

# DESMOND TUTU TB CENTRE ANNUAL REPORT: 2021



*Every breath counts*



**Stellenbosch**  
UNIVERSITY  
IYUNIVESITHI  
UNIVERSITEIT

forward together  
sonke siya phambili  
saam vorentoe

## 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

## Contents

Letter from the Director .....	1
Desmond Tutu TB Centre Research Focus Areas.....	2
DTTC Governance.....	6
DTTC Executive Committee (ExCo).....	6
Risk Management.....	4
Desmond Tutu TB Centre: Highlights for 2021 .....	7
Research Updates .....	9
1. Paediatric tuberculosis and lung health.....	9
2. Health systems strengthening and operational research .....	19
3. HIV prevention research .....	24
4. Sociobehavioural science research (SBR) .....	25
Research Grants Awarded: 2021 .....	28
DTTC Academic meetings .....	30
TB Clinical Forum 2021 .....	32
Advocacy .....	32
DTTC Community Advisory Board (CAB) .....	32
Conferences, academic meeting, and events.....	35
International events.....	35
Local conference and events .....	36
Scientific Meetings, Workshops, and training events.....	37
Visitors during 2021 .....	45
Employees .....	46
DTTC Staff appointments .....	46
Students graduated .....	46
Acknowledgements and Funders .....	48

Appendix I. Research outputs – peer-reviewed scientific publications.....	50
Appendix II. Students.....	59
Appendix III. Media interaction (television, video, radio, printed media) .....	64

## Letter from the Director

I am grateful to be able to report on another successful year for the Desmond Tutu TB Centre. Despite the ongoing challenges posed by the COVID-19 pandemic, and escalating poverty in South Africa, the centre has managed to retain its focus on research excellence and capacity building which is transforming policy, practice and access in South Africa and globally.

Internal and external research collaborations have grown despite limited international travel, funding has been stable, and we have seen increased collaboration between research focus areas, career tracks of younger investigators flourish, and a record number of publications.

Most importantly this year, we reflect on the wonderful legacy of our patron, Archbishop Desmond Tutu, who passed away at the age of 90 on 26 December 2021.

The Arch, who survived tuberculosis as an adolescent, was a dedicated activist to raise awareness about the tuberculosis epidemic in South Africa. He also spearheaded advocacy campaigns about childhood tuberculosis, which was, largely neglected until recently, despite the dramatic morbidity and mortality it caused in children and adolescents.

Sadly, tuberculosis remains a leading cause of death in South Africa, fueled by HIV, and poverty. Health inequalities remain. We are humbled to pay tribute to our beloved patron. May the Arch's love, his many messages of hope and encouragement, and his true humility always stay with us.

We continue to be thankful for the opportunity to serve our communities affected by tuberculosis and HIV.



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**Anneke C Hesselning**

*Distinguished Professor in Paediatrics  
and Child Health*

*Director: Desmond Tutu TB Centre*

*SARChi Chair in Paediatric Tuberculosis*

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Desmond Tutu TB Centre

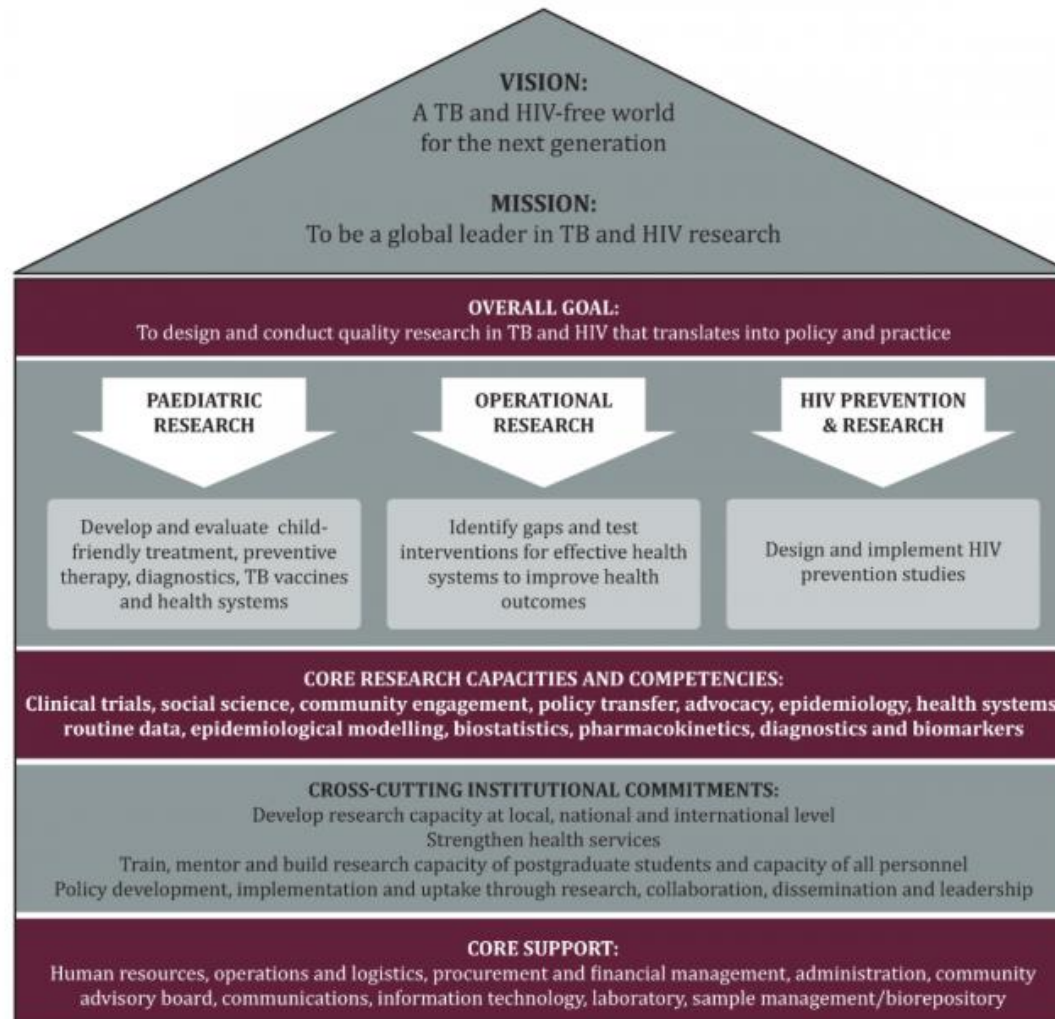
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Fakulteit Geneeskunde en Gesondheidswetenskappe /

Faculty of Medicine and Health Sciences

Universiteit Stellenbosch University

## Desmond Tutu TB Centre Research Focus Areas



## SCIENTIFIC FOCUS AREAS

**DTTC DIRECTOR: PROF ANNEKE HESSELING**

### Paediatric Research

#### Investigators/Clinicians

Prof Simon Schaaf  
Prof James Seddon  
Prof Anthony Garcia-Prats  
Dr Jana Winckler  
Dr Louvina van der Laan  
Dr Elisabetta Walters  
Dr Anne-Marie Demers  
Dr Marieke van der Zalm  
Dr Megan Palmer  
Dr Sue Purchase  
Dr Jennifer Hughes  
Dr Rolanda Croucamp  
Dr Gezila de Beer  
Dr Elri Nortier  
Dr Isabelle De Wandel  
Dr Samke Nyamathe

#### Study Coordinators/Nurse Manager/Project Managers

Tina Sachs  
Petra de Koker  
Mosidi Mapule  
Margaret van Niekerk  
Adelaide Carelse  
Elise Batist  
Ingrid Courtney

#### Nurses/Counsellors

Staff component including support  
staff – n=91

### Operational Research

#### Investigators

Dr Karen du Preez  
Dr Muhammad Osman  
Dr Sue - Ann Meehan  
Dr Florian Marx

#### Research + Project Coordinators

Nosivuyile Vanqa  
Dzunisani Baloyi  
Portia Hendricks

Staff component including support  
staff – n= 7

### HIV Prevention Research

#### Investigators

Prof. Peter Bock

#### Investigators/Clinicians

Dr Kerry Joubert  
Dr Brian Esterhuizen

#### Study Coordinator/Community Engagement Officer

Vikesh Naidoo  
Michelle Scheepers  
Yvonne Saunders  
Jabu Mantantana

#### Nurses

Counsellors  
Community Mobilizers

Staff component including support  
staff –n= 22

### Sociobehavioural Research

#### Investigators

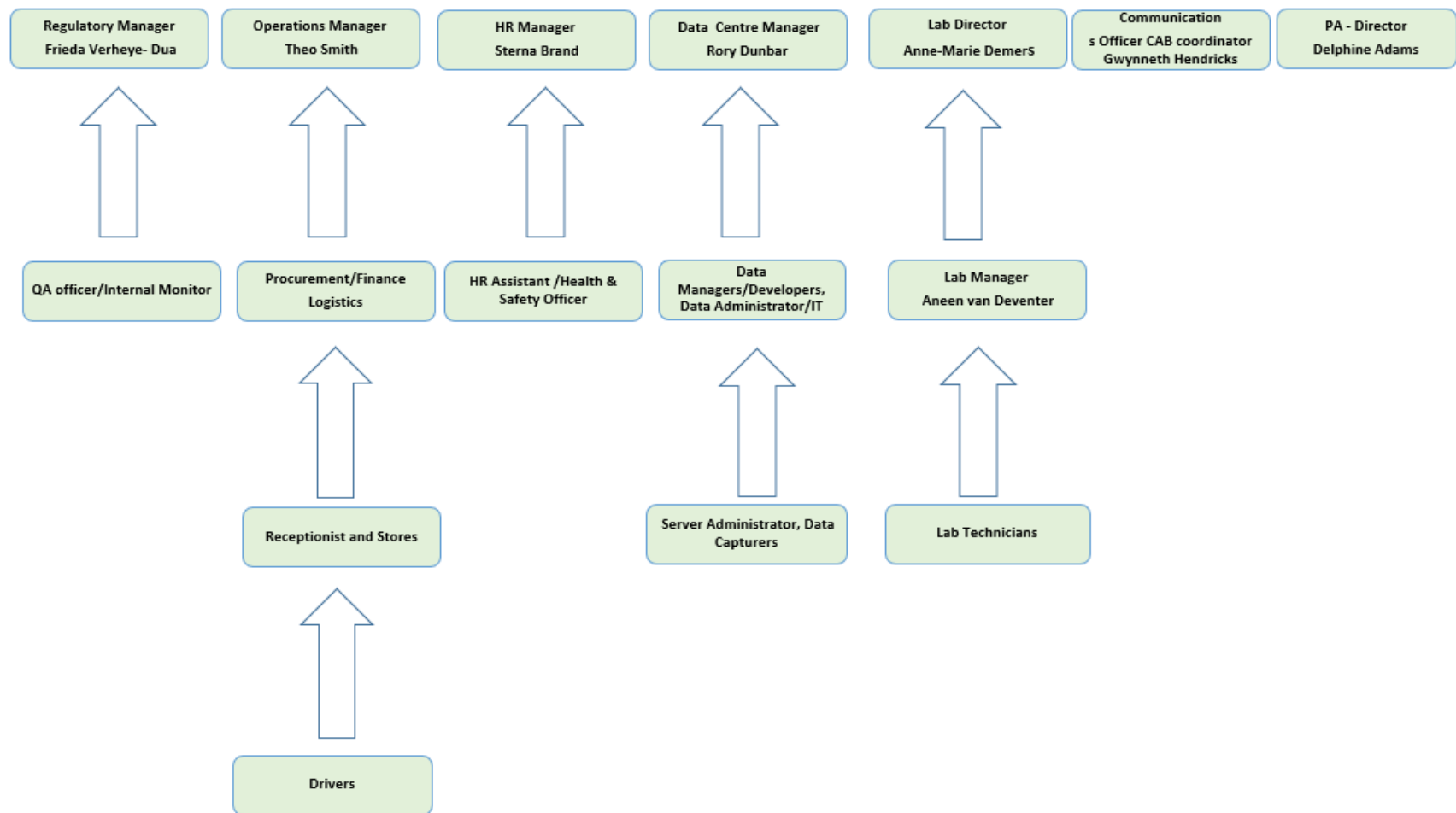
Dr Graeme Hoddinott  
Dr Lario Viljoen

#### Research + Projects Coordinators

Hanlie Myburgh  
Michaile Anthony  
Dillon Wademan  
Melissa Nel

#### Graduate Research Assistants

Staff component including support  
staff – n=12



## **DTTC Governance**

### *DTTC Executive Committee (ExCo)*

The DTTC is led by the Director, Anneke Hesselning, 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 as well as 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 2021 during the COVID 19 pandemic the DTTC ExCo met once every two weeks.

