



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Study shows the high rates of sub-clinical TB infections in PLWHA

In this Issue

In this issue we report on new TB studies from the CAPRISA team and collaborators to commemorate World TB Day observed in March.

On page 1 we feature a study published in *Clinical Infectious Diseases* that shows high rates of subclinical TB infections in people living with HIV.

We report on a proposed multi-centre, multi-country TRIAD study, and the CAPRISA TB community collaborative outreach event, on page 2.

On page 3 we feature the CAP 093 INSIGHT study to investigate INSTI's for enhanced TB-HIV integration and we congratulate Profs Mlisana & De Oliveira on their SAMRC awards.

On page 4 we report on the NICD's study on the Ad26.COV2.S breakthrough infections and the CAPRISA study which aims to identify TB transmission hotspot areas.

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A recent CAPRISA-led study highlighted the inadequacies of symptom-based TB screening in high TB-HIV burden settings resulting in the high incidence rates of recurrent subclinical TB in people living with HIV and AIDS (PLWHA).

The study, "Recurrent subclinical tuberculosis among ART accessing participants: Incidence, clinical course, and outcomes, published in the journal *Clinical Infectious Diseases*, set out to determine the incidence, progression, and outcomes of subclinical TB in anti-retroviral therapy (ART) accessing PLWHA with known previous successful TB treatment outcomes in South Africa.

A total of 402 adult participants living with HIV and AIDS were screened for TB with 3-monthly clinical and bacteriologic evaluation and bi-annual chest radiographs over 3 years.

A total of 48/402 (11.9%) bacteriologically confirmed incident recurrent TB cases was identified, comprising 17/48 (35.4%)

subclinical TB cases and 31/48 (64.5%) clinical TB cases.

Age, sex, and body mass index (BMI) were similar among subclinical, clinical, and no TB groups.

Incidence rates of recurrent TB overall; in clinical TB; and subclinical TB groups was 2.3 [95% CI: 1.7-3.0]; 1.5 [95% CI: 1.1-2.2]; and 0.9 [95% CI: 0.5-1.4] per 100 person-years, respectively. In the subclinical TB group, 14/17 (82.4%) was diagnosed by TB culture only, 11/17 (64.7%) received TB treatment, and 6/17 (35.3%) resolved TB spontaneously.

Undiagnosed asymptomatic subclinical tuberculosis (TB) remains a significant threat to global TB control and accounts for a substantial proportion of cases among people living with HIV/AIDS (PLWHA).

The researchers called for an update of the symptom-based screening guidelines to control the scourge of TB infections in PLWHA.

For further reading see: *Naidoo K, et al. Recurrent subclinical tuberculosis among ART accessing participants: Incidence, clinical course, and outcomes. Clin Infect Dis. 2022. doi: 10.1093/cid/ciac185. <https://pubmed.ncbi.nlm.nih.gov/35247054/>*

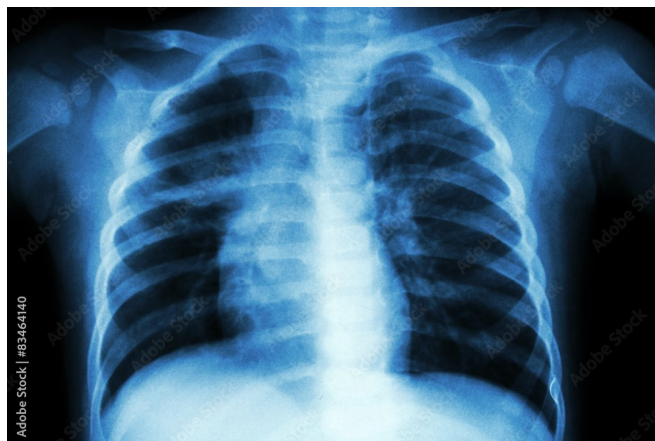


Image left: Undiagnosed asymptomatic subclinical TB remains a threat to global TB control. Photo credit: Adobe Stock



Optimizing DR TB Outcomes—TRIAD study

CAPRISA is one of nine clinical research sites, and lead co-ordinator for the TRIAD study, a multi-center, multi-country Prospective Pragmatic Cohort study to assess the effectiveness, feasibility, acceptability, and cost-effectiveness of implementing the Xpert MTB/XDR (Xpert XDR; Cepheid) assay for rapid triage-and-treatment with a shorter, all-oral drug resistant tuberculosis (DR-TB) treatment regimen.



isoniazid, fluoroquinolones and second-line injectable agents to provide rapid genotypic susceptibility testing to detect DR-TB. Participants that test positive for *Mycobacterium tuberculosis (M.tb)* with rifampicin resistance will be enrolled into *Cohort 1* (n=880). Participants that test positive for *M.tb* that are rifampicin susceptible with isoniazid mono-resistance will be enrolled into *Cohort 2* (n=400).

