

DESMOND TUTU TB CENTRE ANNUAL REPORT: 2018



Every breath counts



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Letter from the Director

The past year was exciting and challenging for our centre. Large trials like HPTN 071 (PopArt) have come to an end, resulting in much smaller staff component and reduced funding.

At the same time, we have become more efficient, more internally collaborative and our three “research pillars” in our centre have become more integrated. We have pursued new endeavours, notably in paediatric therapeutics and in adult HIV prevention trials.

We continue to build capacity at all levels and have had a record 6 PhD students graduate from our centre during 2018. There is now a strong cadre of young and mid-level career researchers who are not only supporting our scientific agenda, but are mentoring and supporting other researchers.

We have established new local, South African, Africana and global collaborations and continue to be the global leader in paediatric tuberculosis clinical research.

We have opened two new research sites to support TB and HIV prevention trials, and have grown in key core support areas including regulatory, data, laboratory, logistics and communications.

We are thankful for a highly productive year and look forward to going from strength to strength in 2019.



Professor Anneke C. Hesseling

Director: Desmond Tutu TB Centre

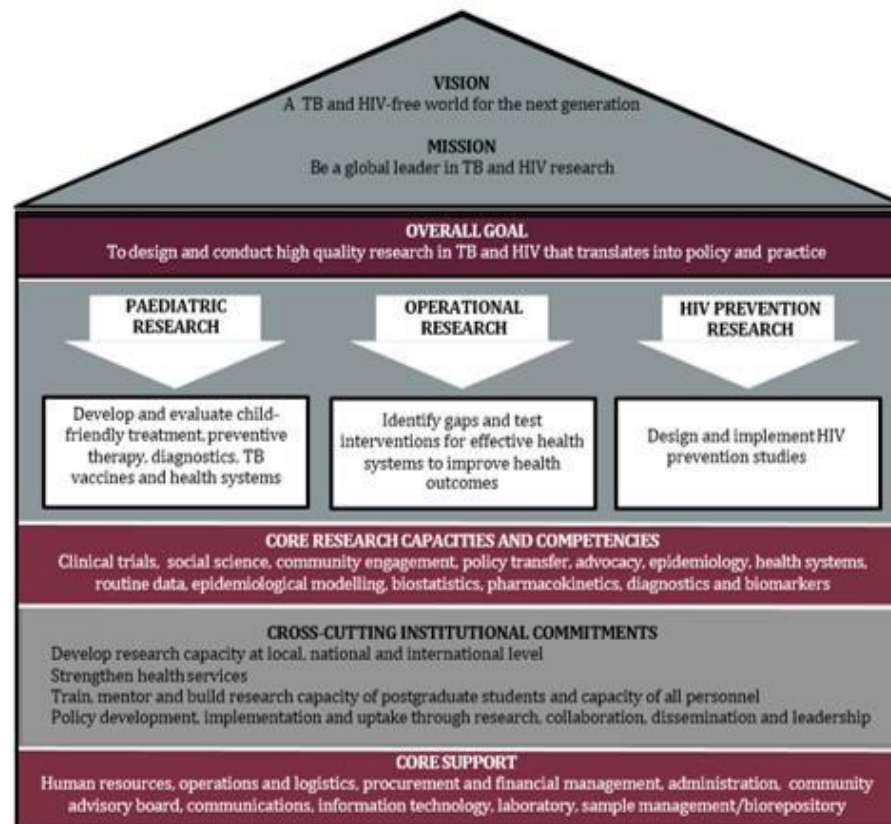
Distinguished Professor in Paediatrics and Child Health

SARcHi Chair in Paediatric Tuberculosis

DTTC Strategy House



Desmond Tutu TB Centre Strategy House



Glossary of Terminology

ACTG	AIDS Clinical Trials Group
AE/AER/EAE	Adverse Event / Adverse Event Report / Expedited Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
ART/ARV	Antiretroviral Therapy / Antiretroviral
BMC	BioMed Central
BMRC	British Medical Research Council
CAB/CAG	Community Advisory Board/Community Advisory Group
CD4	Cluster of Differentiation 4
CDC	US Centers for Disease Control and Prevention
CHIP	Community HIV Care Providers
CRS	Clinical Research Site
CTU	Clinical Trials Unit
CXR	Chest X-ray
DAIDS	Division of AIDS, NIAID
DFID	Department for International Development
DR-TB	Drug-Resistant Tuberculosis
DS-TB	Drug-Susceptible Tuberculosis/Drug-Sensitive Tuberculosis
DST	Drug Susceptibility Testing
EC	Ethics Committee
DTTC	Desmond Tutu TB Centre
EDCTP	The European & Developing Countries Clinical Trials Partnership
FAMCRU	Family Clinical Research Unit
FDA	Food and Drug Administration
FHI 360	Family Health International and Academy for Educational
FMHS	Faculty of Medicines and Health Science
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HR	Human Resources
HREC	Health Research Ethics Committee
HTS	HIV Testing Services
IMPAACT	International Maternal Pediatric Adolescent AIDS Clinical Trials
IT	Information Technology
LAB	Laboratory
MA	Master of Arts
MCC	Medicines Control Council
MDR-TB	Multidrug-Resistant Tuberculosis
MPH	Master of Public Health
MRC	Medical Research Council
MS	Mass Spectrometry
MSF	Médecins sans Frontières

<i>M.tb</i>	<i>Mycobacterium tuberculosis</i>
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
OR	Operational Research
ORAP	Operational Research Assistance Project
PC	Population Cohort
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary Health Care
PI	Principal Investigator
PK	Pharmacokinetics
PMTCT	Prevention of Mother To Child Transmission
RIF	Rifampicin
RGMO	Research grants management office
QA	Quality Assurance
SACEMA	South African Centre for Epidemiological Modelling & Analysis
STI	Sexually transmitted infections
SU	Stellenbosch University
TBTC	TB Trials Consortium
VMMC	Voluntary Male Medical Circumcision
ZAR	South African Rand (currency)

