Melinda Suchard

Plasma kynurenine-to-tryptophan ratio, a highly sensitive blood-based diagnostic tool for tuberculosis in HIV-infected pregnant women

Adu-Gyamfi C, *Savulescu D, Makhatini L, Otwombe K, Salazar-Austin N, Chaisson R, Martinson N, George J,* ***Suchard MS***

Clinical Infectious Diseases
Impact Factor: 8.313

Background: For pregnant women living with human immunodeficiency virus (HIV), concurrent active tuberculosis (TB) disease increases the risk of maternal mortality and poor pregnancy outcomes. Plasma indoleamine 2,3-dioxygenase (IDO) activity, measured by kynurenine-to-tryptophan (K/T) ratio has been proposed as a blood-based TB biomarker. We investigated whether plasma K/T ratio could be used to diagnose active TB among HIV-infected pregnant women.

Methods: Using an enzyme-linked immunosorbent assay (ELISA), we measured K/T ratio in 72 HIV-infected pregnant women with active TB and compared to 117 HIV-infected pregnant women without TB, matched by age and gestational age.

Results: Plasma K/T ratio was significantly elevated during pregnancy compared to sampling done after pregnancy ($p < 0.0001$). Pregnant women who had received isoniazid preventive therapy (IPT) before enrolment had decreased plasma K/T ratio compared to those who had not received IPT ($p = 0.0174$). Plasma K/T ratio was elevated in women with active TB at time of diagnosis compared to those without TB ($p < 0{\cdot}0001$). Using a cut-off of 0.100, plasma K/T ratio gave a diagnostic sensitivity of 94% (CI 82-95), specificity of 90% (CI 80-91), PPV 85% and NPV 98%. A receiver operating characteristic curve (ROC) gave an area under the curve of 0.95 (CI 0.92-0.97, $p < 0.0001$).

In conclusion: plasma K/T ratio is a sensitive blood-based diagnostic test for active TB disease in pregnant women living with HIV. Plasma K/T ratio should be further evaluated as an initial TB diagnostic test to determine its impact on patient care.

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, de Plessis M, McMorrow ML, Treurnicht FK, Hellferscee O, Dawood H, Variava E,* ***von Gottberg A***

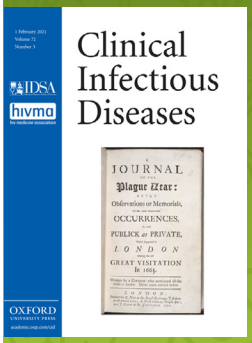
Clinical Infectious Diseases
Impact Factor: 8.313

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 HIV prevalence and routine pertussis vaccination for six decades, including use of the acellular vaccine since 2009.

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

Results: Over the six-year period 19429 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 Mazvita Muchengeti

Cervical cancer in sub-Saharan Africa: a multinational population-based cohort study on patterns and guidelines adherence of care

Griesel M, Seraphin TP, Mezger NC, Herl L, Feuchtner J, Joko,Fru WY, et al. ***(Dr Mazvita Muchengeti is a co-author)***

Oncologist
Impact Factor: 5.025

Background: Cervical cancer (CC) is the most common female cancer in many countries of sub-Saharan Africa (SSA). We assessed treatment guideline adherence and its association with overall survival (OS).

Methods: Our observational study covered nine population-based cancer registries in eight countries: Benin, Ethiopia, Ivory Coast, Kenya, Mali, Mozambique, Uganda, and Zimbabwe. Random samples of 44-125 patients diagnosed from 2010 to 2016 were selected in each. Cancer-directed therapy (CDT) was evaluated for degree of adherence to National Comprehensive Cancer Network (U.S.) Guidelines.

Results: Of 632 patients, 15.8% received CDT with curative potential: 5.2% guideline-adherent, 2.4% with minor deviations, and 8.2% with major deviations. CDT was not documented or was without curative potential in 22%; 15.7% were diagnosed with International Federation of Gynecology and Obstetrics (FIGO) stage IV disease. Adherence was not assessed in 46.9% (no stage or follow-up documented, 11.9%, or records not traced, 35.1%). The largest share of guideline-adherent CDT was observed in Nairobi (49%) and the smallest in Maputo (4%). In patients with FIGO stage I-III disease (n = 190), minor and major guideline deviations were associated with impaired OS (hazard rate ratio [HRR], 1.73; 95% confidence interval [CI], 0.36-8.37; HRR, 1.97; CI, 0.59-6.56, respectively). CDT without curative potential (HRR, 3.88; CI, 1.19-12.71) and no CDT (HRR, 9.43; CI, 3.03-29.33) showed substantially worse survival.