The proposed study, led by Prof Kogie Naidoo, Study PI and Head of HIV-TB Treatment Research at CAPRISA (*in the photo*), aims to screen approximately 4800 GeneXpert MTB/RIF or Ultra MTB-positive participants (irrespective of rifampicin resistance status) from clinical research sites in South Africa, Nigeria and Ethiopia to enrol 880 rifampicin resistant and 400 isoniazid mono-resistant participants over a period of 12-18 months.

“This research will provide information about the feasibility, acceptability and cost-effectiveness of the DR TB triage-and-treat model, to inform policies and guidelines for programmatic implementation” said Prof Naidoo. The Xpert XDR assay will be used to guide selection of appropriate, evidence-based, all-oral DR-TB treatment regimen of shortest possible duration. The TB molecular bacterial load assay (TB-MBLA) will be used as an adjunct to provide bacillary load monitoring over the course of treatment to assess real-time DR TB treatment response.

The Xpert XDR assay, a rapid genotypic test, will be implemented as a reflex test to detect resistance to

A build-up session to World TB Day: A collaborative partnership to end TB

“Invest in Action to End TB Now! Get Screened. End Stigma. Save Lives”



Photo: (L-R) : Mr Patrick Mdletshe, CAPRISA Head of Community Programme; Ms Ntombifuthi Luthuli, TBHIV Care; Ms Sthembile Dlamini, Office of the Premier; Ms Nelly Madikizela, Gugu Dlamini Foundation; Ms Siphelele Gabokhuttle, Community Liaison Officer TBHIV Care



A collaborative World TB Day Build-Up Session was held on 16 March in the community of Ntuzuma, north of Durban, in KwaZulu-Natal. The event of multiple stakeholders included CAPRISA, TB-HIV Care, the Gugu Dlamini Foundation, eThekweni Municipality, KZN Department of Health and the community of Ntuzuma.

Themed: “Invest in Action to End TB Now! Get Screened. End Stigma. Save Lives”, the event was led by Mr Patrick Mdletshe, Chair of the CAPRISA Community Programmes. Guest speakers included representatives from CAPRISA, TB HIV Care, the Office of the Mayor, the Office of the Premier, Department of Health and an MDR TB survivor who gave a personal testimony of her journey with TB. “I learned from the CAPRISA community and support groups that TB is treatable and completely curable. Perseverance will save your life,” said Phindile Vilakazi a Multidrug-resistant TB (MDR TB) survivor.

The common theme amongst the speakers, was a need for greater collaboration to combat the three major public health threats: HIV, TB and Covid-19, and a call for greater strides to be made in ending TB, which is a preventable, treatable and curable disease.

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INSTI'S for enhanced TB-HIV Integration

The CAPRISA 093 INSIGHT study to evaluate the antiviral efficacy, safety and pharmacokinetics of twice daily Biktarvy® in ART-naïve adults with HIV/TB coinfection receiving Rifampicin based TB treatment is underway at the CAPRISA Springfield Research clinic.

The study will provide evidence to introduce Biktarvy® as an alternative safe, effective and cost effective INSTI option to Africa in patients with HIV-associated TB. The study is led by Dr Anushka Naidoo CAPRISA Scientist and PI and Co-PI's, Prof's Kelly Dooley, Professor of Medicine at John Hopkins University & Kogieleum Naidoo, Head of HIV-TB Research at CAPRISA. This ground-breaking study will provide the opportunity to determine the use of Biktarvy for people with HIV-TB co-infection in areas where the drug is not already licensed, including low and low middle income countries where lack of safety and efficacy information is a barrier to the drug's introduction.



(L-R): Dr Anushka Naidoo (PI), Prof's Kelly Dooley (Co-PI)

The study may also pave the way for TAF roll-out, said Dr Anushka Naidoo, "a drug that has a better bone and renal safety profile than TDF, which has been hindered, in part, by lack of data in HIV-TB co-infected individuals." Co-treatment of HIV and TB, although ideal due to significant morbidity and mortality benefits, "has its challenges, explained Naidoo. "This is mainly caused by drug-drug interactions with the rifamycin's, higher pill burden and overlapping toxicities."

