



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Newsletter

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Study findings show that genital inflammation can shape genital antibody responses

In this Issue

Our feature story this month highlights the study, 'Higher mucosal antibody concentrations in women with genital tract inflammation' published in *Scientific Reports-Nature Portfolio*.

We pay tribute to Prof Zena Stein's extraordinary legacy on pages 2, 3 and 4.

On page 5, we report on three events to commemorate World AIDS Days co-hosted by CAPRISA, the China CDC, the Treatment Action Campaign and the National Research Foundation.

On page 6 we announce the Moderna mRNA vaccine trials—the Ubuntu study which gets underway at two CAPRISA research sites; and the appointment of research pulmonologist, Dr Rubeshan Perumal.

We congratulate CAPRISA's Statistics & Data Management team on their Excellence award; and Prof Salim Abdool Karim who received the UNISA's Chancellor's Calabash Public Servant award, on page 7.

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Using vaginal specimens from CAPRISA's 004 and 008 clinical trials, this article published in *Scientific Reports-Nature Portfolio* entitled 'Higher mucosal antibody concentrations in women with genital tract inflammation' by CAPRISA's post-doctoral fellow Dr Parveen Sobia and principal investigator, Dr Dersere Archary provides further dissection on the interaction between pre-existing genital inflammation and genital antibodies.

Genital inflammation modifies HIV risk. However, there is a paucity of data on whether genital inflammation can modify antibody profiles and affect the antibodies' ability to block infection or impact vaccine efficacy in especially vulnerable populations of young women in sub-Saharan Africa.

Women with genital inflammation gauged by elevated levels of genital cytokines had significantly higher levels of genital IgG subclasses (IgG1, IgG3 and IgG4) and isotype IgM compared to women without inflammation. We also observed

strong significant associations between cytokines defining genital inflammation and antibodies in the genital tract. Our findings suggest that genital inflammation can shape genital antibody responses.

Therefore, from a biological perspective, it is important to understand if pre-existing genital inflammation presets the antibody footprint at the vulnerable sexual surface that may undermine HIV prevention strategies including both PrEP and vaccines.

The researchers iterate that further investigation is required to verify a plausible link between the local inflammatory milieu and the effect on genital antibodies and their functions.

- Parveen Sobia (PhD)

For further reading see: Sobia P, et al. Higher mucosal antibody concentrations in women with genital tract inflammation. *Scientific Reports* 2021; 11:23514. <https://doi.org/10.1038/s41598-021-02954-0>

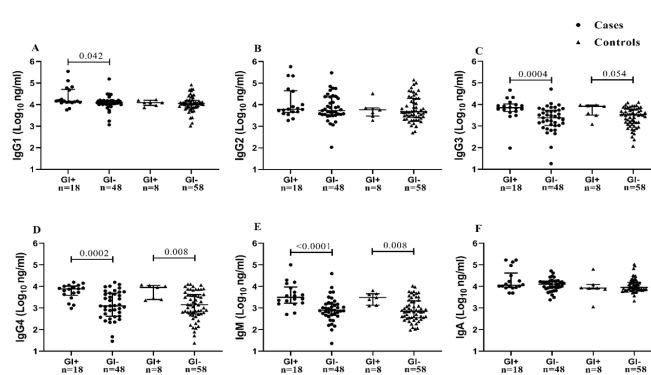


Figure. Comparison of mucosal IgG subclasses and isotypes in women stratified for presence of genital inflammation (GI+) or absence of genital inflammation (GI-) within cases [GI+ (n = 18) and GI- (n = 48)] and controls [GI+ (n = 8) and GI- (n = 58)] pre-HIV infection. Each data point represents an individual sample, the line-bars represents medians and interquartile ranges. Black circle represents cases and black triangle represents controls.



Professor Zena Stein – a champion for social justice and an extraordinary *epidemiologist*

It was the moralistic drive to help others that underpinned all the work Stein did, recognising the need to address inequality as a core means to improve health.