Conclusion: We found that only one in six patients with cervical cancer in SSA received CDT with curative potential. At least one-fifth and possibly up to two-thirds of women never accessed CDT, despite curable disease, resulting in impaired OS. Investments into more radiotherapy, chemotherapy, and surgical training could change the fatal outcomes of many patients.

Implications for practice: Despite evidence-based interventions including guideline-adherent treatment for cervical cancer (CC), there is huge disparity in survival across the globe. This comprehensive multinational population-based registry study aimed to assess the status quo of presentation, treatment guideline adherence, and survival in eight countries. Patients across sub-Saharan Africa present in late stages, and treatment guideline adherence is remarkably low. Both factors were associated with unfavorable survival. This report warns about the inability of most women with cervical cancer in sub-Saharan Africa to access timely and high-quality diagnostic and treatment services, serving as guidance to institutions and policy makers. With regard to clinical practice, there might be cancer-directed treatment options that, although not fully guideline adherent, have relevant survival benefit. Others should perhaps not be chosen even under resource-constrained circumstances.

Dr Melinda Suchard

Dr Dana Savulescu

Nicotinamide pathways as the root cause of sepsis – an evolutionary perspective on macrophage energetic shifts

Suchard MS *and* ***Savulescu DM***

FEBS Journal
Impact Factor: 4.7

Divergent pathways of macrophage metabolism occur during infection, notably switching between oxidative phosphorylation and aerobic glycolysis (Warburg-like metabolism). Concurrently, macrophages shift between alternate and classical activation. A key enzyme upregulated in alternatively activated macrophages is indoleamine 2,3-dioxygenase, which converts tryptophan to kynurenine for de novo synthesis of nicotinamide. Nicotinamide can be used to replenish cellular NAD^+ supplies. We hypothesize that an insufficient cellular NAD^+ supply is the root cause of metabolic shifts in macrophages. We assert that manipulation of nicotinamide pathways may correct deleterious immune responses. We propose evaluation of nicotinamide (vitamin B3) and analogues, including isoniazid, nicotinamide mononucleotide and nicotinamide riboside, as potential therapy for infectious causes of sepsis, including COVID-19.

Dr Sabelle Jallow

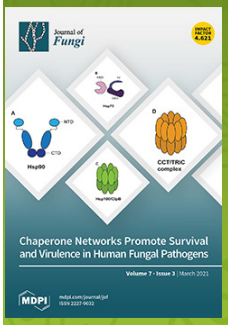
Prof Nelesh Govender

Ibrexafungerp: A First-in-Class Oral Triterpenoid Glucan Synthase Inhibitor

Jallow S, Govender NP

J Fungi (Basel)
Impact Factor: 4.621

Ibrexafungerp (formerly SCY-078 or MK-3118) is a first-in-class triterpenoid antifungal or 'fungerp' that inhibits biosynthesis of β-(1,3)-D-glucan in the fungal cell wall, a mechanism of action similar to that of echinocandins. Distinguishing characteristics of ibrexafungerp include oral bioavailability, a favourable safety profile, few drug-drug interactions, good tissue penetration, increased activity at low pH and activity against multi-drug resistant isolates including C. *auris* and C. *glabrata*. In vitro data has demonstrated broad and potent activity against *Candida* and *Aspergillus* species. Importantly, ibrexafungerp also has potent activity against azole-resistant isolates, including biofilm-forming *Candida* spp., and echinocandin-resistant isolates. It also has activity against the asci form of *Pneumocystis* spp., and other pathogenic fungi including some non-*Candida* yeasts and non-*Aspergillus* moulds. In vivo data have shown IBX to be effective for treatment of candidiasis and aspergillosis. Ibrexafungerp is effective for the treatment of acute vulvovaginal candidiasis in completed phase 3 clinical trials.



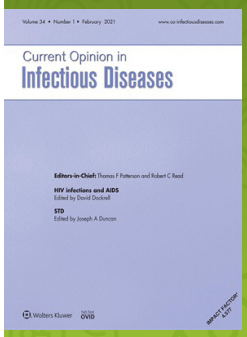
Dr Mazvita Muchengeti

Ms Tafadzwa Dhokotera

Conjunctival cancer in people living with HIV

Muchengeti, Mazvita; *Bohlius, Juliac; Dhokotera,* ***Tafadzwa G.***

Current Opinion in Infectious Diseases
Impact Factor: 4.577



Purpose of review: Historically, conjunctival cancer has been associated with HIV, particularly in sub-Saharan Africa. The human papilloma virus (HPV) has been implicated as a potential causative agent without conclusive evidence. This review covers recent evidence of the epidemiology, diagnosis and treatment of conjunctival cancer in people living with HIV (PLWH).