The DTTC also established a COVID-19 Task team that met weekly during 2020, evaluating and implementing COVID 19 strategies in line with Department of Health and Stellenbosch University and managing staff on site during COVID 19 and those who tested positive for COVID 19. In 2021 the DTTC successfully applied to remain within the TBTC networks, which will ensure core and study specific funding over a 7-year period. In addition, the DTTC is actively applying for further research opportunities to strengthen the core funding for the centre.

## DTTC Executive Committee Roles and Responsibilities



Anneke Hesseling:  
DTTC Director and Chair of DTTC ExCo



Megan Palmer:  
Medical Director at DTTC BCH Paediatric  
Pharmacokinetics Unit



Marieke van der Zalm: Clinical Lead:  
Paediatric Lung Health Studies



Frieda Verheye-Dua:  
Regulatory Manager



H Simon Schaaf: Lead investigaor:  
Paediatric MDR-TB Studies



Sue-Ann Meehan:  
Project Manager and Co-Investigator



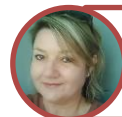
Peter Bock:  
Lead HIV Prevention Research



Muhammad Osman:  
Lead Implementation Research



Graeme Hoddinott:  
Lead Sociobehavioural Science



Sterna Brand:  
Human Resource 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 and evaluated on a regular basis.

Risks related to Human Resources, Finance and Regulatory are being monitored and evaluated on a regular basis.

The DTTC regulatory office will ensure that no study is commenced without appropriate regulatory approval.

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 (SA-GCP, 3<sup>rd</sup> Ed dated 2020) and Human Subject Protection (HSP) prior to any study commencement. Through constant data monitoring by dedicated centre staff, dual entry of any research information as well as GCP and HSP 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 2021, 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 place staff and patient safety at risk. 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 2021 DTTC continued f Infection prevention control (IPC) training virtually. In 2021 the IPC training was upscaled to train more than 40 staff members virtually. The DTTC ensures that all staff receive bi-annual health screenings. During 2021 additional guidelines were included in the screening process in line with COVID 19 regulations. 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 were part of category 1 of the national vaccine rollout and most staff were vaccinated during 2021.

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. 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.

## **Desmond Tutu TB Centre: Highlights for 2021**

### **Key Achievements and Awards**

- The TBTC 10-year grant was re-awarded to DTTC, Stellenbosch through a competitive renewal process.
- The SARChI 5-year grant in Paediatric Tuberculosis was re-awarded to Anneke Hesseling (tier 1).
- Anneke Hesseling and Simon Schaaf received the output award for publications from Stellenbosch University.
- Mareli Claassens was awarded a Harvard LEAD fellowship as part of the Harvard Global Health Institute (HGHI) and the Women and Health Initiative (W&HI) within the Global Health and Population Department at the Harvard T.H. Chan School of Public Health.
- The ICAB (IMPAACT Network) elected Gwynneth Hendricks (the DTTC CAB Liaison Officer) and Siphosethu Nco (the CAB representative) to serve on the ICAB Leadership Group (ILG) for a period of 2 years.
- Simon Schaaf was invited to present at the Paediatric Day of Excellence and reflected on his career in TB care in a talk titled "A Journey of Grace".
- Anneke Hesseling was awarded the title of Honorary member of the International Union Against Tuberculosis and Lung Disease. This title is awarded to persons who have made significant contributions to advance and support the work of The Union. The Award was presented at the virtual General Assembly on the 22<sup>nd</sup> of December 2021.
- Lario Viljoen received her PhD degree in Sociology at the Department of Sociology and Social Anthropology, and Muhammad Osman received his PhD from the Department of Paediatrics and Child Health, both at Stellenbosch University.

### **DTTC on international platforms**

- The DTTC made significant contributions in the Paediatric and Adolescent Tuberculosis (TB) guideline meeting which was organised by the World Health Organization (WHO). This meeting focused on new recommendations regarding the diagnosis and treatment of children with TB.
- James Seddon and Simon Schaaf were invited as speakers at the Peruvian Network of Paediatric Tuberculosis where more than 580 participants attended virtually.
- Marieke van der Zalm was invited as a speaker at the ISGlobal in Spain, which was a research meeting on 6 May 2021. Title: Post-TB lung disease: The forgotten child.

- Graeme Hoddinott and Lario Viljoen presented at The London School of Hygiene and Tropical Medicine (LSHTM), and at the Bill and Melinda Gates Foundation webinar series on HIV stigma in sub-Saharan Africa.
- The DTTC Community Advisory Board was featured in the AIDS Clinical Trials Group (ACTG) CAB newsletter.
- The BENEFIT Kids Project, and PETITE specifically, was highlighted in the World Health Organisation (WHO) GAP-f newsletter.
- A team filmed footage for the SHINE project, focusing on how to convey the study findings and what it means in the field. Anneke Hesseling and Megan Palmer presented.
- Staff from the DTTC presented at various national and international conferences and contributed to 65 publications in peer-reviewed academic journals in 2021.

### **Key Events**

- On the 24<sup>th</sup> of March, the Desmond Tutu TB Centre hosted a virtual event for the World TB Day with the theme, “The Clock is Ticking”. Several speakers, including James Seddon, Lenny Naidoo, and Rabia Cariem presented. A video competition was launched, and Taahirah Davids won the prize for the best video.
- The DTTC held a virtual dissemination meeting on the 8<sup>th</sup> of December. Key speakers included Judy Caldwell (City of Cape Town) and Wolfgang Preiser. Other teams at the Centre held smaller in-person events throughout December.

### **Other highlights at the Centre**

- More than 100 staff members at the DTTC were able to receive the Johnson & Johnson COVID-19 vaccine at Tygerberg hospital.
- Several staff members at the Centre were promoted in 2021, including Muhammad Osman and Karen du Preez to Senior Researcher, and Marieke van der Zalm to Associate Professor in the Department of Paediatrics and Child Health.
- A large group of employees completed Infection Prevention Control training during 2021.

### ***In memoriam***

The DTTC is deeply saddened by the passing of Mrs Evelyn Fielies on the 7<sup>th</sup> of May 2021. Mrs Fielies was a professional nurse who joined the Desmond Tutu TB Centre in 2015.

The DTTC mourned the death of Archbishop Desmond Tutu on the 26<sup>th</sup> of December 2021. Nulda Beyers, Anneke Hesseling, and Mariana Kruger paid tribute to the archbishop through several press releases and media interactions.

## Research updates

### 1. Paediatric tuberculosis and lung health

*Prevention and treatment: Drug resistant TB*

**BENEFIT Kids (Better Evidence and Formulations for Improved MDR-TB Treatment for Children):** This project is designed to address critical gaps in research and products in order to improve the treatment and prevention for children affected by MDR-TB. The project was made possible with support and funding from Unitaid. The overall goal is to reduce morbidity and mortality of children affected by MDR-TB through better access to improved MDR-TB prevention and treatment options. The Project consists of two systematic reviews, five clinical trials, and the targeted formulation and market shaping work to improve the availability of child-friendly formulations of 2nd-line TB drugs.

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 was 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 was 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. The study had their FPFV in October 2020 and all of the 24 participants were enrolled by April 2021. Preliminary results have been shared with the WHO to assist the guidelines and handbook development for management of TB. Final PK analysis results will be available in early 2022.
- Trial 2, **PERFORM** trial (Pharmacokinetics of lEvoFloxacIn FORMulations in children with MDR-TB exposure) (Site PI: Louvina E. van der Laan). The is evaluating the

pharmacokinetics and acceptability of 100mg dispersible compared to 250mg non-dispersible tablets of levofloxacin in children with MDR-TB exposure. The trial is sponsored by UNITAID. This was a single site study which was implemented at the DTTC BCH PK Unit. Recruitment started in Nov 2020 and the study was fully enrolled by the end of 2021. A total of 25 children were enrolled to obtain 24 complete evaluable crossover pharmacokinetics profiles. HIV-uninfected children receiving MDR-TB preventive therapy, for at least 2 weeks duration, were eligible. Children were randomized 1:1 to receive one dose of either the dispersible or non-dispersible levofloxacin formulation on the pharmacokinetic (PK) sampling day 1, followed by the other formulation on the second PK sampling day. Following the second PK sampling day, children were referred to routine TB care programmes. Both levofloxacin formulations are by Macleods Pharmaceutical, Ltd., Mumbai, India. Data analysis is underway with final results planned in Q2/Q3 of 2022. The primary aims would be to compare the model-based estimation of the relative bioavailability of the dispersible formulation compared to the non-dispersible formulation of levofloxacin dosed according to recommended weight-banded dosing, to describe the pharmacokinetics and developmental pharmacology (allometry and maturation) of levofloxacin, to characterize the short-term safety of the dispersible and non-dispersible levofloxacin formulations and to characterize the acceptability of the dispersible versus the crushed non-dispersible levofloxacin formulations.

- Trial 3, **CATALYST** (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 DR-TB. These two second-line TB drugs are key components of WHO-recommended DR-TB treatment regimens in children. The formulations of moxifloxacin and clofazimine used on the trial are child-friendly dispersible tablets which are easier to dose in young children than the standard formulations currently available in routine care, and which we propose are more acceptable and tolerable for children. This is a multi-site study which will recruit at the DTTC Brooklyn Chest Hospital Pharmacokinetic (BCH PK) 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. The study opened to accrual in all sites in 2021 and aims to enrol 36 children across the three sites. By the end of 2021, 12 children had been enrolled, 7 of these at DTTC. Recruitment is ongoing and enrolment is expected to be complete in Q3/Q4 2022.

The SBR component of the **CATALYST** study (SBR: Graeme Hoddinott and Lario Viljoen) was designed to explore the acceptability and palatability of the novel dispersible formulation of clofazimine and moxifloxacin for children. As part of the study, children and/or their caregivers in India, the Philippines, and South Africa were recruited to take part in four interviews over the course of 24 weeks to document their treatment journey. The aim is to recruit 21 participants across the three countries over the study period. In 2021, the SBR team recruited 10 participants and data collection was ongoing.

- Trial 4, the TB Therapeutic Trials: Prevention of **MDR-TB TB-CHAMP** (MDR-TB preventive therapy trial): (DTTC PIs: Anneke Hesselning, 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. (see details below).
- Trial 5, the **PETITE** study (Pharmacokinetic and safeTy of the 4-In-1 granules in neonates) 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 outcome of PK interim analysis resulted in a revision of the protocol including adaptations of the study formulation. Cohort 1B had to be repeated under the new protocol with PPFV August 2021 and LPLV in September 2021. Another interim analysis has been conducted to determine the proceedings of Cohort 2, which is planned for early 2022.

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. Contracts with 2 manufacturers have successfully been signed at the end of 2021 to complete the work set out. Additionally, the **ChilPreF ML** (Children's preferences between six novel moxifloxacin and linezolid formulations – a 'swish-and-spit' taste panel evaluation in children in South Africa) (Site PI: Dr Graeme Hoddinott) is being implemented. The study aims to inform pragmatic recommendations about which formulation(s) of moxifloxacin and linezolid to recommend for commercial manufacturing based on palatability profile. The main objective of the study is to characterize the relative (ranked) taste preferences between formulation blends each of moxifloxacin and linezolid amongst children and disaggregated by manufacturer. This is a cross-sectional 'swish-and-spit'

taste panel evaluation to be conducted at two sites in South Africa. Eligible healthy child volunteers between ages 5 and 17 years will be invited to participate in this evaluation of the palatability of six different versions each of moxifloxacin and linezolid. The study will be implemented between December 2021 and May 2022.

**IMPAACT P1108** (PI: Jennifer Hughes). 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 enrolls children in age-based cohorts in an age de-escalation strategy and is being undertaken in South Africa, India, and Haiti. The overall target sample size is 75 and 23 of the 42 children enrolled thus far were enrolled at DTTC. DTTC enrolled 7 children on the trial in 2021, across cohorts 1-3 and recruitment is ongoing.

