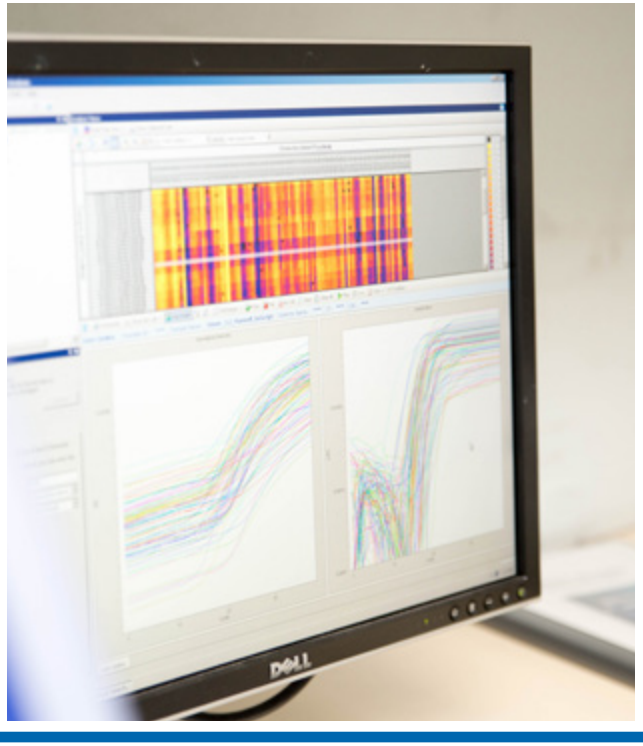
20 YEARS OF TB RESEARCH | satvi

TOWARDS A WORLD WITHOUT TB

University of Cape Town • iYunivesithi yaseKapa • Universiteit van Kaapstad

ANNUAL REPORT 2021



vision and mission

Our Vision

A World Without TB

Our Mission

Innovative and High-Quality
TB Vaccine Research to impact
the Global Epidemic

Our Values

Innovation I Respect I Employee
Recognition | Accountability
Communication | Commitment | Honesty

Vaccines

Drugs

Diagnostics

Epidemiology

Immunology

www.satvi.uct.ac.za

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director's foreword

2021 was a headline year that marked the 20th anniversary of the first SATVI clinical trial and the start of a diverse TB research programme that spanned epidemiology, diagnostics, therapeutics, immunology and vaccines over two decades. Research highlights amid the COVID-19 pandemic included participation in two efficacy trials of vaccines against SARS-CoV-2, and a key role as the Cape Winelands regional site for the Sisonke implementation trial of a SARS-CoV-2 vaccine for health workers. Despite the challenges of accessing health facilities and working in the community during COVID-19 restrictions, six clinical trials of five different TB vaccines (VPM-1002; BCG; MTBVAC; H56:IC31 and M72/AS01E) continued recruitment of infant, adolescent, adult, and TB and HIV-co-infected populations.

A notable publication in the field of TB therapeutics reported the success of a four-month treatment regimen in an ACTG network trial. Other high-impact publications reported findings from TB biomarker studies, including several arising from the CORTIS project, and this research focus is reflected in ongoing studies of novel diagnostic and predictive biomarkers in children and adults.

Our research is made possible through a strong partnership with the Cape Winelands community, which is slowly recovering from the social and economic impacts of the COVID-19 pandemic, but the effects of that pandemic on the burden of TB in our community are yet to be understood. For helping SATVI to pursue our vision of A World Without TB during these difficult times, we salute our participants, their families, and our staff, and we remain grateful for the continued support of our collaborators and funders.

Professor Mark Hatherill
Director, SATVI

celebrating 20 years of TB research

Click *here* to download the SATVI History booklet.

On 26 March 2021 SATVI celebrated its 20th year, commemorating the day on which the first participant was enrolled in the first TB vaccine trial conducted at SATVI: a randomised controlled trial of intradermal vs percutaneous BCG vaccination (*Hawkridge et al., 2008*).

SATVI has made a substantial contribution to the global **TB vaccine** development effort, including key **epidemiological studies** that have laid the groundwork for the development of new TB biomarkers; **immunology studies** that have informed potential correlates of vaccine-mediated protection against TB; the first infant efficacy trial of a novel TB vaccine candidate in 50 years; and two pivotal efficacy trials of BCG revaccination and the sub-unit vaccine candidate M72/AS01$_E$. Our strong partnerships with the Breede Valley community, the Departments of Health and Education, and our collaborators and funders have been critical to that effort.

The 20th Birthday event was preceded by a year-long effort to capture the early history of SATVI, which involved interviewing former staff, students and stakeholders for their recollections, the highlights of which were recorded in a commemorative booklet available on the SATVI website.

First participant in the BCG RCT trial vaccinated

governance

PROFESSOR MARK HATHERILL, DIRECTOR

Dr Mark Hatherill (MD, FCPaed) is a specialist paediatrician and clinical triallist who is active in the design and implementation of innovative trials of new TB vaccines and TB preventive therapy strategies, through several consortia. His academic focus includes evaluation of biomarker-targeted TB interventions, and clinical trials of novel TB vaccine candidates. He is a full member of the Institute of Infectious Disease & Molecular Medicine (IDM) at the University of Cape Town (UCT), and lead investigator of the Regional Prospective Observational Research in Tuberculosis (RePORT) South Africa consortium.

Dr Hatherill is funded by institutional research grants from the Gates Medical Research Institute, the SA Medical Research Council (SAMRC), the US National Institutes of Health and Civilian Research and Development Foundation (CRDF), the European & Developing Countries Clinical Trials Partnership, and Aeras/IAVI.

PROFESSOR TOM SCRIBA,
DEPUTY DIRECTOR IMMUNOLOGY

Dr Tom Scriba (PhD) directs the Clinical Immunology Laboratory at SATVI. He was trained in biological sciences at Stellenbosch University and obtained a DPhil (PhD) in T-cell immunology at Oxford University. He returned to South Africa in 2006 to complete a postdoctoral fellowship in paediatric and clinical immunology in TB and vaccinology at the IDM, UCT. Dr Scriba's research interests include immunopathogenesis of infectious disease, and in particular *M. tuberculosis*, development of immuno-diagnostics, development of novel TB vaccines, discovery of immune correlates of risk of TB disease and correlates of protection against M.tb infection and TB disease. Dr Scriba is a full member of the IDM and of the Collaboration for TB Vaccine Discovery of the Bill and Melinda Gates Foundation (BMGF), and is funded by competitive grants from the BMGF, the National Research Foundation (NRF), SAMRC, US National Institutes of Health (NIH) and the European Union.

DR MASOODA KASKAR,
CHIEF OPERATIONS OFFICER

Dr Masooda Kaskar joined SATVI's senior leadership team in 2016 to advance organisational excellence and drive innovation and growth. Her leadership experience spans the corporate, public and philanthropic sectors, with a focus on strategic business development, governance and operations. In her current role she is a key driver of SATVI's transformation efforts and risk management plans to ensure the growth and long-term sustainability of the organisation. Dr Kaskar previously occupied several senior leadership positions within the pharmaceutical industry. At Novartis she was instrumental in developing and implementing transformational growth plans that resulted in establishing Novartis's leadership position within the industry. She holds an MBChB degree from UCT and an MBA degree from UCT's Graduate School of Business.