7 July 1922 – 7 November 2021

It is with deep sadness that we learned of the passing of Zena Stein – our family friend, a friend of CAPRISA and mentor who passed away peacefully on 7th November this year leaving a formidable legacy of her life dedicated to science and social justice.

Stein was an extraordinary leader in the field of public health and epidemiology, with a deep and unwavering commitment to improve the health of the most vulnerable. Zena Stein together with her husband, Mervyn Susser, formed the Susser-Stein duo that built an impressive legacy of evidence-based advocacy to highlight and address inequalities in society.

Stein was born on 7 July 1922 in Durban, South Africa, completed her primary schooling at Gordon Road Girl’s School, and high school at Durban Girls High in Glenwood. She began her career by studying history at the University of Cape Town, graduating with a Master of Arts degree. It was after serving as a nurse during World War II and seeing the toll of the war that Stein and Mervyn Susser (who she knew from childhood) decided to enter a profession where she could make a difference to society. She began studying medicine in 1945 at the University of Witwatersrand in Johannesburg, motivated by the goal of helping poorer and more disadvantaged populations.

In [the citation for her an honorary doctorate from Wits](#), Stein was described as “one of the most notable medical graduates of the University of Witwatersrand.” It was the moralistic drive to help



Zena Stein. Photo credit: New York Times

others that underpinned all the work Stein did, recognising the need to address inequality as a core means to improve lives of the most vulnerable whether it was in apartheid South Africa, among coal miners in the United Kingdom or mental health issues; or reconciling grandmothers with lost grandchildren in Latin America or the gap in women-initiated technologies in response to HIV.

[In a 2003 interview](#), about racial disparities in health outcomes in South Africa, Stein recalled: “There was a mismatch between our formal lectures and what we knew was happening in our own country. We knew something was wrong and we would have to go beyond our formal training to address it.”

Stein was a pioneer in the field we have now come to know as epidemiology, which at the time of her studies didn’t exist. Acknowledging the severe gaps in the curriculum offered, Stein and Susser sought to bring in a more human element to health and began joining in study groups outside of school.

She wanted more than what textbooks could offer, wanting to learn more about diseases that were having a direct impact on people right on their doorstep. Stein didn’t want to learn about “public health” in the abstract — but rather how to actively help prevent problems that people were facing at a community level.

This is eloquently captured in the 1955 Susser-Stein article in *The Lancet* entitled “*Medical care in a South African township*” (*The Lancet* 1955; 265: 912–915). Consequently, much of Stein and Susser’s early work in the 1950s in South Africa laid the foundation for robust scientific research on maternal and child health and was central in creating awareness about the impact of environmental factors on reproduction.

Her approach to science has been credited as making science more practically useful while maintaining rigour and academic robustness. She never compromised on academic rigour, even when highlighting a social problem, as illustrated by the article published in 1959 in *The Lancet* on the problem of Ortho-cresyl phosphate poisoning in Cato Manor township in Durban.

Stein and Susser left South Africa for political reasons but continued their fight against the inequalities in health through their research and the creation of CHISA (Committee for Health in South Africa). Stein never lost her love for South Africa — or its treats. The Abdool Karims would always visit her in New York bearing Peppermint Crisp chocolate bars and rooibos tea, much to her delight.

Continued on page 3...



Professor Zena Stein – a champion for social justice and an extraordinary *epidemiologist*

Hers was a life well lived and full of meaning right to the very end! Hamba kahle Zena....

We will always remember Stein for her warmth as this gentle, caring, highly energetic, and friendly person who always had time for all with whom she met.

Stein (together with Mervyn Susser) used to go swimming every morning on their annual visits to South Africa that they resumed post-democracy. Indeed, Zena's passion for swimming comes from her years of coaching by the famous swimmer Rachel Finlayson and goes back to her days in primary school at Gordon Road Girl's Primary School.