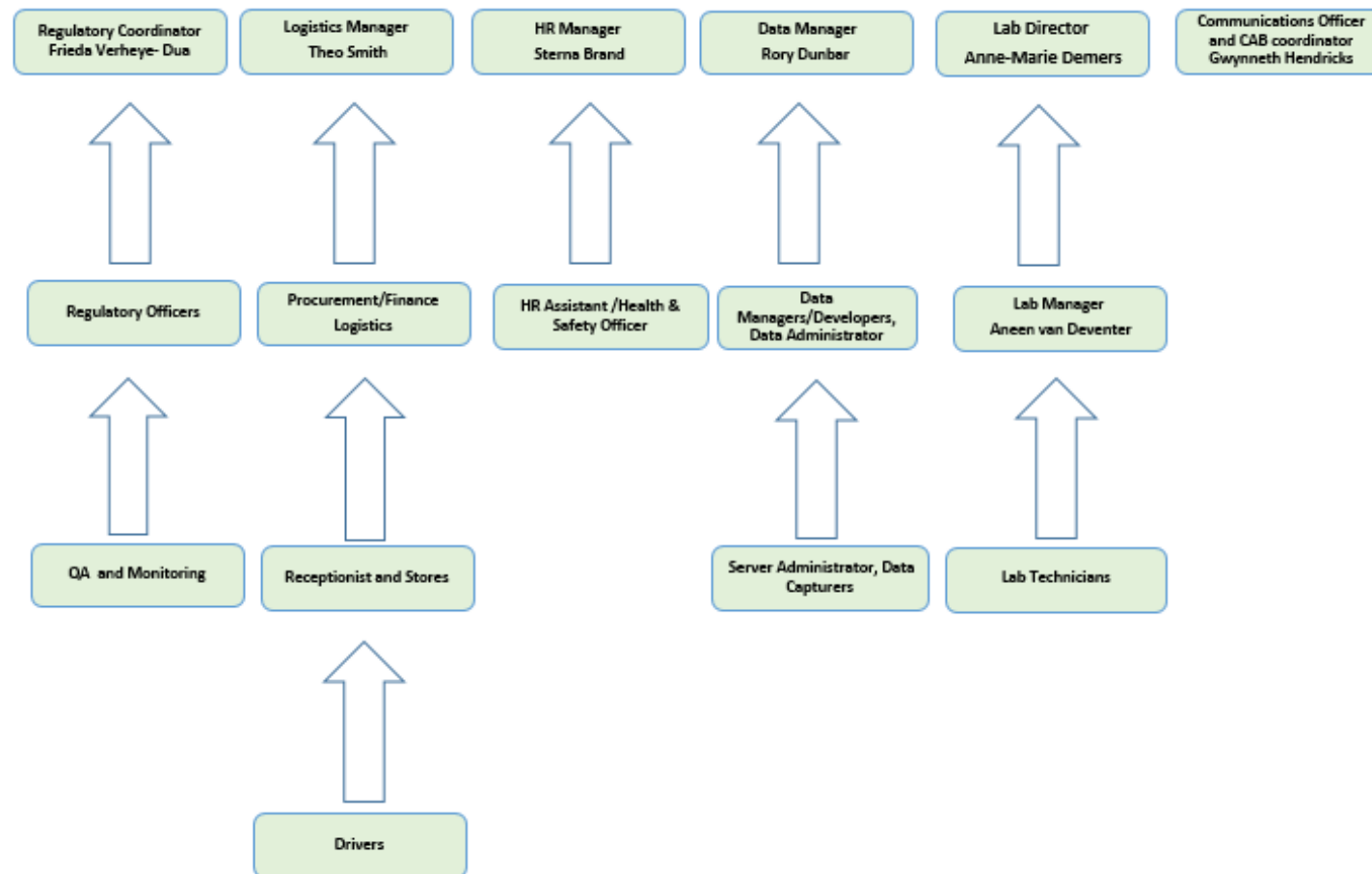
Organogram

SCIENTIFIC FOCUS AREAS

DTTC DIRECTOR: PROF AC HESSELING



SUPPORT COMPONENT



DTTC TOTAL STAFF COMPONENT 152

Research Updates

Research Focus Area One: Paediatric Tuberculosis

The DTTC initially has established its reputation based on its strong track record of clinical research in paediatric tuberculosis (TB). The DTTC is now the global leader in therapeutics for the prevention and treatment of TB in children, especially in the context of drug-resistant TB.

This paediatric TB research programme at the DTTC is led by Anneke Hesseling, centre director, SARCHI Chair in Paediatric Tuberculosis and Distinguished Professor in Paediatrics and Child Health, Stellenbosch University. Key focus areas include 1) therapeutics for Drug Susceptible (DS) and Drug Resistant TB (DR-TB) in children (leads; Anthony Garcia-Prats, Megan Palmer), 2) preventive trial for TB in children (lead: Anneke Hesseling, 3) Lung health, diagnostics and biomarkers in children (lead: Elisabetta Walters, Marieke van der Zalm and Anne-Marie Demers), 4) underpinned by in-depth epidemiological and operational research (leads: Karen du Preez, Muhammad Osman). Major areas of interest specifically include the evaluation of novel therapeutic strategies for Multidrug resistant TB (MDR-TB) in children, where it is a global leader in its field and is generating seminal data on an ongoing basis. The DTTC officially opened its upgraded state of the art paediatric pharmacokinetics clinical research unit at Brooklyn Chest Hospital (medical director: Tony Garcia-Prat) in July 2016 (refer to highlights, 2016), where it has been working since 2011. This unit has been expanded twice since then, reflecting the urgent need for clinical research in this domain, with 9 trials for antituberculosis treatment (including novel drugs like delamanid and bedaquiline) currently ongoing.

During 2018, the paediatric group (n=84 personnel) has specifically actively pursued linking and collaborating with the Sociobehavioural science group at DTTC (lead: Graeme Hoddinott), and on high quality operational research. The group has also expanded to collaborations at the Tygerberg campus on the role of viral pathogens in TB disease pathogenesis in children (Professor Gert van Zijl, Medical Virology), antimicrobial resistance in children and the biome and Medical Microbiology (Professor Andrew Whitelaw) and at the Stellenbosch campus, including health economics (Professor Ronelle Burger) mathematical modelling (SACEMA, Dr. Alex Welte, Eduard Grebe and Juliet Pulham), and basic scientists including biochemists (Professor Jacky Snoep), to support its expanding research agenda.

Expanding national collaboration have included Shandukani (Dr. Lee Fairlie, WHRI), and PHRU (Professor Neil Martinson) and new international collaboration have included the Uppsala pharmacometrics modelling group and Professor Tony Hu, Arizona State University and Professor Bob Husson (Boston Children's). The DTTC is also increasingly collaborating with other African research groups including in Uganda, Zambia, Mozambique and Namibia. During 2018, one of the pediatric team clinicians, Dr Karen du Preez, has been selected and trained as an epidemiological TB program review consultant for the World Health Organization, strengthening our existing collaboration

to support pediatric TB at both national and international level.

The DTTC paediatric group is a well-performing clinic site for the DAIDS-funded International Maternal, Paediatric, Adolescent AIDS Clinical Trials (IMPAACT) where it is currently conducting 5 IMPAACT TB trials and also for the US Centres for Disease Control (CDC) TB Clinical Trials Consortium (TBTC), where it leads Study 35, a TB prevention trial of rifapentine and isoniazid, in children.

The paediatric TB research group at the DTTC has been exceptionally productive during 2018. They have graduated 2 Master's degree and 2 PhD students, with 2 new PhD students registered, 1 postdoctoral fellow from Spain (Elise Lopez), and a BMRC-funded research fellow from Imperial College London, James Seddon (who has received an extraordinary appointment at the DTTC as Senior Researcher).

The group's research has resulted in >50 publications in international peer-reviewed journals (Appendix I), participation in several national and international TB treatment guideline meetings, including with WHO, and with the SA National DOH.

The group has had 3 major international grants awarded, and several local grants.

The group has embarked on new collaborations with Imperial College London, Rutgers University, BJMC, Pune, India and La Salle Medical Health Sciences Institute College of Medicine, De La Salle University Medical Center, the Philippines. The group has also developed new national partners in South Africa, and new collaborative partners in Africa (Uganda and Zambia).

The therapeutics group has been shaping the science and implementation of paediatric TB treatment trials through leadership in the National Institutes of Health (NIH) funded IMPAACT and the CDC TBTC trial consortia.