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 IMPAACT P1108 has already informed WHO paediatric dosing guidelines and bedaquiline is available in South Africa for children 6 years of age and older in the routine TB programme. The WHO will release updated TB guidelines in 2022 which are expected to include guidance for dosing of bedaquiline in children <6 years based on data from the IMPAACT P1108 trial.

**IMPAACT 2005** (PI: Louvina van der Laan). 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 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. 48 participants, aged 0-17 years, will be enrolled into 4 age-based cohorts over a period of 72 weeks and will receive delamanid for 24 weeks. PK and safety data will be collected. This is a multi-site study implemented at DTTC, Sizwe Johannesburg, PHRU Matlosana Klerksdorp, Gaborone Botswana and the BJ Medical College in India. The trial initially opened to accrual in Feb 2019 but was temporarily paused to implement a protocol revision implementing revised dosing for younger children, and additional monitoring following the discovery of psychiatric adverse events linked to delamanid. Recruitment is reopening soon on the revised approved protocol.

**IMPAACT 2026** (PI: Jennifer Hughes). IMPAACT 2026 is a phase IV prospective observational PK study that was designed on the same basis as P1026s which closed in December 2019 – pharmacokinetic analyses for the last cohorts enrolled on P1026s are still ongoing. Both studies

have multiple arms and multiple research sites. The primary aim of the 2026 study overall is to describe pharmacokinetic (PK) properties of selected antiretroviral (ARV) and anti-tuberculosis (TB) drugs administered during pregnancy and postpartum. The DTTC is registered as a site for Components 4 and 5 of the 2026 study and therefore will enrol women receiving specific second-line TB medications (bedaquiline, delamanid, linezolid, clofazimine, fluoroquinolones) used to treat RR-TB during pregnancy (Component 4), as well as HIV-infected women without TB who have chosen to breastfeed after birth while receiving selected ARVs (atazanavir, darunavir or lopinavir). As well as describing the PK properties of the selected drugs in plasma of women and their infants during the perinatal period, this study also aims to describe the transfer of these drugs to the infant through breastmilk among women who choose to breastfeed while on treatment. The target sample sizes for the relevant arms of the 2026 study are: up to 28 mother-infant pairs for component 4, and up to 15 mother-infant pairs for component 5. The study opened to accrual in mid-2020 for component 1 and the other arms are due to open in Q1/Q2 of 2022 once relevant sites have been successfully activated.

**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 DR-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. The target sample size for the study is 40 participants. The study opened to accrual in September 2020 and 50% of the cohort was enrolled by the end of 2021 after which the trial was paused for interim analysis. We expect to start enrolling the second half of the cohort in Q2/Q3 2022.

The SBR component of the **Clofazimine PK Study** (SBR: Graeme Hoddinott, Ziphelele Saule, Arlene Marthinus) will characterise the palatability and acceptability in children of clofazimine given in combination with an OBR for the treatment of RR-TB. The aim is to explore the acceptability of Clofazimine on the participant/patient and caregiver's household, including patient/caregivers' experiences of practical administration and adherence support practices. Researchers will describe how the participants' physical (home), social and psychological context impact on their treatment experience. By the end of 2021, the SBR team recruited and interviewed 13 of 16 participants and conducted 36 interviews amongst this group. Once data collection is reported a report will be compiled, and manuscripts developed in 2022.

### *Therapeutic trials: Prevention of drug-susceptible TB*

**TBTC Study 35** (PI Anneke Hesselning). 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 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 acceptability of this novel FDC of Rifapentine and Isoniazid. The first patient was enrolled on Study 35 in October 2019 and DTTC contributed 13 of the 16 participants that were enrolled across all sites in the first two cohorts. Enrolment was paused for interim analysis in March 2020. Cohorts 2 and 3 opened to accrual in September 2021 after the interim analysis was complete, and DTTC had enrolled 6 children into these cohorts by the end of 2021. Recruitment is ongoing.

The SBR component of **Study 35** (SBR: Graeme Hoddinott) was designed to understand children's, caregivers', and health workers' experiences of utilising the 3HP regimen. Data collection started in 2020 and will continue until 2022. The study comprised two components. Component 1 involves qualitative, in-depth interviews with health workers involved in Study35. As of December 2021, 5 health workers participated in their first set of interactions for Study35A. Component 2, involves qualitative, serial, in-depth interviews with children (and caregivers where appropriate) enrolled in Study 35. Before study pause between May and December 2021, six caregivers and nine children were recruited to Study35A. Each participated in three interviews over the course of 12 weeks to document their treatment journey. Data collection is ongoing, with follow-up interviews planned for healthcare workers and another 16 child and caregiver participants planned for 2022.

### *Therapeutic trials: Treatment of drug-susceptible TB*

**SHINE:** the main results of this trial were disseminated during 2021. In brief, 4 months of standard TB treatment in children was non-inferior to standard 6-month treatment. These data have informed the WHO updated guidelines for the treatment of TB in children.

**A5300B/Phoenix trial** (PI Peter Bock). The DTTC are implementing the PHOENIX trial from the Kuilsrivier community site. The study is run jointly by the IMPAACT and ACTG networks and the study purpose is to compare how safe and effective 26 weeks of Delamanid (DLM), a medicine used to treat TB, is versus 26 weeks of isoniazid (INH), a standard medicine to treat or prevent TB, for preventing infection with TB in household contacts of people with confirmed MDR TB. DTTC was activated for PHOENIX in October 2021. Through Nov/Dec 2021 transfer in participant was received from another site and enrolment of new participant will start in early 2022.

#### *Lung health, diagnostic, and biomarker studies*

**Umoya study** (TB diagnostics/ biomarkers and lung health). Umoya is a unique ongoing prospective observational cohort of children presenting with symptoms of presumptive PTB. All children are systematically investigated for M. tuberculosis and other respiratory pathogens. Several diagnostic samples are collected at enrolment and during the first 6 months of follow-up. Long-term follow-up until 4 years after enrolment allows us to characterize the long-term effects of PTB on lung health in young children in the context of other common pathogens. Umoya provides a unique opportunity to investigate diagnostic tests/ biomarkers and lung health in children with presumptive PTB. Umoya started recruitment November 2017 and currently has 426 children enrolled. The SBR component (Graeme Hoddinott and Michael Anthony) of the study will be to investigate the short-term and long-term impact of respiratory illnesses on the quality of life of children. By the end of 2021 the SBR team recruited 15 participants and conducted 30 interviews amongst the group. The team also administered (n=426) quality of life questionnaires. In addition, the SBR team developed a diagnostic and acceptability questionnaire which was used to investigate the feasibility and acceptability of TB diagnostic samples such as respiratory samples (NPA, GA & Induced sputum) blood serum, urine, stool, saliva, and TB Diagnostic investigations such as chest radiography and Butterfly ultrasound, among children in the study. By the end of 2021, the SBR administered (n=104) questionnaires. Lastly, towards the end of 2021 the SBR team implemented 51 household socioeconomic status questionnaires to assess the economic and social impact of respiratory illness and TB treatment on households. Quality of life and household socioeconomic status data collection will be continued in 2022.

The study is funded by:

- NIH- R01 grant (PI G Alter, Harvard), to investigate serum-based biomarkers for TB diagnosis in children under the age of 5 years.
- NIH-K43 & EDCTP senior fellowship (PI M vd Zalm), to investigate the long-term impact of PTB and other respiratory pathogens (including SARS-CoV-2) on lung health in South African children.
- South African Medical Research Council (PI M vd Zalm), to investigate the role of respiratory viruses in children with PTB, including SARS-CoV-2.
- NIH-subaward (PI Megan Shaw, UWC), to investigate the role of influenza and SARS-CoV-2 in children with PTB.

**COVID Kids** (PI Marieke vd Zalm, Helena Rabie, and Andrew Redfern). The COVID-kids study aims to investigate the clinical impact of COVID-19 on South African children. This research project includes a 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. Clinical assessment and data collection are done at enrolment and during follow-up 3, 12 and 18 months later. In addition, all cases of the paediatric inflammatory multisystem syndrome (PIMS-TS) temporarily associated with COVID-19 are captured. This research was initially supported by SEED funding from Stellenbosch University special vice-rector fund for COVID research. Since November 2021, the study is part of the VERDI study. VERDI (SARS-CoV-2 variants Evaluation in pRegnancy and paeDIatrics cohorts), is funded by the European Commission with a contribution of 10 million euros, devotes an international and collaborative effort to analyse the impact of new variants in these vulnerable populations.

The research group, made up of 22 Centers of excellence in Europe, USA, South Africa, the Caribbean, the Middle East and Asia, coordinated by the University of Padua and Penta Foundation (Italy)

The SBR component (Graeme Hoddinott and Michaile Anthony) of the study aims to understand the relative impact of COVID-19 on the quality of life of children and their families. By the end of 2021, the SBR team interviewed 21 caregivers and administered (n=86) quality of life

questionnaires. In addition, the SBR team implemented 166 questionnaires to identify households' risks, beliefs and perceptions associated with the COVID-19 pandemic. Two manuscripts will be produced from the data collection in 2022. The quality-of-life questionnaires administration will continue 2022.

**Teen TB:** Understanding the biology, morbidity, and social contexts of adolescent tuberculosis (PI James Seddon). Teen TB is an observational study examining multiple components of adolescent TB. The study is funded by The Global Challenges Research Fund. The study was delayed in starting due to COVID-19 but began recruitment in November 2020. 50 adolescents (10 to <20 years) with TB disease were recruited by July 2021, and 50 controls were recruited by August 2021. At baseline, all individuals had blood samples taken, a chest x-ray and all had their lung function (spirometry, oscillometry, diffusion and plethysmography). For participants with TB disease, a PET/CT scan was done, they underwent chest ultrasound and were seen at 2, 8 and 48 weeks. Sociobehavioural science (SBR) questionnaires were done in all 50 participants with TB disease, with in depth interviews in a sub-set of 20 adolescents. Analysis of imaging and lung function data is underway, and the blood samples are being evaluated to look at pubertal status, evidence of previous viral infection and to measure protein inflammatory markers. Some participants are still being followed up, with the final visits due to complete in July 2022.

The SBR component (SBR: Graeme Hoddinott) of the **TeenTB** study was designed to explore the social context of adolescents affected by DS TB and MDR TB. The life course experiences of this sub-group will be characterised, including familial/peer social contexts, experiences of TB disease including disability, sexual experiences and time of sexual debut, HIV, smoking, substance abuse, violence, processes of peer support and socialisation, impact on education, episodic and chronic threats to mental well-being, accessing health services, TB treatment adherence, and quality of life. In 2021, qualitative data were collected in a nested, sub-sample of 17 adolescents and their families, with four interactions per participant. Data collection was completed, and a concept note towards manuscript development has been drafted.

**TB-CHAMP** (MDR-TB preventive therapy trial): (DTTC PIs: Anneke Hesselning, 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. The main trial opened to accrual in Quarter 4 of 2017. As of the end of 2021, 1006 children had been screened and 795 enrolled in the study. TB-CHAMP protocol version 3.0 was approved by HREC and SAHPRA in March 2021, and expanded eligibility criteria to include all children in the household under 5 years and all children from 5-

17 years who are either HIV or TB infected. Two new sites (THINK, KZN and Isango Lethemba TB Research Unit, Gqeberha) joined the TB-CHAMP team at the end of 2021. Research investigating the challenges faced in recruiting children to TB-CHAMP (led by Dr Susan Purchase) was published in the International Journal of Tuberculosis and Lung Disease in May 2021. Recruitment progressed relatively well despite COVID-19 and community unrest and will end in July 2023. The trial, led by the DTTC, was previously funded by the BMRC/Wellcome Trust/DFID, and received funding for completion from Unitaid as part of the BENEFIT Kids grant.