Stein had great insight in applying for an US NIH grant to establish the Columbia University-Southern African Fogarty AIDS International Research and Training Program in 1994 that laid the foundations for building the science capacity in South Africa to enhance responses to HIV and TB. In fact, there are few HIV/TB organisations in South Africa that do not have at least one scientist from this programme; often in a leadership role.

Stein was an inspiration to all who were fortunate to have met her and privileged to have been mentored by her. A true visionary, brilliant scientist, exemplary and inspiring role model for women scientists and for global health practitioners.

Post-apartheid, when Stein and Susser were in their 70s they returned to South Africa at the request of the Abdool Karims to serve as co-Directors of the Africa Centre for Health and Population Studies in northern KwaZulu-Natal while the search for a Director was underway.

Indeed, the University of KwaZulu-Natal recognised the phenomenal

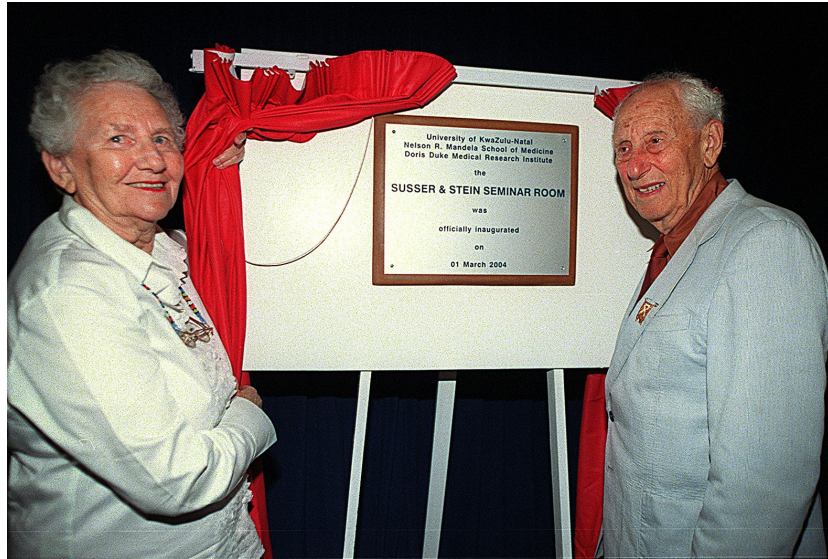


Photo: (L-R) Professor Zena Stein & Professor Mervyn Susser unveil the plaque at the naming of the Susser & Stein Seminar Room, in the Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, on 1 March 2004.

contributions that they made to primary healthcare and named a lecture hall in the Doris Duke Medical Research Institute at the Nelson R Mandela School of Medicine the 'Susser-Stein Seminar Room'.

Determined to improve the lives of women and children, the humble start to her medical career began with serving the disadvantaged community in Alexandra, South Africa and ended in the hallowed halls of Columbia University where she was: Professor and Head of the Department of Epidemiology and Professor in Psychiatry at Columbia University and co-director of the HIV Center for Clinical and Behavioural Studies at the New York State Psychiatric Institute.

Stein received numerous accolades for her many contributions to the field of epidemiology.

She received the John Snow Award from the American Public Health Association, and honorary doctorates from Columbia University in the US and the University of Witwatersrand in South Africa and the SAMRC President's Award.

Her unwavering legacy of social justice will always be remembered.

Our thoughts are with her son Ezra Susser, and daughters Ida Susser and Ruth King, her grandchildren, and great grandchildren.

Hers was a life well lived and full of meaning right to the very end!

Hamba kahle Zena....

- Salim & Quarraisha Abdool Karim



Professor Zena Stein – a champion for social justice and an extraordinary *epidemiologist*

A selection of photographs captures Professor Zena Stein’s memorable moments with Professor Salim and Quarraisha Abdool Karim and CAPRISA



Photo: (left): Zena Stein and Mervyn Susser visiting the Abdool Karims when they were students in 1988 in New York.; (photo right): Zena Stein participates in discussion at the 2015 CAPRISA Strategic Planning meeting held in , Durban, South Africa.