Profs Koleka Mlisana and Tulio de Oliveira receive SAMRC awards



The SAMRC honoured the scientific contributions of CAPRISA Research Associates, Professors Koleka Mlisana and Tulio de Oliveira, at the 8th SAMRC Scientific Merit Awards held on 10th March.

The prestigious President's Award is made to 'scientists who have made exceptional lifelong contributions to medical research and public health' was presented to microbiologist, Professor Koleka Mlisana for her research in HIV.

She has over 40 years' experience in health sciences and currently co-chairs the Ministerial Advisory Committee on Coronavirus (MAC). Mlisana was head of the HIV Pathogenesis and Vaccine Research Programme at CAPRISA.



A Gold medal award was presented to bioinformatics scientist Professor Tulio de Oliveira, who facilitated the identification of the SARS-CoV-2 variants of concern – Beta and Omicron in South Africa and led the creation of the Network for Genomic Surveillance in South Africa (NGS-SA).

Oliviera is the Director of the newly established Centre for Epidemic Response and Innovation (CERI) and Professor of Bioinformatics, School for Data Science and Computational Thinking, Faculty of Science and Faculty of Medicine and Health Sciences, Stellenbosch University. According to the SAMRC the Gold Medal category, is awarded to 'researchers who have made substantial and influential contributions that have impacted

on health especially in the developing world'.

Continued from page 2..

A build-up session to World TB Day...continued

Services offered for the attendees on the day included HIV testing, TB screening, mobile chest x-rays and transport to KwaMashu Poly Clinic was offered to guests who requested Covid vaccine jab.

Dr Busi Ntsalaze, CAPRISA Research Clinician said "Covid-19 had a devastating impact on the End TB goals. The gains made in TB over many years have been eroded with reports of 100 000 more TB deaths per annum in the 2020-2021 reporting period compared to previous years. We need increased investments to get back on track with TB", she said.



Ad26.COV2.S breakthrough infections induce high titers of neutralizing antibodies against Omicron and other SARS-CoV-2 variants of concern

Drs Dale Kitchin (*bottom photo*) and Simone Richardson (*top photo*) of the NICD published a study entitled “Ad26.COV2.S breakthrough infections induce high titers of neutralizing antibodies against Omicron and other SARS-CoV-2 variants of concern” in *Cell Reports Medicine*.



tude to humoral immune responses measured in convalescent donors who had been hospitalized with severe illness, and are cross-reactive against diverse SARS-CoV-2 variants, including the neutralization resistant Omicron (B.1.1.529) variant that currently dominates global infections, as well as SARS-CoV-1.

The study confirms that neutralizing and binding antibody responses to Ad26.COV2.S vaccination are stable for 6 months post Janssen (Johnson & Johnson) Ad26.COV2.S non-replicating viral vector vaccination, when tested against multiple SARS-CoV-2 variants. Secondly, using longitudinal samples from individuals who experienced clinically mild breakthrough infections 4 to 5 months after vaccination, they show dramatically boosted binding antibodies, Fc effector function, and neutralization. These high titer responses are of similar magni-



These data have implications for population immunity in areas where the Ad26.COV2.S vaccine has been widely deployed, but where ongoing infections continue to occur at high levels. [https://www.cell.com/cell-reports-medicine/pdfExtended/S2666-3791\(22\)00035-0](https://www.cell.com/cell-reports-medicine/pdfExtended/S2666-3791(22)00035-0)

Holly Spencer awarded MSc with Distinction



Congratulations to Holly Spencer (*in the photo*) from the National Institute for Communicable Diseases (NICD) who obtained her MSc degree with distinction. Holly studied the Functional Impact of *IGHG3* Genetic Variation in HIV-1 Infection and was supervised by Dr. Cathrine Scheepers, Dr. Simone Richardson and Prof. Penny Moore.

Finding TB

The CAPRISA 095 TARGET TB study aims to identify TB transmission hotspot areas within a defined community, and leverage that information to design and advance effective, and efficient TB case-finding interventions.