MARWOU DE KOCK,
FIELD SITE MANAGER

Marwou de Kock holds a master's degree in Clinical Research Administration from UCT, as well as degrees in biomedical science and laboratory management. She has worked at SATVI since 2002 and has intricate knowledge of the site, the people and procedures in the laboratory, clinical operations, and community engagement. She helped establish the SATVI Field Site Laboratory and developed it into a world-class facility that received SANAS accreditation in 2010. Ms de Kock is responsible for managing the SATVI Field Site, overseeing and managing service delivery for all operations, and coordinating and implementing multiple research projects.

senior clinical research team

ASSOCIATE PROFESSOR ELISA NEMES, PRINCIPAL INVESTIGATOR & IMMUNOLOGIST

Dr Elisa Nemes completed a PhD in HIV-specific T-cell immunology in Italy and France in 2008. She then worked on paediatric immune responses to HIV and TB in Cameroon.

Dr Nemes joined SATVI in 2011, where she has been involved in basic immunology studies, development of immuno-diagnostics and clinical trials of new TB vaccines; studies of host correlates of risk of TB disease and correlates of protection from *M.tb* infection and TB disease in infants, adolescents and adults; and studies of BCG/TB immune reconstitution inflammatory syndrome (IRIS) in HIV+ children. She is funded by competitive grants from the US National Institutes of Health. Dr Nemes was promoted to Associate Professor ad hominem in 2019 and became a full member of the IDM in 2020.

DR MICHÈLE TAMERIS, CLINICAL INVESTIGATOR

Dr Michèle Tameris graduated from UCT with an MBChB degree in 1980. She worked for many years in the public health sector, in Cape Town and in Worcester. In 2003 she joined SATVI as a clinical researcher, and was promoted ad hominem to senior clinical researcher in January 2019. Since 2005 she has been an investigator on all 27 vaccine trials of nine candidate TB vaccines that have been conducted at SATVI, including 10 as Principal Investigator.

Dr Tameris has been awarded two Wellcome Trust International Engagement awards (2012 and 2014) for projects using drama to improve community understanding of TB research and remains actively involved in community engagement and advocacy programmes.

She is a member of the Stop TB Partnership Working Group on New Vaccines, leading the Advocacy sub-committee.

DR ANGELIQUE KANY KANY LUABEYA, CLINICAL INVESTIGATOR

Dr Angelique Kany Kany Luabeya graduated as a medical doctor in 1996 from the University of Kinshasa (Democratic Republic of Congo), and holds a master's degree in epidemiology from the London School of Hygiene and Tropical Medicine (LSHTM).

She joined SATVI in 2009 as a clinical investigator from the Africa Centre for Health and Population Studies at the University of KwaZulu-Natal, and has been involved as principal investigator in the implementation and conduct of clinical trials of several TB vaccines (AERAS C035-456, IDRI-TBVPx-203, VPM1002-ZA-2.13TB, BCG REVAX, and MTBVAC) in healthy adults and adolescents, TB patients and newborn infants. More recently she led as investigator on two COVID-19 vaccine trials, the ENSEMBLE study and the SISONKE trial, which vaccinated healthcare workers in South

Africa. She also contributed to the implementation of the NOVAVAX COVID-19 vaccine study.

Dr Luabeya has a research interest in healthcare systems and in the design and conduct of novel diagnostic and immunology studies. She is investigator on several studies – including TB case-finding by oral swab PCR, molecular confirmation of TB treatment and Mycobacterium tuberculosis correlates of risk using molecular epidemiology – conducted in collaboration with the University of Washington and the Columbia University Mailman School of Public Health. She has authored or co-authored several publications appearing in peer-reviewed journals.

DR JUSTIN SHENJE, CLINICAL INVESTIGATOR

Dr Shenje graduated as a medical doctor from the University of Zimbabwe in 2004, then completed a master's degree in clinical epidemiology at the University of Pretoria, before joining the SATVI team as a clinical investigator in 2015.

He has been investigator on two groundbreaking TB drug clinical trials, the A5343 and A5349 studies. The A5343 study showed that delamanid and bedaquiline, two new anti-TB drugs, can be safely combined in the treatment of MDR TB; and the A5349 study showed that a four-month rifapentine-based drug-sensitive TB regimen was non-inferior to the standard six-month drug-sensitive treatment regimen. He is principal investigator on a number of ongoing studies, including the A5400B study, which evaluates the effectiveness of the use of delamanid in TB prophylaxis of MDR TB household contacts; the A-055 study, which investigates the efficacy of the novel TB vaccine H56:IC31 for prevention of post-treatment TB recurrence; and two diagnostic studies, ENDxTB and CORTIS KIDS, which seek to find non-sputum-based diagnostic tests in household contacts above the age of 12 years and under the age of five years respectively.

DR SIMON MENDELSOHN, CLINICAL INVESTIGATOR

Dr Simon Mendelsohn graduated from the University of Cape Town as a medical doctor in 2011. On a Rhodes Scholarship, he read for two master's degrees at the University of Oxford, in Immunology (2015) and International Health and Tropical Medicine (2016), and obtained a Diploma in Tropical Medicine and Hygiene from the Royal College of Physicians (London).

Dr Mendelsohn joined SATVI on a PhD Fellowship in 2017 and works as a part-time clinical investigator. He has experience in HIV and TB clinical medicine; most recently with Médecins Sans Frontières, implementing an HIV and TB programme in Malawi prisons. He was awarded the NIH Fogarty HIV-associated TB Training Program Clinician Scientist PhD Fellowship in 2019, and the South African Medical Research Council Clinician-Researcher Programme PhD Fellowship in 2020.

DR NICOLETTE TREDOUX, CLINICAL INVESTIGATOR

Dr Nicolette Tredoux graduated from the University of Stellenbosch in 1998 with an MBChB degree. She worked for many years in the public and private sector in Worcester and Robertson, both as a general practitioner and as a research medical officer. She obtained a postgraduate diploma in occupational medicine at Stellenbosch University in 2015.

Dr Tredoux joined SATVI in 2021 as a clinical investigator.

research highlights

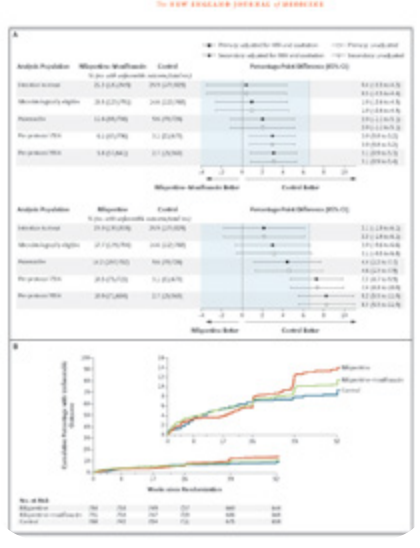
NEW TB REGIMENS AND TREATMENT

RIFAPENTINE-CONTAINING TREATMENT SHORTENING REGIMENS FOR PULMONARY TUBERCULOSIS: A RANDOMISED, OPEN-LABEL, CONTROLLED PHASE 3 CLINICAL TRIAL (ACTG 5349)

SATVI Principal Investigator: Justin Shenje
Sponsor: Aids Clinical Trials Group (ACTG) Division of AIDS (DAIDS), Tuberculosis Trials Consortium (TBTC)

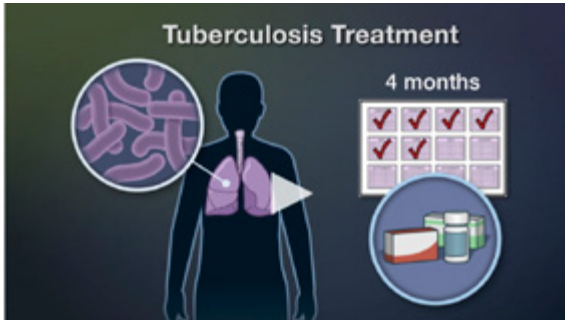
The results from this randomised phase 3 clinical trial, which was conducted between 2016 and 2018, were published in *The New England Journal of Medicine* (*Dorman et al., 2021*) and show that a four-month rifapentine-based regimen containing moxifloxacin is equivalent to the standard six-month regimen in the treatment of tuberculosis.