Photo: (left): Photo (L-R): Dr Deborah Birx, former US Ambassador; Prof Salim Abdool Karim Director CAPRISA; Prof Zena Stein; Prof Quarraisha Abdool Karim Associate Scientific Director, CAPRISA; Miss Aisha Abdool Karim Senior Journalist, Bhekisisa; and Mr Mitchell Warren Executive Director, AVAC. Photo: (right): Prof Kogie Naidoo Deputy Director, CAPRISA; Dr Ida Susser, Prof Zena Stein; and Prof Ayesha Kharsany Senior Scientist, CAPRISA.



Photo: (left) Zena Stein & Mervyn Susser with Salim Abdool Karim at the Nelson R Mandela School of Medicine; (centre); a portrait of Zena & Mervyn in the Susser & Stein Seminar Room; and Zena Stein delivers an address at the CAPRISA awards dinner in 2015.



World AIDS Day - A call for global solidarity, community partnerships & leadership to end AIDS

End inequalities. End AIDS. End pandemics

A clarification and unanimous call for strong leadership, political will, global solidarity, and a bold plan to attain the UNAIDS target to end AIDS was made by eminent scientists, government officials and civil society, at three events co-hosted by CAPRISA to commemorate World AIDS Day. The events were held in partnership with the Chinese Centres for Disease Control (China CDC), the Treatment Action Campaign in South Africa and the National Research Foundation (NRF).

The China CDC and CAPRISA co-hosted a webinar on Monday 29th November which brought together the world's foremost HIV scientists and HIV activist, Ms Sibongile Tshabalala Chairperson of TAC. Scientists acknowledged the significant gains made in treatment and raised concern that HIV prevention measures was 'lagging' behind, with an estimated 1.5m new infections in 2020. They called for a rejuvenation of the strategy in line with realities on the ground. [Watch the webinar here](#)

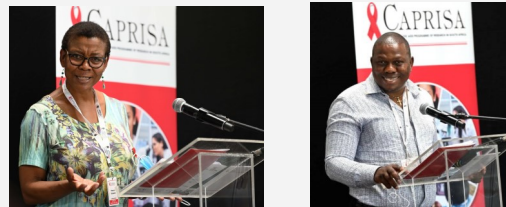
TAC and CAPRISA and Vulindlela Community leadership co-hosted a community-based event on Tuesday, 30th November at CAPRISA's Vulindlela Research Clinic. The event brought together participants, community leadership and scientists who recognised the power of partnerships, excellence and science in responses to HIV to date and called for renewed effort to enhance responses to HIV and Covid-19. [Watch the video recording here](#)

The NRF hosted the NRF Science for Society World AIDS Day lecture on Wednesday, 1st December in partnership with CAPRISA themed: HIV/AIDS and COVID-19 – navigating the intersect of the two pandemics. The lecture explored lessons learned from the Covid-19 vaccine development; the HIV vaccine research; the interplay between HIV/AIDS and COVID-19 and its impact on communities; and the inequities that have emerged from the pandemics. Speakers included: Salim Abdool Karim, Penny Moore (NICD), (in the bottom photo) Mark Heywood (Maverick Citizen Editor), (in the top photo) and Patrick Mdletshe (CAPRISA Head of Community Programmes). [Watch the lecture here](#)



Speakers at the WAD webinar co-hosted by the China CDC and CAPRISA. Top row (L-R): Prof Adeeba Kamaluzaman President of the International AIDS Society; Prof Peter Piot, Handa Professor of Global Health at the London School of Hygiene and Tropical Medicine; Prof George Gao, Director General of the Chinese Centre for Disease Control and Prevention (China CDC); Ms Sibongile Tshabalala, Chairperson of the Treatment Action Campaign (TAC) South Africa;

Bottom row (L-R): Prof Salim S. Abdool Karim, Director, CAPRISA; Dr Peter Hayward Editor-in-Chief, The Lancet HIV (Moderator); Prof Quarraisha Abdool Karim, Associate Scientific Director, CAPRISA; and Prof Mengjie Han, Director National Centre for AIDS/STD Control and Prevention, at the China CDC.