As part of the economic evaluation of TB-CHAMP, it is essential to quantify the cost of treating children with MDR-TB preventive therapy from a health system and societal perspective as well as quantifying the cost of treating children with MDR-TB disease from both these perspectives (**MDR TB Kids Study**). In addition, it is essential to quantify the socioeconomic status of families exposed to MDR-TB and with children treated for MDR-TB disease. Finally, the health-related quality of life (HRQoL) needs to be assessed to determine the impact of MDR-TB diagnosis and treatment on life quality. This is necessary to determine parameters such as QALYs and DALYs. MDR-TB Kids recruited 50 children (<13 years) who had been treated for MDR-TB between 1 January 2018 and 1 July 2021. Questionnaires were completed on all children to capture HRQoL, socioeconomic status and costs to family of MDR-TB treatment for the child and a sub-set of families (n=20) underwent in depth SBR interviews. Finally, for the 50 individuals recruited, health service utilization (hospital admissions, investigations, treatment etc.) were extracted from the provincial health information exchange. These data are being analysed by Thomas Wilkinson towards his PhD.

The qualitative SBR component of the MDR-TB Kids study (SBR: Graeme Hoddinott) comprises two components. Component 1 involved a cross-sectional interviewer-led questionnaire that seeks to gather information from the parents and caregivers of infants, children, and young people between the ages of 0-14 years old. The questionnaire sought to understand the household impact and experience of MDR-TB and was delivered electronically. Component 2 comprised serial, activity-based, in-depth interviews with primary caregivers of children aged 0-14 years who have been diagnosed with MDR-TB. In 2021, participants were recruited to complete Component 1, and 17 participants were recruited to and completed Component 2.

## **2. Health systems strengthening and operational research**

**Evaluating 10 years of TB control in South Africa** (PIs: Muhammad Osman; and Karen du Preez; co-investigators: Anneke Hesselning, 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 2021, 3 manuscripts were published. These manuscripts documented case finding and outcomes with an emphasis on mortality in children, adolescents, and adults.

Ongoing work includes epidemiological analyses and contributions to mathematical modelling work.

**LINKEDin:** reducing initial loss to follow up among tuberculosis patients in South Africa (PIs: Anneke Hesselning 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. The study was implemented in 6 hospitals and 31 primary health care facilities in 3 provinces of South Africa in the Western Cape, Gauteng, and KwaZulu Natal from January 2019 to December 2020. The DTTC worked 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 aimed to measure the proportion of TB patients who are ILTFU at baseline and again at the end of the implementation phase. In the WCP, 4 sub-studies were 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.

During 2021, data cleaning and data analysis for the primary aim for WCP and KZN were completed. ILTFU is higher among hospital diagnosed patients compared to those diagnosed at PHC level. While hospitals account for a modest proportion of diagnosed TB patients they have a high TB-associated mortality. We found that 17% of TB patients died with 70% of deaths being within 30 days of their diagnosis. Most deaths occurred among patients diagnosed in hospital. A hospital-based TB diagnosis is a critical opportunity to identify those at high risk of early and overall mortality and a manuscript documenting these findings was published in 2021. Two additional sub-studies were completed and published in peer reviewed journals. A qualitative study to understand linkage from the patients' perspective identified 4 key factors that influenced participants' decisions around linkage, including a lack of communication from healthcare workers which delayed linkage and a need to reduce the impact of their illness on self and others, which was a motivation to link. The sub-study on the use of interactive messaging to reduce pre-diagnosis loss to follow-up for TB care found that enrolment in a WhatsApp-based communication intervention among presumptive TB patients was low, mainly due to low availability of WhatsApp-compatible phones, but for those who did participate, the majority returned to the clinic for their TB test result, suggesting potential for interactive messaging services to support TB care along the TB care cascade.

**LINKED-UP:** Reducing initial loss to follow up among tuberculosis patients in South Africa (PIs: Anneke Hesselings and Muhammad Osman). The overall aim of LINKED-UP is to implement activities that have been developed in the LINKEDin study to improve the use of routine TB data to reduce ILTFU and increase HIV testing among TB patients in KZN. LINKED-UP will scale up LINKEDin activities through 1) expanding LINKEDin activities geographically and 2) including additional activities to increase the appropriate use of routine TB and HIV data, to reduce initial loss to follow up among TB patients and in parallel, to also increase HIV testing among TB patients. LINKED-UP was built on the existing LINKEDin project, to increase the availability and effective use of routine TB and TB/HIV data and reports by Department of Health personnel to improve patient care and outcomes. Jointly, with the development of the KZN provincial health data centre (PHDC), this work aimed to ensure effective transition to scale-up of our original LINKEDin intervention as a well-established data use-case. The DTTC implemented LINKED-UP activities in collaboration with multiple established stakeholders, each with specific roles and responsibilities in Ugu and Umkhanyakude health districts. The DTTC provides overall grant

management, technical guidance, and support for implementing partners and ensure meaningful joint collaborations with other stakeholders at all levels to achieve proposed project outcomes. The LINKED-UP study includes a qualitative sub-study to address a secondary aim, to determine an optimal process of change management that maximizes health workers experiences of support, facilitates rapid transition, supports training tools, and minimizes potential organisational barriers. The specific objectives are to: i) Describe health worker experiences of using the electronic systems to identify TB patients and trace ILTFU TB patients at the facility level ii) Explore health workers' experiences of delivering services before and after implementation of the PHDC. iii) To determine an optimal process of change management that maximizes health workers experiences of support, facilitates rapid transition, supports training tools, and minimizes potential organisational barriers. Data will be collected in the 1st six months of 2022, through key informant telephonic interviews across health facilities and across staff levels. We will recruit and enrol 42 key informants in total from both districts.

**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 (5 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 2021, mentees have continued work on understanding the results and started the process of drafting manuscripts

Epidemiological impact and intersection of the COVID-19 and tuberculosis pandemics in Brazil, Russia, India, and South Africa - **IMPAC19TB** (Overall PI: Anneke Hesselning and South African PI: Muhammad Osman). This study is funded by the South African Medical Research Council through the South African Department of Science and Innovation. This multilateral international collaborative project aims to evaluate the epidemiological impact and intersection of the COVID-19 and tuberculosis pandemics in Brazil, Russia, India, and South Africa. The overall project includes 5 interlinked objectives:

1. To estimate differential losses along the TB care cascade attributable to COVID-19 by each country

2. To estimate the impact of COVID-19 on trends in MTB population structure
3. To determine the effect of TB on patient level COVID-19 outcomes
4. To determine programme and other in-country response measures to mitigate the negative impacts of COVID-19 on TB healthcare services
5. Using mathematical modelling to estimate the impact of COVID-19 and COVID-19 response measures on TB incidence and TB-associated mortality, and model the impact of recovery measures

South Africa is leading the co-ordination of the overall study across all four countries and implementing activities for objectives 1, 4 and 5 in South Africa. This 2-year study started in April 2021. The study has all necessary approval in place. For objective 1, we have developed a comprehensive list of indicators including TB case finding and outcomes, TB prevention, TB and HIV, and COVID-19 and requested the data from Department of health. For objective 4, we completed data collection for the healthcare worker and TB patient surveys (64 health worker questionnaires and 125 patient questionnaires in Eastern Cape, KwaZulu-Natal and Western Cape provinces). For objective 5, we have worked on setting up the model, which will utilise the data collected from objectives 1 and 4. We contributed toward a scoping review publication on 'The COVID-19 and tuberculosis syndemic: The way forward'.

**An assessment of the impact of the COVID-19 epidemic and nationwide lockdown on public tuberculosis healthcare service provision and epidemiology in South Africa** (PI: Florian Marx). This consultancy has been commissioned by the South African TB Think Tank. The study will conduct an epidemiological analysis of the TB care cascade during the period of the COVID-19 pandemic at a subnational level in South Africa. Data collected and analysed in the first part of the project will inform a transmission-dynamic mathematical model of TB calibrated to the subnational (provincial) level. We will use this model to estimate the impact of the COVID-19 epidemic on TB in South Africa at the provincial level. The consultancy was awarded in the last quarter of 2021 and the agreement is being finalised. The work will happen during 2022.

**Value proposition of novel diagnostic tools for TB** (PI: Florian Marx): This project, funded by the Bill and Melinda Gates Foundation (BMGF), is conducted in collaboration with Imperial College London and the Clinton Health Access Foundation. It aims at using mathematical modelling to estimate the population-level impact of introducing two novel TB diagnostic tools (currently in the development stage) in South Africa and India. The project will be finalized in June 2022. A manuscript is in preparation.

**Care4TBMkids** (PI: Dr Karen du Preez). The Care4TBMkids study aims to estimate the disease burden and outcomes of TB meningitis in children at a global, and a national and sub-national level in South Africa. Funded through an NIH K43 Emerging Global Leader career development award from the Fogarty International Centre, the study will help identify opportunities for prevention, earlier diagnosis and treatment for children with TB meningitis, providing evidence for future interventions to improve prevention and care. During 2021, we also received an administrative supplement award to investigate the impact of COVID-19 on paediatric TBM care in South Africa.

Achievements for 2021 include finalisation of a mathematical model to estimate the total number of children with TB meningitis globally, including a literature review of the pre-chemotherapy to determine the risk of disease progression following infection. Routine TB surveillance data from South Africa, Brazil, the United States, and the European Centre for Disease Control will be included in a meta-analysis.

Preliminary results of paediatric TBM case notification rates and TB treatment outcomes in the context of age and HIV in South Africa were accepted for presentation at the World Society of Paediatric Infectious Diseases conference (WSPID) in February 2022. The analysis included 1,668 children and adolescents with a 1/2<sup>nd</sup> diagnostic code of TBM in routine TB surveillance data, highlighting the high burden of TBM and HIV-associated TBM in children and adolescents in South Africa with high mortality.

A large investigative team consisting of multiple key stakeholders within Department of Health representing multiple levels of the healthcare system were established and developed the protocol for a prospective paediatric TBM cohort study in the Western Cape Province. Ethical and regulatory approvals from three hospitals and primary healthcare facilities in two sub-districts in Cape Town were obtained and enrolment will start in 2022. Formative research to describe the TBM health system and the impact of COVID-19 is nearly complete and will be submitted for publication in 2022. The study team has also worked closely with the Western Cape Department of Health Provincial Health Data Centre to perform operational verification of a TBM algorithm to support ongoing surveillance of TBM in the province.

### **3. HIV prevention research**

**HPTN 084 (LIFE)** (PI: Peter Bock). The HPTN 084 aim was to evaluate the safety and efficacy of the injectable agent, cabotegravir (CAB LA) compared to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), for pre-exposure prophylaxis (PrEP) in HIV-uninfected women. In November 2020, preliminary results showed that 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 (TDF/FTC) for HIV prevention among cisgender women in sub-Saharan Africa. The DSMB recommended stopping the blinded phase of the trial and moving all participants to open label. In Dec 2021 cabotegravir was approved by the US FDA. The HPTN 084 study will continue to implement an open label extension through 2022 where participant can choose which medication (CAB or Truvada) they wish to take, and researchers will continue to gather further key information including amongst pregnant women.

#### **4. Sociobehavioural science research (SBR)**

During 2021, the sociobehavioural science team continued to contribute complimentary research activities across various studies at the DTTC. This includes research as part of Study 35, TeenTB, MDR-TB Kids, the clofazimine PK study, and CATALYST and ChilPref ML under the BENEFIT Kids umbrella. In the operational pillar, the team also conducted research as part of the Care4TBM study and contributed to the LinkedIN study and its follow-up project – LinkedUP. In addition to these nested components, the team also conducted several other studies, including those listed below:

**TPT DCE:** The Preferences for TB preventive therapy (TPT) in South African children and adolescent study (SBR: Graeme Hoddinott and Abenathi Mcinziba). Tuberculosis preventive therapy (TPT) for the prevention of drug-susceptible TB is highly effective in preventing TB and if implemented effectively, can prevent many TB cases and deaths in children, particularly in high TB burden countries. This study determined children's and caregivers' preferences relating to the most important characteristics of different TB preventive treatment regimens (including 3HR, 3HP and 6H) and service delivery models, using the Discreet Choice Experiment (DCE) model and qualitative interviews to understand the preferences of users. The DCE was administered children, adolescents, and caregivers (n= 125 per each group) from 25 primary health care facilities located in the Cape Metropolitan District of the Western Cape Province. In-depth interviews were conducted with 18 participants: healthcare workers (n= 5), caregivers (n= 5), children and adolescents (n= 8), sampled purposively for diversity in gender and age. Field staff also completed daily semi-structured field note forms (n= 180 forms from ~12 weeks of DCE administration by four fieldworkers and to 464 participants) to reflect on their interactions with participants. Data collection took place between September 2021 – January 2022. The study was supported by the TB Think Tank. We drafted and submitted a technical report and policy brief to TB Think Tank as part of our deliverables. We are also in the process of writing a manuscript of the whole study results and to formulate pragmatic recommendations to guidelines and practices for TPT offered to children and adolescents in South Africa.