> "These results are a game-changer for shortening treatment of TB patients in developing countries."
> Professor Mark Hatherill, SATVI Director



The New England Journal of Medicine, 2021.

The study involved 2 154 participants with newly-diagnosed drug-susceptible pulmonary TB, who were randomised into three groups. The first, control group (Arm 1) received the standard six-month treatment consisting of rifampicin, isoniazid pyrazinamide and ethambutol. In the other two groups, one (Arm 2) received a four-month regimen with rifampicin replaced with rifapentine; and in the other group (Arm 3), rifampicin was replaced with rifapentine, and ethambutol was replaced with moxifloxacin. The study included people living with HIV, which was controlled through antiretroviral therapy.



The New England Journal of Medicine, 2021.

SATVI 5349 study team.

This clinical trial was conducted as part of an international multicentre trial within the International Trials Consortium Study 31/AIDS Clinical Trials Group (ACTG), funded by the National Institutes of Health.
Click *here* to view a NEJM video summary of the trial.
ClinicalTrials.gov Identifier: NCT02410772.

STUDY TO ASSESS THE EFFICACY AND SAFETY OF THE AD26.COV2.S VACCINE FOR THE PREVENTION OF SARS-COV-2 MEDIATED COVID-19 IN ADULTS (ENSEMBLE)

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Sponsor: Janssen Vaccines and Prevention

This randomised, double-blind, placebo-controlled phase 3 trial aimed to evaluate the effectiveness and safety of the Ad26.COV2.S vaccine in preventing molecularly-confirmed moderate to severe/critical COVID-19, compared to a placebo, in adult participants. The study had two arms: one in which participants received the experimental Ad26.COV2.S vaccine, and the other in which participants received a placebo. The last participant was screened in quarter 4 of 2020, and participants were followed over a two-year period to evaluate the occurrence of SARS-CoV-2 infection and mild, moderate or severe COVID-19 disease. A single-dose regimen at 5 X 10^{10} viral particles (VP) per vaccination dose level was scheduled to be given in this phase 3 study.

Ensemble COVID-19 study team.

Click *here* to view a video summary of the trial.

Preliminary results, published in *The New England Journal of Medicine* (*Sadoff et al., 2021*), showed that Ad26.COV2.S protected against moderate to severe/critical COVID-19 with onset at least 14 days after administration (116 cases in the vaccine group vs 348 cases in the placebo group; 66.9% efficacy; adjusted 95% confidence interval [CI], 59.0 to 73.4; and at least 28 days after administration (66 vs 193 cases; efficacy 66.1%; adjusted 95% CI, 55.0 to 74.8). Vaccine efficacy was higher against severe/critical COVID-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days).

The New England Journal of Medicine

While a single dose of Ad26.COV2.S vaccine was immunogenic and highly efficacious against severe COVID-19-related hospitalisation and death, the effect only lasted for at least eight months. Signs of waning immunity were observed in terms of the number of participants with undetectable antibodies – especially in the older population, where as many as 28% have no detectable neutralising antibodies at six months post-vaccination.

To address this problem, the protocol was amended in quarter three of 2021 to add an open-label phase of the study, in which a one-dose booster vaccination with Ad26.COV2.S was offered to all enrolled participants, even to those who did not adhere to the protocol and received other authorised COVID-19 vaccines (a single or two-dose regimen of an mRNA vaccine or protein, inactivated, and adenovector-based vaccines). The booster vaccination was administered in the open-label phase of the study (preferably six months but at least three months after their last COVID-19 vaccination). Participants are in follow-up.

The trial will conclude in quarter one of 2023.
ClinicalTrials.gov Identifier: NCT04505722

STUDY TO EVALUATE THE EFFICACY, IMMUNOGENICITY AND SAFETY OF A SARS-COV-2 RECOMBINANT SPIKE PROTEIN NANOPARTICLE VACCINE WITH MATRIX M1 ADJUVANT IN SOUTH AFRICAN ADULTS LIVING WITH AND WITHOUT HIV

SATVI Principal Investigator: Michèle Tameris
Sponsor: Novavax

This phase 2a/b trial aimed to evaluate the efficacy, immunogenicity and safety of the Novavax COVID-19 vaccine, SARS-CoV-2 rS with Matrix-M1 adjuvant in HIV-negative (n=4 422) and HIV-positive adults on stable antiretroviral therapy (n=240). 146 participants, between the ages of 18 and 84, were enrolled at SATVI. The preliminary findings, published in *The New England Journal of Medicine* (*Shinde et al., 2021*) showed that the NVX-CoV2373 was efficacious against all forms of COVID-19, including the B.1.351 (beta) variant. These preliminary findings hold important public health implications for pandemic modelling, control strategies and vaccine development. Subsequent to these positive results, a protocol amendment was approved to implement a blinded crossover vaccination period starting at the month six visit. This crossover allows all previous placebo recipients to receive two doses of Novavax three weeks apart, and all previous Novavax recipients to receive a third dose of Novavax and three weeks later a dose of placebo. Follow-up visits were completed in quarter four of 2021.
ClinicalTrials.gov Identifier: NCT04533399

EFFECTIVENESS AND SAFETY OF A SINGLE DOSE OF THE AD26.COV2.S (JANSSEN) COVID-19 VACCINE FOLLOWED BY A BOOSTER DOSE (SISONKE 2 STUDY)

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Sponsor: Janssen and Janssen, South African Medical Research Council (SAMRC)
Funder: South African Medical Research Council (SAMRC)

This phase 3b is evaluating the effectiveness and safety of a single dose of the Janssen Ad26.COV2.S COVID-19 vaccine combined with a homologous boost of the same vaccine among participants in the Sisonke vaccination programme. Vaccine efficacy is being compared with that of Sisonke participants who did not receive a booster dose.

Data from the ENSEMBLE study of the same vaccine as the single dose, and conducted on four continents, demonstrated 66% efficacy in preventing moderate and severe COVID-19 disease, 28 days post-vaccination (72% in the USA; 64% in South Africa).

Sisonke Study team, Worcester.

It was 85% efficacious overall in preventing severe disease, and there were no COVID-19-related hospitalisations or deaths in vaccine recipients, including in South Africa. Importantly, a high level of protection was observed against severe disease caused by the SARS-CoV-2 B.1.351 (beta) variant observed in South Africa (89% after 28 days post vaccination) (*Bekker et al., 2021*).

The target group of the SISONKE 2 study are healthcare workers, in both the public and private health sector, who are older than 18 years and who had received the Ad26.COV2.S (Janssen) COVID-19 vaccine in the previous SISONKE 1 trial. SATVI acted as the implementation agent for this clinical trial, aimed at protecting healthcare workers through vaccination.

Sisonke2
PROTECTING HEALTHCARE WORKERS

Clinical investigators, Worcester.

During this SISONKE 2 study, participants received a homologous Ad26.COV2.S (Janssen) booster dose at least two months after the initial dose. The study is estimating the incidence of symptomatic SARS CoV-2 infections in Sisonke participants, and monitoring the genetic diversity of breakthrough SARS CoV-2 infections.