Group photo top: (L-R): Community leadership Mrs. Sithole & Reverend Sithole; Ms Marie Francoise Marie-Nelly Country Director Africa, The World Bank; Dr Reshma Sheoraj Member of the Board at the World Bank Group; Prof Quarraisha Abdool Karim, CAPRISA Associate Scientific Director; Mr Patrick Mdletshe, CAPRISA Head of Community Programmes 2nd Row: Photo (L): Dr Mamosa Tshabalala, Acting Chief Director Strategic Health Programmes, Department of Health (R): Pastor Mlotshwa, Chairperson, CAPRISA Community Research Support



CAPRISA enrolls first participant into the CoVPN 3008 ‘Ubuntu’ trial for people living with HIV

On 2 Dec 2021, CAPRISA enrolled the first participant into the Ubuntu trial which evaluates the efficacy of the Moderna mRNA-1273 vaccine in people living with HIV.

“The Ubuntu study will provide safety data to regulators, assess correlates of protection from COVID-19 and it will answer important questions on mRNA vaccine dosage regimens among people living with HIV,” explained Dr Nigel Garrett, co-Chair of the study and Head of Vaccine and HIV Pathogenesis Research at CAPRISA (*left in the photo*). It is also the first study to evaluate the efficacy of Moderna mRNA-1273 against the Omicron variant.

The trial is being conducted in Eastern and Southern African regions and is expected to enroll about 14,000 volunteers at 54 clinical research sites in South Africa, Botswana, Zimbabwe, Eswatini, Malawi, Zambia, Uganda, and Kenya, where adult HIV prevalence ranges from 4.5% to 27%.

The study aims to enroll 12,600 people living with HIV and 1,400 who are HIV-negative. About 5,000 of the volunteers will have previously had COVID-19, with confirmation based on blood antibody tests done at initial enrollment. Study participants living with HIV will receive optimal HIV treatment through the course of the trial.



(L): Dr Nivashnee Naicker Research Clinician & Dr Nigel Garrett at the CAPRISA eThekweni Research Clinic.

All participants will receive the Moderna vaccine, but dosages and schedules will vary depending on previous SARS-CoV-2 infection. Those with past infection will receive fewer doses of vaccine, based on evidence that prior immunity may be markedly enhanced by vaccination.

Research pulmonologist joins CAPRISA

CAPRISA welcomes specialist physician and research pulmonologist, Dr Rubeshan Perumal (*left in the photo*), who will join CAPRISA as a senior scientist in the Treatment Research Programme. Perumal will provide mentoring to research clinicians and fellows and advance the treatment scientific agenda. He led the Post-COVID-19 Lung Disease clinical service and research programme at Groote Schuur Hospital and at the University of Cape Town’s Centre for Lung Infection and Immunity (UCT) and has been a panellist on the WHO Working Group on Care Pathways for Long COVID. He presently serves as a consultant pulmonologist at Inkosi Albert Luthuli Central Hospi-



tal. He holds master’s degrees in Public Health (MPH), Internal Medicine (MMed), and Pulmonology (MPhil in Pulmonology) and is currently completing a PhD focused on the pharmacokinetic-pharmacodynamic optimisation of tuberculosis treatment.

Perumal joined CAPRISA as a clinical research placement in 2006, “to explore the fascinating world of clinical research and to gain a more objective understanding of clinical problems”, he says. “Fifteen years later, I am immensely grateful for the countless opportunities to expand my skills...CAPRISA continues to push the boundaries of medicine, and is overflowing with inspirational scientific capacity and leadership.”

He is a past recipient of the Fogarty International Clinical Research Scholarship, the South African Thoracic Society Research Fellowship and was named a Global Young Physician Leader by the Inter Academy Partnership.