Recent findings: HIV infection has been attributed to 33% of squamous cell carcinoma of the conjunctiva in sub-Saharan Africa. Although clear evidence of the effect of immunodeficiency on conjunctival cancer risk has been demonstrated, the role of HPV on conjunctival cancer development is still unclear. Biomarkers such as the p16 protein are not always indicative of HPV infection. The Epstein-Barr virus (EBV) might potentially be another infectious agent of interest in the development of conjunctival cancer. There is some evidence of increased conjunctival cancer recurrence post treatment as well as increased probability of metastasis in PLWH.

Summary: Immunodeficiency increases the risk of conjunctival cancer in PLWH. Symptomatic screening of conjunctival cancer in PLWH should be encouraged. Research on HPV involvement should remain a priority and EBV considered as another etiologic agent of interest. More studies on treatment modalities in PLWH should be considered.

Ms Faith Moyo

Dr Tendesayi Kufa-Chakezha

Achieving maternal viral load suppression for elimination of mother-to-child transmission of HIV in South Africa

Moyo, Faith; *Mazanderani, Ahmad Haeri; Murray, Tanya; Sherman, Gayle G ;* ***Kufa, Tendesayi***

AIDS
Impact Factor: 4.534

Objective: To describe changes in maternal viral control over time in South African women living with HIV (WLHIV) using surveillance data from the National Health Laboratory Service's Corporate Data Warehouse (NHLS CDW).

Design: A retrospective cohort analysis of maternal viral load during pregnancy and up to 15 months postpartum was performed amongst WLHIV (15-49 years) within the public-health sector between 2016 and 2017.

Methods: HIV and pregnancy-related test data were used to create a synthetic cohort of pregnant WLHIV from the NHLS CDW. Syphilis-screening, in association with ward type and/or postpregnancy cervical screening and/or birth HIV test and/or positive β-hCG, was used as a proxy for pregnancy. The syphilis-screening date marked the first antenatal care visit (fANC). Fractional polynomial models described viral load evolution from fANC up to 15 months postdelivery. Piecewise linear regression models determined factors associated with viral load decline.

Findings: Among 178 319 pregnant WLHIV, 345 174 viral load tests were performed [median = 2 (IQR: 2-3) per woman]. At fANC, 85 545 (48%) women were antiretroviral therapy (ART) experienced; 88 877 (49.8%) were not and 3897 (2.2%) unknown. Proportions of viraemia (viral load ≥50 copies/ml) were 39 756 (53.6%) at first viral load performed during pregnancy, 14 780 (36.9%) at delivery and 24 328 (33.5%) postpartum. Maternal age at least 25 years, CD4+ cell count at least 500 cells/μl and viral load less than 50 copies/ml at baseline predicted sustained viral load suppression during follow-up.

Conclusion: Despite high-ART coverage among pregnant women in South Africa, only 63% of WLHIV achieved viral load less than 50 copies/ml at delivery. Maternal viral load monitoring requires prioritization for maternal health and eMTCT.

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

Meredith L. McMorrow, Liza Rossi, Susan Meiring, Katherine Bishop, Raphaela Itzikowitz, Washiefa Isaacs, Faakhiera Stellenboom, Sibongile Walaza, Orienka Hellferscee, Florette K. Treurnicht, Heather J. Zar, Stefano Tempia, ***Cheryl Cohen***

Influenza Other Respi Viruses
Impact Factor: 3.288

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 Shaheed Vally Omar

Bedaquiline resistance and genetic resistance associated variants: South African National Bedaquiline Surveillance Program 2014-2019

Omar SV, *Ismail F, Joseph L, Ngcamu D, Okozi N, van der Meulen M, Gwala T, Bhyat Z, Sicwetsha A, de Abreu C, Makubalo L, Ismail NA*

Antimicrobial resistance / International Journal of Infectious Diseases
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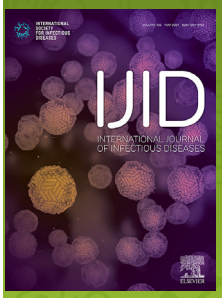