**DIMPLE** (SBR: Graeme Hoddinott, Dzunisani Baloyi, Caitlin October). The DIMPLE project (Developing simple, cost-efficient Interventions to Manage Psychosocial distress associated with Long-term hospitalization in children affected by TB) aims to determine the challenges that the children face at Brooklyn Chest Hospital (BCH) and to gain insight on how these challenges can be managed. Once this has been done, interventions that may help in managing these challenges

will be developed. The project is funded by a small grant (ECRF) from Stellenbosch University (2020-2021). The project included a scoping review in which interventions to manage psychosocial distress in hospitalized children are identified and described. Following this, observations and interviews were conducted with staff members (n= 5), hospitalised children (n= 5), and caregivers of children who are in-patients at BCH (n= 3) to determine the challenges that the children at BCH face due to caregiver-child separation. A narrative story telling tool intervention to manage psychosocial distress was developed based on the findings of the scoping review and primary data.

**INPUTT** (Site PI: Graeme Hoddinott). Secondary analyses of the HPTN 071 (PopART) trial data toward understanding the primary outcomes in greater detail and informing ART-related policy and practice. The project is funded by the Bill and Melinda Gates Foundation. Activities included were (a) ~monthly protocol team meetings that included a closed webinar series, (b) co-authorship to three manuscripts reporting on these secondary analyses submitted to the “Lancet HIV” journal, and (c) contribution to two further manuscripts in development.

**The Urine Tenofovir Rapid Assay (UTRA)** (SBR: Graeme Hoddinott and Abenathi Mcinziba). A newly developed Urine Tenofovir Rapid Assay (UTRA) assesses tenofovir in urine at point-of-care and is a novel tool to test and immediately respond to adherence levels of people living with HIV (PLHIV). We explored PLHIV and health workers’ initial perceptions about integrating the UTRA into routine medical care for adherence support. This qualitative evaluation is a nested sub-study in the ongoing cross-sectional study that investigates the sensitivity of a urinary assay test (the UTRA) to detect virologic failure and measure the correlation of the assay with long-term TFV exposure and recorded adherence in South Africa. The parent study enrolled 120 patients on ART who are at risk of virologic failure at a primary care health facility in Cape Town, South Africa. As part of qualitative work, a series of once-off in-depth qualitative interviews were conducted with PLHIV (n= 25) and health workers (n= 5) between October 2020 and March 2021. Findings showed that the point-of-care UTRA is acceptable to patients and health workers and its integration into the adherence support system is perceived by PLHIV and health workers to be appropriate, feasible, and actionable. The study was supported by the U.S. National Institutes of Health and South African Medical Research Council through its U.S.-SA Program for Collaborative Biomedical Research (R01AI152119). A manuscript was produced based on the qualitative results and is under review.

**MH4H** (Site PI: Graeme Hoddinott). A consultation project to support USAID implementing partners to review the mental health needs of their TB/HIV staff’s mental health support needs.

Data collection included in-depth interviews with 91 health workers (across cadres) in 6 provinces in South Africa. The data were collected successfully, a set of tools to support improving mental health among USAID implementing partners' staff's mental well-being which was shared with these partners in a booklet. We also co-authored an academic manuscript reporting the findings that is under review at a journal and presented the findings at an oral presentation to the 2021 "PATA" (Paediatric-Adolescent Treatment Africa) conference.

**UseMyVoice2EndTBStigma** (Site PI: Graeme Hoddinott). Supporting TB Proof (advocacy NGO) in implementing a survey and in-depth qualitative work on people who have had TB's stigma experiences toward informing the development of community-based TB stigma reduction intervention. The project was funded by the StopTB partnership. Activities included (a) the design and support for implementation (training / mentorship) and then contributing to analysis of a survey among ~120 participants at sites in Khayelitsha and Hammanskraal, (b) similar support for in- depth interviews with ~20 participants, (c) participation in two stakeholder consultation workshops, and (d) co-authorship of a scoping review manuscript.

**RINSS:** Rapid assessment of urban communities to optimise Public Health Interventions: water infrastructure in sub-Saharan Africa (Site PI: Graeme Hoddinott, Melissa Nel). The study aims to build on a rapid qualitative assessment approach called 'Broad Brush Surveys' (BBS), specifically developed to rapidly document and convey both visible and invisible features of urban communities, including formal, informal structures and infrastructures, to optimise design and implementation of water infrastructure interventions for urban contexts. The project is sponsored by Global Challenges Research Fund (GCRF) with the British Academy (BA) and the Royal Academy of Engineering (RAE). The project started in 2020 with fieldwork commencing in May 2021 in two urban communities of Cape Town, South Africa and two in Lusaka City, Zambia. The third wave of COVID-19 has shortened the length of the fieldwork in the study communities, with additional delays due to National elections in Zambia and provincial/local elections in South Africa. In Cape Town, fieldwork was completed by June 2021 and in Lusaka City by December 2021. A combination of observational and qualitative data was collected within the communities. The data collection process entailed conducting a sequence of activities to describe the local context: discussion and social mapping with relevant community leadership; transect walk of the community; structured observations of transport hubs, entry/exit points, gathering places, relevant amenities, markets, nights and weekends; group discussions with leaders, appropriate stakeholders, different age and gender groups; key informant interviews with individuals knowledgeable about the topic. Outputs include short

community profiles, community maps, a RINSS BBS manual for implementing the approach, publications, and dissemination. Community and stakeholder dissemination is set to take place in April-May 2022.

**Psi-LOW:** Piloting HIV stigma indicators amongst law enforcement officers and health workers (PI: Lario Viljoen). The aim of the study is to pilot two stigma indicators (on gender-responsiveness of HIV services and attitudes of police officers toward key populations) to strengthen global efforts to monitor progress towards the societal enabler targets. In order to do this, the study uses a mixed methods research study design, combining qualitative cognitive interviews and quantitative surveys, toward developing two stigma indicators for use in health facilities and police stations. The project is being conducted in collaboration with an international health consultancy firm (Hera Solutions; co-investigator Anne Stangl) and is being conducted for the purpose of reporting to UNAIDS. In 2021, the team applied for ethics approval.

#### **Research Grants Awarded: 2021**

<b>Grant</b>	<b>Title</b>	<b>PI/ recipient</b>
International Union against Tuberculosis and Lung Disease	Diagnostic Atlas for Paediatric TB – Megan: An Update	Megan Palmer
CDC Tuberculosis Trials Consortium	Grant to continue participating in the CDC Tuberculosis Trials Consortium through the Veterans Affairs group	Anneke Hesseling for the Desmond Tutu TB Centre
EDCTP grant	Title: Collision of three global pandemics: The effect of tuberculosis and HIV on the epidemiological, clinical, virological, and immunological trajectory of COVID-19 in Botswana and Namibia (Core-NB)	Mareli Claassens
Tuberculosis Trials Consortium (TBTC)	TBTC 10-year grant re-awarded to DTTC, Stellenbosch through a competitive renewal process.	Anneke Hesseling for the Desmond Tutu TB Centre

National Research Foundation: South African Research Chairs Initiative (SARChI)	SARChI 5-year grant in Paediatric Tuberculosis re-awarded to Anneke Hesseling.	Anneke Hesseling
South African Medical Research Council (SA MRC)	IMPAC19TB: Epidemiological impact and intersection of the COVID-19 and tuberculosis pandemics in Brazil, Russia, India, and South Africa	Anneke Hesseling for the Desmond Tutu TB Centre
World Health Organization	WHO for MDR TB IPD data curation for 5 years: Children and adolescents.	Anneke Hesseling, Tony Garcia-Prats, Vivian Cox.
Horizon 2020	VERDI (SARS-CoV-2 variants Evaluation in pRegnancy and paeDiatrics cohorts)	Marieke van der Zalm
NIH- K-43	Supplement grant application: The long-term consequences of SARS-CoV-2 on lung health in young South African children	Marieke van der Zalm
NIH- K43	Supplement grant application: The impact of COVID-19 on children with tuberculous meningitis	Karen Du Preez
Bill & Melinda Gates Foundation (via Imperial College)	Assessment of the value proposition of new TB diagnostic tools – Epidemiological Modelling for South Africa (costed extension)	Florian Marx
TB Think Tank (SA DoH)	Modelling the impact of COVID on TB epidemiology (Consultancy)	Florian Marx, Muhammad Osman
UNAIDS Societal Enablers	Pilot study: Societal HIV stigma enablers	Lario Viljoen Graeme Hoddinott

## DTTC Academic meetings

Date	Presenter	Topic
1 Apr.	Muhammad Osman	TB-associated mortality in South Africa
15 Apr.	Caryn Upton	BCG for COVID-19: Study Design and Preliminary Data
27 May	Lario Viljoen	Social narratives of sex and intimacy in the context of universal testing and treatment of HIV/AIDS
10 June	Nomtha Mandla	Determinants, strategies, and cost implications for participant recruitment and retention in an HIV prevention cohort, perspectives from HPTN 071 (PopART)
4 Feb.	Vivian Cox	WHO guidance for paediatric TB/RR-TB: Recent and upcoming developments for 2021
18 Feb.	LM Verhagen	Respiratory tract infections in children: Let's look at the respiratory mucosal immune system
24 Feb.	1. Mariana Kruger 2. Sharon Kling	Theme: Ethics  1. Ethics in health  2. Conflicting duties during the COVID-19 pandemic.
10 Mar.	Speakers  1. J Lawrenson  2. J Janson  3. C. Cilliers  4. NM Parker	Mini-symposium on Peri-operative care of Paediatric Cardiac Patients with ASD, VSD, AVSD and Tetralogy of Fallot  Speakers and Topics:  Presentation and Pre-op Management  Surgical Management  Anaesthetic Management

		Postoperative PICU Care
18 Mar.	Chante Brand	Antimicrobial resistance in the TB-CHAMP children – What does this mean?
5 Aug.	Peter Donald	The Lübeck Disaster
2 Sept.	Eric McCollum	COVID-19 in Lesotho & Introducing Phefumla
16 Sept.	Megan Palmer	Interim analysis butterfly ultrasound
14 Oct.	Karen du Preez	Paediatric tuberculous meningitis: A forgotten public health emergency
28 Oct.	Simon Schaaf	TB drug resistance surveillance in children 2017 – 2019
25 Nov.	Liz Walters	Clinical and bacteriological spectrum of disease in a cohort of children investigated for intrathoracic TB in Cape Town
9 Dec.	Jeff Starke	The WHO End TB Strategy – Will it work for Children and Adolescents?

## TB Clinical Forum 2021

Date	Presenter	Topic
14 May	Megan Palmer, James Seddon, Eric McCollum	Interpreting CXRs to diagnose paediatric TB
11 June	Anneke Hesseling and Susan Dorman	DSTB shortening regimen trials update
12 Mar.	Judy Taylor (CCT) and Keertan Dheda (UCT)	Covid-19 and impact on TB/HIV services in Cape Metro
9 July	Gary Maartens (UCT) and Jenny Hughes (DTTC)	QT issues in DRTB Management. Approach to management of low HB in clients with Rifampicin-Resistant TB
13 Aug.	Helena Rabie (SU) Graeme Meintjies (UCT)	Paediatric TB/HIV update   Adult TB/HIV update
10 Sept.	Harry Hausler (THC) and Ashraf Kagee (SU)	Mental Health and TB-the neglected epidemic   Mental Health impact of COVID-19 on HCW and communities
8 Oct.	Ranks Lehloenya Francesca Conradie	Management of CADR associated with first and second-line TB drugs and/or ART.  BPAL regimen and Clinical Access programme in Cape Metro.
12 Nov.	Anneke Hesseling, Jenny Hughes, Jana Winckler, Sue Purchase, and Peter Bock	Update on Paediatric treatment and prevention trials
10 Dec.	James Seddon	Highlights from 52 <sup>nd</sup> Union World Conference

## Advocacy

### DTTC Community Advisory Board (CAB)

*HIV Prevention Trials Network (HPTN):*

The CAB was represented by G. Hendricks at the HPTN 084 Community Working Group (CWG) calls (21 January, 10 February, 10 March) and HPTN Global CWG calls (18 Feb, 25 March). The HPTN Annual Meeting was held from 17 – 21 May and G. Hendricks, G. Tabata, Z. Mtshamba, B. Ntanga attended. The CAB also contributed to the development of the HPTN084 OLE protocol through CAB consultations with community representatives and the CAB task team in May (28) and June (8 and 12).