CAPRISA Data Management team recognised for service excellence

CAPRISA's Statistics and Data Management department served as the Data Management Centre (DMC) providing data management and statistical support for the PEPFAR PROMOTE (**P**ROMise **O**ngoing **T**reatment **E**valuation) study.

At the final PROMOTE annual meeting held in Kampala, Uganda on 15th -16th November, the DMC team received an award in recognition of the excellent statistics data management services provided. The presentation was made by study protocol co-chairs Dr Taha Taha and Dr Mary Glenn Fowler.

The PEPFAR PROMOTE study was a follow-up study to the IMPAACT PROMISE (Promoting Maternal and Infant Survival Everywhere) clinical trial.

During the 5-year study a total of 4619 mothers and children were enrolled in 8 PROMOTE sites across 4 African countries (Uganda, Malawi [2 sites], Zimbabwe [3 sites] and South Africa [2 sites]).

"A primary aim of the study was to investigate the long-term impact of maternal ART interventions through extended follow-up of HIV-infected wom-



Seated L-R ; Dr Nonhlanhla Yende-Zuma: Head of Statistics and Data Management and Ms Precious Radebe: Data Manager Standing L-R; Mr Mthobisi Zondi: Junior Statistician, Ms Indra Grigalionyte: Clinical Data Encoder and Mr Aslam Jeewa: Chief Data Manager

en and their children," explained Dr Nonhlanhla, head of Statistics & Data Management at CAPRISA.

CAPRISA Director awarded UNISA's 2021 Chancellor's Public Servant Award



UNISA.

We congratulate Professor Salim Abdool Karim, CAPRISA's Director, who received the University of South Africa's (UNISA) Chancellor's Calabash 2021 Public Servant Award on Friday, 26 November 2021.

"Unisa takes pride in its association with people who continue to shape futures in the service of humanity and in supporting education," said Prof Puleng LenkaBula, Vice-Chancellor of

The presentation was made by the Chancellor of the University of South Africa (UNISA), His Excellency Dr Thabo Mbeki who hosted the Chancellor's Calabash Dinner. The Chancellor's Calabash Awards are Unisa's way of recognising its alumni and/or persons who have shown exemplary achievements and service to our society, said the Vice-Chancellor.

Penny Moore delivers the 12th James Gear Lecture

Prof. Penny Moore at the NICD delivered the virtual 12th James Gear Lecture, entitled: "Pivoting from HIV vaccine research to COVID - Lessons for the next pandemic", on 15 November 2021. This annual lecture is hosted by the Poliomyelitis Research Foundation (PRF) in memory of one of South Africa's pioneers in the field of virology and infectious, James Henderson Sutherland Gear, in support of research and knowledge sharing aimed at furthering the development of Medical Virology in South Africa.



Moore highlighted how investments in HIV vaccine research had enabled the rapid contribution of SA scientists to the COVID-19 research effort, and the need to translate the same sense of urgency back to HIV prevention research.



