DESMOND TUTU TB CENTRE ANNUAL REPORT

2020

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Letter from the Director

This past year has brought unprecedented challenges to South Africa and the world, with the emergence of a new global pandemic in addition to the pandemics of tuberculosis and HIV already affecting South Africans.

Major gains made in tuberculosis and HIV control globally have been reversed. Yet, South Africa, in true spirit, is showing signs of resilience and recovery.

We are grateful that no lives have been lost due to COVID-19 at our centre but are deeply sad with those who have lost loved ones. We recognize that the COVID-19 pandemic has had a lasting impact on all of our lives, and on the lives of people we serve through our research.

We have learnt to be increasingly appreciative of each other, to be more innovative and flexible, and have become more resilient – qualities that will serve us well beyond COVID-19.

We are grateful to have been able to continue our research, and in new and increasingly meaningful ways, to ensure lasting positive impact which is needed now more than ever to combat tuberculosis, HIV and poverty. We are also extremely grateful to our funders, and also the University, for supporting us during this past challenging year.

We look to the future with hope and with a great sense of privilege to be able to continue and expand on our work, to serve communities in South Africa and globally.

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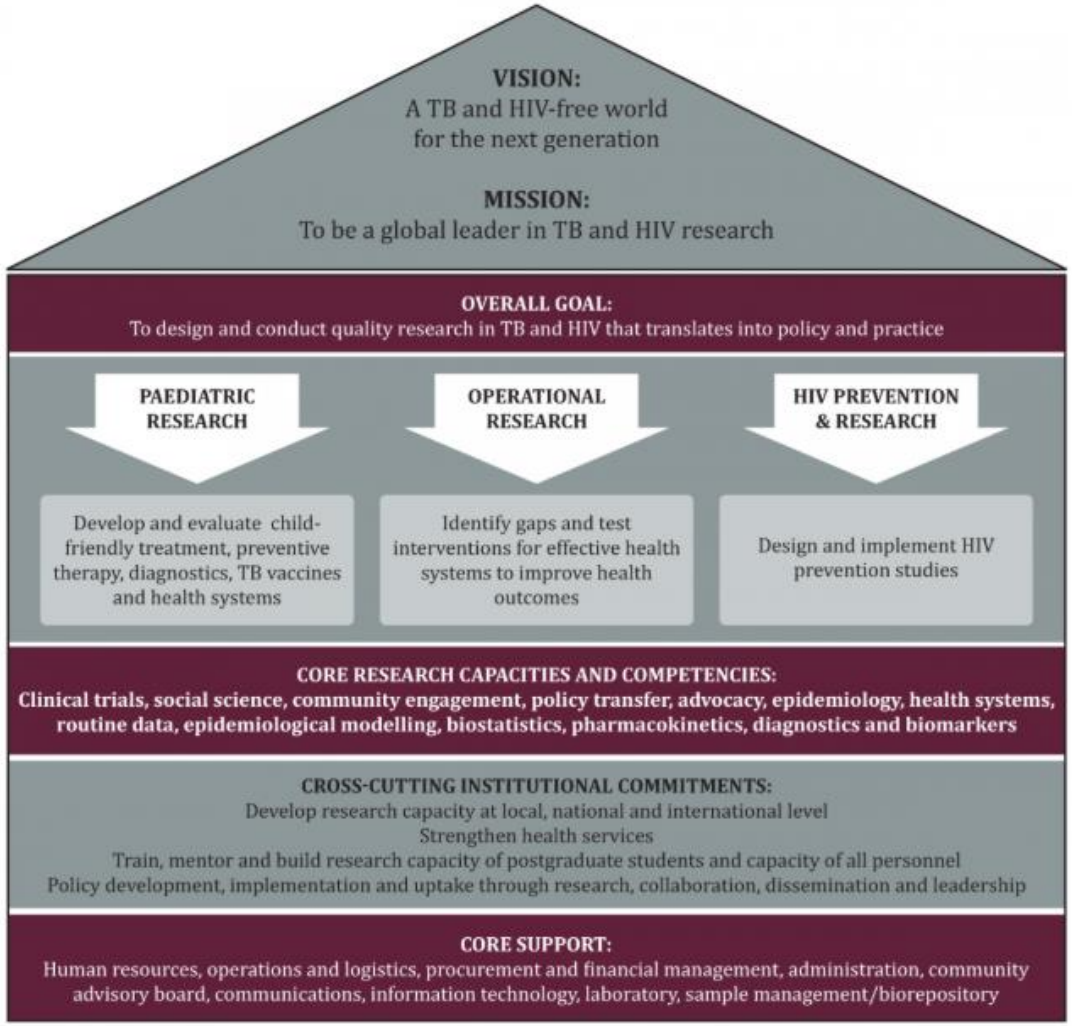
Desmond Tutu TB Centre Research Focus Areas



Glossary of Terminology

AIDS	Acquired Immunodeficiency Syndrome
ART/ARV	Antiretroviral Therapy / Antiretroviral
BCH	Brooklyn Chest Hospital
BMC	BioMed Central
BMRC	British Medical Research Council
CAB	Community Advisory Board
CD4	Cluster of Differentiation 4
CDC	US Centers for Disease Control and Prevention
CIDER	Centre for Infectious Disease Epidemiology and Research
CTU	Clinical Trials Unit
CWG	Community Working Group
CXR	Chest X-ray
DAIDS	Division of AIDS, NIAID
DFID	Department for International Development
DoH	South African National Department of Health
DR-TB	Drug-Resistant Tuberculosis
DS-TB	Drug-Susceptible Tuberculosis/Drug-Sensitive Tuberculosis
DTTC	Desmond Tutu TB Centre
EDCTP	The European & Developing Countries Clinical Trials Partnership
FAMCRU	Family Clinical Research Unit
FDC	Fixed dose combination
FMHS	Faculty of Medicines and Health Science
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HREC	Health Research Ethics Committee
ICAB	IMPAACT Community Advisory Board
INH	Isoniazid
IPC	Infection prevention control
ILTFU	Initial lost to follow-up
IMPAACT	International Maternal Paediatric Adolescent AIDS Clinical Trials Group
IRD	Interactive Research and development

ISMMS	The Icahn School of Medicine at Mount Sinai
LTBI	Latent TB infection
MA	Master of Arts
MDR-TB	Multidrug-Resistant Tuberculosis
MPhil	Master of Philosophy
MRC	Medical Research Council
MRC CTU	Medical Research Council Clinical Trials Unit
MS	Mass Spectrometry
MSF	Médecins sans Frontières
NHRD	National Health Research Database
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
ORAP	Operational Research Assistance Project
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary health care
PHDC	Provincial Health Data Centre
PI	Principal Investigator
PK	Pharmacokinetics
PrEP	Pre-exposure prophylaxis
RFP	Request for Proposal
RIF	Rifampicin
RGMO	Research grants management office
SAHPRA	South African Health Products Regulatory Authority
SACEMA	South African Centre for Epidemiological Modelling & Analysis
SC	Steering Committee
SU	Stellenbosch University
TBTC	TB Trials Consortium
TPT	TB preventative therapy
UCT	University of Cape Town
WHO	World Health Organisation

Desmond Tutu TB Centre: Highlights for 2020

Key Achievements

- The Desmond Tutu TB Centre (DTTC) was re-awarded, through a competitive grant, status as a DAIDS-funded International Maternal, Paediatric, Adolescent AIDS Clinical Trials (IMPAACT) network trial site through the Stellenbosch Clinical Trials Unit (PIs Anneke Hesseling and Mark Cotton).
- The DTTC was also re-awarded status as a CDC Tuberculosis Trials Consortium, through the Veterans Affairs group (PI Anneke Hesseling), through a competitive grant application process.
- The DTTC co-hosted the first South African National Symposium on Tuberculosis modelling titled "Tuberculosis Modelling Research to Guide Decision-Making for Tuberculosis Control in South Africa".
- A large-scale project at the Centre, the BENEFIT Kids Project, funded by UNITAID, was launched in January. A study video, produced by Damien Shuman, was released globally on World TB day. This award is the largest single direct grant ever awarded to Stellenbosch University. The TB CHAMP study, part of the project, was featured on the Unitaid website to show case the study and the team implementing the research.
- DTTC established one of the African paediatric COVID-19 clinical cohort studies, COVID-Kids.
- The DTTC presented findings at several key virtual meetings, including the World Health Organization (WHO) and The World Union on TB and Lung Disease meetings.
- DTTC staff presented at several virtual conferences, including at the Faculty's 64th Annual Academic Day and the International AIDS Society Conference.
- Centre staff had 5 oral presentations, 8 posters, and 3 symposia accepted to the 51st Annual International Union against Tuberculosis and Lung Disease conference.
- Nomtha Mandla, mentored by Peter Bock, was accepted into the coveted HPTN Scholars Programme and received a scholarship towards her PhD research.

- DTTC staff members from the Sociobehavioural science team participated in the SACEMA virtual FameLab event. Dzunisani Baloyi won 2nd runner up on her presentation of her master's thesis topic.
- Sue-Ann Meehan was promoted to Senior Researcher.
- Eric McCollum, paediatric pulmonologist, joined the DTTC as a Distinguished Associate Professor from Johns Hopkins University.
- Anneke Hesseling was re-awarded the position of Distinguished Professor in Paediatrics and Child Health at Stellenbosch University
- Anneke Hesseling joined the Stellenbosch University COVID-19 Medical Advisory Team, led by the Vice-Rector, Research, Professor Eugene Cloete.
- The DTTC was awarded a Certificate of Excellence for Conduct of HPTN 084 in recognition of enrolling 30% of participants with a Voice Risk Score (VRS) of 8.
- Several of the studies conducted at the DTTC received widespread media coverage, including the SHINE trial, the HPTN 084 (LIFE) study, and both the PETITE Study and TB CHAMP trial as part of the BENEFIT Kids Project.
- Muhammad Osman received the award for the Overall Winner of the best abstract at the South African Medical Research Council 2020 Early Career Scientist Convention.
- The Community Advisory Board (CAB) Member of the Year 2020 was awarded to Siphosethu Nco for outstanding work commitment.
- The DTTC published 71 peer-reviewed manuscripts during the past year.

Postgraduate students

- Ten staff members graduated with graduate or postgraduate degrees.
- Karen du Preez was awarded her PhD in Paediatrics and Child Health at Stellenbosch University.
- Lario Viljoen successfully defended her PhD in Sociology at Stellenbosch University.

Research Updates

1. Paediatric tuberculosis and lung health

The DTTC continued to build upon its world class reputation of clinical research in paediatric tuberculosis (TB) and child lung health. The DTTC hosts a South African National Research Foundation SARcHi Chair in Paediatric Tuberculosis, Anneke Hesseling, who is Centre director and Distinguished Professor in Paediatrics and Child Health, at Stellenbosch University. Key focus areas for paediatric research include 1) therapeutics and treatment of Drug Resistant TB (DR-TB) in children, 2) Therapeutics for Drug Susceptible (DS) TB in children and pregnant women, 3) trials on TB preventive therapy for DS in children, 4) lung health, diagnostics, and biomarkers in children, and 5) epidemiological and implementation research.

Major areas of interest specifically include the evaluation of novel therapeutic strategies for Multidrug resistant TB (MDR-TB) in children, where the Centre is a global leader in its field and is generating seminal data on an ongoing basis. The DTTC has again expanded its state-of-the-art paediatric pharmacokinetics (PK) clinical research unit at Brooklyn Chest Hospital (BCH) over the past year.

Expanding national collaborations have included Dr Suzanne Staples at THINK in KwaZulu Natal, Professor Francesca Conradie at Wits University, through the Isanga Lethemba site in the Eastern Cape Province, and Dr Tamara Kredo at the South African Cochrane Centre. New international collaborations have included Professor Galit Alter, Harvard University, Professor Cheryl Day, Emory University, professor Mike Levine, Imperial College London, and Professor Denise Naniche, IS Global (Spain and Mozambique),

The DTTC was re-rewarded a grant to remain part of the IMPAACT network and has remained a well-performing site and where it is currently undertaking four TB trial, including on bedaquiline and delamanid in children, and also for the US Centres for Disease Control (CDC) TB Clinical Trials Consortium (TBTC), where it leads Study 35, a TB prevention trial of short course rifapentine and isoniazid, in children.

The group's research has resulted in more than 40 publications in international peer-reviewed journals (Appendix I), participation in several national and international TB treatment and prevention guideline meetings, including with the WHO, and with the South African National Department of Health (DoH).