Clinical investigators and study coordinators, Worcester.

selection of major clinical and immunology research

PHASE 2A STUDY OF THE SAFETY AND IMMUNOGENICITY OF MTBVAC IN SOUTH AFRICAN NEWBORNS (MTBVAC 202)

SATVI Principal Investigator: Michèle Tameris
Funders: European and Developing Countries Clinical Trials Partnership (EDCTP)
Sponsor: Biofabri

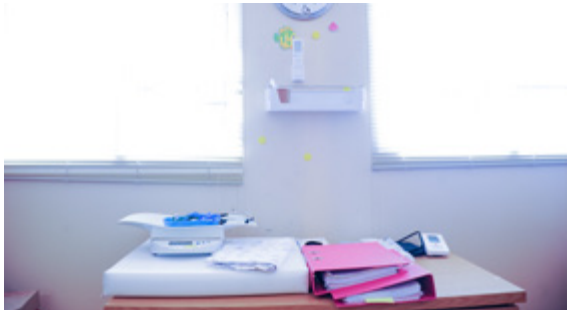
The MTBVAC 202 study is a phase 2a randomised, controlled, double-blind, dose-defining clinical trial of the MTBVAC vaccine which aims to evaluate the safety, reactogenicity, immunogenicity and potential for IGRA conversion and reversion of MTBVAC in HIV-unexposed, BCG-naïve newborns. Enrolment in this study commenced at the beginning of 2019 and was completed during quarter one of 2021. Participants were enrolled into three consecutive cohorts who received 2.5 x 10^4 CFU, 2.5 x 10^5 CFU, or 2.5 x 10^6 CFU of MTBVAC. Participants in cohorts 1 and 2 have completed all their clinical visits, while follow-up visits for cohort 3 participants will continue until quarter three of 2022. A protocol amendment allowed for an independent statistician to analyse the available, unblinded safety and immunogenicity data after completion of study day 182 visits of cohort 3. This analysis has been reviewed by the Data Safety Monitoring Board in order to establish the MTBVAC dose to be used in the phase 3 efficacy trial, which is planned to commence in quarter 2 of 2022.

ClinicalTrials.gov identifier: NCT03536117

PHASE 1B/2A RANDOMISED, DOUBLE-BLIND, ACTIVE-CONTROLLED SAFETY AND IMMUNOGENICITY STUDY OF THE MTBVAC TB VACCINE IN ADULTS

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Funders: National Institutes of Health (NIH), Congressionally Directed Medical Research Programs (CDMRP)
Sponsor: International AIDS Vaccine Initiative (IAVI) and Biofabri

This study aims to evaluate the safety and immunogenicity, and determine the optimal dose, of the novel TB vaccine MTBVAC, compared with BCG. The study enrolled 144 HIV-negative adults between the ages of 18 and 50 years,



with or without evidence of *M.tb* sensitisation assessed by IGRA tests, to receive a single dose of either MTBVAC or BCG (BCG Japan). Participants received MTBVAC intradermally at one of four dose levels: 5 x 10^3 CFU, 5 x 10^4 CFU, 5 x 10^5 CFU, or 5 x 10^6 CFU. Participants were grouped into eight cohorts of 18 participants each, according to dose and *M.tb* sensitisation status. Participants completed their 12-month follow-up by August 2021.

Preliminary study data shows that the vaccination was well tolerated at all dose levels in adults with and without evidence of *M.tb* sensitization in a high-TB-prevalence setting. Evaluation of data is currently underway, and results of the trial are expected to be published during 2022.

ClinicalTrials.gov identifier: NCT02933281

STUDY TO EVALUATE THE SAFETY AND EFFICACY OF THE H56:IC31 TB VACCINE IN REDUCING THE RATE OF TB DISEASE RECURRENCE IN HIV-NEGATIVE ADULTS AFTER DRUG-SUSCEPTIBLE PULMONARY TUBERCULOSIS TREATMENT (A-055)

SATVI Principal Investigator: Justin Shenje
Funders: European and Developing Countries Clinical Trials Partnership (EDCTP)
Sponsor: International AIDS Vaccine Initiative (IAVI)

PREDICT study team, Worcester.

Patients with tuberculosis (TB) have a high risk of recurrence, hence this double-blind, randomised, placebo-controlled phase 2 trial was designed to evaluate the safety, immunogenicity and efficacy of H56:IC31, a TB vaccine, in preventing the recurrence of TB in HIV-negative individuals after completing six months of successful TB treatment. Participants receive two doses of vaccine or placebo, the first at enrolment and the second 56 days thereafter, and are then followed over 421 days. The endpoints for the study are microbiologically confirmed pulmonary TB and probable TB, while other outcome measures include safety and immunogenicity of the H56:IC31 vaccine. The study commenced enrolment in quarter one of 2019 and completed enrolment in March 2022. Follow-up will be completed in quarter one of 2023.

ClinicalTrials.gov Identifier: NCT03512249

PHASE 2B TRIAL OF BCG REVACCINATION IN HEALTHY ADOLESCENTS TO PREVENT SUSTAINED *MYCOBACTERIUM TUBERCULOSIS* INFECTION (BCG REVAX)

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Funder & Sponser: Bill and Melinda Gates Medical Research Institute (Gates MRI)

The purpose of this study is to determine the efficacy of revaccination with BCG vaccine in preventing sustained *M. tuberculosis* infection compared against a placebo.

This phase 2b trial, which commenced in quarter four of 2019, enrolled healthy adolescents who received the BCG vaccine at birth and who are QuantiFERON®-TB Gold Plus (QFT) negative, at multiple sites across South Africa. 584 adolescents of the total study population of 1 800 were enrolled at SATVI. Enrolled participants will be followed for four years. Despite the negative impact of the COVID-19-enforced lockdowns and restrictions, enrolment was completed during quarter three of 2021.

ClinicalTrials.gov Identifier: NCT04152161

SAFETY AND IMMUNOGENICITY OF THE M72/AS01$_E$ TB VACCINE IN PARTICIPANTS WITH WELL-CONTROLLED HIV (MESA-TB)

Investigator: Michèle Tameris
Sponsers & Collaborators: Bill & Melinda Gates Medical Research Institute

The purpose of this study is to determine the efficacy of revaccination with BCG vaccine in preventing sustained *M. tuberculosis* infection compared against a placebo.

The New England Journal of Medicine.

The final results of the phase 2b trial of the M72/AS01$_E$ TB vaccine were reported in *The New England Journal of Medicine* (*Tait et al., 2019*), which showed that two injections of M72/AS01$_E$ given a month apart offered 50% protection against TB during three years of follow-up, compared with a placebo.

MESA_TB study team.

This study will assess the safety and immunogenicity of the M72/AS01$_E$ TB vaccine in virally suppressed, antiretroviral-treated participants with human immunodeficiency virus (HIV) infection, aged between 16 and 35. Participants were enrolled between quarters one and two of 2021. They received two doses of the M72/AS01$_E$ vaccine, on days 1 and 29 of the trial, and were then followed up over 12

months after the second dose (study day 390). Enrolment in this study was challenging mainly because one inclusion criterion was having received tuberculosis preventive therapy (TPT) in the past, as this is not well documented in clinic records. Participant follow-up is ongoing, and results are expected in late 2022.
ClinicalTrials.gov identifier: NCT04556981

PHASE 3 TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF VPM1002 IN COMPARISON TO BCG IN PREVENTION OF MYCOBACTERIUM TUBERCULOSIS INFECTION IN NEWBORN INFANTS

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Sponser: IAVI
Funder: Serum Institute of India

VPM-1002 study team, Worcester.

This study is a double-blind, multicentre, randomised, single-administration, active-controlled phase 3 trial. Newborn infants will receive either VPM1002 or BCG SII (1:1 allocation) to assess the efficacy, safety and immunogenicity of VPM1002 against M.tb infection. The trial hypothesis being addressed is that a single dose of VPM1002 administered intradermally to newborn infants is safer and non-inferior to BCG (Bacille Calmette-Guérin from the Serum Institute of India) in protecting against *Mycobacterium tuberculosis* infection.

Healthy newborn infants will be centrally randomised to receive the allocated vaccine, stratified by the HIV status of the mother.