Background: Bedaquiline (BDQ) is the first new agent for use in treatment of drug resistant tuberculosis (DR-TB). Studies identified the genetic resistance determinants to be the biological pathway target *atpE* and efflux based pathway regulating the mmpS5/L5 efflux pump *Rv0678*. South Africa has been troubled with poor outcomes in drug resistant TB patients prior to the introduction of BDQ. Clinical trials and the compassionate use access program showed improved cure rates for pre-/ extensively drug resistant TB patients. In October 2014, BDQ was registered in South Africa and to date >15,000 drug resistant TB patients have been initiated on a BDQ containing regimen. With its introduction and as part of the national policy framework, the National TB Reference Laboratory implemented a surveillance programme to monitor the emergence of resistance. In 2018, Ismail et al. proposed tentative critical concentrations for phenotypic drug susceptibility, which were later established by the World Health Organization using multi-country data. In addition, they further identified the efflux based pathway as the sole contributor to resistance for isolates detected as being phenotypically resistant. In this study, we aimed to explore the genetic resistance associated variants (RAV) related to BDQ resistance using the proposed critical concentrations.

Methods and materials: Surveillance specimens were prospectively collected from patients initiated on a BDQ treatment regimen at baseline, month 2 and month 6 on treatment between 2014–2019. All mycobacterial cultured isolates from this cohort were phenotypically tested to identify resistance. Phenotypically resistant isolates were then sequenced to identify RAVs in either the Rv0678 or atpE genes.

Results: A total of 8041 unique patients were included in this study. Three percent of these isolates were phenotypically resistant, all of which harboured a RAV in the Rv0678 gene. More than 75% of these RAVs were localized to a 100 bp fragment within the genetic target. The underlying genetic mechanism for BDQ resistance in South Africa still remains exclusively related to the Rv0678 genetic target.

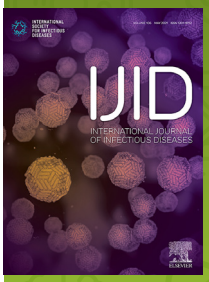
Conclusion: The exploration of efflux pump inhibitors as a conduit remains relevant. Furthermore, the information may prove useful for development of a rapid molecular screening tool for the detection of BDQ resistance

Dr. Jenny Rossouw

First confirmed case of infant botulism in Africa, caused by a dual-toxin-producing *Clostridium botulinum* strain

Vosloo MN, Opperman CJ, Geyer HDW, Setshedi GM, Allam M, Kwenda S, Ismail A, Khumalo THZ, Brink AJ, Frean JA, ***Rossouw J***

International Journal of Infectious Diseases
Impact Factor: 3.202



Botulism, a rare life-threatening toxemia, is probably underdiagnosed in all of its forms in Africa. This study reports the first laboratory-supported case of infant botulism on the African continent. A 10-week-old, previously well infant presented with progressive global weakness, feeding difficulty, and aspiration pneumonia. During a lengthy hospitalization, a rare bivalent *Clostridium botulinum* strain, producing subtype B3 and F8 toxins and with a new multilocus sequence type, was isolated from stool. The infant was successfully treated with a heptavalent botulinum antitoxin infusion and pyridostigmine. Despite the relative rarity of infant botulism, this case illustrates the importance of maintaining a high level of clinical suspicion when assessing hypotonic infants. The value of modern diagnostic modalities in identifying and characterizing this under-recognized condition is also demonstrated.

Ms Lactatia Motsuku

Dr Elvira Singh

Colorectal cancer incidence and mortality trends by sex and population group in South Africa: 2002–2014

Lactatia Motsuku, *Wenlong Carl Chen, Mazvita Molleen Muchengeti, Megan Naidoo, Tamlyn Mac Quene, Patricia Kellett, Matshediso Ivy Mohlala, Kathryn M. Chu,* ***Elvira Singh***

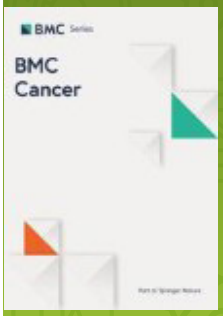
BMC Cancer
Impact Factor: 3.150

Background: South Africa (SA) has experienced a rapid transition in the Human Development Index (HDI) over the past decade, which had an effect on the incidence and mortality rates of colorectal cancer (CRC). This study aims to provide CRC incidence and mortality trends by population group and sex in SA from 2002 to 2014.

Methods: Incidence data were extracted from the South African National Cancer Registry and mortality data obtained from Statistics South Africa (STATS SA), for the period 2002 to 2014. Age-standardised incidence rates (ASIR) and age-standardised mortality rates (ASMR) were calculated using the STATS SA mid-year population as the denominator and the Segi world standard population data for standardisation. A Joinpoint regression analysis was computed for the CRC ASIR and ASMR by population group and sex.