A selection of scientific papers published in 2021

- 65 **Sobia P, Pillay T, Liebenberg LJ, Sivo A, Mansoor LE, Osman F, Passmore JA, Abdool Karim Q, Abdool Karim SS, Baxter C, McKinnon LR.** Higher mucosal antibody concentrations in women with genital tract inflammation. *Scientific Reports* 2021; 11:23514. <https://doi.org/10.1038/s41598-021-02954-0>
- 66 **Lewis L, Sookrajh Y, Gate K, Khubone T, Maraj M, Mkhize S, Hermans LE, Ngobese H, Garrett N, Dorward J.** Differentiated service delivery for people using second-line antiretroviral therapy: clinical outcomes from a retrospective cohort study in KwaZulu-Natal, South Africa. *Journal of the International AIDS Society* 2021; 24:e25802. doi: 10.1002/jia2.25802.
- 67 **San JE, Ngcapu S, Kanzi AM, Tegally H, Fonseca V, Giandhari J, Wilkinson E, Nelson CW, Smidt W, Kiran AM, Chimukangara B, Pillay S, Singh L, Fish M, Gazy I, Martin DP, Khanyile K, Lessells R, de Oliveira T.** Transmission dynamics of SARS-CoV-2 within-host diversity in two major hospital outbreaks in South Africa. *Virus Evolution* 2021; 7(1):veab041. doi: 10.1093/ve/veab041.
- 68 **De Lay PR, Benzaken A, Abdool Karim Q, Aliyu S, Amole C, Ayala G, Chalkidou K, Chang J, Clayton M, Couto A, Dieffenbach C, Dybul M, El Sadr W, Gorgens M, Low-Ber D, Mesbah S, Saveedra J, Sirinirund P, Stover J, Syarif O, Taslim A, Thiam S, Njenga LW, Ghys PD, Izazola-Licea JA, Frescura L, Lamontagne E, Godfrey-Faussett P, Fontaine C, Semini I, Hader S.** Ending AIDS as a public health threat by 2030: Time to reset targets for 2025. *PLoS Medicine* 2021; 18(6):e1003649. doi: 10.1371/journal.pmed.1003649.
- 69 **Jewanraj J, Ngcapu S, Osman F, Ramsuran V, Fish M, Mtshali A, Singh R, Mansoor LE, Abdool Karim SS, Abdool Karim Q, Passmore J-A S, Liebenberg LP.** Transient association between semen exposure and biomarkers of genital inflammation in South African women at risk of HIV infection. *Journal of the International AIDS Society* 2021; 24:e25766. doi: 10.1002/jia2.25766
- 70 **Molatlhegi RP, Ngcobo S, Liebenberg LJP, Ngcapu S, Mabhula A, Leslie A, Mchunu N, Zondi MM, Adamson JH, Govender K, Samsunder N, Abdool Karim SS, Abdool Karim Q, Passmore JS, Sivo A, McKinnon LR.** Genital and systemic immune effects of the injectable, contraceptive norethisterone enanthate (NET-EN), in South African women. *American Journal of Reproductive Immunology* 2021; 86(2):e13411. doi: 10.1111/aji.13411.
- 71 **Abdool Karim Q.** Enhancing HIV Prevention with Injectable Preexposure Prophylaxis. *New England Journal of Medicine* 2021; 385(7):652-653.
- 72 **Garrett N, Mtshali A, Osman F, Masson L, McKinnon LR, Singh R, Mitchev N, Ngobese H, Kharsany ABM, Abdool Karim SS, Mlisana K, Passmore JA, Rompalo A, Mindel A, Liebenberg L.** Impact of point-of-care testing and treatment of sexually transmitted infections and bacterial vaginosis on genital tract inflammatory cytokines in a cohort of young South African women. *Sexually Transmitted Infections* 2021; 97(8):555-565.
- 73 **Gengiah S, Naidoo K, Mlobeli R, Tshabalala MF, Nunn AJ, Padayatchi N, Yende-Zuma N, Taylor M, Barker PM, Loveday M.** A Quality Improvement Intervention to Inform Scale-Up of Integrated HIV-TB Services: Lessons Learned From KwaZulu-Natal, South Africa. *Global Health: Science and Practice* 2021; 9(3):444-458.
- 74 **Abdool Karim SS and Abdool Karim Q.** Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic. *Lancet* 2021. S0140-6736(21)02758-6. doi: 10.1016/S0140-6736(21)02758-6.
- 75 **Ntombela NP, Kharsany ABM, Soogun A, Yende-Zuma N, Kohler HP, McKinnon LR.** Prevalence and Risk Factors for HIV Infection Among Heterosexual Men Recruited from Socializing Venues in Rural KwaZulu-Natal, South Africa. *AIDS Behavior* 2021; 25(11):3528-3537.

**continuation from previous newsletter*



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