The group has several major international grants awarded, including from the NIH, EDCTP, and the TBTC. Several local grants were awarded including from the SA MRC.

The DTTC group is continuing to shape the science and implementation of paediatric TB treatment trials through leadership in the National Institutes of Health (NIH) funded IMPAACT and the CDC TBTC trial consortia.

Exciting new work undertaken by the group during 2020 includes the first African paediatric COVID-19 study, and expansion of its lung health platform, led by Dr Marieke van der Zalm, with unique cohorts investigating the short and long-term impact of TB, respiratory viruses, and COVID-19, on child lung health, and including seminal TB biomarker diagnostic work. Eric McCollum, paediatric pulmonologist, joined the DTTC as a Distinguished Associate Professor from Johns Hopkins University, and will focus on supporting expansion of DTTC's lung health research platform.

The DTTC paediatric group alone contributed 16 presentations to the 51st annual International Union against Tuberculosis and Long Disease conference held virtually in 2020, with 5 oral presentations, 8 poster presentations and 3 symposia.

Prevention and treatment: drug resistant TB

BENEFIT Kids (Better Evidence and Formulations for Improved MDR-TB Treatment for Children): (Project leads: Dr Anthony Garcia-Prats, Prof Anneke Hesseling) This is a Unitaid-funded project which will run over a 3-year period (October 2019 – September 2022) with the aim of developing an evidence-based package of improved prevention and treatment

tools to reduce paediatric MDR-TB morbidity and mortality. This evidence package will be made available for adoption and scale-up. During 2020, there were several delays in the study due to the impact of the COVID-19 pandemic and national lockdown measures. BENEFIT Kids is a large project that is divided into three outputs with multiple partners' and stakeholders' involvement:

- Output 1 aims to provide improved evidence from existing data for better MDR-TB treatment for children through two systematic reviews of the MDR-TB treatment literature in paediatrics and will feed into WHO guideline development. During 2020, the literature search for the review article on the pharmacokinetics and dosing of second-line TB drugs in children and adolescents was complete and analysis is scheduled to begin in the first quarter of 2021.

  For the second review on treatment outcomes, progress has been made on the literature search and the secondary analysis is planned for Q1 2021. Close collaboration with WHO has taken place in order to include the outcomes of the literature review in their 2021 guidelines review on MDR-TB treatment for children.
- Output 2 consists of 5 clinical trials to deliver improved evidence for better MDR-TB prevention and treatment for children:
  - Trial 1, "Delamanid Crush study", which is led by TASK and assesses the relative bioavailability in adults of delamanid dispersed in water compared to whole tablet form. Delamanid is a key new drug used to optimise MDR-TB treatment regimens and is more easily administered to children in a dispersed formulation. Understanding whether dispersing impacts on bioequivalence is important. In 2020 all approvals have been granted and the study opened to accrual in October. At the end of the year, 5 of the 24 participants have been enrolled.
  - Trial 2, the "PERFORM study" (Pharmacokinetics of lEvofloxacin FORmulations in children with MDR-TB exposure) and evaluates the pharmacokinetics and acceptability of 100 mg dispersible compared to 250 mg non-dispersible tablets of levofloxacin in children exposed to MDR-TB. Levofloxacin is used in both MDR-TB treatment regimens and as prevention for children exposed to

MDR-TB and this study aims to look at how formulation may affect drug exposure (which impacts on safety and efficacy). During 2020, World Health Organisation Research Ethics Review Committee (WHO ERC), Health Research Ethics Committee (HREC) and South African Health Products Regulatory Authority (SAHPRA) approvals have been granted. The first patient was screened in October 2020.

- Trial 3, the "CATALYST study" (Clofazimine and moxifloxacin PK, safety, and AccepTAbiLitY for paediatric TB treatment), and is a phase I/II trial of the pharmacokinetics, safety, tolerability, and acceptability of new formulations of clofazimine and moxifloxacin in children treated for rifampicin-resistant TB. These two study drugs are often included in MDR-TB treatment regimens and the trial aims to evaluate new child-friendly formulations. This is a multi-site study which will recruit at the DTTC Brooklyn Chest Hospital (BCH) site as well as in India (partner BJMC and JHU, PI: Dr Aarti Kinikar) and the Philippines (De la Salle Medical Centre, PI: Dr Mel Frias) University. During 2020, the three sites prepared for opening of the study. In South Africa, WHO ERC, HREC, and SAHPRA approval have been granted and the site initiation visit is scheduled for early 2021. India and the Philippines were still awaiting approvals from local authorities.
- Trial 4, the "TB Therapeutic trials: Prevention of MDR-TB TB-CHAMP (MDR-TB preventive therapy trial): (DTTC PIs: Anneke Hesseling, Simon Schaaf, James Seddon). This is the first ever randomized phase III placebo-controlled trial to assess the efficacy of levofloxacin preventive therapy vs. placebo in child contacts of MDR-TB. The target sample size is 1009 children 0-5 years of age. The main trial opened to accrual in Quarter 4 of 2017. As of the end of 2020, 801 children had been screened and 633 enrolled in the study. Recruitment in 2020 was more challenging than usual, due to the COVID-19 pandemic and unrest in communities. Interim analysis took place in Quarter 3 of 2020 after 500 contacts had been followed up for at least 24 weeks. There were no safety concerns, but analysis showed the trial should proceed to recruit the

full number of participants. In December 2020, Unitaid published an article on their website featuring interviews with DTTC team members Susan Purchase, Hazel Davids-Ruiters, Simphiwe Simelane, and Daphne Van Ster. The article highlighted the importance of the work being done as part of the TB-CHAMP study. The trial, led by the DTTC, previously funded by the BMRC/Wellcome Trust/DFID, and received funding for completion from Unitaid as part of the BENEFIT Kids grant. The trial includes 3 South African sites, including Shandukani (WHRI, Johannesburg, Dr Lee Fairlie), PHRU Matlosana, Klerksdorp (Prof. Neil Martinson) and the DTTC.

- Trial 5, the "PETITE study" (PharmacokinEtic and safeTy of the 4-In-1 granules inneonaTEs) which is led by neonatologist Adrie Bekker. This is an open label, single arm, two-stage trial to evaluate the single and multi-dose pharmacokinetics and safety of the abacavir/lamivudine/ lopinavir/ritonavir (30/15/40/10mg) (4-in-1) fixed-dose granule formulation in HIV-exposed neonates. This study opened to accrual in September 2020 and Cohort 1A and Cohort 1B (16 children in total) was completed. The PK interim analysis is in process and its outcome will determine the continuation of the study with Cohort 2.

- Output 3 aims to produce targeted formulation development and market shaping to improve availability of child-friendly formulations of key second-line TB drugs and will be undertaken in partnership with TB Alliance. Some progress has been made with identifying potential manufacturers through a Request for Proposal (RFP) process. Further re-programming will need to be take place in early 2021 to ensure progress with this output.

IMPAACT P1108: (PIs Anneke Hesseling, Simon Schaaf). IMPAACT 1108 is an NIH-funded phase I/II trial to determine the optimal and safe dose of bedaquiline in HIV-infected and HIV-uninfected children with MDR-TB. P1108 is a multi-centre trial which enrols children in age-based cohorts in an age de-escalation strategy and is being undertaken in South Africa, India, and Haiti. The target sample size is 75 and 8 of the 15 children enrolled thus far were

enrolled at the DTTC. Bedaquiline is a critically important treatment option for both adults and children as it allows for the use of shorter, injectable-sparing MDR-TB treatment regimens. Data from P1108 has already informed WHO paediatric dosing guidelines and bedaquiline is now available in South Africa for children 6 years of age and older in the routine TB programme. The opening of Cohorts 2 and 3 (children < 6 years of age) to enrolment was delayed from Quarter 1 2020 to Quarter 4 due to the COVID-19 pandemic and national lockdown. The first child was enrolled in 2020 at DTTC on 13 November. Four children were enrolled from DTTC in 2020 (2 in Cohort 2 and 2 in Cohort 3) and the total number of children enrolled on P1108 since study start in 2017 is 12. Recruitment is ongoing.

IMPAACT P1026s (PI: Jennifer Hughes). IMPAACT P1026s is a phase IV observational PK study that started in November 2017 and closed to recruitment in December 2019. The primary aim of the trial is to describe pharmacokinetics (PK) of selected antiretroviral (ARV) drugs, TB drugs and contraceptives currently used in the clinical care of HIV-infected and HIV-uninfected women with TB or drug-resistant TB. Findings from the second-line TB arm of this study will provide PK data of medications used to treat MDR-TB during pregnancy. PK assays are being prioritised for levofloxacin, linezolid and bedaquiline, the three 'WHO Group A' drugs considered to be the most efficacious for treating MDR-TB. A follow-up study, IMPAACT 2026, which also aims to describe the PK properties of ARV and TB medications administered during pregnancy and postpartum (in blood and also in breastmilk), is due to open to recruitment in 2021. The target sample size for the study is 40 participants and the study opened to accrual in mid-2020.

IMPAACT 2005: (PI Anneke Hesseling). IMPAACT 2005 is an NIH-funded phase I/II open-label, single arm study to evaluate the pharmacokinetics (PK), safety and tolerability of delamanid in combination with an optimized background regimen for MDR in HIV-infected and HIV-uninfected children with MDR-TB. Delamanid is a new drug used for the treatment of MDR-TB in children and adults. Optimizing its use in children is crucial as its inclusion in an MDR-TB treatment regimen allows for the exclusion of painful injectable drugs (and their

unacceptable side effect of permanent hearing loss, among others) and shortening of treatment duration. A total of 48 participants, aged 0-17 years, will be enrolled into four age-based cohorts over a period of 72 weeks and will receive delamanid for 24 weeks. PK and safety data will be collected. This trial was planned to open to accrual in Quarter 2 of 2020 but this was delayed due to the COVID-19 pandemic. Subsequent to this delay a protocol amendment was required and this is awaited before trial opening, expected to be Quarter 3/4 2021.

Clofazimine PK Study (PI: Jennifer Hughes). The DTTC is implementing this single site, industry-funded (Novartis) study sponsored by Stellenbosch University. This is a Phase I/II study of the PK, safety, and tolerability of clofazimine in HIV-infected and uninfected children treated for rifampicin-resistant (RR)-TB. As a 'WHO Group B' drug, clofazimine is used in almost all treatment regimens for people with RR-TB disease however, dosing and PK data for this drug in children is extremely limited. This study aims to assess the safety and tolerability of the smaller 50mg capsule formulation while also establishing optimal weight-based dosing in all children less than 18 years of age.

Therapeutic trials: prevention of drug-susceptible TB

TBTC Study 35: (PI Anneke Hesseling) This multisite study funded by the United States Centre for disease control (CDC) and the CDC Foundation, aims to evaluate the pharmacokinetics (PK), safety and tolerability of rifapentine given in a novel, water-dispersible fixed dosed combination with isoniazid (INH) which is developed and supplied by Sanofi. This fixed dose combination (FDC) of rifapentine and isoniazid which has been shown to be efficacious in preventing progression from latent TB infection (LTBI) to disease, will be given once-weekly, for 12 weeks, in HIV-infected and HIV-uninfected children between the ages of 0-12 years in whom treatment for LTBI is indicated. Current LTBI treatment is daily INH for 6 months, adherence to this regimen is poor as it is not a child friendly regime or formulation. It is important to treat LTBI to prevent progression to disseminated or severe forms of TB in young children, therefore a regimen that improves adherence to LTBI treatment, will

potentially decrease TB related childhood morbidity and mortality. This study hopes to inform dosing (especially in children under two years), provide more safety data, and assess the acceptability of this novel FDC of rifapentine and isoniazid. The first patient was enrolled on Study 35 in October 2019 and the first 2 cohorts were fully enrolled by March 2020. DTTC contributed 13 of the 16 participants that were enrolled across all sites, and the recruitment was paused for interim analysis. Cohorts 2 and 3 will open to accrual in Quarter 3 2021, with the aim to generate data in children below 2 years of age. The group is actively engaged in efforts to support the development of a child friendly rifapentine formulation which will be globally accessible.