The proposed design is an event-based approach that includes variable follow-up time (minimum of 12 months and maximum of 36 months). The trial will continue until 632 cases of M.tb infection, diagnosed by IGRA conversion, have been identified, or until all participants have completed 36 months of follow-up. The duration of the trial will be end-point-driven, using a design targeting accrual of 632 primary endpoints, which will trigger the primary analysis.

A single dose of either the VPM1002 or BCG SII will be administered intradermally in the arm within 14 days of birth.
ClinicalTrials.gov identifier: NCT04351685

TREATMENT STUDIES

USING BIOMARKERS TO PREDICT TB TREATMENT (PREDICT)

SATVI Principal Investigator: Michèle Tameris
Funders: Bill and Melinda Gates Foundation, European and Developing Countries Clinical Trials Partnership (EDCTP), NIH through an International Collaborations in Infectious Disease Research (ICIDR) grant, RePORT South Africa (PI: Walzl)
Sponsors: National Institute of Allergy and Infectious Diseases (NIAID)

This study aims to assess if TB treatment can be shortened to four months in TB patients with moderate disease severity, classified using GeneXpert sputum results, drug-adherence data and PET/CT scan results to assign patients to either

PREDICT study team, Worcester.

standard six-month treatment or a shortened four-month strategy. Participants receiving the shortened four-month strategy completed the standard two-month intensive phase of TB treatment, but the continuation phase was reduced to two months instead of the standard four months. Post-treatment follow-up was for 18 months. The study started in quarter one of 2017 and is anticipated to be completed in quarter two of 2022.
ClinicalTrials.gov Identifier: NCT02821832

STUDY TO COMPARE THE SAFETY AND EFFICACY OF DELAMANID WITH ISONIAZID IN PREVENTING ACTIVE TB DISEASE IN HIGH-RISK HOUSEHOLD CONTACTS (PHOENIX STUDY)

SATVI Principal Investigator: Justin Shenje
Funder: National Institutes of Health (NIH)
Sponsor: Aids Clinical Trials Group (ACTG)

The PHOENIx study aims to compare the safety and efficacy of delamanid, a new anti-TB drug, with that of isoniazid in the prevention of active TB disease in high-risk household contacts (HHC) of patients with MDR TB. The study plans to enrol 3 452 HHC, who will receive either delamanid or isoniazid over a period of 26 weeks and will be followed up for 96 weeks.

HHC of patients with pulmonary TB are at a greater risk of contracting TB than the general population. At even greater risk are children under the age of five years, people living with HIV, and individuals with latent TB infection, who are considered high-risk HHC. Isoniazid prophylaxis is recommended for all high-risk HHC; however, there is concern that in household contacts of patients with MDR TB, isoniazid may not confer sufficient protection.

Recruitment commenced in quarter four of 2019 and is expected to run until quarter three of 2026.
ClinicalTrials.gov Identifier: NCT03568383

STUDY OF HOST BLOOD BIOMARKERS FOR THE DIAGNOSIS, PROGNOSIS AND TREATMENT RESPONSE OF CHILDHOOD TUBERCULOSIS (CORTIS KIDS)

Principal investigator: Justin Shenje
Funder: National Institutes of Health (NIH)

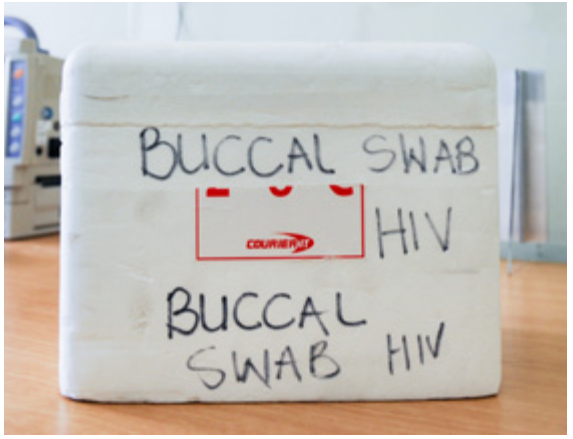
This observational study seeks to evaluate the diagnostic performance of host biomarkers for diagnosing TB in those with disease, and the prognostic performance of these biomarkers for incident TB in children. As a natural follow-up to the CORTIS-01 and CORTIS-HR studies, this study evaluates and compares the performances of an RNA signature, a proteomic risk signature, and a T-cell antigen-specific activation assay (TASA) in children under five years of age. The study seeks to enrol 490 participants, and commenced recruitment in quarter three of 2019. Despite the COVID-19 pandemic and associated challenges, 179 participants had been enrolled by the end of 2021, and we plan to complete recruitment by quarter four of 2022.

DIAGNOSIS

STUDY OF TUBERCULOSIS CASE-FINDING BY ORAL SWAB POLYMERASE CHAIN REACTION (PCR)

SATVI Principal Investigator: Angelique Kany Kany Luabeya
Funders: National Institutes of Health (NIH) via University of Washington, Bill and Melinda Gates Foundation, (PI: Cangelosi) University of Washington

This project evaluates the feasibility of oral swab analysis for the diagnosis of TB disease, using polymerase chain reaction (PCR) to detect *Mycobacterium tuberculosis* DNA from oral swabs collected from TB patients. Previous studies have demonstrated that *M. tuberculosis* DNA and/or cells accumulate in the oral cavity of TB patients in amounts that are sufficient to enable non-sputum-based diagnosis of TB.



This study also evaluates samples collected with tongue swabs as samples for rapid, safe duplex screening for TB and SARS-CoV-2 (COVID-19). The medical response to the COVID-19 pandemic has been highlighted by limitations in the availability of testing for symptomatic people. *M. tuberculosis* and SARS-CoV-2 are biologically dissimilar but share important features, as respiratory pathogens. Both are airborne diseases whose clinical presentations include fever, cough, fatigue, difficulty breathing, and chills. In areas where both diseases are prevalent, it is critical to test for both when patients present with common symptoms. Tongue swabs are extremely easy to collect from any adult or child, in any setting. Therefore, tongue swabbing can potentially be used to simultaneously screen for COVID-19 and TB ('CoTB') in regions of the world where both respiratory diseases are common.

EVALUATION OF NEW DIAGNOSTIC TESTS FOR ACTIVE AND INCIDENT TB IN INDIVIDUALS WITH KNOWN TB EXPOSURE (ENDX-TB: EXPOSED)

Investigator: Justin Shenje
Funder: National Institute of Allergy and Infectious Diseases (NIAID), NIH

END-TB study team, Worcester.

Current diagnostic methods for tuberculosis have poor sensitivity and rely on sputum, which can be difficult to collect in some patients. There is a need to develop non-sputum-based tests, with better sensitivity and quick turnaround times, which perform better, particularly in patients with early disease. There are a number of blood- and urine-based tests that have shown promise, namely lateral flow assays for host proteins, transcriptomic signatures and high-sensitivity urine lipoarabinomannan (LAM) assay. ENDx-TB is a diagnostic study which aims to evaluate the performance of these tests which have shown promise in relation to conventional TB diagnostic tests. The study will recruit adolescent and adult household contacts and follow them up for a duration of 12 months. During this follow-up period, participants will be monitored for TB symptoms and signs and undergo standard TB investigation alongside experimental diagnostic tests, to identify incident TB cases among the study population. The study commenced in quarter two of 2021.

STUDY INTO BIOMARKER APPROACHES FOR SYMPTOMATIC, SUBCLINICAL AND INCIPIENT TUBERCULOSIS (REPORT SA)

Investigator: Michèle Tameris
Sponsor: University of Cape Town
Funder: Report TB International

This study aims to discover and validate novel biomarkers to detect symptomatic, subclinical and incipient TB disease, in people living with and without HIV. Multiple biomarkers will be tested among high-risk individuals, i.e. household contacts of patients recently diagnosed with TB. Participants are screened for subclinical TB and followed for incipient TB. During the study, biomarkers in blood, urine, sputum and oral swab samples will be evaluated.