The DTTC paediatric group hosted its 12th International TB Training Course at Goudini very successfully, with 50 international participants. The DTTC paediatric group alone contributed 13 presentations to the 49th annual International Union against Tuberculosis and Lung Disease conference in The Hague, with 7 oral presentations, including a later breaker session.

Therapeutic trials: prevention of drug-susceptible TB

IMPAACT P1078: This IMPAACT-funded network multisite randomized controlled double blinded trial evaluates the safety and tolerability of isoniazid ante- vs. post-partum in HIV- infected pregnant women. DTTC was the last site to join this trial as a newly funded IMPAACT site, in 2015. Twelve women were enrolled and follow-up visits completed July 2017. The overall trial was closed to accrual in 2016 and follow-up (740 maternal-infant pairs) was completed in September 2017 and the data is being disseminated.

TBTC Study 35: This multisite study, funded by the CDC TBTC (PI: Anneke Hesseling,) will evaluate the optimal dosing and safety of the novel 12 dose combination regimen of rifapentine and isoniazid, shown to be efficacious in prevention of TB in adults and

children. The protocol has been in development for 4 years and has been finalized and approved by the Medicines Control Council (MCC) and local ethics committees. A novel fixed dose paediatric formulation has been developed for the trial. The database is in development and the trial is expected to open in 2019 under an FDA IND.

Therapeutic trials: treatment of drug-susceptible TB

SHINE: (Site PI: Anneke Hesseling). The trial PI and sponsor is the Medical Research Council Clinical Trials Unit (MRC CTU) at University College London (PI: Diane Gibb), with the funders: BMRC, Wellcome Trust, DFID. This multi-site open-label international trial is the first ever to evaluate the efficacy and safety of 4 vs. the standard 6-month WHO-recommended regimen for treatment shortening of non-severe DS-TB in children. Recruitment was completed in July 2018, with 1204 children enrolled in South Africa, Zambia, Uganda and India. DTTC enrolled a total of 315 children. Nested Pharmacokinetics (PK) sampling was completed in 31 children. This trial, if successful, will have a major impact on the current long treatment regimens for paediatric TB, which is usually paucibacillary (smear negative). DTTC has led nested qualitative work to evaluate the acceptability and palatability of the new WHO-endorsed fixed dose combination formula used in the trial. DTTC is also coordinating the process for central expert review of the Chest X-rays (CXR) taken on the SHINE trial – an undertaking which will involve review of approximately 3000 CXR images and will form an important part of the final adjudication of certainty of TB diagnosis and classification of outcomes on the trial. The evaluation of baseline CXRs by central experts is due to be completed in 2019.

Project P1026s: Pharmacokinetic properties of antiretroviral and related drugs during pregnancy and postpartum (Site PI: Anneke Hesseling). The Phase IV, observational Pharmacokinetic (PK) study started in November 2017. The primary outcome is to describe the pharmacokinetic parameters during pregnancy of selected ARV drugs currently used in the clinical care of 25 HIV-infected pregnant women, and to compare these parameters to a) historical pharmacokinetic data from non-pregnant women, and b) postpartum pharmacokinetic data from the same women in the study cohorts. In 2018, one of the study clinicians addressed the clinicians at Brooklyn Chest Hospital and gave an overview of the studies currently run at the unit. This oral presentation was held at the clinicians' weekly clinical meeting at the hospital. The study clinician took this opportunity to meet the newly appointed CEO of the hospital, Waheeda Sonnie, who showed her interest in the unit's work. To date, 8 women have enrolled in the study at the DTTC in the second-line TB drug arm of the protocol. This will provide critically needed information on the pharmacokinetics in pregnant women of medications used for MDR-TB. A follow-up study to 1026s, which will include first and second-line TB drug arms, is in development.

IMPAACT P1101: (Site PI: Anneke Hesseling) this IMPAACT-funded multisite network phase I/II trial is evaluating the PK and safety of raltegravir, a new integrase inhibitor, in combination with first-line TB treatment, including rifampicin. Children must be HIV-

infected, on TB treatment but not currently on ARVs. This patient group has been difficult to enroll in Cape Town, given good HIV prevention and treatment services in children. Three participants have been enrolled to date and interim data analysis is ongoing for the overall trial (5 South African sites). A new cohort of children <2 years of age has been opened for the trial.

OptiRif Kids: (PI Anneke Hesselning) this phase I/II open label multi-cohort dose escalation study to evaluate the pharmacokinetics and safety of increased doses of rifampicin in HIV-negative children with TB disease is funded by TB Alliance. The study utilizes a dose escalation approach in a maximum of 5 dosing cohorts of 20 children aged 0-12 years in each cohort. This trial includes collaboration with the University of Cape Town Clinical Pharmacology Division, Radboud University, Nijmegen, and Uppsala University, Sweden as well as with the Shandukani Research Site, Wits Health Research Institute. This study aims to establish the dose of RMP in children required to match RMP exposure targets in adults, using a 35-40 mg/kg dose, over 15 days. In 2018, Cohorts 1 and 2 closed for enrolment (cohort 2 since July 2018; cohort 1 since November 2018). OptiRif Kids will pave the way for the design and evaluation of shorter course regimens for DS-TB in children using higher doses of rifampicin. The third and final cohort opened for enrolment in Q4 of 2018, and completion of this cohort and closing of the study, with final analyses, is expected in 2019.

Therapeutic trials: prevention of MDR-TB

TB-CHAMP (MDR-TB preventive therapy trial): (DTTC PI: Hesselning, Schaaf, 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 multidrug-resistant (MDR) TB. The sample size is approximately 1500 children 0-5 years of age. The trial, led by DTTC, is funded by the BMRC/Wellcome Trust/DFID and includes 3 South African sites, including Shandukani (WHRI, Johannesburg, Dr. Lee Fairlie), PHRU Matlosana, Klerksdorp (Prof. Neil Martinson) and DTTC.

A formal PK lead-in study was completed in 2017 looking at bio-availability of a novel scored dispersible levofloxacin formulation (to be used in the main trial) in 24 children. This study showed that the paediatric levofloxacin formulation was well tolerated, acceptable, safe, and had adequate exposures in children < 5 years of age. Pharmacokinetic and acceptability data from this study have been recently published in two journal articles. The main trial opened to accrual in Q4 2017 at DTTC, and in Q1 2018 at the other 2 sites. As of 31 January 2019, 393 children had been screened and 3015 enrolled in the study. Additional grant funding has been requested from the The European & Developing Countries Clinical Trials Partnership (EDCTP) and other funders. This trial is likely to have a considerable impact on global and national guidelines and on clinical care.

Therapeutic trials: treatment of MDR-TB

Otuska 232/233: (PI Anthony Garcia-Prats): Along with a site in the Philippines, the DTTC is implementing this industry sponsor-funded (Otuska, Japan) Phase 1 (232) and Phase 2 (233) trials which seek to characterize the pharmacokinetics and safety of delamanid in children with MDR-TB. New drugs are desperately needed for the treatment of children with MDR-TB, and these trials are critical for ensuring timely access to this important new medication. In this age de-escalation trials, all age groups (0 to 17 years) have fully enrolled for both studies. Data from these groups informed WHO guidance in 2016 for the use of delamanid in children 6-17 years of age with MDR-TB, and in 2018 for Group 3 (ages 3-6 years). The 232 study is now closed with final data analysis ongoing, and long-term follow-up of Group 4 (0 to 2 years) completed at the end of 2018, with the final analysis now ongoing.