Furthermore, this study aims to identify undetected TB, to help understand the contribution of undiagnosed subclinical TB to community transmission, the latter being critical to interrupting TB transmission. The TARGET TB study is led by Prof Barun Mathema, Professor of Public Health at Columbia University in New York and study Co-PI, Prof Kogieleum Naidoo, CAPRISA Deputy Director and Head of the TB-HIV Treatment Research Programme.



Prof Barun Mathema

“This study adopts a novel approach of linking transmission dynamics to detecting undiagnosed and subclinical community-level TB,” says Prof Naidoo. “The rapid identification and treatment of infectious individuals with tuberculosis is central to breaking the chain of TB transmission as 40% of incident TB cases globally remain undiagnosed each year, contributing to delayed initiation of treatment, prolonged infectiousness, and ongoing TB transmission, explained Prof Kogie Naidoo. “Undiagnosed cases include symptomatic and asymptomatic TB patients who have not sought care or are missed by the health system, whose potential to transmit TB is unknown.”



Prof Kogie Naidoo



Visitors to CAPRISA

On 29th March Prof Quarraisha Abdool Karim, CAPRISA's Associate Scientific Director hosted officials from the German Embassy. Dr Susanne Kieffer, Head of Education and Research and Ms Elke Wolff, Deputy Head of Cooperation at the Embassy. Abdool Karim provided an overview of CAPRISA's core scientific research programmes and highlighted key research studies on HIV, TB and Covid-19.

CAPRISA's Data Management and Statistics, and Information Technology teams hosted DF/Net Research, Inc. representatives Busisiwe Mpila, Business Development Representative in Africa and Gavin Robertson, Director of Biometrics on 10 March. Discussions focused on the latest technology advancements in healthcare to strengthen CAPRISA's data management systems.



Left Photo (L-R): Ms Elke Wolff, Deputy Head of Cooperation of the Embassy of the Federal Republic of Germany; Prof Salim Abdool Karim, CAPRISA Director; Dr Susanne Kieffer, Head of Education and Research of the Embassy of the Federal Republic of Germany

Right Photo: Front row (L-R): Ms Indra Grigalonyte, Clinical Data Encoder; Dr Nonhlanhla Yende-Zuma, Head of Statistics and Data Management; Ms Precious Radebe, Senior Data Manager; Ms Busisiwe Mpila, Mr Gavin Robertson; and Mr Sibusiso Mbhele, System Engineer.

Back row: (L-R): Mr Khodani Ramakulukusha, Data Manager and Mr Mxolisi Mahlangu, Data co-ordinator.



Ivy to serve as KZN Research Sector representative on provincial AIDS Council

We congratulate Ms Ivy Fikelephi Kaunda (*in the photo*) Community Liaison Officer at the CAPRISA eThekweni Research Clinic (ECRS) on her appointment as the Organiser of the KwaZulu-Natal (KZN) Provincial Council on AIDS Research Sector chaired by the Premier of KwaZulu-Natal.

The KZN Provincial Council on AIDS is the coordinating body of the HIV & AIDS, STIs and TB response in the province. As the research sector organiser, Kaunda is responsible for organising campaigns and interventions



on scientific discoveries, science symposiums, and educational outreach in HIV, TB, and STI's in communities.

Kaunda joined CAPRISA in 2009 as a Counsellor/ Recruiter and was appointed as the site Community Liaison Officer in the Prevention and Vaccine unit at the ECRS. She supports the Community teams and leads the planning and organisation of community engagement events.



A selection of scientific papers published in 2022

12 **Naidoo K, Moodley MC, Hassan-Moosa R, Dookie N, Yende-Zuma N, Perumal R, Dawood H, Mvelase NR, Mathema B, Abdool Karim SS.** Recurrent subclinical tuberculosis among ART accessing participants: Incidence, clinical course, and outcomes. *Clinical Infectious Diseases* 2022. doi: 10.1093/cid/ciac185. <https://pubmed.ncbi.nlm.nih.gov/35247054/>

13 **Naranbhai V, Pernat CA, Gavralidis A, St Denis KJ, Lam EC, Spring LM, Isakoff SJ, Farmer JR, Zubiri L, Hobbs GS, How J, Brunner AM, Fathi AT, Peterson JL, Sakhi M, Hambelton G, Denault EN, Mortensen LJ, Perriello LA, Bruno MN, Bertaux BY, Lawless AR, Jackson MA, Niehoff E, Barabell C, Nambu CN, Nakajima E, Reinicke T, Bowes C, Berrios-Mairena CJ, Ofoman O, Kirkpatrick GE, Thierauf JC, Reynolds K, Willers H, Beltran WG, Dighe AS, Saff R, Blumenthal K, Sullivan RJ, Chen YB, Kim A, Bardia A, Balazs AB, Iafate AJ, Gainor JF.** Immunogenicity and Reactogenicity of SARS-CoV-2 Vaccines in Patients With Cancer: The CANVAX Cohort Study. *Journal of Clinical Oncology* 2022; 40(1):12-23.