Results: Totals of 33,232 incident CRC cases and 26,836 CRC deaths were reported during the study period. Of the CRC cases reported, 54% were males and 46% were females, and among deaths reported, 47% were males and 53% were females. Overall, there was a 2.5% annual average percentage change (AAPC) increase in ASIR from 2002 to 2014 (95% CI: 0.6-4.5, p-value < 0.001). For ASMR overall, there was 1.3% increase from 2002 to 2014 (95% CI: 0.1-2.6, p-value < 0.001). The ASIR and ASMR among population groups were stable, with the exception of the black population group. The ASIR increased consistently at 4.3% for black males (95% CI: 1.9-6.7, p-value < 0.001) and 3.4% for black females (95% CI: 1.5-5.3, p-value < 0.001) from 2002 to 2014, respectively. Similarly, ASMR for black males and females increased by 4.2% (95% CI: 2.0-6.5, p-value < 0.001) and 3.4% (, 95%CI: 2.0-4.8, p-value < 0.01) from 2002 to 2014, respectively.

Conclusions: The disparities in the CRC incidence and mortality trends may reflect socioeconomic inequalities across different population groups in SA. The rapid increase in CRC trends among the black population group is concerning and requires further investigation and increased efforts for cancer prevention, early screening and diagnosis, as well as better access to cancer treatment.

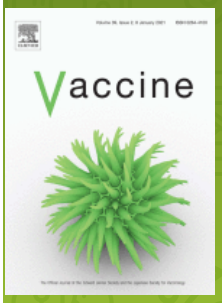


Prof Cheryl Cohen

A cost-effectiveness analysis of South Africa's seasonal influenza vaccination programme

Edoka I, Kohli-Lynch C, Fraser H, Hofman K, Tempia S, McMorrow M, Ramkrishna W, Lambach P, Hutubessy R, ***Cohen C***

Vaccine
Impact Factor: 3.143



Background: Seasonal influenza imposes a significant health and economic burden in South Africa, particularly in populations vulnerable to severe consequences of influenza. This study assesses the cost-effectiveness of South Africa's seasonal influenza vaccination strategy, which involves vaccinating vulnerable populations with trivalent inactivated influenza vaccine (TIV) during routine facility visits. Vulnerable populations included in our analysis are persons aged ≥ 65 years; pregnant women; persons living with HIV/AIDS (PLWHA), persons of any age with underlying medical conditions (UMC) and children aged 6-59 months.

Method: We employed the World Health Organisation's (WHO) Cost Effectiveness Tool for Seasonal Influenza Vaccination (CETSIV), a decision tree model, to evaluate the 2018 seasonal influenza vaccination campaign from a public healthcare provider and societal perspective. CETSIV was populated with existing country-specific demographic, epidemiologic and coverage data to estimate incremental cost-effectiveness ratios (ICERs) by comparing costs and benefits of the influenza vaccination programme to no vaccination.

Results: The highest number of clinical events (influenza cases, outpatient visits, hospitalisation and deaths) were averted in PLWHA and persons with other UMCs. Using a cost-effectiveness threshold of US$ 3400 per quality-adjusted life year (QALY), our findings suggest that the vaccination programme is cost-effective for all vulnerable populations except for children aged 6-59 months. ICERs ranged from ~US$ 1 750 /QALY in PLWHA to ~US$ 7500/QALY in children. In probabilistic sensitivity analyses, the vaccination programme was cost-effective in pregnant women, PLWHA, persons with UMCs and persons aged ≥65 years in >80% of simulations. These findings were robust to changes in many model inputs but were most sensitive to uncertainty in estimates of influenza-associated illness burden.

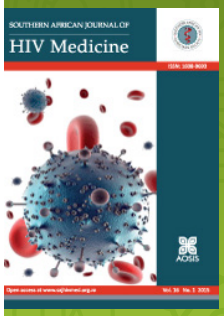
Conclusion: South Africa's seasonal influenza vaccination strategy of opportunistically targeting vulnerable populations during routine visits is cost-effective. A budget impact analysis will be useful for supporting future expansions of the programme.