MDR PK 1: (PI Anneke Hesseling) This NIH-funded (R01 grant) was completed during 2016. This study of the pharmacokinetics and safety of routine doses of existing second-line anti-TB drugs in HIV-infected and uninfected children, was the first study of its kind, in some cases generating some of the only data on the pharmacokinetics and safety of these medications in children with TB. Over 4 years 312 children aged 0-15 years were enrolled and followed long-term for safety and treatment outcome. This study has already resulted in seminal data on the use of levofloxacin, ofloxacin, moxifloxacin, amikacin, high dose isoniazid, and the effect of MDR-TB treatment on the pharmacokinetics of ARVs commonly used in children. Analysis of para-aminosalicylic acid (PAS), ethionamide, terizidone, clofazimine and linezolid are ongoing. Long-term outcome and toxicity data are being analyzed currently. These data are informing international guidance on the dosing of these medications in children. The platform generated from this study has supported 5 PhD students and 6 master's degree students, to date.

MDR PK 2: (PI Anthony Garcia-Prats) Building on the data, experience, and clinical platform of MDR PK1, this NIH-funded (R01 grant) seeks to evaluate the pharmacokinetics and safety of model-optimized doses of the key second-line anti-TB medications levofloxacin, moxifloxacin, and linezolid in children treated for MDR-TB. The study will also characterize the acceptability and palatability of different dosing strategies and will evaluate the effect of formulation manipulation on pharmacokinetics in children. The total sample size is n= 100; to date, 84 children have been enrolled through the end of 2018, and accrual is now closed with long-term follow-up expected to be completed in 2019. Data from the study on linezolid and moxifloxacin pharmacokinetics was shared with the World Health Organisation (WHO) in 2018 and informed revised dosing guidance for these medications. Multiple analyses on the pharmacokinetics, safety and acceptability of linezolid, moxifloxacin and levofloxacin, as well as analysis of treatment outcomes are planned in 2019.

IMPAACT P1108: (PIs Anneke Hesseling, Simon Schaaf) This NIH-funded IMPAACT network phase I/II trial to determine the optimal and safe dose of bedaquiline in HIV-

infected and uninfected children with MDR-TB has been in development for 4 years. The protocol was completely developed and received MCC approval in August 2016. Five international sites, including DTTC, 2 other South African sites, one in India and one in Haiti, opened up to accrual on the 1st of September 2017. Bedaquiline has become a critically important treatment option for adults with MDR-TB, with extensive roll-out of the drug within the routine TB programme setting in South Africa and many other countries; however the lack of data in children has prevented paediatric access. This trial will provide desperately needed data on bedaquiline in both HIV-infected and – uninfected children with MDR-TB in order to ensure paediatric access to this new TB medication. The first participant was enrolled on the 21 September 2017. The first 15 children have been enrolled and the first formal interim analysis has been completed. Interim data was shared with the WHO and informed new dosing recommendations for bedaquiline in children. It is expected that the two youngest cohorts (0 to 2 years, 2 to 5 years) will open in early 2019.

Bedaquiline CRUSH Study (TASK-002): (Protocol Co-Chair – Anthony Garcia-Prats). This study, funded by National Institute of Child Health and Human Development (NICHD) through the IMPAACT network was a randomized, open label, crossover, bioequivalence study to assess the bioavailability of bedaquiline given as whole tablets or suspended (dissolved) in water. The study was conceived in order to facilitate the use of the bedaquiline whole tablets for use in paediatric clinical trials and eventually in routine care, as the paediatric formulation is not available now or expected to become available for some time. Twenty-four healthy male and female volunteers were randomly assigned 1:1 to one of 2 treatment sequences in order to receive either first a single dose of the crushed form of bedaquiline, as the experimental, and secondly a single dose of the whole tablet as the approved dosing form, or vice versa. The study was implemented at TASK Applied Science in Cape Town, and analysis completed in 2017 (E Svensson, Uppsala University). Results, which showed that bedaquiline administered dissolved in water was bioequivalent to whole tablets, were published in 2018 and will inform the practical use of the adult formulation in children in the field, where access to the paediatric formulation is expected to be limited for some time.

Lung health, diagnostic and biomarker studies

(PIs Elisabetta Walters, Marieke van der Zalm and Anne-Marie Demers)

The diagnostic platform nested in the DTTC paediatric programme focuses on improving the diagnosis of TB in children. TB in children is mostly clinically diagnosed as the collection of high- quality sputum samples is resource-intensive and relatively invasive and available laboratory methods are insufficiently sensitive to detect the low organism concentration typically found in samples from children. However, young children are at risk of delayed diagnosis due to poor diagnostic tools, resulting in increased risk of morbidity and mortality from advanced TB. The overall aim of the diagnostic platform is to improve the detection of TB in children using comprehensive strategies that are

feasible, child-friendly and adequately sensitive to detect paucibacillary disease, focusing especially on young children.

UMOYA (“breathe”). Intra-thoracic tuberculosis in children: moving towards better diagnosis and improved lung health: (PIs Liz Walters, Marieke van der Zalm).

A diagnostic cohort study that builds on a previous diagnostic study led by Liz Walters and has leveraged funding from NIH, Thrasher Foundation, EDCTP and the South African MRC. UMOYA started recruitment November 2017 and currently has 102 children enrolled. The aim is to enroll 300 children with suspected TB and 100 healthy sibling controls from Tygerberg hospital and Karl Bremer hospital. The study will continue to evaluate improved diagnostic strategies for paediatric TB, including novel laboratory techniques for both molecular and culture-based diagnosis on respiratory and stool specimens. It will support ongoing evaluation of blood and urine biomarker work. In addition, the study will continue work to evaluate the interaction between viral and bacterial co-pathogens with TB, and plans to assess and monitor lung function longitudinally in all children

Evaluation of novel TB biomarkers in children

Study 1. Urine proteomics: This project aims to identify host-derived urine proteins that are differentially expressed in children with TB compared to children with non-TB illness. The project is in collaboration with US partners Robert Husson and Hanno Steen from Boston Children’s Hospital, USA. This year, the focus of the project has been to optimise the LC-MS/MS platform to achieve a high detection of proteins in urine samples. This is done in the Steen laboratory at Boston Children’s Hospital, Harvard University. Data analysis will include both traditional logistic regression approaches (lead by Harvard University) as well as bio-informatics methods (lead jointly by Harvard and Stellenbosch Universities). A doctoral student, Ashley Ehlers, under the supervision of Prof D Tabb from SU’s Division of Molecular Biology and Human Genetics, has been awarded a scholarship by Boston Children’s Hospital, to work on this project.

Study 2. Serum bio-signatures. This project aims to identify pathogen-derived serum antigen peptides that are differentially expressed in children with TB compared to children with non-TB illness, using a novel NanoShell-MS assay. The project is in collaboration with US partner Tony Hu from Arizona State University.