Therapeutic trials: treatment of drug-susceptible TB

SHINE: (Site PI: Anneke Hesseling). The SHINE trial (Shorter treatment for minimal TB in children) is a multi-site open-label trial that aims to evaluate the efficacy and safety of 4-month vs. the standard 6-month TB treatment regimen for non-severe DS-TB in children. The trial is sponsored by the Medical Research Council Clinical Trials Unit (MRC CTU) at University College London. Recruitment was completed in July 2018, with 1204 children enrolled in South Africa, Zambia, Uganda and India and the last study visit on SHINE was conducted in January 2021. The DTTC enrolled a total of 315 children on SHINE. The new WHO-endorsed dispersible fixed-dose combination of first-line TB drugs was used in this trial: nested pharmacokinetics sampling was completed in 31 children, and the DTTC led the qualitative work around the acceptability and palatability of this formulation. The DTTC also coordinated the process for central expert review of the chest X-rays (CXR) taken on the SHINE trial, interpreting and classifying >1200 CXR images. The SHINE trial results were presented at the 51st Annual International Union against Tuberculosis and Lung Disease – the trial found that 4 months TB treatment was as effective as 6 months treatment in children with non-severe TB. This provides strong evidence that children with non-severe PTB could receive a shorter treatment regimen and there is ongoing work with the WHO regarding how these results could be operationalised. The study has received media coverage on multiple platforms, including a featured article on Spotlight – see Appendix III.

Lung health, diagnostic, and biomarker studies

(PIs Marieke van der Zalm. Investigators: Anne-Marie Demers, Elisabetta Walters) UMOYA ("Breathe"). Intra-thoracic tuberculosis in children: moving towards better diagnosis and improved lung health: (PIs Marieke van der Zalm, Liz Walters). This ongoing prospective observational cohort of children with suspected TB aims to evaluate improved diagnostic strategies for paediatric TB, including novel laboratory techniques for both molecular and culture-based diagnosis on respiratory and stool specimens. This cohort supports ongoing evaluation of blood biomarker work and establish a biorepository of several other samples including nasopharyngeal aspirates, saliva, urine, and stool. In addition, the study will continue work to evaluate the interaction between viral and bacterial co-pathogens with TB and plans to assess and monitor lung function longitudinally in all children. UMOYA started recruitment November 2017 and at the end of 2020, had 313 children enrolled. Recruitment was paused during the COVID-19 pandemic from March to November 2020.

In 2020, three new 5-year grants were awarded for ongoing work on this platform:

- NIH-R01 grant (2020- 2025, $1 455 808) was awarded for research into Multiplexed Antigen-Specific Antibody Fc Profiling on a Chip for Point-of-Care Diagnosis of TB in HIV-infected Children in collaboration with Professor Galit Alter and colleagues at Harvard University. This grant will support the recruitment of an additional group of 300 South African children with suspected TB in order to develop a blood-based point of care test to diagnose tuberculosis in especially the youngest children that are HIV exposed or infected, by investigating host Mycobacterium tuberculosis (M.tb) antibody responses.
- NIH K43 emerging global leader award (career grant Dr vd Zalm, 2020- 2021, $565 867) for research into "The long-term consequences of pulmonary tuberculosis and respiratory viruses on lung health in young South African children".
- EDCTP senior fellowship plus (2021- 2026, euro 750 000) was awarded to Dr vd Zalm to build capacity in research on child lung health in South Africa and Mozambique. Dr Justina Bramugy (early career fellow in this project) will lead the implementation of a

prospective lung health cohort in Mozambique, in collaboration with Dr Elisa Lopez and Professor Quique Basset (IS Global, Spain).

Other key sub-studies nested in the platform are:

- Butterfly ultrasound (PI Megan Palmer) funded by the Bill and Melinda Gates Foundation (BMGF) . The Butterfly ultrasound study is a proof-of-concept study which aims to explore the use of lung ultrasound to discriminate between TB and non-TB lung disease in a paediatric population. The Butterfly study was paused during the lockdown period and re-opened to accrual in October 2020 after a costed extension was received from BMGF to complete the project. In addition to the Butterfly ultrasound probe, a new, portable ultrasound machine with a smaller probe has been purchased so that the team can begin suprasternal notch scanning. The costed extension will give the team the opportunity to reach the planned recruitment target and complete the study by Quarter 2 of 2021.
- Influenza project: subcontract with University of the Western Cape and Professor Megan Shaw to investigate genetic diversity of the influenza virus in children with suspected pulmonary TB. This is a 2-year subcontract; The Icahn School of Medicine at Mount Sinai (ISMMS) holds the contract from NIAID/NIH. The University of the Western Cape (UWC) and Stellenbosch University will receive funds from a subcontract between ISMMS and UWC 2019-2021.
- QOOL kids (Quality of life for children): A second award of Temporary Research Assistance funding (for 2021) from the University of Stellenbosch for Michaile Anthony working towards her PhD (Graeme Hoddinott/ Marieke van der Zalm). This has included substantial development and implementation of standardized quality of life measures for use at multiple study visits.
- Development, programming, and preparation for use of a standardized diagnostics acceptability measure for use at multiple study visits.
- Urine proteomics: This project aims to identify host-derived urine proteins that are differentially expressed in children with TB compared to children with non-TB illness.

The project is in collaboration with USA partners Robert Husson and Hanno Steen from Boston Children's Hospital, USA. This final year, the focus of the project has been to optimize the LC-MS/MS platform to achieve a high detection of proteins in urine samples. This is done in the Steen laboratory at Boston Children's Hospital, Harvard University. Data analysis will include both traditional logistic regression approaches (led by Harvard University) as well as bio-informatics methods (led jointly by Harvard and Stellenbosch Universities). A doctoral student, Ashley Ehlers, under the supervision of Prof Tabb from SU's Division of Molecular Biology and Human Genetics, has been awarded a scholarship by Boston Children's Hospital, to work on this project. Final data-analysis is ongoing and expected Q3-4 2021.

- Serum bio-signatures. This project aims to identify pathogen-derived serum antigen peptides that are differentially expressed in children with TB compared to children with non-TB illness, using a novel NanoShell-MS assay. The project is in collaboration with US partner Tony Hu from Arizona State University and data-analysis is ongoing.

COVID Kids (PI Marieke vd Zalm, Helena Rabie and Andrew Redfern): The COVID-kids study, building on the UMOYA platform, is a collaboration between DTTC and the larger Department of Paediatrics and Child Health. The study investigates the clinical impact of COVID-19 on South African children and includes routine care data collection of children presenting to Tygerberg with possible COVID-19 and a prospective observational cohort of a selected group of children with and without COVID-19. The routine care data collection aims to describe the clinical presentation of children with COVID-19. The COVID-kids cohort study aims to rigorously investigate the clinical impact, immunology, respiratory morbidity, psychological impact, and transmission dynamics of SARS-CoV-2 in South African children. Children younger than 13 years, HIV-/+, are recruited from Tygerberg Hospital, the main referral hospital in the Western Cape. Included are children with acute respiratory illness and high risk for COVID-19; acute respiratory illness of unknown aetiology; household SARS-CoV-2 exposure, or any symptoms and a positive SARS-CoV-2 test. Clinical assessment and data collection are done at enrolment and during follow-up to three months. In addition, all cases of Kawasaki disease or

the paediatric inflammatory multisystem syndrome (PIMS-TS) temporarily associated with COVID-19 are captured. At enrolment, respiratory samples are sent for testing for SARS-CoV-2 and an additional respiratory panel of 16 common respiratory viruses. A saliva sample is also collected and stored for future mucosal immunology and SARS-CoV-2 testing to compare cycle thresholds between saliva and respiratory samples as an indication of infectiousness. Respiratory morbidity is determined at enrolment and three months later. In total 80 children and caregivers are enrolled in the cohort study (with new recruitment closed) and the first children have been seen for their 3-month follow-up visit.

This research was supported by SEED funding from Stellenbosch University special vice-rector fund for COVID research.

Ongoing COVID-19 paediatric study collaborations:

- The South African COVID-19 in Children Research Network is coordinated by the South African Medical Research Council (SAMRC).
- The Cape Town MIS-C Team, with University of Cape Town and paediatricians from Red Cross Children's Hospital.
- The African Forum for Research and Education in Health (AFREhealth), funded by National Institutes of Health.

Teen TB - Understanding the biology, morbidity, and social contexts of adolescent tuberculosis (PI James Seddon): This observational study of adolescent (10 to <20 years) was due to start in March 2020 but was delayed due to COVID-19. Recruitment started in November 2020. The study aims to recruit 50 adolescents with TB disease and 50 healthy controls who have been exposed to TB in their households. There are four main research areas: 1) explore the role of advanced imaging in adolescent TB (PET/CT, lung ultrasound and CXR); 2) understand the impact of TB on lung health and respiratory function in adolescents; 3) understand the impact of puberty on the immune response to TB and how these impact on respiratory morbidity and 4) explore the psychosocial experiences of adolescents affected by DS- and MDR-TB. Recruitment will continue until 31 July 2021 and then follow up for an additional two months. This study is funded by the Global Challenges Research Fund.

2. Health systems strengthening and operational research

The aim of the research in this pillar is to help improve TB and HIV care by building an evidence base for effective programme implementation. Operational research focuses on identifying gaps in health programme quality, efficiency, and effectiveness, evaluating factors that contribute to these, and testing interventions to improve outputs and outcomes.

This research focus area also includes epidemiological and routine data analyses, modelling, and health system strengthening research, all contributing to the overall aim of generating evidence to strengthen program implementation.

1. Evaluating 10 years of TB control in South Africa: (PI: Muhammad Osman; co-investigators: Karen du Preez, Anneke Hesseling, Rory Dunbar). Routine TB surveillance data have been under-utilised in identifying and understanding programme weaknesses and finding ways to address these. The socio-economic determinants that may be contributing to poor TB control have not been adequately evaluated. As South Africa scales up TB control efforts to achieve the even more ambitious "End TB Strategy" goals, a more data-driven approach to TB control efforts is required. This study aims to undertake a comprehensive, in-depth analysis of TB control in South Africa to review epidemiological trends from 2004 to 2016 and to identify achievements and programme gaps where intervention is required. This project is not funded and is being implemented in collaboration with National Department of Health.

During 2020 analysis on case notification and outcomes for paediatrics, adolescents, and adults was completed. Multiple analyses were completed, and three manuscripts produced.

Ongoing analyses include:

1. Case notifications in adults
2. Spatial variability in childhood TB in South Africa
3. TB meningitis in children and adults
4. Key populations: Children and previously treated TB patients

LINKEDin: reducing initial loss to follow up among tuberculosis patients in South Africa: (PIs: Anneke Hesseling and Muhammad Osman). This study is funded by the Bill and Melinda Gates Foundation. Individuals diagnosed with TB, but who are lost to follow up before initiation of TB treatment and/or TB notification are referred to as "initial loss to follow up"

(ILTFU). This study aims to: 1) demonstrate the impact of an automated notification system of TB patients in hospitals on increasing the number of notified TB cases; and 2) demonstrate the impact of the implementation of an automated alert-and-response TB patient management system on increasing the proportion of TB patients who are linked to TB services and who initiate treatment at different levels of health care. Implementation began in 2019 in 6 hospitals and 31 primary health care facilities in three provinces of South Africa: Western Cape, Gauteng and KwaZulu Natal. The DTTC is working closely with implementing partners; Centre for Infectious Disease Epidemiology and Research (CIDER) in the Western Cape Province, Right to Care in Gauteng Province and Interactive Research and development (IRD) in KwaZulu Natal, as well as local and provincial health departments. Using a before/after design, the study will measure the proportion of TB patients who are ILTFU at baseline and again at the end of the implementation phase. In the WCP, four sub-studies are being implemented to; 1) estimate costs associated with the interventions 2) determine patient experiences and social determinants of linkage to care, 3) quantify mortality among ILTFU TB patients and 4) pilot an innovative strategy for linkage to TB care.

Implementation continued during 2020. Field work was interrupted due to COVID-19 and a national lockdown. To accommodate this, the funder awarded a costed 6-month extension to the study, effectively moving the end of the study implementation period to 31 December 2020. The field teams resumed tracing in the field from August 2020 with all relevant IPC protocols in place and continued until 31 January 2021 to follow up all TB patients diagnosed until 31 December 2020.

Preliminary analysis during 2020 identified that ILTFU is higher among hospital diagnosed patients compared to those diagnosed at primary health care (PHC) level. We noted hospitals account for a modest proportion of diagnosed TB patients but had high TB-associated mortality. A hospital-based TB diagnosis is a critical opportunity to identify those at high risk of early and overall mortality. To address this, the team implemented an intervention at Khayelitsha district hospital in the Western Cape Province that aimed to engage with TB patients prior to their discharge from hospital to ensure they had a good understanding of the importance of continuing their care at PHC level. These results have also highlighted that interventions to diagnose TB before hospital admission should be prioritised. An additional

lesson learned during 2020 has been the importance of having the correct patient contact details captured in the electronic system and this has been conveyed to health services.