Prof Nelesh Govender

Skin and mucosal manifestations of an AIDS-related systemic mycosis

Boswell MT, Robinson L, ***Govender N***

Southern African Journal of HIV Medicine
Impact Factor: 2.500



A human immunodeficiency virus (HIV)-positive male from Cameroon who had recently started antiretroviral therapy presented with a new rash, night sweats and loss of weight. On examination, erythematous to flesh-coloured papules were noted on the trunk. Intraoral examination revealed granular-appearing lesions of the hard and soft palate, with areas of pigmentation in keeping with HIV-associated mucosal hyperpigmentation. A full blood count showed a pancytopenia, with a moderate neutropenia. He had a severe lymphopenia, and his CD4+ T-cell count was 46 cells/microlitre (µL). Serum (1-3)-β-d-glucan and ferritin levels were markedly elevated at > 500 picograms per millilitre (pg/mL) and 5533 micrograms per litre (µg/L), respectively. Periodic acid–Schiff with diastase (PAS-D) and Grocott-Gomori histochemical stains of a skin punch biopsy showed numerous small, round intracytoplasmic organisms within histiocytes, consistent with histoplasmosis. A pan-fungal polymerase chain reaction (PCR) assay confirmed infection with either *Histoplasma capsulatum* or *Emergomyces africanus*. This PCR assay cross-reacts with *Blastomyces* species; however, the yeast phase of this pathogen has a different histological appearance.

Prof Cheryl Cohen

Housing quality in a rural and an urban settlement in South Africa

Mathee A, Moyes J, Mkhencele T, Kleynhans J, Language B, Piketh S, Moroe E, Wafawanaka F, Martinson N, McMorrow M, Tempia S, Kahn K, ***Cohen C***

International Journal of Environmental Research and Public Health
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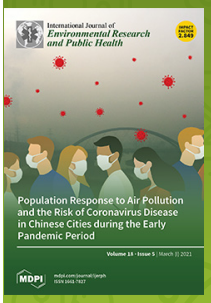


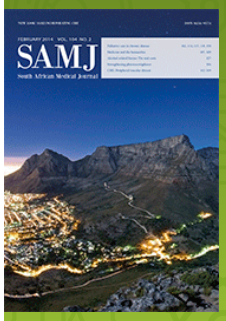
During 2016 to 2018, a prospective household cohort study of influenza and respiratory syncytial virus community burden and transmission dynamics (the PHIRST study) was undertaken to examine the factors associated with influenza and other respiratory pathogen transmissions in South Africa. We collected information on housing conditions in the PHIRST study sites: rural villages near Agincourt, Bushbuckridge Municipality, Mpumalanga Province, and urban Jouberton Township in North West Province. Survey data were collected from 159 and 167 study households in Agincourt and Jouberton, respectively. Multiple housing-related health hazards were identified in both sites, but particularly in Agincourt. In Agincourt, 75% (119/159) of households reported daily or weekly interruptions in water supply and 98% (154/159) stored drinking water in miscellaneous containers, compared to 1% (1/167) and 69% (115/167) of households in Jouberton. Fuels other than electricity (such as wood) were mainly used for cooking by 44% (70/159) and 7% (11/167) of Agincourt and Jouberton households, respectively; and 67% (106/159) of homes in Agincourt versus 47% (79/167) in Jouberton were located on unpaved roads, which is associated with the generation of dust and particulate matter. This study has highlighted housing conditions in Agincourt and Jouberton that are detrimental to health, and which may impact disease severity or transmission in South African communities.

Dr Jaishree Raman

Maintaining focus on administering effective malaria treatment during the COVID-19 pandemic

Raman J, *Baker L, Blaylock M, Blumberg L, Frean J, Misiani E, Ukpe IS*

South African Medical Journal
Impact Factor: 2.238



As September marks the start of the malaria season in South Africa (SA), it is essential that healthcare professionals consider both COVID- 19 and malaria when a patient who lives in or has recently travelled to a malaria area presents with acute febrile illness. Early diagnosis of malaria by either a rapid diagnostic test or microscopy enables prompt treatment with the effective antimalarial, artemether-lumefantrine, preventing progression to severe disease and death. Intravenous artesunate is the preferred treatment for severe malaria in both children and adults. Adding single low-dose primaquine to standard treatment is recommended in endemic areas to block onward transmission. Use of the highly effective artemisinin-based therapies should be limited to the treatment of confirmed malaria infections, as there is no clinical evidence that these antimalarials can prevent or treat COVID-19. Routine malaria case management services must be sustained, in spite of COVID-19, to treat malaria effectively and support SA's malaria elimination efforts.