Study 3. TB lipoprotein biomarkers. This exploratory study aims to identify whether TB lipoprotein is a useful diagnostic biomarker of active TB disease in children. Results of an initial analysis are in progress. TB Lipoprotein (TLP) is a specific mycobacterial modification of low density lipoprotein (LDL), a host biomolecule.

Epidemiological and operational research for pediatric TB

Please refer to [Research focus Area Two: Health Systems and Operational Research](#) for updates of pediatric focused epidemiological and operational research studies.

Research focus Area Two: Health Systems and Operational Research

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

This research focus area also include epidemiological and routine data analyses, modelling, and health system strengthening research, all contributing to the overall aim of generating evidence to strengthen program implementation. Outputs for 2018 are listed under the following headings: Health systems Research and Operational Research (including TB mortality and childhood TB as specialized focused areas).

Health Systems and Operational Research

LINKEDin: reducing initial loss to follow up among tuberculosis patients: (PIs: Anneke Hesseling and Muhammad Osman). This study is funded by the Bill and Melinda Gates Foundation and will be implemented in 2019. Individuals diagnosed with tuberculosis (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 will be implemented in 6 hospitals and 31 primary health care facilities in 3 provinces of South Africa; Western Cape (WC), Gauteng (GP) and Kwa-Zulu Natal (KZN). The study will include all laboratory-diagnosed TB patients in the identified study sites as well as clinically diagnosed TB patients in the WC. Using a before/after design, the study will measure the proportion of TB patients who are ILTFU at baseline and again after the 12th month, following the implementation of the study interventions. Between July and December 2018, the study received ethics approval with the Stellenbosch University Health Research Ethics Committee (HREC) and approvals from the relevant health departments/authorities. Numerous stakeholder engagement meetings were held to introduce the study and get buy-in at all levels. Interviews were held for key staff. A baseline data collection tool was designed.

Operational Research

Evaluating 10 years of TB control in South Africa: (PIs: A.C. Hesseling/Muhammad Osman). 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 2018 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.

Abstracts presented at the 49th Union World Conference on Lung Health in The Hague in October 2018

1. Trends in the South African tuberculosis epidemic with scale up of TB-HIV integration services (poster) (Muhammad Osman, Karen du Preez, Rory Dunbar, Alex Welte, Pren Naidoo, Anneke C. Hesselning). This poster highlighted HIV testing and ART coverage in SA have improved substantially over 10 years. The burden of TB amongst HIV-infected individuals is declining but remains substantially greater than among HIV uninfected. The overall declining trend in the TB epidemic appears less significant among the HIV-uninfected population.
2. Mortality amongst HIV-positive female tuberculosis patients in South Africa (short oral) (MM Claassens, C van Schalkwyk, R Dunbar, M Osman, P Naidoo, M Borgdorff). This short oral presentation focused on data between 2009 and 2013. It demonstrated a substantial decline of mortality in HIV-positive TB patients, while among HIV-negative TB patients, mortality was stable. Limitation regarding the time of ART initiation, CD4 count or ART adherence were recognized and updated analyses including data through to 2017 is in progress.
3. Ten years of routine paediatric TB surveillance data in South Africa - high disease burden and poor treatment outcomes (oral) (K Du Preez, M Osman, P Naidoo, S Dlamini, AC Hesselning). This oral presentation showed the significant number of children treated for TB and reported in ETR.net in South Africa. The proportion of children overall (11-13%), and proportion of these <5 years of age (62%) are consistent with that expected in high burden TB settings. Documentation of HIV testing has improved over time but the pre-treatment microbiological confirmation of TB disease remains low (9%). Ongoing analysis is exploring age, TB disease spectrum, HIV co-infection and treatment and reasons for poor treatment outcomes in children.

Operational Research Assistance Program: 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 3 independent study protocols for research to be undertaken. Five mentors from DTTC are supporting the trainees through protocol development, study implementation and publication of their findings.

All 3 projects have completed the mentored protocol development stage and were approved for implementation by the Stellenbosch University HREC.

1. Comparing early treatment outcomes in multidrug resistant (MDR) tuberculosis (TB) patients treated with conventional MDR-TB regimens is being implemented by Dr L Naidoo and Dr D Da Costa and supervised by M Osman and A Garcia-

Prats. Data collection and capture is complete and 177 records are in the process of data cleaning before analysis. Abstracts were presented at the South African TB Conference in Durban in June 2018 and the 49th Union World Conference on Lung Health in The Hague in October 2018.

2. Identifying risk factors associated with unfavourable treatment outcomes amongst patients treated for Isoniazid mono-resistant TB in Cape Town, South Africa is being implemented by Dr K Joseph and Dr F Solomon-Da Costa supervised by K du Preez. Data has been received on 370 patients and preliminary analysis is in progress. An abstract was presented at the 49th Union World Conference on Lung Health in The Hague in October 2018.
3. Motivations For, Anxieties And Preferences (MAP) About Transitioning To Community-Based Art Adherence Clubs (CAC) Among Patients Attending Facility-Based Art Adherence Clubs is being implemented by Dr R Mabezue and supervised by R Dunbar and M Osman. Data collection is in progress and over 200 participants have been consented and interviewed.

Operational Research focused on TB mortality

Former TB patients as a high-risk group for TB-associated morbidity and mortality in high-incidence communities in Cape Town – a pilot study (PIs: Florian Marx and Muhammad Osman). A high risk of TB, chronic lung disease and mortality have been reported among people with a history of previous TB treatment, but data from high-incidence settings remain limited. This study aims to locate adults who had successfully completed TB treatment in the past five years, and to characterize general morbidity and mortality. Routine electronic TB treatment register data was used to randomly select 256 adults (≥ 18 years) who successfully completed pulmonary TB treatment between 2013 and 2017. Household visits were conducted in a high-incidence community in suburban Cape Town to locate and survey former TB patients. Individuals who could produce sputum were bacteriologically investigated for TB. Household interviews and vital registration data were used to estimate mortality among patients who could not be traced.

We have interviewed 51 former TB patients and 52% (19/36) were living with HIV. Approximately half had self-reported symptoms indicative of chronic lung disease and of 28 participants who provided a sputum sample, one (3.6%) had culture-positive TB and another two reported currently being on re-treated for TB treatment, providing 3/51 prevalent cases of TB. Among 256 former TB patients, there were 15 (5.9%) confirmed deaths were confirmed (5.9%) with a median time of 1.43 (IQR: 0.48-2.16) years between the successful completion of the previous TB treatment episode, and death. The mortality rate among former TB patients was 2.7 deaths (95% CI: 2.5-3.0) per 100 person years with a standardized mortality ratio of 4.1 (95% CI: 3.6-4.7) compared to the general local population.

Our preliminary results are consistent with a high prevalence of respiratory disease including prevalent TB among former TB patients, and higher mortality.

The abstract: *Finding former tuberculosis patients - a high-risk group for tuberculosis-associated morbidity and mortality in Cape Town, South Africa: A pilot study*, was published as part of SA MRC 12th annual Early Career Scientist Conference and presented as a poster at the SACEMA Research days 2018.