Operational Research Assistance Program (ORAP): The overall aim of ORAP is to undertake operational research as an integral component of health programmes in South Africa to contribute to improved quality and performance of the health system.

In November 2016, a new miniature version of ORAP was implemented in the Western Cape. Participants (five from health services) have embarked on an experiential learning course to develop three independent study protocols for research to be undertaken. Five mentors from the DTTC are supporting the trainees through protocol development, study implementation and publication of their findings. All three projects are approved for implementation by the Stellenbosch University Health Research Ethics Committee (HREC).

During 2020, mentees have been working on analyses and started the process of drafting manuscript. Finalisation of these three projects is planned for 2021.

Epidemiological Modelling of TB and control interventions

Modelling of TB and the impact of TB control interventions constitutes an additional core competency to be built at the DTTC in the forthcoming years. Central to this effort is the DTTC-SACEMA TB Modelling Partnership established in 2019 and the joint TB modelling group. In January 2020, DTTC co-hosted the First National Symposium on Mathematical Modelling Research to Guide Decision Making For Tuberculosis Control in South Africa, a first meeting of its kind to create a platform for collaboration between mathematical modellers and key decision makers in TB control. The joint DTTC-SACEMA TB Modelling Group, led by senior researcher Florian Marx, has continued its work on a joint research project to build a South African TB model to project TB incidence and mortality in South Africa and the impact of control interventions. Muhammad Osman and Florian Marx are also members of the new Task Group “TB Epidemiology and Modelling” of the TB Think Tank (National Department of Health). Current key research priorities for the partnership are the population-level impact of scaling up antiretroviral therapy in South Africa, rational use of novel diagnostics for TB case detection, interventions along the TB care cascade, and TB prevention in high-risk groups such as young children and former TB patients.

3. HIV prevention research

The DTTC has made great strides in the field of HIV prevention with the completion and implementation of two large community-based seminal trials as part of the HIV Prevention Trials Network (HPTN).

HPTN 071 (PopART): The HPTN 071 (PopART) trial assessing the impact of a community-based HIV prevention trial on HIV incidence was concluded in 2019. In order to refine analyses of available data, funding was received from the Bill and Melinda Gates Foundation. A total of 23 PopART related articles were published during 2020. Refer to the Sociobehavioural Sciences section below.

HPTN 084 (LIFE): (PI: Peter Bock) HPTN 084 (LIFE) is a phase 3, double blind, safety, and efficacy study of long-acting injectable cabotegravir compared to daily oral TDF/FTC for HIV Pre-Exposure Prophylaxis (PrEP) in HIV negative women aged 18 to 45 at high risk for HIV acquisition. By the end of March 2020, the DTTC Kuilsriver site had enrolled 159 participants. On the 9th of November 2020, researchers from the HIV Prevention Trials Network (HPTN) announced that data from the HPTN 084 clinical trial showed a pre-exposure prophylaxis (PrEP) regimen of long-acting cabotegravir (CAB LA) injections once every eight weeks was safe and superior to daily oral tenofovir/emtricitabine (FTC/TDF) for HIV prevention among cisgender women in sub-Saharan Africa. During the planned review of study data, an independent Data and Safety Monitoring Board (DSMB) recommended the study sponsor—the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health—stop the blinded phase of the trial and share the results, which are outlined below (Extracted from the HPTN website, https://www.hptn.org/news-and-events/press-releases/hptn-084-study-demonstrates-superiority-of-cab-la-to-oral-ftctdf-for):

Overall, HPTN 084 enrolled 3,223 cisgender women at research sites in Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, and Zimbabwe. The average age of study participants was 26 years and 57% of participants were 18-25 years old. A total of 38 HIV infections occurred during follow-up, with four infections in the CAB LA arm (incidence rate 0.21%) and 34 infections in the FTC/TDF arm (incidence rate 1.79%). The hazard ratio in the CAB LA versus FTC/TDF arm was 0.11 (95% CI 0.04-0.32).

Approximately nine times more incident HIV infections occurred in the FTC/TDF arm than in the CAB arm. These results meet the statistical criteria for superiority of CAB LA compared to FTC/TDF in the HPTN 084 study population. The higher-than-expected level of adherence to FTC/TDF throughout the study and overall low incidence rate in both arms of the study clearly demonstrate both drugs were highly effective at preventing HIV acquisition.

4. Sociobehavioural science research

Despite challenges related to the COVID-19 pandemic, the Sociobehavioural Science team continued to successfully implement a broad range of research including new data collection and analysis activities as components of the wider DTTC research portfolio in 2020. The team has made strong contributions to all three research focus areas at the Centre. These activities range from determining the acceptability and palatability of TB treatment for children in several paedaitric studies (S35A; CATALYST); people' experiences of linking (or not linking) to TB treatment or care (LINKEDin); and exploring methods to rapidly assess communities prior to the implementation of interventions (RINSS Study), along with other projects for the South African TB Think Tank. Across activities, all data collection, management, processing, and preparation for analyses are standardised and managed by a dedicated data quality team. In 2020, the team continued to transcribe and translate many hours of recorded interviews/discussion data.

The team had several highlights during the year, including the completion of one PhD thesis, the graduation of two master's students, and the graduation of three honours students. In addition, several team members have made significant progress on their PhD projects.

The team led on or contributed to several major research grant applications for the Centre. In total, team members co-authored 11 academic manuscripts, leading on 5 manuscripts and authoring one book chapter during 2020.

A priority for 2021 is to support staff in building capacity to lead in project implementation and to secure further funding. A further priority is to continue to encourage post-graduate studies, and in doing so, building on the culture of academic learning and publication.

Sociobehavioural science and TB, including paediatric TB.

Study 35A: This is a qualitative study nested within Study35 - a Phase I/II, open-label, single arm, exposure-controlled dose finding study, evaluating the pharmacokinetics, safety, and tolerability of rifapentine given in a new, water-dispersible fixed dose combination formulation with isoniazid once- weekly, for 12 weeks. The primary aim of Study 35A is to

understand the acceptability of this novel formulation 3HP TPT among health workers, children, and their caregivers. The team acquired HREC clearance in preparation of interviews with children, caregivers, and health workers. Although the parent study, Study35, was paused at the end of 2020, Study35A will continue data collection in February 2021 with the children and caregivers already recruited to the parent study. The first round of data collection and data processing is expected to be complete within the first quarter of 2021. A preliminary report will be prepared for distribution to the larger study team.

H3TB: Is a collaboration with Imperial College London and the University of Namibia to understand ways of contact tracing (and then early intervention) for people with MDR-TB in two districts in Namibia. The project includes evaluating the feasibility and yield of contact tracing in hospitals, households, and 'hotspots' (identified as high transmission/use areas in the community). Our contribution to the project is facilitating the social and spatial network data collection. The protocol has been submitted to the University of Namibia's Research Ethics Committee for review and tool development is underway. Data collection is expected to begin in 2021 with the project to continue until 2024.

Extemporaneous formulations: In consultancy with the TB Alliance, this project is to develop simple-to-implement ways of preparing four current formulations of MDR-TB drugs to facilitate accurate dosing and easier administration to children. Our role is to inform the local dynamics that inform acceptability and the home conditions in which these extemporaneous formulations (suspensions) will be stored to enable evaluation of their stability under those 'real-world' conditions. The project has developed a mechanism for crushing, suspending, and taste masking these formulations and next steps are to develop a user (child and caregiver) acceptability evaluation with protocol for this evaluation expected to be submitted to Stellenbosch University HREC in the first quarter of 2021 and the project completed by the end of 2021.

TPT DCE (The Preferences for TB preventive therapy (TPT) in South African children and adolescent study): This study, funded by the TB Think Tank, utilises a descriptive approach, combining of qualitative in-depth interviews with discrete choice experiments to understand children's, adolescents', their caregivers', and health workers' preferences for TPT in South

Africa. Specifically, it aims to provide insight into the most preferred factors of TPT regimens. The team acquired HREC clearance in 2020. Data collection is set to start Q1 of 2021.

TEEN TB: The aim of this nested study is to develop an understanding of social context of adolescent TB to inform the larger interventional study aimed at TB therapy and services suited to adolescents at risk of, or affected by, DS- and DR-TB. The nested component consists of in-depth interviews to understand the experiences of adolescents living with tuberculosis as well as a survey. Data collection started in November 2020 and will proceed into 2021. For this component of the study, we will interview 30 adolescents, aged 10-20 years, who are living with TB.

Urine tenofovir point-of-care assay (UTRA): UTRA is a treatment adherence monitoring tool developed to detect patients with inadequate adherence in order to avert subsequent virologic failure. We have conducted serial in-depth qualitative interviews with purposively selected patients (n~25) and health workers (n~5) to describe perceptions of UTRA and the processes and challenges of integrating UTRA into existing care systems. The interviews of the study were conducted between October 2020 and will be completed in the first quarter of 2021. The results of the study will inform the overall study of investigating the utility, feasibility, and acceptability of UTRA as an adherence support tool.

Sociobehavioural Science and Operational Research

LINKEDin (Reducing initial loss to follow up among tuberculosis patients in South Africa) – Three sub-studies:

- Patient Experiences: This qualitative sub-study of the LINKEDin study was conducted to explore patient experiences of linking (or not linking) to care following TB diagnosis. We conducted repeated interviews (qualitative cohort) and semi-structured observations with TB patients in one sub-district within the Cape Town Metro district between June 2019 and January 2020. We included TB patients who linked without intervention (n=5), who linked after an SMS or phone call (n=5), those who linked after a home visit from a community care worker (n=5), and those who failed to link to care (n=5). Data analysis was completed, and a manuscript has been submitted to a journal.

- WIARS: The 'WhatsApp-based interactive alert and response system (WIARS)' sub-study aimed to pilot and evaluate an innovative interactive communication strategy to prevent loss to follow-up among presumptive TB patients who submitted sputum for diagnosis at the local clinic in a high-incidence community in suburban Cape Town. The intervention consisted of three levels of communication: (1) WhatsApp-based interactive reminders to attend scheduled clinic visits, (2) the inclusion of proxy contacts in a WhatsApp chat to support attendance, and (3) prompts to share location information and receive a phone call for participants who missed a scheduled appointment. Of the 341 people approached to enrol in the study, 223 (65%) were ineligible to enrol because they did not own a WhatsApp compatible phone or own a phone at all. Of those enrolled, 95/112 (85%) were very interested to know their TB test result and 78/112 (70%) thought it was very likely or likely that they had TB. Most participants (70%) came for their appointment on the scheduled day or the day after.
- Finding TB patients not linked to care: The systematic tracing and referral to linkage of TB patients was conducted in the Khayelitsha sub-district of Cape Town. These were patients recorded as diagnosed with TB but not initiated on TB within the provincial routine health data system. We included all initial loss to follow up (ILTFU) TB patients who were diagnosed in thirteen primary health care (PHC) facilities and the Khayelitsha District Hospital (KDH) between January and December 2020. We attempted to locate all the ILTFU patients and refer them to care. We recorded our process electronically using the REDCap tool. Analysis is ongoing.

Sociobehavioural science and HIV prevention research

HPTN 071 (PopART) - Post-PopART evaluation: HPTN 071 (PopART) was a 3-arm cluster-randomized trial that measured the impact of a combination prevention package, including universal testing and treatment (UTT), on HIV incidence during 2014-2018. The primary results of the trial were reported in March 2019. The study has shown that it is feasible and acceptable to implement a combination prevention intervention including UTT, delivered by community HIV-care providers at scale in urban environments in Southern Africa. Further analyses, funded by the Bill and Melinda Gates Foundation, is ongoing with the aim of

understanding the results of the trial; unpacking and extrapolating the effects of the PopART intervention; understanding and addressing the challenges and limitations in the PopART strategy; and gaining a clearer understanding of the drivers of HIV transmission and acquisition. As part of the Socio-behavioural component of the grant, the aim is the completion of the in-depth analysis of data from the HPTN 071 (PopART) trial and a completed manuscript for publication. During 2020, the team finalized the first concept note.