Performance of the most promising biomarkers will be compared head to head, and benchmarked against target product profiles (TPP) for triage, diagnostic and incipient TB tests. Recruitment at SATVI commenced in quarter one of 2021, and participants are followed up for one year.

This study is part of a multisite clinical study involving other research sites such as the University of Cape Town Lung Institute (UCTLI), Stellenbosch University (SUN), the Immunology Research Group (SUN-IRG), the University of the Witwatersrand, the Perinatal HIV Research Unit (PHRU), the Africa Health Research Institute (AHRI) and the University of Pretoria (UP), as well as international partners and collaborators in the RePORT TB consortium.

COMPLETED OBSERVATIONAL

MOLECULAR DETECTION OF AIRBORNE MYCOBACTERIUM TUBERCULOSIS IN SOUTH AFRICAN HIGH SCHOOLS

Investigator: Mark Hatherill, Erick Bunyasi
Funder: National Institutes of Health, Stanford University

The study aimed to establish whether high schools are high-risk settings for TB transmission, because research has shown that a significant proportion of adolescents acquire TB infection outside their households. In South Africa, up to 47% of TB cases are either undiagnosed or untreated.

In this observational study, air quality data were obtained from 72 classrooms at two participating Worcester high schools, and compared with air quality data sampled from seven rooms frequented by patients at three public health clinics in Worcester and an open air space (grass lawn) not occupied by people. The study was a collaboration between scientists from the South African Tuberculosis Vaccine Initiative (SATVI), the Desmond Tutu HIV Centre, the Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa), Stanford University, the South African Medical Research Council, the South African National Health Laboratory Services and UCT's Molecular Mycobacteriology Research Unit.

The study found that:

- Airborne *M.tb* genomic DNA was frequently detected in high-school classrooms, and instantaneous risk of exposure in classrooms was similar to the risk in public health clinics.
- 40% of classrooms were inadequately ventilated, although classrooms were sampled mostly during the winter months when windows and doors were more likely to be closed.

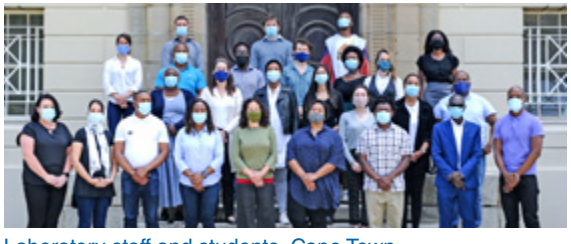
Bunyasi et al., 2021.

"These findings show that air sampling for *M.tb* DNA may be a useful tool for TB transmission research in schools and other places where people gather."

selection of immunology studies

HEAD-TO-HEAD VALIDATION OF TRANSCRIPTOMIC SIGNATURES OF TB IN CORTIS STUDIES

Principal Investigator: Tom Scriba
Project Scientist: Simon Mendelsohn
Funders: Bill and Melinda Gates Foundation; South African Medical Research Council



Laboratory staff and students, Cape Town.

The aim of this study is to evaluate the diagnostic and prognostic performance for pulmonary TB of multiple host transcriptomic signatures in the CORTIS studies. Eight concise transcriptomic signatures were prospectively measured, head to head, by microfluidic real-time qPCR on blood samples from 2 923 HIV-negative and 861 HIV-positive adults from five TB-endemic communities in South Africa. All participants were microbiologically tested for TB disease at baseline and at end-of-study visits, and screened for TB through 15 months of follow-up.

Most signatures performed well in diagnosing symptomatic pulmonary TB, but none met the WHO Target Product Profile criteria for a triage test to diagnose subclinical TB. Prognostic performance for incident TB occurring within six to 12 months in HIV-negative participants was higher for all signatures than for TB occurring through 15 months, with several signatures meeting WHO benchmark criteria for prognostic tests in the six-month window.
Results will be published early in 2022.

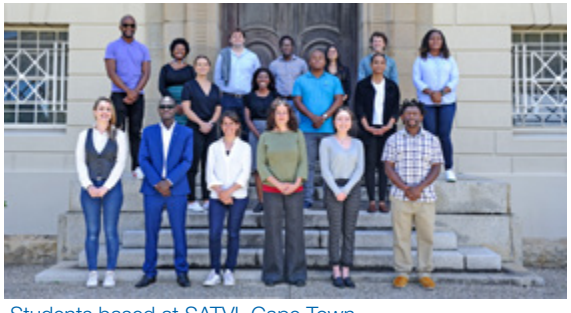
> "The study highlights the potential that small TB transcriptomic signatures hold for triage of symptomatic adults seeking care, screening of antiretroviral clinic attendees and other high-risk groups for further investigation, and prediction of short-term risk of TB for initiation of targeted preventive therapy, and warrants translation to point-of-care testing platforms."

IMMUNE CORRELATES OF PROTECTION FROM SUSTAINED *M.TB* INFECTION AND TB DISEASE

Principal Investigators: Elisa Nemes, Tom Scriba
Project Scientists: Claire Imbratta, Stanley Kimbung, Denis Awany, Munyaradzi Musvosvi
Funders: Gates Medical Research Institute, Bill & Melinda Gates Foundation and US National Institutes of Health

SATVI is involved in several aspects of an international and multi-laboratory effort to discover immune correlates of protection against sustained *M.tb* infection mediated by BCG revaccination in adolescents (*Nemes et al., 2018*) as well as protection against TB disease mediated by M72/AS01$_E$ vaccination in adults (*Tait et al., 2019*). We are conducting pilot studies to measure whole blood cellular composition and phenotype the main cell subsets by 27-colour flow cytometry (both trials, Claire Imbratta); whole blood gene expression profiles by RNA sequencing (M72/AS01$_E$ trial, Stanley Kimbung and Denis Awany); and *M.tb*-specific single cell TCR and RNA sequencing (M72/AS01$_E$ trial, Munyaradzi Musvosvi in collaboration with Alex Shalek at MIT). Results will be inte-

grated with data generated in other laboratories to provide a rational, data-driven selection of assays to analyse samples stored from protected and unprotected participants from the two efficacy trials. Outcomes of this programme will identify immune correlates of protection against TB, which will be validated in ongoing larger trials of BCG revaccination and M72/AS01$_E$ vaccination.



Students based at SATVI, Cape Town.

COMPLETED

BIOMARKERS OF RECENT *M.TB* INFECTION

Principal Investigator: Elisa Nemes
Project Scientists: Cheleka Mpande, Tessa Lloyd, Pia Steigler
Funders: US National Institutes of Health

Individuals who acquired *M.tb* infection recently are at higher risk of progression to TB disease compared to those with remote, established *M.tb* infection. We aimed to identify host biomarkers that can distinguish individuals with recent or remote *M.tb* infection, measured by QuantiFERON-TB conversion in a longitudinal cohort of adolescents. We conducted multidimensional profiling of *M.tb*-specific conventional T-cells and *M.tb*-reactive innate cells, and applied statistical modelling to describe immunological changes induced by *M.tb* infection (*Mpande et al., 2021*) and to identify candidate biomarkers (*Lloyd et al., 2021*.). *M.tb*-specific T-cell activation was the most striking feature of recent *M.tb* infection, and the excellent performance of this biomarker to distinguish between infection states was reproducible in separate cohorts (*Mpande et al., 2021*). If further validated in different settings, this simple biomarker has the potential to guide targeted preventative treatment for TB to those at higher risk of progression.