*ICAB (IMPAACT Network Community Advisory Board):*

The first ICAB Network call of the year was held in March (11), with a follow-up meeting on the 26th of March. At this meeting, the ICAB (IMPAACT Network) elected G. Hendricks, the DTTC CAB Liaison Officer, and S. Nco, the CAB representative, to serve on the ICAB Leadership Group for a period of 2 years. From 7-8 June, G. Hendricks attended the TBTC Annual Meeting in preparation for CRAG/community participation.

*AIDS Clinical Trials Group (ACTG):*

As the newly elected AIDS Clinical Trials Group CAB representative S. Khonkwane, attended the Global ACTG Meetings in July (22), August (26), and September (23). G. Hendricks had two articles featured in the 2nd Edition of the ACTG CAB Newsletter, in June (16th), one of which introduced S. Khonkwane as the DTTC-CAB representative.

*CAB Contributions and Highlights:*

The CAB also provided regular input on various studies throughout the year, including: The Phoenix Study (13 March); the TeenTB study (12 June) and the BRICS Study (IMPAC19TB) (12 June and 30 September). The CAB also issued letters of support (iThemba Study) and in June the CAB provided input on community dissemination for the SHINE study. Two DTTC-CAB members applied to be recruited for the HANC Community Partners (CP). Additionally, the UNION & The Union Community Connect Programme awarded 3 scholarships to the DTTC CAB members. Goodman Makanda presented a session of the Community Connect Programme on 19 October 2021 for a study led by DTTC. On the 2nd of September Graeme Hoddinott and Gwynneth Hendricks presented, the “Role of community advisory boards and their role as gatekeepers in research” at the Stellenbosch University: Social, Behavioural and Education Research Ethics Workshop. Gwynneth Hendricks also attended the IMPAACT Complications Scientific Committee Meeting, HIV & Common Mental Health Disorders (2nd September). On the 14th of September 6 CAB members attended TB Champion Training, hosted by TB Proof. Goodman

Makanda was appointed to serve as community advisor on the Stellenbosch University Health Research Ethics Committee (SU-HREC) (5th October). On the 13th of October 2021, DTTC CAB member and Mathematics educator, Hopolang Lekhetha, featured in Die TygerBurger and on SABC 3's 'Insider,' highlighting his outstanding accomplishments at the Curro Delft High School and the Capitec Foundation's Maths Tutoring Programme. G. Hendricks, Z. Mtshamba, M. Ngqwule and R. Clarke participated, in the UNAIDS 2021 Ethical Recommendations on the inclusion of Adolescents in Clinical Trials. Five CAB members also attended a WHO Information Session for civil society representatives regarding updated TB guidelines (10 December 2021).

#### CAB Administration:

The CAB welcomed and appointed 3 new members in March (2nd). The CAB held Steering (4 February, 9 March), and General committee meetings over the course of the year (13 Feb, 13 March, 12 June, 17 July, 21 August, 11 September, and 13 November). The CAB run a series of Strategy Review Workshops for the upcoming 2022/2023 year, in September (7, 14, 21 and 28). The CAB held the DTTC-CAB EXCO Meeting on the 10th of June, and its Annual General Meeting on the 27th of November 2021. An Award Ceremony and team building was held at Devonvale Golf Estate. Some notable Awards include the SUN-CTU Shield of Excellence 2021 awarded by site management and staff to Godfrey Mbulelo Tabata and the DTTC-CAB Member of the Year 2021 (voted by CAB members), awarded to Siphokazi Khonkwane. ACTG attendance certificates and the HPTN HIV Information Workshop certificates were presented to all CAB members. CAB members enjoyed the rest of the day, playing volleyball, soccer, table tennis and board games. On the 29th of November Blanche Pretorius from HREC met with Graeme Hoddinott and Gwynneth Hendricks to discuss possible collaboration with additional community representation from CABs on the SU-HREC. The proposal is to be discussed with CAB members in January 2022.



(1) DTTC CAB Annual Award Ceremony; (2) Siphokazi Khonkwane: DTTC-CAB Member of the Year 2021; (3) Godfrey Mbulelo Tabata: SUN-CTU CAB Shield of Excellence Award 2021.

## Conferences, academic meeting, and events

### *International conferences and events*

#### London School of Hygiene and Tropical Medicine virtual webinar series, June 2021.

Graeme Hoddinott and Lario Viljoen presented at the London School of Hygiene and Tropical Medicine virtual webinar series, funded by the Bill and Melinda Gates Foundation, on HIV stigma in sub-Saharan Africa.

Webinar 1. Is HIV stigma decreasing in sub-Saharan Africa? 8 June 2021.

Webinar 2. Is HIV stigma changing in sub-Saharan Africa? 15 June 2021.

Webinar 3. Is HIV stigma still an important barrier to control of the HIV epidemic in sub-Saharan Africa? 22 June 2021.

#### PAGE – Population Approach Group in Europe, 2-3; 6-7 September 2021

1. Pharmacokinetics and dose optimization strategies of para-aminosalicylic acid in children with rifampicin-resistant tuberculosis. L van der Laan (Poster presentation).

#### The 52<sup>nd</sup> Union World Conference on Lung Health, 19 – 22 October 2021. Virtual event

##### Oral presentations

1. Surveillance of childhood tuberculosis and drug resistance in the COVID-19 era. HS Schaaf, MM van der Zalm, R Croucamp, M Palmer, P Goussard, H Rabie, L Smith, AC Hesselring
2. The diagnostic accuracy of chest radiographic features for paediatric pulmonary tuberculosis. M Palmer, KS Gunasekera, MM van der Zalm, HS Schaaf, J Morrison, AC Hesselring, P Goussard, E Walters, JA Seddon
3. Lung ultrasound for the diagnosis of paediatric pulmonary tuberculosis: interim analysis. M Palmer, E Lopez-Varela, MM van der Zalm, AC Hesselring, A Redfern, P Goussard, M Fentress and R Pitcher
4. Incidence, causes, and outcome in cases of hepatocellular injury in children on multidrug-resistant tuberculosis therapy. J Duvenhage, HS Schaaf, AC Hesselring, AJ Garcia-Prats. HR Draper, J Winckler

### Poster presentations

1. Reducing initial loss to follow-up amongst people with tuberculosis in Cape Town, South Africa. M Osman, S Meehan, A von Delft, A Boule, R Dunbar, M Smith, FM Marx, P Naidoo, AC Hesselring

### Symposia

1. Advancing TB prevention in children during the COVID-19 pandemic (Chair: AC Hesselring)
2. Engaging communities, health workers, and policy makers to address TB stigma (Chair: G Hoddinott)
3. Incorporating patient values and preferences as a solution to preventing TB (Chair: G Hoddinott).
4. Presentations: Caregiver experiences of TB prevention therapy in children in South Africa – implications for dose-frequency preferences. G Hoddinott
5. Closing the gap on paediatric TB diagnosis: improving bacteriological diagnosis and evidence-based treatment decision algorithms.
6. Presentation: Time for a paradigm shift: the role of paediatric TB Treatment Decision algorithms. J Seddon
7. Computer aided detection of pulmonary tuberculosis on paediatric chest x-rays: using old tools in new ways. M Palmer.

### Community Connect at the Union

1. Use MY Voice to End TB: empowering community health workers to contribute to person-centered, gender-responsive, stigma-free TB care in South Africa (Goodman)

### *Local conference and events*

### UKWANDA Rural Research Day, Worcester, South Africa. 13 May 2021.

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, South Africa. N Vanqa, G Hoddinott, B Mbenyana, M Osman and SA Meehan.

2. 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.
3. Early experiences of people living with HIV and health workers about a point-of-care urine test for tenofovir: a qualitative study on acceptability. A Mcinziba.
4. Exploring how the management of household incomes impact on antiretroviral therapy adherence behaviour of people living with HIV in the Western Cape, South Africa. A Mcinziba.

#### Stellenbosch University 65th Annual Academic Day, 2021-August 2021 (virtual event)

1. 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 G, P Hendricks, L Viljoen, M Osman, SA Meehan
2. The global burden of tuberculous meningitis in adults: a modelling study. P Dodd, F Cresswell, A Stadelman, M Osman, J Seddon
3. Panbio rapid antigen test not useful in hospitalised paediatric patients. M Claassen, MM Van der Zalm, G Van Zyl, W Preiser, H Rabie
4. Acute Respiratory illness admissions in children during the COVID-19 pandemic. A Redfern, Rabie H, MM van der Zalm, J Lishman, L Verhagen
5. Low burden of viral respiratory infections in children presenting to Tygerberg hospital during the COVID-19 pandemic in Cape Town, South Africa. I Dewandel, R Croucamp, M van Niekerk, M Anthony, A Redfern, M Claassen, G van Zyl, H Rabie, MM van der Zalm
6. Family dynamics, socioeconomic contexts, and treatment journeys of children living with TB in the Western Cape, Cape Town: case studies of qualitative data. M Anthony, van der Zalm M, A Hesseling, G Hoddinott
7. Lung ultrasound for the diagnosis of paediatric pulmonary tuberculosis: interim analysis. M Palmer E Lopez-Varela MM van der Zalm M, AC Hesseling, A Redfern, PGoussard, M Fentress, R Pitcher

#### **Scientific Meetings, Workshops, and training events**

### *January - March*

- Muhammad Osman, Karen Du Preez, Lario Viljoen, and others from the DTTC attended the National Department of Health (NDOH) virtual feedback meeting on the South African TB prevalence survey results on the 10<sup>th</sup> of March.
- James Seddon attended the Update on the Global Burden of TB in Children and a Whistle - Stop Tour of Developments in Diagnostics. 29 Feb 2021. Organised by The Union – North American Region. (Virtual event).
- Infection prevention control (IPC) training started on the 1<sup>st</sup> of March 2021, facilitated by Dr Jennifer Hughes. Twenty employees were enrolled for the first course from March to June 2021. Classes include: 1 & 15 March, module 1 - Roles and Structure of IPC; 29 March, module 2 - Micro-organisms of relevance to IPC.
- On the 17<sup>th</sup> of March, the DISRUPT Consortium studies (TUTT, LINKEDin and TB Mate) presentation on findings took place. The results for TUTT were shared by Neil Martinson. Muhammad Osman and Sue-Anne Meehan shared initial results for the LINKEDin, and TB Mate reported on interim findings from adherence support.
- On the 24<sup>th</sup> of March, the Desmond Tutu TB Centre World TB Day 2021 Virtual event was held.
- On the 24<sup>th</sup> of March, Melissa Nel presented at a Mapping workshop (British Academy Urban Infrastructures of Well-Being Programme) on “A method for rapidly assessing context in urban communities to optimise public health interventions: the case of water infrastructure in sub-Saharan African cities (RINSS).”

### *April – June*

- In April, Marieke van der Zalm presented at the World Society for Paediatric Infectious Diseases (WSPID) virtual webinar - Managing children with HIV and tuberculosis in the shadow of a global pandemic. Title: The diagnosis of childhood TB during a global pandemic.
- James Seddon attended the MSF Paediatric Day on the 16<sup>th</sup> of April (virtual event). Theme: A common-sense approach to diagnosing TB in children.