HPTN 071a (Stigma Ancillary Study) - Post-PopART evaluation: Additional funding was received from the Bill and Melinda Gates Foundation to do analyses on data collected as part of the HPTN 071a Stigma ancillary study. With the additional funding, the team will be able to undertake extended analyses of longitudinal data from the HPTN 071 PopART trial; develop research synthesis and convening to develop a "state of the art" understanding of HIV stigma that can lead to action; design an "HIV STigma REduction and Mitigation implementation science network (STREAM). In 2020, the team continued to contribute and publish several manuscripts and held regular meetings and several virtual workshops.

Other sociobehavioural science research

MH4H: Is a study working with USAID/PEPFAR implementing partners in 14 districts in South Africa to understand the mental health experiences and services needs of health workers given the COVID-19 pandemic as an additional stressor. The protocol has been approved by Stellenbosch University HREC and submitted to the National Health Research Database (NHRD). Staff who will conduct the interviews have been hired and trained. Data collection is scheduled to be completed by April 2021 with a preliminary report expected in July 2021.

UseMyVoice2EndTBStigma: Is a collaboration with TB Proof to assess TB stigma in two communities in South Africa and to then work with community health workers in those communities to develop TB stigma reduction interventions. The project includes a survey (quantitative questionnaire) and nested qualitative data collection with a purposively selected sub-sample of survey participants. The protocol has been approved by Stellenbosch University HREC and is under review by the PHRCs in two provinces. The survey tool and qualitative discussion guides have been developed and field staff trained on their use. Data collection is expected to be completed early 2021 with analysis and reporting for Q3 2021.

RINSS (Rapid assessment of urban communities to optimise Public Health Interventions: water infrastructure in sub-Saharan Africa) is a formative research project that will entail 15 days of participatory and observational activities to investigate the water and sanitation infrastructure in two communities in the Western Cape. This project is collaborative with the University of Zambia and the Department of Engineering at Stellenbosch University. We aim to create a manual for doing the Broad Brush Survey (BBS) approach to formative research - the methodology used for RINSS - to inform community-based trials and interventions. The BBS manual will guide researchers to conduct rigorous and reproducible studies. Data collection will start in March/April 2021 in South Africa and Zambia, with the aim of producing four community-level case-reports (two communities in each country) by May 2022. Finer data analysis will be carried out for publications, further disseminations and a draft policy brief and recommendations all produced by December 2022.

Research Grants Awarded: 2020

During 2020, DTTC was received several grants from multiple international and national funding institutions and by the University. Several students at the DTTC were also successful in their funding applications.

Grant	Title	PI/ recipient
TBTC, CDC	Tuberculosis Trials Consortium,	Anneke Hesseling
NIH RO1	FASTERKids: Biomarker diagnostic Grant	Marieke van der Zalm with Harvard University
NIH K43	Burden of Tuberculosis Meningitis in children	Karen du Preez
NIH K43	Long term impact of TB and respiratory viruses on lung health in children.	Marieke van Der Zalm
European and Developing Countries Clinical Trials Partnership (EDCTP): Senior fellowship	The long-term consequences of pulmonary tuberculosis and respiratory viruses on lung health in young South African children	Marieke van der Zalm (working in collaboration with ISGlobal - Spain)
Bill and Melinda Gates Foundation	The post-PopART stigma ancillary team were funded for 18 months to produce a list of additional analyses and policy guidance based on data collected as part of the HPTN 071a (PopART) stigma ancillary study.	HPTN 071a (PopART) stigma ancillary study leadership with Graeme Hoddinott
HPTN Scholars Program	Predictors of participant retention in an HIV prevention trial population cohort: perspectives from the HPTN 071(PopART) study	Nomtha Mandla (Peter Bock as mentor)

Stellenbosch University: COVID-19 Project Seed Funding: Special Vice-rector (RIPS) Fund	COVID-Kids - Defining the presentation, immunology, and respiratory morbidity of respiratory virus infections, including COVID-19, in South African children.	Marieke van der Zalm
Stellenbosch University: Postgraduate Support Bursary	Mphil in Transdisciplinary Health and Development Studies: Exploring ways in which the management of household incomes affect antiretroviral therapy (ART) adherence of people living with HIV in the Western Cape	Abenathi Mcinziba
TB Think Tank	A review of patient-centred care initiatives for tuberculosis care in South Africa and beyond Identify and describe patient-centred initiatives for TB care and treatment, to enhance TB services in South Africa.	Graeme Hoddinott

DTTC Academic meetings

The DTTC Academic Meetings, usually held fortnightly at the Faculty of Medicines and Health Science (FMHS) target academic researchers to engage in ground-breaking research initiatives. In 2020, due to the COVID-19 pandemic, meetings were suspended in March 2020 and resumed in July 2020 on a virtual platform. Several national and international researchers presented their findings.

Date	Presenter	Topic
30 Jan.	Florian Marx Chris Dye Brian Williams	Summary of the 1st National TB Modelling Symposium ''Why do we spend so little on preventing ill-health and so much on treating it''? Priorities for TB Control globally and in South Africa''
27 Feb.	Richard Pitcher	Update on Ultrasound of the Paediatric lung and Mediastinum
12 Mar.	Rosa Sloot	Interpretation of serial interferon-gamma results to measure new tuberculosis infection among household contacts in Zambia and South Africa
23 Jul.	Sue-Ann Meehan Muhammad Osman	Initial loss to follow up among TB patients-preliminary findings from the LinkedIn study.
6 Aug.	Peter Donald	Anthon Ghon and his colleagues and the primary focus and complex of tuberculosis.
20 Aug.	Veronique de Jager	Update on early phase adult TB drug trials

17 Sep.	Karen Du Preez	PhD: Complimentary surveillance strategies and interventions to inform a tuberculosis care cascade for children.
8 Oct.	Ken Gunasekera Juli Switala	Development of a treatment-decision algorithm for HIV-uninfected children evaluated for pulmonary tuberculosis. Treatment of children and adolescents with RR-TB and reasons for hospital admission in the injectable-free era
29 Oct.	Muhammad Osman	TB and sudden unexpected deaths in Cape Town.
19 Nov.	Abenathi Mcinziba	Exploring how the management of household income affect ART adherence behaviour of people living with HIV in the Western Cape.
3 Dec.	Muhammad Osman	Mortality in Initial Loss to Follow up TB patients: Findings from LINKEDin

TB Clinical Forum 2020

The TB Clinical Forum 2020, hosted by the DTTC at the Stellenbosch University Faculty of Medicines and Health Science (FMHS) and organized by the City of Cape Town officials, is usually held on a monthly basis to create an interactive platform for academic researchers and government official in health services. However, due to the global COVID-19 pandemic, clinical form meetings were cancelled after February 2020, and were resumed in 2021.

Date	Presenter	Topic
14 February	Brian Allwood(SU) \ Marieke Van Der Zalm	Life after TB-the neglected part of the emergency
13 March	Ali Esmail (UCT)	MOTTS/NTM-A practical approach to diagnosis and management

Advocacy

During World TB Day in 2020, the DTTC launched the BENEFIT Kids promotional video, directed by Damien Schuman. The video highlighted the challenges for children affected by MDR-TB and showed how the various studies as part of the BENEFIT Kids Project will address these concerns. The video was shared on several platforms, including the DTTC website and BENEFIT Kids Project page.

The DTTC Community Advisory Board (DTTC CAB)

Since the DTTC Community Advisory Board (CAB) was established in November 2015, the CAB assisted with the prioritisation and development of research protocols. The CAB assists in driving the research agenda of the DTTC by guiding and sensitising researchers to the issues within the community. They provide guidance on documentation and participant recruitment strategies. During 2020, the DTTC CAB had to adapt their schedule to address urgent concerns related to the COVID-19 pandemic. In March, during a virtual meeting, it was decided that the communications platform, WhatsApp, has proven to be the most reliable channel for both the DTTC and a TASK team member. In May 2020, the DTTC-CAB coordinator establish that most CAB members could access Zoom to attend future virtual meetings. The DTTC EXCO approved the use of the transport funds so that members can purchase internet data.

CAB members were also active in effort to combat the COVID-19 pandemic with two members sharing information during the June meeting about volunteering with contact tracking and tracing with the University of Cape Town (UCT) and Médecins sans Frontières (MSF).

DTTC CAB activities: January to December 2020

Governance: On the 10th of September, the Steering committee meeting was held to discuss finances and to update the Constitution of the CAB. In November, the CAB held a Constitution Review Workshop.

International meetings: On the 20th of October 2020, CAB member, Goodman Makanda participated (virtually) in the Union Meeting: Survivor's Summit & Community Connect Programme.

Local and other meetings: The DTTC CAB held regular general meetings and quarterly Steering Committee (SC) meetings for the executive body. Although meetings had to shift to an online platform, the CAB's ICAB (IMPAACT Community Advisory Board) representative continued to participate in the IMPAACT network bi-monthly teleconference calls and the CAB HPTN network representative participated in the HPTN Community Working Group (CWG) monthly teleconference calls, including the HPTN Global Community Working Group conference calls. Throughout the year, the CAB also attended several SUN-CTU CAB Leadership Group (SCCLG) meetings. In October, CAB members attended the 10th Annual International Desmond Tutu Peace Lecture with the focus on Climate Change.

Dissemination events: CAB members attended several study dissemination events during 2020. In May, Gwynneth Hendricks attended the HPTN 083 Preliminary Study Results Webinar and in June, the NIH/NIAID Networks invited community representatives to join a presentation with Anthony Fauci for a question-and-answer session. Gwynneth Hendricks and Godfrey Tabata attended.
Several studies from the Centre also shared findings with the CAB. In November, the Sue-Ann Meehan and Nosi Vanqa presented the LINKEDin Preliminary Results and Peter Bock and Jabu Mantantana presented the HPTN 084 debriefing. In December, the SHINE Results were shared by Anneke Hesseling, Megan Palmer, Marieke van der Zalm, Annemarie Demers, Graeme Hoddinott and Dillon Wademan.
In addition, in July 2020, Marieke van der Zalm gave a talk on COVID-19 and research being conducted to the CAB.

Study and grant input: The DTTC CAB provided input for several studies, including issuing a letter of support for the re-opening of the P1108 and P2005 studies in July 2020 and for the iTHEMBA (TB Meningitis) R01 grant application in August 2020.
Extramural: CAB Member of the Year 2020 was awarded to Siphosethu Nco for outstanding work commitment, strong work ethic and leadership in her role as Secretary and going beyond the call of duty to support the development and professionalism of the DTTC-CAB.
In March 2020, the CAB had a uniform photoshoot and participated in the #EndTB campaign

in collaboration with the StopTB Partnership 2020. On the 5th of December, the CAB held a virtual Teambuilding Lunch and Event: Sharing the lessons learnt in 2020 with dreams and aspirations for 2021. Members were invited to get their favourite, food, drink or snack and tell others what it is and dress up for fun. Additionally, on the 10th of December, CAB members attended and presenting at the DTTC Annual Virtual Dissemination Event.

BENEFIT Kids CAB

The first BENEFIT Kids project community advisory board CAB meeting was held on Tuesday, 8 September 2020, with all 4 board members attending (Arne von Delft, Blessi Kumar, Jeff Acaba, Ciara Sage Goslet). The project was presented to the board by the project's DTTC members (Anneke Hesseling, Tony Garcia-Prats, Vivian Cox, Megan Palmer, Tina Sachs) and a colleague from the partner TB Alliance (Sarah Cook-Scalise). It was a successful start to a 3-year collaboration between the community members and the project team."

Conferences, academic meeting, and events

During 2020, team members from the DTTC participated in and presented at several (mostly virtual) local and international conferences, including the Union World Conference on Lung Health; the AIDS Impacts conference in London; the South African TB conference in Durban; the first International Post-Tuberculosis Symposium at Stellenbosch University; the Stellenbosch University Research Day; and several other events.

International conferences and events

23rd International AIDS conference (IAS). Virtual Meeting. 06-10 July 2020

Poster presentation.

- Predictors of initial loss to follow up amongst hospital-diagnosed HIV-infected tuberculosis patients in Cape Town, South Africa. S Meehan, AC Hesseling, A Boulle, M Smith, A Heekes, A von Delft, P Hendricks, M Osman.

IAS Pre-conference: "Turning Threats into Opportunities: Implementing and Continuing Quality TB Services in the Time of COVID-19 and Beyond". 3 July 2020.

Organizer: USAID, IAS, STOP TB Partnership

Oral presentation

- State of the art of new TB/HIV tools: updates on RR/MDR-TB treatment. V Cox.