M.TB-SPECIFIC T-CELL FUNCTIONAL, MEMORY AND ACTIVATION PROFILES IN QUANTIFERON REVERTERS ARE CONSISTENT WITH CONTROLLED INFECTION

Principal Investigator: Elisa Nemes
Project Scientists: Cheleka Mpande, Tessa Lloyd, Pia Steigler
Funders: US National Institutes of Health

We performed a multi-dimensional analysis to identify immunological features that could distinguish QuantiFERON-TB (QFT) reverters from persistent QFT positive and persistent QFT negative adolescents in a longitudinal cohort. Features of *M.tb*-specific conventional T-cells and *M.tb*-reactive innate cells did not change over time in reverters. Statistical modelling revealed that immune responses in reverters were more similar to those detected in persistent QFT-negative individuals than to responses in those who were persistent QFT-positive.

> "Reversion of immune sensitisation tests, such as the tuberculin skin test (TST), has been associated with self-cured *M.tb* infection in humans and animal models."

Overall, findings from this study suggest that QFT reversion occurs in a heterogeneous group of individuals with low *M.tb*-specific T-cell responses. In some individuals QFT reversion may result from assay variability, while in others the magnitude and differentiation status of *M.tb*-specific Th1 cells are consistent with well-controlled *M.tb* infection.

DISCOVERY OF PROTECTIVE *M. TUBERCULOSIS*-SPECIFIC T-CELLS THROUGH T-CELL RECEPTOR REPERTOIRE PROFILING

Principal Investigator: Tom Scriba
Project Scientist: Munyaradzi Musvosvi
Funder: Bill and Melinda Gates Foundation

The aim of this research project is to discover the array of T-cell receptors (TCR) used by *M. tuberculosis*-specific T-cells, from individuals who successfully controlled *M. tuberculosis* infection (controllers) or from those who progressed to TB disease (progressors). Together with Mark Davis, Huang Huang and other colleagues at Stanford University, we isolated and sequenced the TCRs of thousands of *M. tuberculosis*-specific T-cells and compared their abundance

in the blood from controllers and from progressors. We then examined whether controllers used different TCRs from progressors, and identified different groups of TCRs that were much more abundant in controllers than in progressors, which we interpret as 'protective' T-cells. Importantly, we also identified the bacterial targets (protein fragments) that these 'protective' T-cells recognise, and we are working on a follow-up project that aims to incorporate these targets into new TB vaccine candidates.

T-cells are an essential component of the adaptive immune system, which detects and defends against infections. To recognise and attack a germ, T-cells use a diverse set of cell surface receptors known as T-cell receptors (TCR), which recognise small protein fragments from the germ that are presented to T-cells by cells infected with the germ. T-cells that recognise protein fragments from the bacterium that causes TB are called *M. tuberculosis*-specific T-cells. When *M. tuberculosis*-specific T-cells recognise such bacterial protein fragments, they become activated and expand clonally, essentially producing thousands of identical copies of themselves, so that an army of *M. tuberculosis*-specific T-cells can fight the infection.

LONGITUDINAL DYNAMICS OF RISK11, A TRANSCRIPTOMIC SIGNATURE OF TB

Principal Investigators: Mark Hatherill, Tom Scriba
Project Scientist: Humphrey Mulenga
Funder: RePORT SA

We previously developed an 11-gene blood transcriptomic TB signature, RISK11, with promising diagnostic performance for identifying those with TB disease and prognostic performance for identifying those who will progress to TB within six to 12 months after testing. This study evaluated the longitudinal kinetics of RISK11 and the effects of TB-preventative therapy (TPT) and respiratory organisms on RISK11 signature scores in HIV-uninfected and HIV-infected individuals. RISK11 was measured in a longitudinal study of RISK11-guided TPT in HIV-uninfected adults (the CORTIS-01 study), and in a longitudinal study of people living with HIV (PLHIV, the CORTIS-HR study). We also measured RISK11 in a cross-sectional respiratory organisms cohort, along with detection and quantification of respiratory viruses and bacteria in nasopharyngeal and oropharyngeal swabs by qRT-PCR.

The study found that RISK11-positive status is often transient, and that reversion from RISK11-positive to RISK11-negative status is more common in HIV-uninfected individuals than in PLHIV. We also found that RISK11 scores were higher in participants with viral organisms in the nasopharynx and oropharynx, or those with prevalent TB, than in those with bacterial organisms other than TB in the nasopharynx and oropharynx, or with no organisms. Thus, RISK11 could not discriminate between prevalent TB and viral organisms, highlighting some important limitations of blood transcriptomic signatures for distinguishing between viral infections and TB.

Laboratory staff,Cape Town.

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Burger R, Maughan-Brown M, Kohler T, English R, Tameris M.
Increased openness to accepting a COVID-19 vaccine is a shot in the arm for South Africa: Evidence from the NIDS-CRAM Wave 5 Survey.

awards, honours & accreditations

Dr Michèle Tameris was promoted ad hominem to Associate Professor.

Dr Angelique Luabeya was promoted ad hominem to Chief Research Officer.

Mzwandile Erasmus was promoted ad hominem to Chief Technical Officer.

The SATVI laboratories received renewed accreditation from the South African National Accreditation System.

Associate Professor Michèle Tameris.

Dr Angelique Kany Kany Luabeya.

Mzwandile Erasmus.

SANAS accreditation.

postgraduate students & postdoctoral fellows

Cheleka Anne-Marie Mpande graduated with a PhD degree (UCT); her research topic focused on the characterisation of T-cell specificity, functional, activation and memory profiles associated with QuantiFERON TB Gold conversion and reversion.

Dr Cheleka Mpande with Professor Tom Scriba, Mrs Mpande (Cheleka's mother) and Associate Professor Elisa Nemes.

Agano Kiravu graduated with a PhD which focused on characterising differences in the birth transcriptome and cellular immune ontogeny between HIV-exposed and their un-exposed peers.

Dr Agano Kiravu.

Kelvin Vollenhoven graduated with a master's degree (Stellenbosch) on the knowledge, attitudes and practices (KAP) of TB among various community groups in the Cape Winelands district.

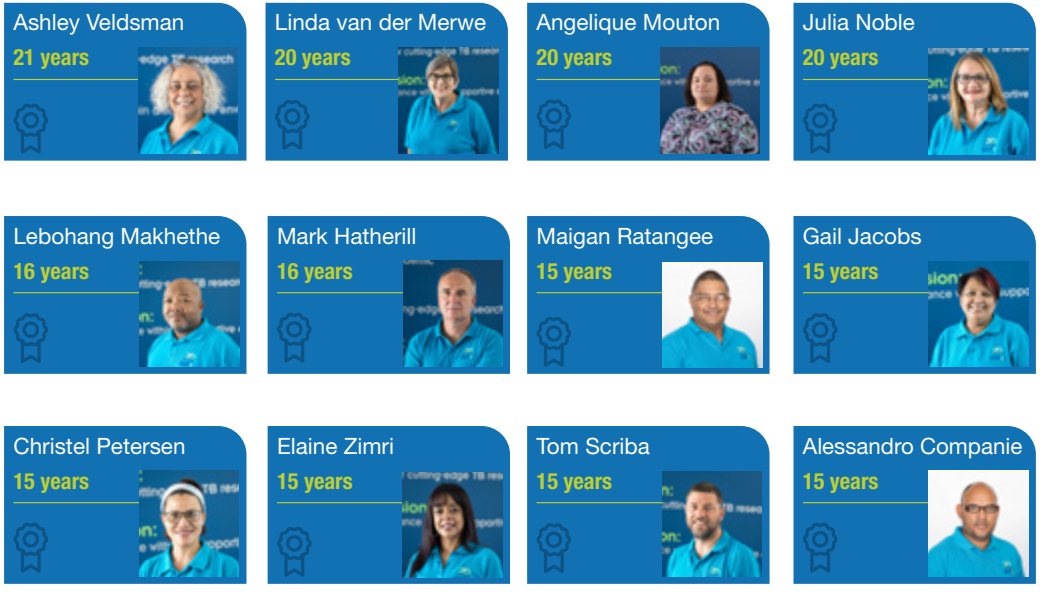
Kelvin Vollenhoven.

our staff

During the year under review, despite the trying circumstances brought about by the COVID-19 pandemic, staff morale has remained high; and we remain committed to the focus of researching improved strategies to curb TB. We are proud that we could also contribute to the fight against COVID-19 through COVID-19 vaccine development, as well as through diagnostic testing for SARS-CoV-2 as part of the NHLS COVID-19 surge testing.