14 **Naranbhai V, Viard M, Dean M, Groha S, Braun DA, Labaki C, Shukla SA, Yuki Y, Shah P, Chin K, Wind-Rotolo M, Mu XJ, Robbins PB, Gusev A, Choueiri TK, Gulley JL, Carrington M.** HLA-A*03 and response to immune checkpoint blockade in cancer: an epidemiological biomarker study. *Lancet Oncology* 2022; 23(1):172-184.

15 Cele S, Jackson L, Khoury DS, Khan K, Moyo-Gwete T, Tegally H, San JE, Cromer D, Scheepers C, Amoako DG, Karim F, Bernstein M, **Lustig G, Archary D**, Smith M, Ganga Y, Jule Z, Reedoy K, Hwa SH, Giandhari J, Blackburn JM, Gosnell BI, **Abdool Karim SS**, Hanekom W; NGS-SA; COMMIT-KZN Team, von Gottberg A, Bhiman JN, **Lessells RJ**, Moosa MS, Davenport MP, **de Oliveira T, Moore PL**, Sigal A. Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. *Nature* 2022;602(7898):654-656.

16 Cele S, Karim F, Lustig G, San JE, Hermanus T, Tegally H, Snyman J, Moyo-Gwete T, Wilkinson E, Bernstein M, Khan K, Hwa SH, Tilles SW, Singh L, Giandhari J, Mthabela N, Mazibuko M, Ganga Y, Gosnell BI, **Abdool Karim SS**, Hanekom W, Van Voorhis WC, Ndung'u T; COMMIT-KZN Team, **Lessells RJ, Moore PL**, Moosa MS, **de Oliveira T**, Sigal A. SARS-CoV-2 prolonged infection during advanced HIV disease evolves extensive immune escape. *Cell Host Microbe* 2022;30(2):154-162.

17 Mielke D, Stanfield-Oakley S, Borate B, Fisher LH, Faircloth K, Tuyishime M, Greene K, Gao H, **Williamson C, Morris L**, Ochsensbauer C, Tomaras G, Haynes BF, Montefiori D, Pollara J, deCamp AC, Ferrari G. Selection of HIV Envelope strains for standardized assessments of vaccine-elicited antibody-dependent cellular cytotoxicity (ADCC)-mediating antibodies. *Journal of Virology* 2022; 96(2):e0164321.

18 **Dookie N, Padayatchi N, Naidoo K.** Tuberculosis Elimination in the Era of COVID-19: A Moving Target. *Clinical Infectious Diseases* 2022; 74(3):509-510.

19 Spooner E, Reddy S, Ntoyanto S, Sakadavan Y, Reddy T, **Mahomed S, Mlisana K**, Dlamini M, Daniels B, Luthuli N, Ngomane N, Kiepiela P, Coutsooudis A. TB testing in HIV-positive patients prior to antiretroviral treatment. *International Journal of Tuberculosis and Lung Disease* 2022; 26(3):224-231.

20 van Dorsten RT, Reh L, Trkola A, **Morris L, Moore PL.** Single-chain variable fragments of broadly neutralizing antibodies prevent HIV cell-cell transmission. *Journal of Virology* 2022; 96(4):e0193421. doi: 10.1128/jvi.01934-21.

21 Zayats R, Murooka TT, **McKinnon LR.** HPV and the Risk of HIV Acquisition in Women. *Frontiers in Cellular and Infection Microbiology* 2022; 12:814948. doi: 10.3389/fcimb.2022.814948.

22 Mulenga H, Fiore-Gartland A, Mendelsohn SC, Penn-Nicholson A, Mbandi SK, Borate B, Musvosvi M, Tameris M, Walz G, **Naidoo K**, Churchyard G, Scriba TJ, Hatherill M; CORTIS Study Team. The effect of host factors on discriminatory performance of a transcriptomic signature of tuberculosis risk. *EBioMedicine* 2022; 77:103886. doi: 10.1016/j.ebiom.2022.103886.