The 51st Union World Conference on Lung Health virtual event, 20-24 October 2020.

Oral presentations

1. A WhatsApp-based interactive communication strategy to reduce initial loss to follow-up among presumptive TB patients in a high-incidence setting. FM Marx, D Jivan, SA Meehan, R Dunbar, AC Hesseling, M Osman.
2. Challenges and solutions for the recruitment of children to an MDR-TB prevention trial: Early experiences from TB-CHAMP. S Purchase, E Batist, N Mmile, S Nkosi, J Workman, N Martinson, L Fairlie, DM Gibb, JA Seddon, AC Hesseling
3. The magnitude of interferon gamma release assay response among children with household contact in a high-burden setting is associated with tuberculosis exposure and active disease. L Ronge, R Sloot, K Du Preez, AW Kay, HL Kirchner, AM Mandalakas, AC Hesseling.
4. Moxifloxacin pharmacokinetics and cardiac safety in children with multidrug-resistant tuberculosis. KK Radtke, AC Hesseling, JL Winckler, HR Draper, BP Solans, S Thee, LE van der Laan, HS Schaaf, RM Savic, AJ Garcia-Prats

5. Development of a treatment-decision algorithm for HIV-uninfected children with presumptive pulmonary tuberculosis. Kenneth Gunasekera, Elisabetta Walters, Marieke van der Zalm, Joshua L. Warren, Anneke C. Hesseling, Ted Cohen, James A. Seddon

Poster presentations

1. Fine needle aspiration biopsy of peripheral lymph nodes in children in a high TB incidence setting: Practical experience in a referral hospital. HS Schaaf, C Richardson, CL Sher-Locketz, PT Schubert, AR Redfern.
2. Excess mortality in TB patients diagnosed at hospital vs at primary health care in South Africa – M Osman, S Meehan, A von Delft, A Boulle, R Dunbar, M Smith, A Heekes, FM Marx, P Naidoo, AC Hesseling.
3. Poor linkage to care and high mortality among pregnant women with tuberculosis in South Africa. SA Meehan, AC Hesseling, J Hughes, A Boulle, M Smith, A von Delft, FM Marx, M Osman.
4. How can we find TB patients not linked to care? Lessons learned from a systematic tracing process implemented in the Western Cape Province, South Africa. N Vanqa, G Hoddinott, P Hendricks, M Osman and SA Meehan.
5. Caregivers' beliefs in anti-tuberculosis medicines in the African/Indian SHINE trial. J Workman, M Van Der Zalm, M Palmer, R Mboizi, V Mulenga, B Joseph, V Mave, K LeBeau, G Hoddinott.
6. A method for baseline adjudication of tuberculosis diagnosis in children in a therapeutic clinical trial: experience from SHINE: GH Wills, SM Graham, JA Seddon, S Welch, C McGowan, A Turkova, M Palmer, AC Hesseling, AM Crook and SHINE Team.
7. Routine South African tuberculosis data: Are we doing enough for children and adolescents? K du Preez, M Osman, J Seddon, HS Schaaf, P Naidoo, R Dunbar, L Mvusi, S Dlamini, AC Hesseling.
8. An adaptive decision-making approach to efficiently deploy tuberculosis case finding in high-burden communities. A de Villiers , C Dye , R Yaesoubi , S Floyd , FM Marx.

Symposia

1. Role and contribution of algorithm and score for diagnosis of paediatric
    - Contribution of chest X-ray in the paediatric diagnostic algorithm? James Seddon
2. Advancing TB prevention in children during the COVID-19 pandemic: Anneke C. Hesseling, Yael Hirsch-Moverman (Chair: AC Hesseling) Responsible use of BCG in the context of COVID-19 pandemic and presented by Prof HS Schaaf.
3. Approaches to improve TB case finding and treatment outcomes in children.
    - Epidemiology of childhood TB (James Seddon)
    - Research agenda to improve TB treatment outcomes in children (Anneke Hesseling)

Local academic conferences and events

SACEMA/DTTC: 1st National Tuberculosis Modelling Research to Guide Decision-Making for Tuberculosis Control in South Africa Symposium, Stellenbosch, 27 – 28 January 2020.

The symposium was organized jointly by DTTC, the DSI/NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) and the Centre for Infectious Disease Epidemiology and Research (CIDER, University of Cape Town) with financial support provided by the South African Medical Research Council, the TB Think Tank (National Department of Health) and SACEMA. The two-day symposium was attended by 52 delegates from 21 institutions including governmental institutions, universities and research centres, non-governmental/non-profit organizations and other professional associations. The meeting was opened by the Deputy Director of the National Department of Health, Dr Yogan Pillay.

DTTC Attendees:

Florian Marx, James Seddon, Muhammad Osman, Anneke Hesseling, Sue-Ann Meehan, Rory Dunbar, Rosa Sloot, Karen du Preez and Ken.

City of Cape Town Health Research day, Cape Town, 27 February 2020.

Presentations

1. TB patient's experiences of linking to care – findings from the LINKEDin study to reduce initial loss to follow up in Khayelitsha, Cape Town. Nosivuyela Vanqa.
2. 'P1108 – Improving access to bedaquiline for adolescents and children with RR-TB'. Bridgett Mtshiselwa.

Round table discussion

1. Peter Bock represented DTTC as a panellist for round table discussions on HIV and TB services research.

64th Annual Academic Year Day of the Faculty of Medicine and Health Sciences. Virtual Conference. 26 - 27 August 2020.

- State of the ART speaker: Graeme Hoddinott. Toward a conceptual model of 'the act' – theory generation in the problematic space of school-based HIV prevention through behaviour change.
- Marieke Van Der Zalm (DTTC), Helena Rabie (FAMCRU) and Andrew Redfern presented "COVID-19 disease in children and some preliminary results on COVID kids".

Scientific Meetings, Workshops, and training events

January 2020

- Three research sites (DTTC, Matlosana, Shandukani) completed P1108 protocol training in Johannesburg from 6 – 7 January.
- James Seddon and Graeme Hoddinott travelled to Windhoek, Namibia to attend the 2nd International TB Conference & Grant Application Meeting with Mareli Claassens from 20 - 24 January 2020.
- P1108 Webinar training was conducted on the 24th and 29th of January 2020.

February 2020

- The inception meeting for the MPHil Transdisciplinary Health and Development Studies methods course was facilitated by Graeme Hoddinott on the 7th of February.
- TB CHAMP Protocol training was held in Johannesburg from the 6th to the 7th of February.

- The IMPAACT Leadership Retreat was held in Washington from the 3rd to the 4th of February 2020. Anneke Hesseling joining remotely.
- Rolanda Croucamp and Marieke van der Zalm attended the UCT clinical refresher course from the 10th to the 14th of February 2020.
- The CTU Academic meeting took place on the 13th of February. Shaun Barnabas (FAMCRU) presented on Genital inflammation and HIV risk in young and adolescent women.
- Vivian Cox attended the National TB annual meeting held in Paris from the 10th to the 11th of February 2020.
- The Prevention Therapy Group Think Tank Meeting with TB HIV Care was attended by Graeme Hoddinott on the 12th of February 2020.
- The first of six seminars for the Methods, MPhil Transdisciplinary Health and Development Studies took place on the 13th of February. The facilitator was Graeme Hoddinott.
- Florian Marx attended a symposium on Finding Missing TB Cases on the 14th of February 2020.
- The TB Think Tank Mortality Symposium took place at the Hotel Verde in Cape Town on the 20th of February 2020. Muhammad Osman presented, and Sue-Ann Meehan attended.
- The Western Cape TB Consortium Working Group Meeting with the LINKEDin study was held on the 21st of February 2020.
- Tina Sachs attended the Stellenbosch University finance course in February 2020.

March 2020

- The University of Cape Town Division of Social Sciences BRIDGES Symposium was held at Goedgedacht, Malmesbury from 9 to 13 March 2020. Graeme Hoddinott, Dillon Wademan, Michaile Anthony, Dzunisani Baloyi, and Hanlie Myburgh attended.

April 2020

- None reported.

May 2020

- Portia Hendricks and Lario Viljoen completed Good Clinical Practice training on the 5th of May 2020.
- James Seddon presented to the WHO HIV-TB implementation for impact Working Group on 20 May 2020 on Diagnosing and treating paediatric MDR-TB infection and disease in the context of HIV.

June 2020

- On the 2nd of June, Anneke Hesseling presented at the World health Organization Child & Adolescent TB Working Group virtual meeting (hosted by Sabine Verkuijl) on TB preventive therapy trials updates and COVID-19.
- On the 3rd of June, Anneke Hesseling and Grania Brigden from The International Union Against Tuberculosis and Lung Disease presented (virtually) on the Impact of COVID-19 on TB care cascade in children and suggested recommendations. Karen du Preez also attended virtually.
- On the 10th of June, Karen du Preez attended the UNION webinar on monitoring the COVID-19 pandemic in sub-Saharan Africa, paying attention to health facility admissions and deaths.
- The LINKEDin study team attended the Western Cape TB consortium working group meeting, held virtually on the 12th of June.
- On the 17th of June, Anneke Hesseling presented at The World health Organization-hosted Global accelerator for paedaitric formulations (GAP-f) virtual meeting on the remaining gaps for TB formulations and research in children for prevention and treatment.
- The LINKEDin team attended (virtually) the Provincial Occupational Health and Safety Measures for COVID-19 presentation (Presented by Dr Meintjies) as part of the Webinar series: Future proofing Public Health Covid-19 on the 18th of June, in preparation for resuming field activities.

July 2020

- James Seddon presented lectures at the European Respiratory Society School of Adult and Paediatric Respiratory Medicine on multidrug-resistant tuberculosis in children. He also chaired one case-based discussion on tuberculosis on the 2nd of July 2020.

August 2020

- None reported.

September 2020

- Adelaide Carelse, Ragmat Saul, Brigette Mtshiselwa, Mapule Mosidi attended the Building Effective Relationships training on 10 and 11 September 2020.
- Anneke Hesseling, Tony Garcia-Prats, and James Seddon participated in and presented at the WHO TB Paediatric Drug Optimization Virtual Meeting (TB PADO) on the 22nd of September 2020.
- Tony Garcia-Prats represented the BENEFIT Kids team with a presentation at the Third WHO stakeholders meeting to enable implementation of Unitaid supported innovative TB projects.

October 2020

- Virtual Infection Prevention Control (IPC) Training focusing on hand hygiene was conducted on the 12th of October. Presenter: Leverne Barends, Asikhangele Mtshabe.
- Portia Hendricks from the LINKEDin study took part in the making of a video for the Provincial Health Data Centre (PHDC) for their innovative presentation at the Population Data Linkage Network (PDLN) conference in November.

November 2020

- Four DTTC staff members from the Sociobehavioural science team participated in the SACEMA virtual FameLab event. Dzunisani Baloyi won 2nd runner up in the “heat” where she presented her master's thesis topic.

- Virtual Infection Prevention Control (IPC) Training focusing on Environment Cleaning & Waste Management was conducted on the 3rd and 17th of November. Presenters: Anneen Van Deventer and Jenny Hughes.
- Anneen van Deventer attended the Stellenbosch University virtual leadership training from 3 - 4 and 10 - 11 November 2020.
- The HPTN 084 Primary Study Results were disseminated via webinar on the 13th of November.
- Several staff members presented at the South African Medical Research Council 2020 Early Career Scientist Convention.

December 2020

- The Virtual Infection Prevention Control (IPC) Training assessments were conducted on the 2nd of December.
- Data safety and monitoring Board (DSMB) results and participant responses to outcome for the HPTN 084 trial were reported on the Community Working Group (CWG) call on the 9th of December.
- The DTTC Annual Dissemination event was held on the 10th of December on a virtual platform. Attendees included CAB members.

Ongoing 2020

- Joint SUN-CTU CAB Leadership Group Meetings (DTTC CAB EXCO; TASK CAB EXCO; FAMCRU ExCo). Meetings held throughout the year, mostly on a virtual platform.
- Working Group for Data Analysis & Modelling (WGDAM). WGDAM is a working that aims to produce research outputs related to TB and health. The Working Group held online meetings during the year.
- The Research Methods for Transdisciplinary Health and Development Studies short course is offered by the Desmond Tutu TB Centre and the Sociology & Social Anthropology Department, presented by Graeme Hoddinott and Lario Viljoen.