This study was funded through a research grant (R64 000) provided by the Günther Labes Foundation and the Oskar Helene Heim Foundation (Berlin, Germany) to FMM and an Emerging Research Award (R35 000) provided by DST-NRF South Africa Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA), Stellenbosch University to MO.

Retrospective descriptive study of sudden and unexpected deaths related to TB in Cape Town: (PI: Muhammad Osman). Undiagnosed TB as a final or contributing cause of death is difficult to quantify but has been estimated through post mortem studies. In a low TB incidence setting (Ireland), only 15 cases of TB were diagnosed in a series of 4930 autopsies while in India, a high TB burden setting, 8.7% of autopsy cases were diagnosed with active tuberculosis and 60% of these were not diagnosed before death. The under ascertainment of both TB and TB mortality in a high burden TB/HIV setting warrants further evaluation. We aimed to estimate TB disease as a final or contributory cause of death among sudden unexpected death in adults and children in Cape Town. We have undertaken a collaborative project with SU Forensic Pathology Services (FPS) and have retrieved and captured data on 719 cases of sudden and unexpected death in 2016. 79 records are expected to be complete in Q1 2019. This study has been supported by Prof Anneke Hesselning through SA NRF SARChI funding.

Operational research focused on childhood TB

The aims of this research area are to firstly evaluate and identify gaps in the current health systems preventing and providing care to children with TB, and secondly to pilot and measure the impact of innovative solutions through rigorous implementation science methodology.

This research area is led by Dr Karen du Preez, and current projects focusses on optimizing pediatric TB surveillance strategies and strengthening prevention and routine data for children with TB, including HIV co-infected children.

Hospital focused surveillance strategies for childhood TB

The results of three studies related to hospital surveillance for childhood TB were published in 2018 – two focused on TB surveillance at tertiary hospital level, specifically children with TB meningitis (TBM) and spinal TB, and the other focused on TB surveillance at a district level hospital.

1. The impact of BCG shortages on the burden of childhood TBM (*Published in The Lancet Global Health, January 2019, see Appendix I*)

During 2017, we have observed a substantial increase in the number of children admitted for diagnosis or management of TBM or tuberculomas to the paediatric neurology ward at Tyberberg Hospital. Birth cohort analyses of admitted children <2 years of age with TBM/tuberculomas found nearly three times as many children born in 2015 compared to the mean number of children born in 2012 to 2014. We hypothesize that this increase is related to the global BCG shortages, which has impacted substantially on the number of BCG available during 2015 in the Western Cape Province.

2. The burden and trend of spinal TB in children (*Published Epidemiology and Infection, 2018, see Appendix I*)

This retrospective study, led by Dr Theresa Mann from the Division of Orthopedic Surgery, assessed the overall burden and trend in spinal TB at tertiary hospitals in the Western Cape Province during 2012-2015. A total of 74 children and 319 adults were identified. The study found a substantial burden of spinal TB cases with a high proportion of children presenting with severe disease and requiring corrective spinal surgery. Although spinal TB affects a relatively small proportion of TB cases, the burden on public health services remains substantial in high TB burden settings, and earlier diagnosis particularly for child cases are needed.

3. The burden, spectrum and outcomes of childhood TB disease at a district level hospital (*Published IJTLD, 2018. See Appendix I*)

This retrospective cohort study aimed to characterize the burden, spectrum and TB treatment outcomes of children managed at a district level hospital in Cape Town. Nearly 100 children were managed at the district level hospital over a 7 month period in 2014. The majority (85%) were very young (≤ 2 years), a third (34%) were malnourished and a fifth (19%) had HIV co-infection. Although 96% of children successfully continued care after hospital discharge, favorable TB treatment outcomes (cured/treatment completed) were only recorded for 78%. This study found a substantial burden of paediatric TB are managed at district hospital-level, with patients often being very young and frequently presenting with comorbid diseases. TB prevention opportunities and treatment outcomes could be further improved.

Routine TB treatment surveillance at national level:

Within the study, “**Evaluating 10 years of TB control in South Africa**”, multiple analyses have been completed and are planned to specifically look at the TB epidemic in

children in South Africa over time. One abstract was accepted for an oral presentation at the 49th Union World Conference on Lung Health in 2018: Ten years of routine paediatric TB surveillance data in South Africa - high disease burden and poor treatment outcomes (oral) (K Du Preez, M Osman, P Naidoo, S Dlamini, AC Hesselning). Main findings of the abstract have been detailed earlier in this section.

Research Focus Area Three: HIV Prevention Research

The DTTC has made great strides in the field of HIV prevention with two studies as part of the HIV Prevention Trials Network (HPTN) conducted during 2018. While the HPTN 071 (PopART) study concluded in 2018, the HPTN 084 (Life) was initiated early in the year.

HPTN 071 (PopART): (Lead: Nulda Beyers, Peter Bock). The HPTN 071 or PopART study is a cluster-randomized trial which aimed to determine the impact of two community-level combination prevention packages, both of which included universal HIV testing and intensified provision of HIV/ART care, on population-level HIV incidence. The study was conducted in 9 communities in South Africa and 12 in Zambia. Communities were randomized to arms A (full intervention prevention package plus ART regardless CD4 count), B (full intervention prevention package plus ART according to government guidelines) or C (standard of care). Following changes to ART guidelines during the study, Arm A and B both offered ART regardless of CD4 count from Oct 2016 onwards. Despite this change the study was still well powered to evaluate the primary outcome, HIV incidence. At each of the arm A and B sites, interventions were delivered to the entire community by a cadre of Community HIV-care providers (CHiPs) with referrals to government Primary Health Care (PHC) clinics. CHiPs provided clients with condoms, screen and refer relevant clients to government clinics for HIV, TB and STI treatment and voluntary male medical circumcision (VMMC). Primary outcomes were measured in a randomly selected individual level cohort of approximately 2000 individuals in each community (including the Arm C communities) over 36 months referred to as the population cohort (PC).

Field work for PopART began in January 2014 and finished in June 2018. For the CHiPs intervention, by the end of 2017 152,454 households had been visited in South Africa and Zambia and 168,556 individuals tested for HIV. At the end of PC follow up, in June 2018, more than 38 000 participants had completed the final round of the PC follow up PC36. The PopART data were revealed in Seattle in December 2018 where the team completed the primary analysis comparing HIV incidence across study arms. The primary results will be presented at CROI in March 2019. Dissemination of primary results to key stakeholders including study communities will be completed in March 2019.

HPTN 084 (Life) trial: (PI: Dr PA Bock) The HPTN 084: A Phase 3 Double Blind Safety and Efficacy Study evaluating Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women. The primary end point is HIV incidence. Participants will be followed up for 3 to 4 years. Overall the study aims to enroll 3,200 participants across the 20 sites (approximately 160 participants per site).

The Kuilsriver site office was newly established from January 2018. DAIDS site

assessment visit was completed in March 2018, the DAIDS laboratory assessment in April 2018 and the site was activated by DAIDS & HPTN by August 2018. The team enrolled their first participant in September 2018 and by end December 2018 had enrolled a total of 16 participants. The team also successfully completed a further audit in December 2018. The focus in the first two quarters of 2019 will be scale up community activities and recruitment.