LONG-SERVICE RECOGNITION

During 2021, we marked the following long-service awards made to various SATVI colleagues who have served SATVI for many years.



SATVI staff, Cape Town.

SATVI staff, Worcester.

Casual Day, September 2021.

our community

The community in which we conduct our research – a rural area – is faced by challenges of vast geography, a serious disease burden and high poverty levels, which make improved health outcomes challenging. Despite these challenges SATVI has established itself firmly in this community, not just through the research agenda which tackles the burden of TB disease, but also through various community engagement programmes and initiatives.

COMMUNITY ADVISORY BOARD

The Community Advisory Board is the link between SATVI and the local community, providing input on planned research and completed research, across the disease spectrum researched by SATVI. During the past year we have had to scale down on in-person events, opting for virtual engagement through online communication platforms to ensure the safety of this stakeholder group.

Engagement with the CAB has included discussing new research studies, including new TB and COVID-19 vaccine studies, research literacy materials and the TB research agenda, and participating in providing feedback on materials developed by the participants in the UCT Honours Vaccinology course, in partnership with EhWoza!

At the end of 2021, we collaborated with the UCT Lung Institute in hosting a joint CAB meeting, which included training in clinical research studies, as well as a session on personal well-being and taking care of oneself. Hilda Fredericks, a CAB member, was elected to an ACTG subcommittee. Sadly, a longstanding CAB member, Avril Williams, passed away from COVID-19 in July 2021.

CAB meeting June 2021.

CAB meeting October 2021.

CAB meeting October 2021.

TB educational workshop, Zwelethemba Community Centre.

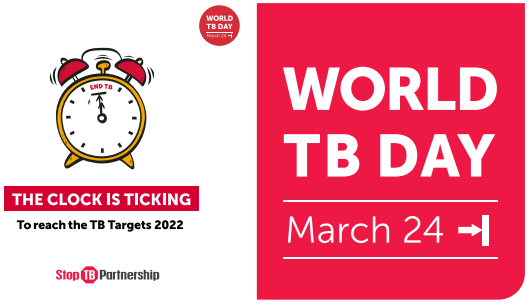
ONGOING WORKSHOPS WITH COMMUNITY GROUPS

We have continued our partnership with the local community, targeting vulnerable groups including HIV- and TB-affected people and the youth. One such workshop was with a patient support group at a Zwelethemba community centre; there was also a series of monthly workshop sessions presented with participants in a substance abuse rehabilitation programme at a local community centre.

Peer educators' workshop, October 2021.

WELLCOME TRUST-FUNDED YOUTH 'LET'S TALK TB' PEER EDUCATION PROGRAMME

During the year we have continued with the 'Let's Talk TB' peer education programme, which commenced in 2020 in Robertson. This year the programme was expanded to two schools in Worcester. Under this programme, participants were trained in radio production and had to complete various assignments – interviewing youth peers, health workers and patients who had been affected by either TB or COVID. The training partner RX Radio packages these programmes for use through local community radio stations. A follow-up project will include documenting the experiences of participants in this programme over the two years.

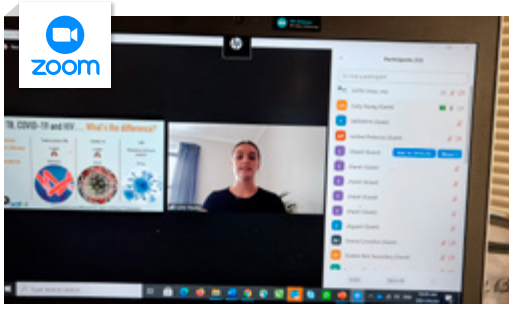


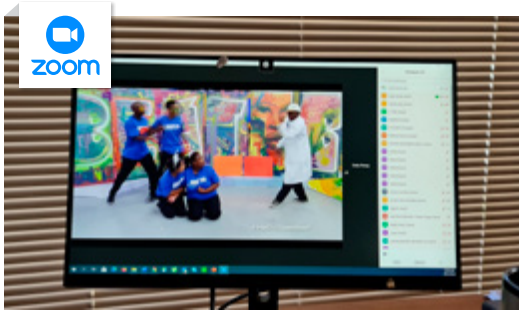
WORLD TB DAY

For World TB Day 2021, SATVI collaborated with the department of Education and the UCT Rural Students network in hosting two separate events to raise awareness of TB and the TB research agenda.

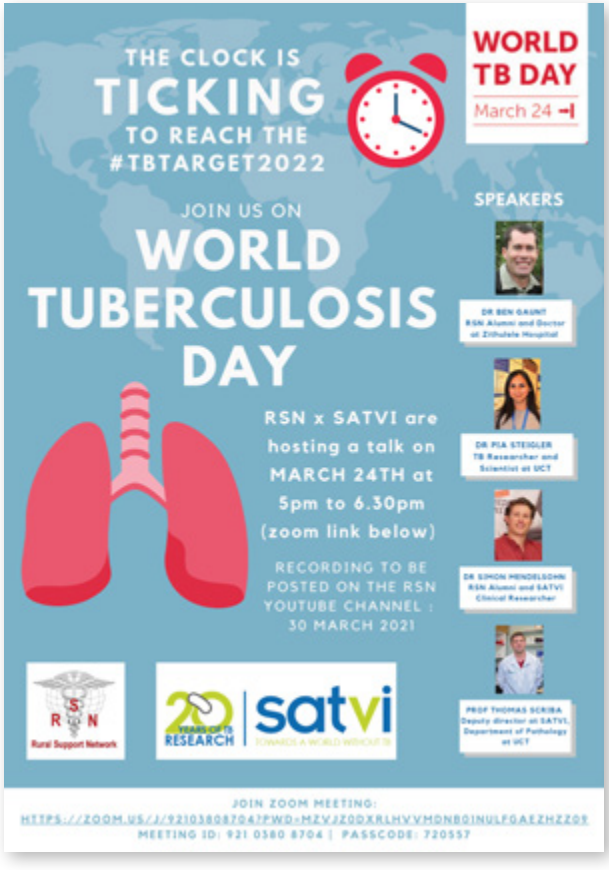
TB ADVOCACY WORKSHOP

During quarter one of 2021, SATVI hosted a two-day TB vaccine advocacy workshop with delegates from various community groupings, which included medical students, community advisory board members and health workers. The programme, which was conducted online, covered an introduction to advocacy, an overview of the TB vaccine research pipeline, and patient perspectives. It was organised by Kelvin Vollenhoven from SATVI and Zani de Witt from the UCT Lung Institute, with the support of Dr Michèle Tameris; it was funded by a grant from the Stop TB Partnership Working Group on TB Vaccines.





World TB Day Schools Programme: SATVI facilitated a programme on World TB Day, with a presentation by Carly Young (a SATVI postdoctoral student) and a play developed by SATVI, which featured a five-minute drama which was performed on SABC 2's *Hectic Nine 9*.



World TB Day-UCT Rural Support Network (RSN): SATVI co-hosted a special World TB Day programme with the UCT Rural UCT Rural Support Network, a student chapter for UCT health students. The programme featured input from Professor Tom Scriba on the current TB research agenda, and a patient perspective from an affected health student.

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