- The following staff attended and advanced driving and hi-jack prevention course. On the 16<sup>th</sup> of April, Wayne Green, Waylin Wenn, Craig Steyn, Anele Gqabuza, and Lusanda Gigi attended. On the 30<sup>th</sup> of April, Nevel Kay, Tukelo Sithole, David Nikani, Amos Gumede, Asikhangele Mtsahbe, Vuyo Peti, John Wolmerans, Lindelane Mavume, and Sabelo Zighu attended.
- On the 26<sup>th</sup> of April, a group from the DTTC attended the Virtual Infection Prevention Control (IPC) training, focusing on hand hygiene.
- The following staff attended HIV training from 28 – 30 April 2021: Asanda Mfazwe, Beauty Bavuma, and Babalwa Gomba.
- Marieke van der Zalm was invited as a speaker at the ISGlobal in Spain, which was a research meeting on 6 May 2021. Title: Post-TB lung disease: The forgotten child (virtual event).
- James Seddon attended the Peruvian Network of Paediatric Tuberculosis virtual event from 17-18 June 2021 Theme: New advances in the treatment of childhood tuberculosis.
- James Seddon and Simon Schaaf were invited as speakers and presented on the role of IGRAs in the diagnosis of paediatric TB disease at the Qiagen Latent TB Paediatric Advisory Meeting from 6-7 May 2021 (virtual event).
- A group from the DTTC attended the IPC training, focusing on Environmental Cleaning and Waste Management (10<sup>th</sup> of May) and Tuberculosis infection prevention and control (24<sup>th</sup> of May).
- LINKEDin training in accessing and using the SPV and drawing of TB cascade was completed for relevant staff at Khayelitsha Day Hospital (KDH), including staff appointed by TB/HIV Care through the Global Fund.
- The IMPAC19TB study engaged with NICD and NDoH during May 2021 to provide an overview of the project, discuss TB, HIV and COVID-19 indicators required for the project.
- The World Health Organization (WHO) convened a Paediatric and Adolescent Tuberculosis (TB) guideline meeting in June 2020 resulting in 9 new recommendations regarding the diagnosis and treatment of children with TB. DTTC led literature reviews

and analyses, provided key data, and coordinated several aspects leading to the recommendations directly. In addition, James Seddon, Anthony Garcia-Prats and Anneke Hesseling served as technical experts at the virtual event.

- James Seddon attended the Peruvian Network of Paediatric Tuberculosis virtual event from 17-18 June 2021. Theme: Recent developments in the diagnosis of paediatric tuberculosis.
- The South Africa TB/COVID conference was held virtually from 5 – 7 June 2021 - Anneke Hesseling was an invited plenary speaker regarding the Impact of COVID-19 on Tuberculosis in Children.
- James Seddon and Simon Schaaf were invited as speakers at the Peruvian Network of Paediatric Tuberculosis, held from 17-18 June 2021. James Seddon spoke on the “Recent developments in the diagnosis of paediatric tuberculosis”, and Simon Schaaf spoke on the “Radiological diagnosis of pulmonary tuberculosis in children: Is there a role for chest tomography?” and “Experience in the development of drug-resistant tuberculosis treatment regimens in children.” (Virtual event attended by 580 participants).
- Anneke Hesseling served on the JnG Global TB Strategy Task team for TB drug development in June 2021.
- DTTC IPC training final assessments were held on the 7<sup>th</sup> of June.
- The TBTC Virtual Meeting was held from 7 - 8 June.
- The ACTG annual meeting was held from 14 – 20 June and several members from the DTTC attended.
- On 24 June, the IMPAACT Scientific Committee meeting was held.
- The IMPAACT Annual Meeting was held from 21 – 25 June 2021.
- The Supervisory Leadership Programme was held from 22 – 24 June 2021. Sue Purchase, Marilyn Mentor, Bryan Esterhuizen, Adelaide Carelse, Daphne van Ster, and Rosemary Brown attended.
- Muhammad Osman presented the SACEMA Seminar on TB-associated mortality in South Africa, looking at the longitudinal trends and the impact of health system interventions on the 18<sup>th</sup> of June 2021 (virtual event).

- Postgraduate Supervision in Health Sciences e-Workshop was hosted by the Research Development and Support, Faculty of Medicine and Health Sciences at SU (11 & 12 June 2021). The workshop was attended by Muhammad Osman, Sue-Ann Meehan, and Graeme Hoddinott.
- The employee wellness programme e-workshop (25 June 2021) was attended by Sue-Ann Meehan and Graeme Hoddinott.
- The London School of Hygiene and Tropical Medicine (LSHTM) and Bill and Melinda Gates Foundation hosted a webinar series in June 2021 on HIV stigma in sub-Saharan Africa, and Graeme Hoddinott and Lario Viljoen presented in two of the sessions.

#### *July - September*

- Several staff members attended a webinar focused on TB and TB research in the Eastern Cape, presented by the Eastern Cape AIDS Council in collaboration with the Desmond Tutu Health Foundation on the 8<sup>th</sup> of July 2021.
- Marieke van der Zalm attended a virtual European Respiratory Society (ERS) course on paediatric respiratory illnesses from the 8-9<sup>th</sup> of July 2021.
- On the 28<sup>th</sup> of July 2021, Anneke Hesselting participated as an invited speaker at the American Thoracic Society and International Union Against Tuberculosis and Lung Disease (The Union), presenting: "Finding the missing tuberculosis cases in children."
- All staff at the DTTC received training on the updated Good Clinical Practice (GCP) guidelines in South Africa on the 25<sup>th</sup> of August, 1<sup>st</sup> of September, and 8<sup>th</sup> of September 2021.
- Staff members attended the South African Paediatric Association Virtual Congress: SAPA 2021 from 13 – 15<sup>th</sup> of August 2021.
- A group from the DTTC attended the Virtual Infection Prevention Control (IPC) training, focusing on hand hygiene (6<sup>th</sup> of September) and Environmental Cleaning, Waste Management (20<sup>th</sup> of September).
- James Seddon attended a session on "Understanding the complex and neglected world of adolescent tuberculosis" as part of the Mohn Centre for Children's Health and Wellbeing

and Centre for Paediatrics and Child Health Seminar Series at the Imperial College in London, held on the 16<sup>th</sup> of September 2021 (virtual event).

- From 16 – 17<sup>th</sup> of September the conference and WHO CC Webinar took place in Novosibirsk, looking at TB in modern epidemiological conditions: TB screening and prevention, in which latest updates of WHO recommendations were discussed. Anneke Hesselning attended.
- James Seddon attended the 3<sup>rd</sup> International Meeting on Childhood Tuberculosis (Research updates virtual event), hosted from Sofia, Bulgaria from 23-24 September 2021.
- On 24 September, Simon Schaaf presented “Treatment of multidrug-resistant tuberculosis in children – 2020 and beyond” as an invited speaker to the 3<sup>rd</sup> International Meeting on Childhood Tuberculosis (PTBNET). (Virtual Meeting).
- James Seddon attended the 2021 Global TB Clinical and Educational Summit (virtual event) from 28-30 September 2021. Theme: Recent developments in the diagnosis and treatment of children with tuberculosis.
- On the 30<sup>th</sup> of September, the IMPAC19TB dissemination event was held.

#### *October - December*

- The Virtual Annual INTERTB Symposium was held on the 1<sup>st</sup> of October. Members from the DTTC attended.
- A group from the DTTC attended the Virtual Infection Prevention Control (IPC) training, focusing on Tuberculosis Infection, Prevention and Control (4<sup>th</sup> of October) and Environmental Cleaning (11<sup>th</sup> of October).
- The 4<sup>th</sup> WHO stakeholders meeting to enable implementation of Unitaaid supported innovative TB projects was held from the 14 – 15<sup>th</sup> of October. Anneke Hesselning, Tina Sachs, and Tony Garcia-Prats attended.
- On the 14<sup>th</sup> of October, James Seddon presented at the Liverpool TB Research Group (LIV TB). Topic: The changing landscape of multidrug-resistant tuberculosis in children.
- 47 staff members wrote the assessment and completed the IPC course in October.

- The 54<sup>th</sup> Annual South African Society for Basic and Clinical Pharmacology Conference was held on the 22<sup>nd</sup> of October (virtual event). Members from the DTTC attended.
- From the 26 – 28<sup>th</sup> of October, the TBTC Fall virtual meeting was held and Anneke Hesseling, Simon Schaaf, and Tony Garcia-Prats attended.
- On the 22<sup>nd</sup> of October, the 54<sup>th</sup> Annual South African Society for Basic and Clinical Pharmacology Conference was held virtually. Members from the DTTC attended.
- Expert consultation on dosing of bedaquiline and delamanid as part of regimens to treat paediatric DR-TB and for a shorter treatment regimen for paediatric TBM was held on the 26<sup>th</sup> and 27<sup>th</sup> of October, in which James Seddon, Anneke Hesseling, Tony Garcia-Prats and Simon Schaaf attended.
- From the 17<sup>th</sup> – 21<sup>st</sup> of October, The European & Developing Countries Clinical Trials Partnership (EDCTP) Forum took place. On the 21<sup>st</sup>, the EDCTP Fellow meeting took place, and Marieke van der Zalm attended both.
- From the 18 – 19<sup>th</sup> of October, the Clinical management of drug sensitive and resistant TB course was hosted by Stellmed. Isabelle Dewandel presented the coursework at the Tygerberg training Centre to primary health care clinics.
- On the 28<sup>th</sup> of October, the Boston TB Interest Group meeting was held. Karen du Preez presented on interdisciplinary and multi-level approaches to estimate the disease burden and outcomes of childhood tuberculous meningitis.
- On the 2<sup>nd</sup> of November, Karen du Preez attended a Research Indaba Webinar on research data management.
- On the 5<sup>th</sup> of November, Understanding Vaccines: COVID-19 Vaccine Webinar was held and Marieke van der Zalm & Carla McKenzie attended.
- International Workshop on Clinical Pharmacology of Tuberculosis Drugs was held from the 11 – 12<sup>th</sup> of November and members from the DTTC attended.
- The Scientific BENEFIT Kids Advisory Board Meeting was held on the 17 November.
- On the 19<sup>th</sup> of November, the WHO and Stop TB Partnership hosted the #EndTB Webinar to mark International Men's Day 2021. Lario Viljoen attended.

- Michaile Anthony, Melissa Nel, and Dzunisani Baloyi attended a course on gender and health presented at the Sociobehavioural Research Unit at the University of Cape Town from the 16<sup>th</sup> to 18<sup>th</sup> of November.
- An annual meeting of the Child and Adolescent TB Working Group was held on the 30<sup>th</sup> of Nov 2021. Members from the DTTC attended.
- On the 25<sup>th</sup> of November, a delegation from IRD Global and South Africa (led by Dr Aamir Khan) met with a team from DTTC at the Kuilsriver site. The objective was to discuss areas of mutual interest and explore the possibility of future collaborations and funding opportunities.
- The BENEFIT Kids Community Advisory Board Meeting was held on 2 December.
- The DTTC held a virtual dissemination meeting on the 8<sup>th</sup> of December. Other teams at the Centre held smaller in-person events throughout December.
- The Centre mourned the passing of Archbishop Desmond Tutu and Nulda Beyers, Anneke Hesseling, and Mariana Kruger paid tribute to the Archbishop on the Stellenbosch University website.
- Anneke Hesseling paid tribute to the Archbishop on RSG radio station on the 28<sup>th</sup> of December.

#### *Ongoing 2021*

- DTTC virtual paediatric team meetings took place every Friday throughout the year.
- DTTC scientific meetings and TB clinical forums occurred on a regular basis throughout the year on a virtual platform.

### **Visitors during 2021**

- Due to the COVID-19 pandemic, no visitors were allowed at the DTTC initially (in the first quarter) and all meetings were held on digital platforms.
- Dr Justina Bramugy from Mozambique and Dr Eliza Lopes were at the DTTC from Monday, 17<sup>th</sup> of May 2021 for approximately 4 weeks as a part of the EDTCP grant and collaboration with UMOYA team.
- Several trial monitors visited the DTTC site offices.
- Dr Lucia Carratalà visited the UMOYA Study as well as BCH during her visit from the 25<sup>th</sup> of October to the 8<sup>th</sup> of November 2021.
- A delegation from IRD Global/IRD South Africa visited the DTTC (Kuilsvier research site) on the 25<sup>th</sup> of November 2021.