Crosscutting Research (Supporting all three research focus areas)

Sociobehavioural Sciences

The Sociobehavioural science team have successfully implemented a broad range of data collection and analysis activities as components of the wider DTTC research portfolio and contributed to all three research focus areas. These activities ranged in scope from innovative ways to assess children's experiences of TB treatment palatability (Project Masterchef) to an exploratory analysis of the potential of technology for TB treatment adherence support (TB PAKS). Across activities, all data collection, management, processing and preparation for analysis is standardised and managed by a dedicated data quality team. In 2018, the team transcribed approximately 780 hours of recorded interview/discussion data and translated over 3000 pages of these transcripts from Xhosa or Afrikaans to English. Further, the team again proved to be highly innovative in designing and refining novel methods to answer research questions with greater sophistication. A priority for 2019/2020 is to support staff in post-graduate studies, and in doing so, building on the culture of academic learning and publication.

Sociobehavioural Science and Paediatric TB

SHINE: In-depth acceptability interviews and observations with caregivers and children about a novel, child-friendly formulation of a fixed-dose combination of first-line TB treatment to be used in the SHINE trial. The SHINE trial offers participants a fixed-dose combination child-friendly formulation of first-line TB treatment. This set of 20 days of semi-structured observations and discussions with 16 caregiver/child dyads informs the acceptability of this formulation for use and clarifies potential misunderstandings by participants about administration of the treatment on trial. A manuscript reporting findings has been developed with submission for publication anticipated in early 2019.

TB-CHAMP: In-depth acceptability interviews and observations with caregivers and children about novel formulation of levofloxacin to be used in the TB-CHAMP trial: The TB-CHAMP trial uses a novel, child-friendly formulation of levofloxacin. This set of 30 days of semi-structured observations and discussions with 17 caregiver/child dyads informs the acceptability of this formulation for use and clarifies potential misunderstandings by participants about administration of the treatment on trial. Data processing is ongoing, and a manuscript is in preparation for submission in 2019 as part of Dillon Wademan's PhD.

Impact of MDR-TB on children: Exploring caregivers' and health workers' perceptions on the effects of caregiver-child separation during long-term hospitalisation for MDR-TB in the Western Cape: A qualitative study. This qualitative project, conducted by Kyla Meyerson in completion of her MA in Psychology (SUN), addressed the third objective of MDR-PK II namely, to characterise the acceptability of DR-TB treatment. MDR-TB treatment requires extended hospitalisation which currently entails caregiver-child separation. Caregiver-child separation has been shown to cause behavioural and emotional problems in children. We explored caregivers' and health workers' perceptions of the effects of caregiver-child separation during long-term hospitalisation for MDR-TB treatment. We conducted 19 semi-structured, in-depth interviews with caregivers and health workers of children (aged zero to five years) who were receiving hospital-based treatment for MDR-TB. A thematic analysis was conducted to organise and interpret the data. Three major themes were identified: (i) MDR-TB treatment was a traumatic experience; (ii) Children's behavioural and emotional states during MDR-TB treatment included excessive crying, aggression, hyperactivity, and withdrawal; (iii) Caregivers' and health workers' behavioural and emotional management strategies included deception, threat, and prioritisation of biomedical health over psychological health. Children's, caregivers', and health workers' problems that emerged during MDR-TB treatment most likely result from a complex interplay between various factors; including precipitating factors of MDR-TB treatment and caregiver-child separation, and predisposing factors of poverty and exposure to violence.

MDR-PK - Masterchef: To understand children's and caregivers' experiences of acceptability (including palatability) of the key second-line tuberculosis drugs, within the MDR-PK II project. Over a four-week period, we conducted interviews with 16 paediatric participants (and where appropriate their caregivers). Our research consisted of a semi-structured interview schedule and various participatory research activities. In the latter, we asked children to rate various tastes, forms of medicine (for example, tablet, capsule, syrup, chewable pill and injection) and colours and forms of medicine packaging in an attempt to design the ideal MDR-TB medication. We wrote a report on the preliminary findings and disseminated these preliminary findings to DTTC health workers at Brooklyn Chest Hospital. Data has been processed to prepare for an in-depth analysis.

Lung health in Africa across the life course (LuLi): The purpose of this project is to describe the prevalence and clinical characteristics of post-tuberculosis lung disease among former tuberculosis patients in Cape Town, South Africa. The project utilised a multi-disciplinary approach, forming a collaboration between the Departments of Physiotherapy, Pulmonology and Paediatrics and Childhealth (DTTC). Our team at DTTC were involved in the recruitment and implementation of the project in one community in the Western Cape of South Africa. A total of 45 participants were recruited to the project. Participants underwent several physiological and lung function tests, as well as completing a few psycho-social surveys to provide a holistic overview of the participants' health. The project aims to define the burden of symptoms and functional deficits in non-healthcare seeking patients who have completed TB treatment in order to build a platform to address potential interventions for those affected.

TB PAKS: Paediatric Adherence, Knowledge and Support: The TB PAKS project aims to develop and refine an 'app' suitable for smartphones to be used by children (and their caregivers) who are on TB prophylaxis or treatment in order to improve their

experience by supporting learning about TB, provide adherence reminders/virtual rewards, and facilitate management of the social impact of TB such as disclosure. Preliminary work on the as-of-yet unfunded project began in 2018, with the Sociobehavioural team hosting two students whose work is helping inform development of the app.

Ava Archey, high-school student and daughter of HIV/TB researcher Kelly Dooley (honourary associate professor, Department of Paediatrics and Child Health), visited the DTTC for two weeks during her summer break to develop a prototype of a TB mobile application (app) for children following a literature review of TB disease and technology. She presented the prototype to stakeholders at the DTTC. Rachel Morse, an undergraduate student from King's College London, interned at the Centre for two months as part of a larger collaboration between Stellenbosch's Faculty of Medicine and Health Sciences and their Department of Global Health and Social Medicine. In her dissertation, which drew on qualitative data and observations collected across various TB projects at the Centre, she explored factors that influence children's adherence to TB treatment and considered ways in which a mobile 'app' could be used to address them. Both these outputs are providing an important foundation for the project.

Sociobehavioural Science and Operational Research

TB-TREATS: Tuberculosis Reduction through expanded antiretroviral therapy and TB screening: The overall aim of this project is to measure the impact of a combined TB/HIV intervention of population level screening for TB, combined with universal testing and treatment (UTT) for HIV on TB incidence, prevalence and incidence of TB infection. The study is a collaboration between Zambart in Zambia, Health Systems Trust in South Africa, the London School of Hygiene and Tropical Medicine, Imperial College and the University of Sheffield in the UK and KNCV in the Netherlands. Given that the TREATS study is being conducted in the same communities as the HPTN 071 (PopART) in South Africa and Zambia, the Sociobehavioural Sciences Team at the Desmond Tutu TB Centre was contracted by the Health Systems Trust to conduct nested qualitative research as part of the formative work towards the TB-TREATS study. The first part of this research was conducted between October and December 2018. We conducted four in-depth interviews with key TB staff to describe their experience with TB service delivery and the role of other stakeholders (n=1 in each arm A and C site). Further research with TB patients is underway and will contribute to a broader understanding of the impact of TB in people's lives in South Africa.