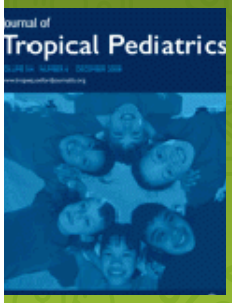
Ms Rudzani Clementine Mathebula

Dr Tendesayi Kufa-Chakezha

Trends in RPR seropositivity among Children Younger than 2 Years in South Africa, 2010–2019

Mathebula R, *Kuonza L, Musekiwa A, Kularatne R, Puren A, Reubenson G, Sherman G,* ***Kufa T***

Journal of Tropical Pediatrics
Impact Factor: 0.940



A positive rapid plasma reagin (RPR) result in children under the age of 2 years indicates either passive transplacental transfer of maternal antibodies or active infection with syphilis (possible congenital syphilis). We describe trends in RPR seropositivity in this population using centralized laboratory data. A secondary analysis of laboratory data collected through the National Health Laboratory Service Corporate Data Warehouse from 2010 to 2019 was conducted. Of the 127 150 children <2 years included in the analysis, 10 969 [8.6%; 95% confidence interval (95% CI) 85-88]) were RPR seropositive. RPR seropositivity increased from 6.5% to 13.0% between 2010 and 2019. Overall, the annual rate of RPR seropositivity was relatively stable between 2010 and 2018 with a range of 89-127/100 000 live births, increasing sharply to 165/100 000 livebirths in 2019. KwaZulu-Natal and North West provinces recorded the largest increases in annual seropositivity rate, while Eastern Cape and Western Cape had the most significant declines. Although this analysis is limited to laboratory results, in the absence of major changes in testing practices, there may be a rise in the burden of antenatal syphilis exposure in utero indicating an increase in maternal syphilis and syphilis transmission in the general population. South Africa needs to intensify mother-to-child transmission of syphilis elimination efforts to reach the WHO target of ≤50 cases per 100 live births by 2030.

Dr Ahmad Mazanderani

Prof Gayle Sherman

Paediatric & Adolescent HIV Viral load Monitoring, 2014-2020

Mazanderani AH, Sherman GG

NICD Bulletin
Impact Factor: n/a

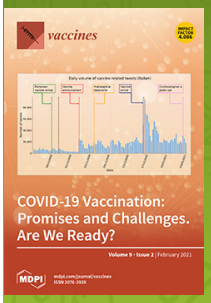
Between July 2019 and June 2020, HIV viral load testing coverage among children and adolescents living with HIV aged <15 years and 15-19 years was approximately 51% and 57%, respectively. Among all children and adolescents (0-19 years of age) with an HIV viral load, 49.7% (130 952) were virally suppressed (<50 RNA copies per millilitre [cps/ml]), 22.7% (59 779) had low-level viraemia (50–<1 000 RNA cps/ml) and 27.6% (72 774) had a VL >1 000 RNA cps/ml. Over the past six and half years, improvement in the overall paediatric and adolescent suppression rate (<50 RNA cps/ml) has been modest at only 7.3%, although some sub-populations (<1 years and 15-19 years) have demonstrated greater improvement than other age groups. Differences in HIV viral load suppression between males and females were apparent among all paediatric and adolescent age groups, with 51.8% of females compared with 46.8% of males 0-19 years of age suppressed between July 2019 and June 2020. There are considerable differences in the volume of HIV viral load testing and suppression rates among South Africa's nine provinces. Whereas KwaZulu-Natal Province has the second highest viral suppression rate, it remains the province with the highest number of unsuppressed children and adolescents living with HIV.

Dr Villyen Motaze

The Impact of Rubella Vaccine Introduction on Rubella Infection and Congenital Rubella Syndrome: A Systematic Review of Mathematical Modelling Studies

Nkengafac Villyen Motaze , *Zinhle E. Mthombothi , Olatunji Adetokunboh , C. Marijn Hazelbag , Enrique M. Saldarriaga , Lawrence Mbuagbaw and Charles Shey Wiysonge*

Vaccines
Impact Factor: n/a



Introduction: Rubella vaccines have been used to prevent rubella and congenital rubella syndrome (CRS) in several World Health Organization (WHO) regions. Mathematical modelling studies have simulated introduction of rubella-containing vaccines (RCVs), and their results have been used to inform rubella introduction strategies in several countries. This systematic review aimed to synthesize the evidence from mathematical models regarding the impact of introducing RCVs.