Visitors during 2020

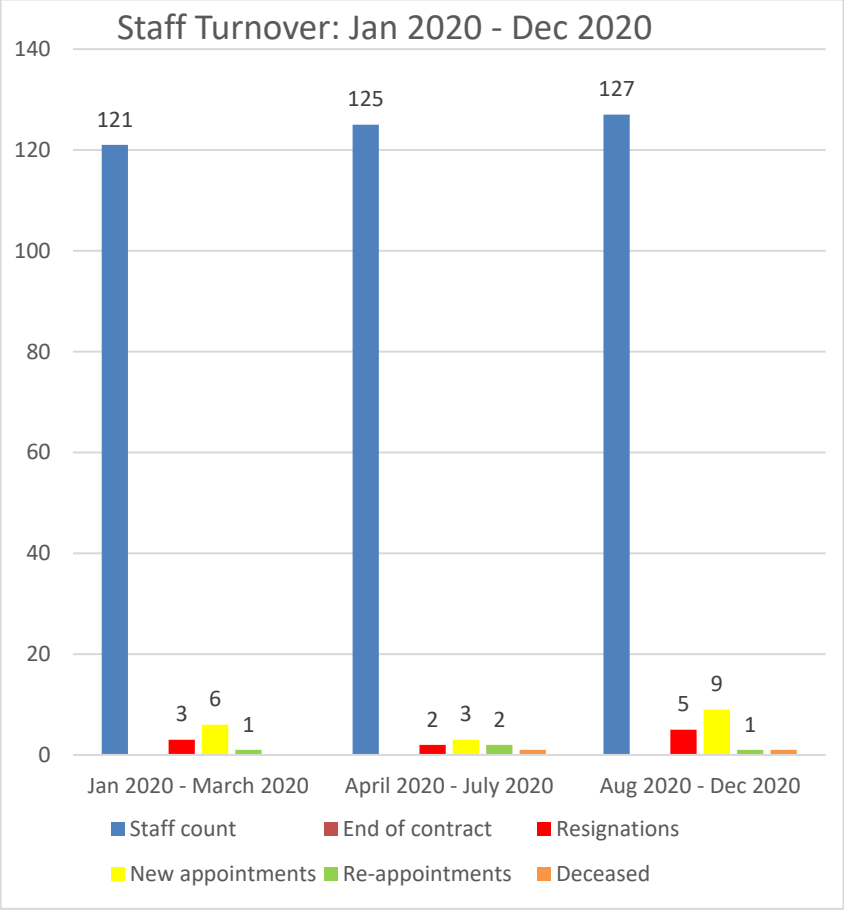
In light of travel restrictions and lockdown measures related to the COVID-19 pandemic, most planned visits had been suspended after March 2020 and meetings were held on virtual platforms. Visitors at the DTTC included:

Date	Visitor	Reason
Jan. – Jun.	Sarah Johnson – Research fellow	Implementation of the Teen TB Study
21 Jan.	Mary Glenshaw, & Director Maureen Goodenow, NIH Office of AIDS Research in Washington.	Site visit for the HPTN 084 study.
22 Jan.	Daniel Chin, Deputy Director for TB Services for GATES Foundation, Seattle, USA	Meeting with LINKEDin study team members
30 Jan.	Chris Dye, former Science Advisor to the WHO Director General and Brian Williams, former Senior Epidemiologist, Global TB Programme, WHO	Visiting DTTC to participate in a field trip with the LINKEDin study teams and to meet with the TB Modelling Working Group
2 – 14 Feb.	Andrew Handel, Paediatric Infectious Diseases Fellowship from Stonybrook University, Long Island, USA	Prof Simon Schaaf , Anneke hesseling for clinical peadiatrics - TB and HIV and reseaech training
13-14 Feb.	Visitors from MRC CTU: Charlotte McGowan and Marta Campos, London, UK	TB-CHAMP monitoring and planning meetings
27 Feb.	Eric McCollum, Johns Hopkins University, USA	Collaboration meeting with Anneke Hesseling and Marieke van der Zalm
3-5 Feb.	Gavin George, Michael Strauss (HEARD), Kwa Zulu Natal	Joining the TB modelling meeting and visited Khayelitsha District Hospital and the Provincial Health Data Centre (as part of the LINKEDin study).

Employees

During 2020, a total of 10 employees resigned, seeking employment elsewhere. The Centre employed 18 new staff members on different studies, linked to different post levels. Four staff members could be re-employed, ensuring that skilled staff are retained, as set out in our comprehensive HR retention strategy. Unfortunately, two of our staff members passed away during 2020.

Employee wellness remains one of our main priorities, including TB and other infectious disease screening and prevention, and infection control training. Psychosocial support and EAP referrals of individuals and teams were expanded during the 2020 COVID-19 epidemic.



DTTC Governance

DTTC Executive Committee (ExCo)

The DTTC is led by the Director, Anneke Hesseling, who is assisted by an Executive Committee (EXCO) of 12 senior scientific and core support DTTC staff members. The Director, who chairs the EXCO, reports to the Executive Head of the Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences and the DTTC Governing Board, which is responsible for oversight of the DTTC's strategic management. The governing board is chaired by Professor Andrew Whitelaw, Dept. Medical Microbiology and NHLS, Tygerberg; vice-chair: Professor Wolfgang Preiser: Division Head: Medical Virology. All members of the ExCo committee play an active role in the management of DTTC, making key decisions to ensure the vision and mission of DTTC are maintained and expanded. Members also form part of the scientific strategy team and are responsible for driving the research agenda at DTTC forward, in line with the 3 DTTC research pillars. The role of this team is to provide scientific input into research ideas put forward to the team and collaborate on potential research proposals.

In 2020 during the COVID 19 pandemic the DTTC ExCo met every two weeks and more frequently as required.

The DTTC established a COVID-19 Task team that met weekly during 2020, evaluating and implementing evidence-based COVID 19 strategies in line with Department of Health and Stellenbosch University and also managing staff on site to mitigate risk and ensure personnel and study participant safety.

DTTC Executive Committee Roles and Responsibilities

Name	Role
Anneke Hesseling	DTTC Director and chair of DTTC ExCo
Megan Palmer	Lead: Paediatric pharmacokinetic studies, Medical director Brooklyn Chest Hospital Paediatric Pharmacokinetics Unit
Marieke van der Zalm	Lead: Paediatric lung health studies
Frieda Verheye-Dua	Regulatory Manager and CRS coordinator
Simon Schaaf	Lead: Paediatric MDR-TB studies
Sue-Ann Meehan	Project Manager and investigator
Peter Bock	Lead: HIV Prevention research
Muhammad Osman	Lead: Implementation Research
Graeme Hoddinott	Lead: Sociobehavioural Sciences
Sterna Brand	Human Resources Manager
Theo Smith	Operations Manager
Rory Dunbar	Data centre manager
Anne-Marie Demers	Laboratory Director

Risk Management

Risks related to Human Resources, Finance and Regulatory are being monitored.

The protection of study participant confidentiality remains a high priority for the DTTC in our aim to deliver high quality reputable research outputs. The DTTC will continue to support staff training in good clinical practice (GCP) and research confidentiality prior to any study commencement. Through constant data monitoring by dedicated data centre staff, dual entry of any research information as well as GCP training, the DTTC will continue to mitigate against data fabrication. The regulatory office will also monitor the import of drugs or export of any materials to research partners to ensure no transfer is commenced without appropriate documentation.

During 2020 , the centre further improved communications platforms, including the regular

updating of the DTTC website. The DTTC is also involved in ongoing efforts to improve marketing and communications efforts in order expand our local and global footprints and to further develop relationships with new and current external stakeholders. The website news and events page is updated on a regular basis and several studies from the Centre have received widespread media attention (See Appendix III).

Accessibility to communities for recruitment and retention of study participants is still a potential risk. The DTTC continues to support various DTTC Field offices in various communities. The DTTC has also invested in developing community advisory boards (CABs). The DTTC has also invested in establishing a Community Advisory Board (CAB) since 2015, and now consisting of 26 community members from various areas across the Cape Metro. The aim of the CAB is to provide input and support in terms of research study protocol development, protocol reviews and study updates across the three research focus areas; paediatric TB research, health systems and operational research and HIV prevention research. The group meets on a monthly basis at the Tygerberg campus. However, since June 2020, the CAB has met monthly via the Zoom communication platform due to the COVID-19 lockdown restrictions. These members are serving on a voluntary basis. However, the DTTC re-imburses community members for travel to and from meetings or with a data allowance, whichever is applicable; and DTTC will sponsor any relevant training requirements for members.

There are ongoing efforts to obtain core funding to ensure the sustainability of core support staff and to decrease related risks. Due to the successful securing of funding for several new projects, several staff had contracts renewed. The aim is to link support functions across different studies to secure sustainability. As such, there was a significant risk reduction in terms of human resources and lower staff turnover rates were ensured.

Political instability and violence or unrest in study communities placed staff and patient safety at risk during 2020, with ongoing challenges during and after the initial lockdown periods. The DTTC has implemented many safety measures in collaboration with SU Security Management Services but have also identified various other measures to provide safe working conditions for staff. During 2021 all DTTC drivers will be retrained in defensive

driving, including highjack prevention and evaluation. The high burden of COVID-19, TB disease and HIV infection among the population served, poses a health risk to DTTC staff. The DTTC has taken many infection control measures through modification of vehicles by installing screens to separate drivers and participants and additional installation of extraction filtration systems at site offices.

In 2020 DTTC continued Infection prevention control (IPC) training virtually. 16 staff members were trained successfully. In 2021 the IPC training will upscaled to train at least 40 staff members virtually. The DTTC ensures that all staff receive bi-annual health screenings. During 2020 additional guidelines were included in the screening process in line with COVID 19 regulations. New staff are being vaccinated for Hepatitis B in line with national guidelines. Names and information have been given through for staff to be vaccinated with the COVID 19 vaccine in the first quarter of 2021. Nurses, doctors, and counsellors will form part of category 1 of the national vaccine rollout.

The DTTC is committed to adhere to SU management code of conduct which includes diversity aspects and identifying candidates from disadvantaged backgrounds for internal promotion. In 2021 there will be a strong emphasis on transformation especially on management level.

Ongoing formal training linked to supervision programs o supports master's and PhD students and will be maintained.

The DTTC employs a cadre of finance staff who work closely with the faculty research grants management office (RGMO) to ensure no misappropriation of research funds takes place. Regular expenditure allocation, reporting and finance meetings are held to mitigate against any misappropriation. Correct budgeting in collaboration with RGMO will also mitigate against large exchange rate losses. In addition, compliance with the University's Anti-Corruption and Anti-Bribery policy is strictly adhered to in collaboration with the Legal department which scrutinises all contracts which we undertake with funders and service providers.

Financial reporting

A detailed financial report is available upon request.

Acknowledgements and Funders

South African Collaborators | Funders | Partners

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In memoriam

Sadly, two much-loved members of the Desmond Tutu TB Centre team passed away in 2020 due to non-COVID-19 related illness. Both Noludwe Mabandlela and Riaan Rowan will be missed, not only by their families and other loved ones, but by their colleagues at the Centre as well.

Appendix I. Research outputs – peer-reviewed scientific publications

Manuscripts (PubMed listed)

1. Ahmed S, Mvalo T, Akech S, Agweyu A, Baker K, Bar-Zeev,N, … Hesseling AC … Seddon JA, … van der Zalm M …. and Cunningham S. 2020. Protecting children in low-income and middle-income countries from COVID-19. BMJ Global Health, 5(5). PMID: 32461228. PMCID: PMC7254117.
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Research Reports

1. Researchers at the DTTC (Megan Palmer, Karen du Preez, James Seddon, Marieke van der Zalm and Anneke Hesseling) contributed to the following research report: Van der Berg, S & Spaull, N. 2020. Counting the Cost: COVID-19 school closures in South Africa & its impacts on children. Research on Socioeconomic Policy (RESEP). Stellenbosch University. Stellenbosch.

2. Bock, P. Primary results of the HPTN 071 Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART) Trial. Research Newsletter: Public Health Matters in the Western Cape, South Africa. Issue 13. January 2020, page 9.

Book Chapters

1. Viljoen L, Myburgh H, Reynolds, LJ. A family affair: Managing comorbidities and the spaces between the private and the public in Connected Lives: Families, Households, Health and Care in Contemporary South Africa (eds. Nolwazi Mkhwanazi and Lenore Manderson), Cape Town, HSRC Press.