## Employees

### *DTTC Staff appointments*

Name	Study/CP Name	Cadre
Pienaar, A.	UMOYA	Counsellor
Mgemane, Y.S.	HPTN084	Professional Nurse
Mpengesi, L.	RINSS	Driver
Mckenzie, C.	UMOYA	Medical Officer
Wanza, O.	BCH	Counsellor
Samsodien, A.	HPTN084	Data Capturer
Mpengesi, L.	UMOYA	Driver
Louw, G.	TB Champ	Data Capturer
Hendricks, W.	HPTN084	Professional Nurse
Nelani, R.	UMOYA	Driver
Rafique, M.	UNITAID	Research Assistant
Jola, L.	UNITAID	Research Assistant
Linganiso, Y.	UNITAID	Research Assistant

### *Students graduated*

Sterna Brand	BCom Honours Industrial and Organisational Psychology (UNISA)
Melissa Nel	MPhil Transdisciplinary Public Health and Development Studies (SU)
Wayne Green	BA of Administration – Licensing Practice (Lyceum College)
Chanda Mwamba	MPhil Transdisciplinary Public Health and Development Studies (SU)

Lario Viljoen	PhD Department of Sociology & Social Anthropology (SU)
Muhammad Osman	PhD Department of Paediatrics (SU)
Abenathi Mcinziba	MPhil Transdisciplinary Public Health and Development Studies (SU)
Tembeka Mhlakhaphalwa	MA Psychology (UKZN)
Ntombenhle Mkhize	MPhil Transdisciplinary Public Health and Development Studies (SU)
Chantel Streicher	MA Research Psychology (SUN)
Caitlin October	BA Honours Psychology (UWC)
Deepika Moti	MSc in Medical Virology

## Acknowledgements and Funders



# South African Collaborators | Funders | Partners



SARChI Chair in Paediatric TB (Hesseling)



Department  
for International  
Development



National  
Research  
Foundation



WITS REPRODUCTIVE HEALTH & HIV INSTITUTE



BETTER TOGETHER.



Funded by Evidence for HIV Prevention in  
Southern Africa (EHPSA), a DFID programme  
managed by Mott MacDonald.



## **Appendix I. Research outputs – peer-reviewed scientific publications**

Manuscripts (PubMed listed)

1. Allwood, B.W., Byrne, A., Meghji, J., Rachow, A., van der Zalm, M.M. and Schoch, O.D. Post-tuberculosis lung disease: Clinical review of an under-recognised global challenge. *Respiration*. 2021 Jan 5;100(1):11-23. PMID: 33401266.
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## Appendix II: Students

Registered Master's Degree (21)				
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.
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.  Graduating dec
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.
Khanyisa Mcimeli	Research Assistant	MPhil Transdisciplinary Public Health and development studies (SU)	Lario Viljoen	Exploring social media use of adolescents living with TB and the effects towards their health perception.
Nozizwe Makola	Community Liaison Officer	MPhil in Applied Ethics specializing in Bioethics (SU)	Nicola Barsdorf Graeme Hoddinott	The role of Community Advisory Boards in protecting human subjects in large-scale community-randomised control trials – a case study of HPTN 071 (PopART).
Christopher Mahwire	Medical Officer, DOH	MSc Epid (SU)	Pren Naidoo	Has the use of Xpert <sup>®</sup> MTB/RIF diagnostic assay improved MDR-TB treatment success rates in KwaZulu Natal?

Marcel Kanyinda Kitnge	Student	MSc Epid (SU)	Pren Naidoo	Did the introduction of an Xpert MTB/RIF-based algorithm increase the proportion of bacteriologically confirmed PTB cases in Cape Town: An Interrupted Time Series Design?"
Khanya Mama	Student	MCom (SU)	Ronelle Burger Graeme Hoddinott	TB patients with confirmed diagnoses who decline/delay taking up treatment – exploring why.
Gwynneth Hendricks	Communications Officer	MTECH: Public Relations Management (CPUT)	Nirvana Bechan Graeme Hoddinott	The role of a Community Advisory Board in public health research from a stakeholder engagement perspective.
Tarshlyn Herandien	Social Science	MA Sociology (SU)	Khayaat Fakier Hanlie Myburgh	Exploring intimacy and the usage of anti-retroviral treatment (ART) in heterosexual relationships of individuals living with HIV.
Joanie Duvenhage	Dep Paediatrics	MMed	Simon Schaaf Anneke Hesselning	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 Sue-Ann Meehan	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	Graeme Hoddinott	Residents' experiences of a rural health service-learning centre's activities – a historical and ethnographic review.

		development studies (SU)		
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.
Bukeka Sawula	Student	MA (SU)	Laing de Villiers Lario Viljoen	Young women living with HIV's experiences of care and caring for children.
Amina Abdullah	Internal Monitor	MPhil: Health Systems and Services Research (SU)	Lungiswa Nkoki	
Chantel Streicher	Student	MA (SUN)	Anthony Naidoo Stephan Rabie	Feasibility and acceptability of the self-directed career guidance project for Grade 9 learners
Mohhadijah Raffique	Student	MA (SUN)	Anthea Lesch	Hip Hop music's footprint on codeine culture
Ayanda Mthiyane	Student	MA (UKZN)	Thabo Sekhesa Mary can der Riet	How female university students construct the concept of love
Samke Nyamathe	Medical Officer	MPH (UCT)		
Registered PhD degree				
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, Physio	Research Officer	PHD (SU) Dep of 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 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.
Megan Palmer	Paediatrician	PhD (SU)	Anneke Hesseling Pierre Goussard James Seddon	Validity of chest radiographic reading methods in children with suspected tuberculosis.
Nosivuyile Vanqa	Social Science Research Officer	PhD (SU)	Graeme Hoddinott Sue-Ann Meehan	Health workers as mediators of RR-TB information and how it affects treatment readiness – an exploratory study in the Khayelitsha sub-district of the Western Cape Province, South Africa.
Michaile Anthony	Junior Study Coordinator	PhD (SU)	Graeme Hoddinott Marieke van der Zalm Anneke Hesseling	Measuring health-related quality of life amongst children with respiratory illnesses in LMIC settings – A mixed-method project toward developing a scale in Cape Town, South Africa.
Postdoctoral Fellow				
Elisa Lopez	Postdoctoral fellow	Postdoc (SU)	Anneke Hesseling	Improving TB treatment outcomes in children.
Currently registered - Undergraduates (8) + Hons (2) + PGD's				
Theo Smith	Honours Public Admin (SU)			

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)
Asikhangele Myshabe	BA Supply chain management (MANCOSA)
Shane Maker	BCom in Information and Technology Management (MANCOSA)
John Wolmerans	BA Supply chain management (MANCOSA)
Caitlin October	BA Hons Psychology (UWC)
Klassina Zimri	BA in Theology (SU)
Hazel David- Ruiters	BA in Community Development (UNISA)

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

#### Print media

Date	Newspaper	Title	Staff member
24/03/2021	Cape Times	Children with TB need continued care	Karen du Preez
24/03/2021	Star	Spotlight on TB hospital reporting gap	Karen du Preez
24/03/2021	Cape Times	ARVs and 'sex inhibition' in SA's 7.9 million patients battling HIV  <a href="https://pclientclips.s3.af-south-1.amazonaws.com/20210607/LDP-1623038001404_134663C.pdf#page=1">https://pclientclips.s3.af-south-1.amazonaws.com/20210607/LDP-1623038001404_134663C.pdf#page=1</a>	Lario Viljoen

#### Television

Date	Station	Link	Title
24/03/2021	Newsroom Africa (Channel 405)	<a href="https://storage.googleapis.com/clientclipsr/20210330/3577274-0~16AF854.mp4">https://storage.googleapis.com/clientclipsr/20210330/3577274-0~16AF854.mp4</a>	Stephen Grotes [presenter]; Talking about the issue of childhood TB in SA (Featuring Karen du Preez)
24/03/2021	ENCA news (channel 403)	<a href="https://storage.googleapis.com/clientclipsr/20210330/3563395-0~16AC21D.mp4">https://storage.googleapis.com/clientclipsr/20210330/3563395-0~16AC21D.mp4</a>	Featuring Karen du Preez

## Radio

Date	Station	Link	Title
24/03/2021	Cape Talk	<a href="https://storage.googleapis.com/clientclipsr/20210324/3560936-0~16AB87C.mp3">https://storage.googleapis.com/clientclipsr/20210324/3560936-0~16AB87C.mp3</a>	Afternoon Drive with John Maytham - Mike Wills (Presenter:) - Discussion around a new Stellenbosch University study showing the need for diagnosis, reporting and continued care for children with TB (Featuring Karen du Preez)
24/03/2021	Radio 786	n/a	Discussion around a new Stellenbosch University study showing the need for diagnosis, reporting and continued care for children with TB (Featuring Karen du Preez)
24/03/2021	Radio sonder grense (RSG).	n/a	Spektrum - Suzanne Paxton - Presenter - Today is international TB Awareness Day. Research at Stellenbosch University shows that children do not receive the necessary treatment for TB (Featuring Karen du Preez)

## Internet media

Date	Site	Link	Title
24/03/2021	Stellenbosch University	<a href="http://www.sun.ac.za/afrikaans/Lists/news/DispForm.aspx?ID=8001">http://www.sun.ac.za/afrikaans/Lists/news/DispForm.aspx?ID=8001</a>	Studie wys kinders met TB ontvang nie altyd voorgesette behandeling (Featuring Karen du Preez)
16/03/2021	Stellenbosch University	<a href="http://www.sun.ac.za/afrikaans/Lists/news/DispForm.aspx?ID=7988">http://www.sun.ac.za/afrikaans/Lists/news/DispForm.aspx?ID=7988</a>	Grants enable researchers to study effects of TB in children (Featuring Marieke vd Zalm)
24/03/2021	Stellenbosch University (podcast recording)	<a href="https://anchor.fm/stellenbosch-university/episodes/Improving-TB-care-for-children-etcfq6">https://anchor.fm/stellenbosch-university/episodes/Improving-TB-care-for-children-etcfq6</a>	Improving TB care for children (Featuring Karen du Preez)
24/03/2021	IOL	<a href="https://www.iol.co.za/the-star/news/many-kids-dont-get-tb-treatment-due-to-diagnosis-and-reporting-challenges-expert-6385e2cb-5abd-4803-9ca8-c7d2d324d8d3">https://www.iol.co.za/the-star/news/many-kids-dont-get-tb-treatment-due-to-diagnosis-and-reporting-challenges-expert-6385e2cb-5abd-4803-9ca8-c7d2d324d8d3</a>	Many kids don't get TB treatment due to diagnosis and reporting challenges – experieces (featuring Karen du Preez)
24/03/2021	Yiba	<a href="https://yiba.co.za/study-shows-children-with-tb-desperately-need-continued-care/">https://yiba.co.za/study-shows-children-with-tb-desperately-need-continued-care/</a>	Study shows children with TB desperately need continued care (Featuring Karen du Preez)
24/03/2021	Stellenbosch University	<a href="http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=8318">http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=8318</a>	Lario Viljoen

			Many women still not benefitting from HIV prevention programmes
27/03/2021	News24	<a href="https://www.news24.com/news24/SouthAfrica/News/news-research-shows-children-falling-through-cracks-in-tb-care-process-20210327">https://www.news24.com/news24/SouthAfrica/News/news-research-shows-children-falling-through-cracks-in-tb-care-process-20210327</a>	New research shows children `falling through cracks` in TB care process (Featuring Karen du Preez)
30/03/2021	All4women	<a href="https://www.all4women.co.za/2218848/news/south-african-news/new-study-shows-nearly-10-000-children-did-not-complete-their-tb-treatment-process">https://www.all4women.co.za/2218848/news/south-african-news/new-study-shows-nearly-10-000-children-did-not-complete-their-tb-treatment-process</a>	New study shows nearly 10 000 children did not complete their TB treatment process
07/04/2021	Medical Research Council	<a href="https://www.samrc.ac.za/media-release/south-africa-strengthens-its-fight-against-covid-19-through-international-solidarity">https://www.samrc.ac.za/media-release/south-africa-strengthens-its-fight-against-covid-19-through-international-solidarity</a>	South Africa strengthens its fight against COVID-19 through international solidarity and the BRICS cooperation
12/08/2021	Stellenbosch University	<a href="http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=8469">http://www.sun.ac.za/english/Lists/news/DispForm.aspx?ID=8469</a>	Lario Viljoen #WomenofSU: Negotiating intimacy in a changing HIV landscape