Methods: We registered the review in the international prospective register of systematic reviews (PROSPERO) with registration number CRD42020192638. Systematic review methods for classical epidemiological studies and reporting guidelines were followed as far as possible. A comprehensive search strategy was used to identify published and unpublished studies with no language restrictions. We included deterministic and stochastic models that simulated RCV introduction into the public sector vaccination schedule, with a time horizon of at least five years. Models focused only on estimating epidemiological parameters were excluded. Outcomes of interest were time to rubella and CRS elimination, trends in incidence of rubella and CRS, number of vaccinated individuals per CRS case averted, and cost-effectiveness of vaccine introduction strategies. The methodological quality of included studies was assessed using a modified risk of bias tool, and a qualitative narrative was provided, given that data synthesis was not feasible.

Results: Seven studies were included from a total of 1393 records retrieved. The methodological quality was scored high for six studies and very high for one study. Quantitative data synthesis was not possible, because only one study reported point estimates and uncertainty intervals for the outcomes. All seven included studies presented trends in rubella incidence, six studies reported trends in CRS incidence, two studies reported the number vaccinated individuals per CRS case averted, and two studies reported an economic evaluation measure. Time to CRS elimination and time to rubella elimination were not reported by any of the included studies. Reported trends in CRS incidence showed elimination within five years of RCV introduction with scenarios involving mass vaccination of older children in addition to routine infant vaccination. CRS incidence was higher with RCV introduction than without RCV when public vaccine coverage was lower than 50% or only private sector vaccination was implemented. Although vaccination of children at a given age achieved slower declines in CRS incidence compared to mass campaigns targeting a wide age range, this approach resulted in the lowest number of vaccinated individuals per CRS case averted.

Conclusion and recommendations: We were unable to conduct data synthesis of included studies due to discrepancies in outcome reporting. However, qualitative assessment of results of individual studies suggests that vaccination of infants should be combined with vaccination of older children to achieve rapid elimination of CRS. Better outcomes are obtained when rubella vaccination is introduced into public vaccination schedules at coverage figures of 80%, as recommended by WHO, or higher. Guidelines for reporting of outcomes in mathematical modelling studies and the conduct of systematic reviews of mathematical modelling studies are required.

Dr Nishi Prabdial-Sing

Prof Adrian Puren

The performance of hepatitis C virus (HCV) antibody point-of-care tests on oral fluid or whole blood and dried blood spot testing for HCV serology and viral load among individuals at higher risk for HCV in South Africa

Nishi Prabdial-Sing, *Lucinda Gaelejwe, Lillian Makhathini, Jayendrie Thaver, Morubula Jack Manamela,Susan Malfeld,C. Wendy Spearman, Mark Sonderup, Andrew Scheibe, Katherine Young, Harry Hausler,* ***Adrian J. Puren***

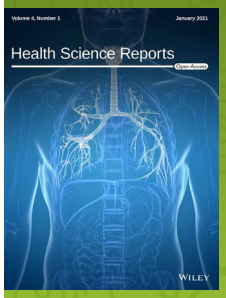
Health Science Reports
Impact Factor: n/a

Human Background and Aims: To enhance screening and diagnosis in those at-risk of hepatitis C virus (HCV), efficient and improved sampling and testing is required. We investigated the performance of point-of-care (POC) tests and dried blood spots (DBS) for HCV antibody and HCV RNA quantification in individuals at higher risk for HCV (people who use and inject drugs, sex workers and men who have sex with men) in seven South African cities.

Methods: Samples were screened on the OraQuick HCV POC test (471 whole blood and 218 oral fluid); 218 whole blood and DBS paired samples were evaluated on the ARCHITECT HCV antibody (Abbott) and HCV viral load (COBAS Ampliprep/COBAS TaqMan version 2) assays. For HCV RNA quantification, 107 dB were analyzed with and without normalization coefficients.

Results: POC on either whole blood or oral fluid showed an overall sensitivity of 98.5% (95% CI 97.4-99.5), specificity of 98.2% (95% CI 98.8-100) and accuracy of 98.4% (95% CI 96.5-99.3). On the antibody immunoassay, DBS showed a sensitivity of 96.0% (95% CI 93.4-98.6), specificity of 97% (95% CI 94.8-99.3) and accuracy of 96.3% (95% CI 93.8-98.8). A strong correlation (R^2 = 0.90) between viral load measurements for DBS and plasma samples was observed. After normalization, DBS viral load results showed an improved bias from 0.5 to 0.16 log10 IU/mL.

Conclusion: The POC test performed sufficiently well to be used for HCV screening in at-risk populations. DBS for diagnosis and quantification was accurate and should be considered as an alternative sample to test. POC and DBS can help scale up hepatitis services in the country, in light of our elimination goals.



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