Appendix II. Students at the Desmond Tutu TB Centre during 2020

Currently Registered Trainees: Master's Degree

Name of trainee	Current position	Degree	Supervisor	Research Topic
Jabulile Mantantana	Community Engagement, Recruitment, and Retention Officer	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott	Continuity of ART for people who experience incarceration.
Nelis Grobbelaar	Programme Director (ANOVA Health)	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott	Integrating change to universal HIV-testing and ART regardless of CD4 - count into routine health services.
Leletu Busakwe	Student	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott	The experiences of paediatric MDR-TB patients' (14-17 years old) hospitalised for treatment in terms of adolescent social and biological development.
Abenathi Mcinziba	Social Science Research Assistant	MPhil Transdisciplinary Public Health and development studies (SU)	Lario Viljoen Peter Bock	Household level management of ART adherence choices in the context of socio-economic pressures.
Stephanie Jacobs	Social Science Research Assistant	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott Dillon Wademan	Families affected by MDR-TB's understanding of disease and treatment.

Dzunisani Baloyi	NRF Intern	MA Psychology (NWU)	MN Van Aardt	Exploring relationships between members of different generations: An older person's perspective.
Joanie Duvenhage	Dep Paediatrics	MMed	Simon Schaaf Anneke Hesseling	Incidence causes and outcome of management in cases of hepatocellular injury in paediatric patients on multidrug-resistant tuberculosis therapy.
Arlene Marthinus	Social Science	MA Psychology (SU)	Graeme Hoddinott Zuhayr Kafaar	School-going adolescents' access to sexual and reproductive health services in the Cape Winelands district
Ntombenhle Mkhize	Student	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott	Adult family members' influences on young people in rural KwaZulu-Natal's experiences of mental health service seeking.
Lindsey-Michelle Meyer	Student	MPhil Transdisciplinary Public Health and development studies (SU)	Graeme Hoddinott	Residents' experiences of a rural health service-learning centre's activities – a historical and ethnographic review
Ziphelele Saule	Social Science	MA Psychology (SU)	Anthea Lesch Graeme Hoddinott	Systems for service provider collaborations for adolescent sexual and reproductive health between department's education, health, and social development.
Ingrid Courtney	Study Coordinator	MSc in Clinical Epidemiology	Marieke van der Zalm Megan Palmer	The impact of pulmonary tuberculosis on lung function in South African Children
Melissa Nel	Social Science Research Apprentice	MPhil Transdisciplinary Public Health and development studies (SU)	Melissa Nel	Social Science Research Apprentice
Blia Yang	Student	MPH (UCT)	Marsha Orgill Graeme Hoddinott	HIV stigma experiences amongst foreign nationals in Cape Town
Bukeka Sawula	Student	MA (SU)	Laing de Villiers Lario Viljoen	Young women living with HIV's experiences of care and caring for children

Tembeka Mhlakhaphalwa	Social Science	MA Psychology (UKZN)	Mary van der Riet	Young women's constructions of sexuality in the context of HIV.
Currently registered PhD's				
Name of trainee	**Current position**	**Degree**	**Supervisor**	**Research Topic**
Muhammad Osman	Research Medical Officer	PhD (SU) Dep of Paediatrics	Anneke Hesseling Pren Naidoo Alex Welte	TB-associated mortality in South Africa: longitudinal trends and the impact of health system interventions.
Dillon Wademan	Social Science Research Officer	PhD (SU) Dep of Paediatrics	Graeme Hoddinott Lindsey Reynolds Ria Reis	Family chronicity and intergenerational syndemics in the chronic management of TB, HIV, and diabetes.
Nomtha Mandla	Research Officer	PHD (SU) Dep Global Health	Lungiswa Nkonki Peter Bock	Recruitment, participation, and retention of research participants in the HPTN 071 Population Cohort, South Africa.
Laing de Villiers	Social Science Research Officer	PhD (SU) Dep of Psychology	Leslie Swartz Graeme Hoddinott	Identity fluidity on the margins of Cape Winelands communities
Hanlie Myburgh	Social Science Researcher	PhD (UVA)	Ria Reis Lindsey Reynolds	The state and the citizen in the scale-up of HIV services in South Africa
Louvina van der Laan	Research Medical Officer	PhD (UCT)	Paolo Denti Anthony Garcia-Prats Anneke C. Hesseling	Pharmacometric modelling as a tool to optimise TB Treatment in children
Rene Raad	Student	PhD (LSHTM)	Justin Dixon Martin Gorsky Graeme Hoddinott	Protection of anti-microbials from resistance – lessons from the case of Tuberculosis in South Africa
Lario Viljoen	Social Science Researcher	PhD (SU)	Lindsey Reynolds	Young women's sexual decision-making in the context of earlier ART-access.
Postdoctoral fellows				
Elisa Lopez	Postdoctoral fellow	Postdoc (SU)	Anneke Hesseling	Improving TB treatment outcomes in children

Currently registered - Undergraduates + Hons + PGD's	
Name	**Degree**
Theo Smith	Honours Public Admin (SU)
Sterna Brand	BCom Honours Industrial and Organisational Psychology (UNISA)
Msondezi Ketelo	BA Honours, Anthropology. (UNISA)
Delphine Adams	BA Social Science (Boston College)
Rubaine Sayers	BA Industrial and Organizational Psychology (UNISA)
Grayson Lamore	BCom Financial Accounting (Boston College)
Shane Maker	BCom in Information and Technology Management (MANCOSA)
Graduates 2020	
Name of trainee	**Degree**
Amina Abdullah	PGD Public Health (UWC)
Nangamso Cawe	PGD Public Health (UWC)
Arlene Marthinus	BA Honours (SU)
Khanyisa Mcimeli	BA Honours(UCT)
Ziphelele Saule	BA Honours (SU)
Michaile Anthony	MA Psychology (UWC)
Nosivuyile Vanqa	MPhil (SU)

Bianca Hamman	MSc (Medical Microbiology)
Lena Ronge	MSc Clin Epi
Karen du Preez	PhD (SU)

Appendix III. Media interaction (television, video, radio, printed media)

Print and online media

- Cape Times. Virus overshadows World TB Day. 25 March 2020.
- Stellenbosch University. Research project bridges treatment gap for children with MDR-TB. 24 March 2020. Available online: http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=7224
- Youtube. BENEFIT Kids: Research project bridges treatment gap for children with MDR-TB. 24 Mach 2020. Available online: https://www.youtube.com/watch?v=0AvwN35R6qY
- Daily Maverick. South Africa: TB in children: Important research being done in Cape Town. 25 March 2020. Available online: https://www.dailymaverick.co.za/article/2020-03-25-tb-in-children-important-research-being-done-in-cape-town/
- Health24, Covid-19: Lockdown takes heavy toll on SA's TB response (James Seddon, Megan Palmer). Available online: https://www.health24.com/Medical/Infectious-diseases/Coronavirus/covid-19-lockdown-takes-heavy-toll-on-sas-tb-response-20200521-4
- Spotlight. TB in children: The amazing research being done in Cape Town - Kathryn Cleary interview with Anneke Hesseling and Megan Palmer. Available online: https://www.spotlightnsp.co.za/2020/03/24/tb-in-children-the-amazing-research-being-done-in-cape-town/
- Saturday Dispatch Weekend Post. Stellenbosch TB trial show children cured much sooner (Featuring the SHINE trial). 30 October 2020.
- Cape Times. Effective shortened treatment for TB (Featuring the SHINE trial). 30 October 2020.
- The Star. Breakthrough in TB Treatment for Children (Featuring the SHINE trial). 4 November 2020.
- Cape Argus. Excitement over HIV drugs for children (Featuring the PETITE Study). 9

December 2020.

- WHO Global TB Programme Newsletter. SHINE trial on shorter treatment for children with minimal TB (Featuring the SHINE Trial). 26 October 2020. Available online: https://mailchi.mp/who/shine-trial-on-shorter-treatment-for-children-with-minimal-tb?e=2ccfbc4a31
- Sowetan Live. Stellenbosch TB trial proves children can be cured much sooner (Featuring the SHINE Trial). 30 October 2020. Available online: https://www.sowetanlive.co.za/news/south-africa/2020-10-30-stellenbosch-tb-trial-proves-children-can-be-cured-much-sooner/
- Times Live. Stellenbosch TB trial proves children can be cured much sooner (Featuring the SHINE Trial). 30 October 2020. Available online: https://www.timeslive.co.za/news/south-africa/2020-10-30-stellenbosch-tb-trial-proves-children-can-be-cured-much-sooner/
- IOL. Breakthrough in treatment of TB in children. (Featuring the SHINE Trial). 4 November 2020. Available online: https://www.iol.co.za/the-star/news/breakthrough-in-treatment-of-tb-in-children-df4a8565-f901-4c18-a593-007ad4a83a0b
- HIV Prevention Trials Network. HPTN 084 Study Demonstrates Superiority of CAB LA to Oral FTC/TDF for the Prevention of HIV (Featuring the HPTN 084 (LIFE) Study). 9 November 2020. Available online: https://www.hptn.org/news-and-events/press-releases/hptn-084-study-demonstrates-superiority-of-cab-la-to-oral-ftctdf-for
- WHO. Trial results reveal that long-acting injectable cabotegravir as PrEP is highly effective in preventing HIV acquisition in women (Featuring the HPTN 084 (LIFE) Study). 9 November 2020. Available online: https://www.who.int/news/item/09-11-2020-trial-results-reveal-that-long-acting-injectable-cabotegravir-as-prep-is-highly-effective-in-preventing-hiv-acquisition-in-women
- Medical Brief: Africa's Medical Media Digest. Trial stopped: Long-acting injectable highly effective in preventing HIV in women (Featuring the HPTN 084 (LIFE) Study). 11 November 2020. Available online: https://www.medicalbrief.co.za/archives/trial-stopped-

long-acting-injectable-highly-effective-in-preventing-hiv-in-women/

- Bizcommunity. Large Africa study makes important breakthrough in HIV prevention (Featuring the HPTN 084 (LIFE) Study). 17 November 2020. Available online: https://www.bizcommunity.com/Article/196/149/210460.html
- Bhekisisa: Centre for Health Journalism. The SHINE trial – hope for shorter, kinder TB treatment for children (Featuring the SHINE Trial). Available online: https://bhekisisa.org/resources/general-resource/2020-11-25-the-shine-trial-hope-for-shorter-kinder-tb-treatment-for-children/
- Yiba.co.za. PETITE study searches for best treatment options for newborns exposed to HIV (Featuring the PETITE Study). 1 December 2020. Available online: https://yiba.co.za/petite-study-searches-for-best-treatment-options-for-newborns-exposed-to-hiv/
- Spotlight. TB in children: Exciting treatment advances, but better tests badly needed (Featuring the SHINE Trial). 3 December 2020. Available online: https://www.spotlightnsp.co.za/2020/12/03/tb-in-children-exciting-treatment-advances-but-better-tests-badly-needed/

Broadcast (Radio and Television)

- RSG. Anneke Hesseling interviewed on RSG at the Woordfees in Stellenbosch. Presenter: S Paxton. Producer: M. Fouché. 9 March 2020.
- Smile FM. BENEFIT Kids Project: The University of Stellenbosch is leading a new R280 million... 4 March 2020.
- Weekend Breakfast Show on Cape Talk Radio: James Seddon discussed the impact of COVID-19 on TB in South Africa. 9 March 2020. Available online: https://www.capetalk.co.za/podcasts/121/weekend-breakfast-with-africa-melane/317176/health-are-covid-19-measures-a-compromise-of-the-tb-epidemic

Stellenbosch University coverage

1. Stellenbosch University Website. Fogarty grant will help put spotlight on TB meningitis in children (featuring Karen du Preez). Available online: http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=7560.

2. Stellenbosch University Website. Dr Redfern shared the virtual platform at the FMHS Academic Day 2020 with Professor Helena Rabie (FAMCRU) and Dr Marieke van der Zalm (DTTC). Covid-Kids study tracks Covid-19's effects in children. Available online: http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=7692
3. Stellenbosch University website. PETITE study searches for best treatment options for newborns exposed to HIV (Featuring Adrie Bekker and the PETITE Study). 27 November 2020. Available online: http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=7848
4. talks@stellenboschuni. PODCAST: PETITE study searches for best treatment options for newborns exposed to HIV (Featuring the PETITE Study). 3 December 2020. Available online: https://anchor.fm/stellenbosch-university/episodes/PETITE-study-searches-for-best-treatment-options-for-newborns-exposed-to-HIV-en6qvs