Sociobehavioural Science and HIV Prevention Research

HPTN 071a (Stigma Ancillary Study) - Health Worker Open Cohort Survey: The Stigma Ancillary Study was a sub-study to the PopART (HPTN071) trial. The stigma study is a mixed method study that nests enquiry about HIV stigma across the PopART study. In particular, it the study examines how health care worker knowledge, attitudes, and experiences of delivering HIV care are influenced by, and influence, the delivery and uptake of the PopART intervention. The quantitative component of the study involved a self-administered questionnaire offered to all health care workers (including CHiPs) working in PopART study communities. Data collection was done in the three waves in 2014, 2015 and 2017. By June 2017, data collection had been completed in South Africa with 797 health workers enumerated. In 2018, the stigma activities included cleaning data from all three rounds and preliminary analysis conducted for health facility

dissemination activities. Several manuscripts are in preparation.

HPTN 071 PopART for Young People (P-ART-Y) Study: Uptake and acceptability of a combination HIV prevention package among young people in Zambia and South Africa. The P-ART-Y study concluded in March, 2018. The primary outcome of the study was the uptake of voluntary HIV counselling and testing, within the previous 12 months at the time of survey administration, amongst adolescents aged 15-19 years. This served as a comparator for the primary outcome of the study (knowledge of HIV status). Other outcomes included acceptance of HIV testing and retesting. Linkage to care, antiretroviral therapy (ART) adherence and retention in care, uptake of prevention of mother and child transmission (PMTCT), voluntary medical male circumcision (VMMC) and condoms. Qualitatively, we looked at the acceptability of the PopART interventions and barriers to access in adolescents. We also looked at the experiences of adolescents living with HIV. The particular needs and vulnerabilities of adolescent girls, including those living with HIV, were also studied. Data collection was completed on 4 November 2017. Data cleaning was completed in 2017 and analysis is ongoing with three manuscripts in development for submission in 2018.

P-ART-Y Dissemination: The study team is worked alongside the Adolescent Advisory Board (ACAB) and Community Engagement Team on the planning of dissemination events. These took place in the Arm C site of the HPTN 071 (PopART) trial and were conducted on the 9, 16 and 23rd March and the 13th of April 2018. Preliminary findings of the cross-sectional survey were shared with young people some of whom participated in the study. These findings included survey uptake frequencies by age and gender and some of the secondary objectives. The primary outcome findings will be disseminated in 2019 together with results from the main trial, the HPTN 071 (PopART) trial. The dissemination events were well received by young people and this forum served as a platform for further discussion on the findings.

Mixed-data in-depth interviews with staff/stakeholders and operational review of clinic-based components of the HPTN 071 (PopART) intervention package: The PopART intervention package included a large number of health system innovations and implementation lessons from the health-facility delivery of universal testing and treatment. Specific focus areas were (a) preparation for transition to treatment regardless of CD4-count, (b) health-facility based HIV testing services, (c) explaining ART regardless of CD4-count to clients, and (d) implementing adherence support structures. Between February and April, 26 in- depth interviews with key informants were collected.

Mixed data observational and discussions with field staff of the community-based components of the HPTN 071 (PopART) intervention package – annual round 5: A set of structured observations and discussions with implementers conducted annually in 9 study communities between January and March. The final round of data were collected without issue in 2018.

HPTN 071 (PopART) Research Collective (PRC): PRC is a collaborative project lead by Dr P Bock, composed of DTTC PopART staff and PopART implementing partners (City of Cape Town, Western Cape DoH, ANOVA Health Institute, Kheth' Impilo and Cape Winelands DoH). This consortium is aimed at formulating lessons learned of implementing the HPTN 071 study at health facilities, over trial period. The PRC consists of five groups each with an aim of developing a manuscripts related to the implementation of the PopART intervention. Data collection was completed in November 2017. A total of 51 interviews were conducted with health services staff at a provincial, district, regional and clinic level. Manuscripts are under development.

Sociobehavioural Science Students Graduated

1. Rene Raad – MA in Anthropology at SUN
2. Hermine Kruger – Honours in Psychology at SUN
3. Arlene Marthinus – Honours in Psychology at UWC
4. Msondezi Ketelo – BA in Anthropology at UWC

Epidemiological Modelling

Modelling of tuberculosis and the impact of TB control interventions constitutes an additional core competency to be built at DTTC in the forthcoming years. In 2018, a DTTC Working Group Data Analysis and Modelling (WGDAM) was established to build and strengthen capacity for in-house modelling (see below). A strategic TB modeling partnership and research programme between DTTC and the South African Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) was prepared in 2018 and is set to take off in 2019. This novel initiative is intended to provide a platform for mathematical modelling and intervention research to inform decision making for TB control at national level in South Africa as well as internationally.

Working Group: Data Analysis & Modeling (WGDAM)

A DTTC Working Group Data Analysis and Modelling (WGDAM) was established to build and strengthen capacity in mathematical modeling of TB and related control interventions. The working group is led by Dr Florian Marx and holds weekly meetings at DTTC. It currently consists of 10 members with backgrounds in medicine, epidemiology/public health, data management and statistics. In 2018, WGDAM initiated a joint research project which aims to project the population-level impact of ART scale up on TB in incidence and mortality in the nine South African Provinces. Prior to this project, the group reviewed data from the National Antenatal Sentinel HIV Prevalence Survey and the District Health Barometer to compare rates of TB and HIV in the 52 South African health districts. This study highlighted poor association between HIV prevalence estimates and rates of reported TB at subnational level, which has important implications for TB control in South Africa. Efforts are needed to better understand the

determinants of local variation in TB and HIV rates in South Africa. Other modelling projects involving WGDAM members in 2018 include studies estimating the impact of TB household contact investigation and preventive therapy, of rolling out novel rapid diagnostic tests in South Africa, and of targeting TB case finding and prevention to previously treated people. The following manuscripts have been published:

1. Sloat R, Maarman GJ, Osman M, Marx FM. Variation in HIV prevalence and the population-level effects of antiretroviral treatment for reducing tuberculosis incidence in South Africa. (Correspondence), on behalf of the Desmond Tutu TB Centre Working Group Data Analysis and Modelling (DTTC-WGDAM). South African Medical Journal 2018; 108(8): 606.
2. Dunbar R, Naidoo P, Beyers N, Langley I. Improving rifampicin-resistant tuberculosis diagnosis using Xpert((R)) MTB/RIF: modelling interventions and costs. Int J Tuberc Lung Dis 2018; 22(8): 890-8.
3. Marx FM, Yaesoubi R, Menzies NA, Salomon JA, Bilinski A, Cohen T. Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: a modelling study. The Lancet Global Health 2018; 6(4): e426-e35.

The potential impact of household contact management on childhood tuberculosis: a mathematical modelling study (*Published Lancet Global Health*):

This study evaluated the impact of carrying out household contact management strategies on the global burden of childhood TB disease and childhood TB mortality. By modelling the current situation for children following household exposure to infectious TB and assuming no household interventions, and then comparing it with two scenarios in which exposed children were screened for disease and then treated for TB infection, the impact of these interventions could be evaluated. Full implementation of household activities could result in a reduction of 160,000 cases of childhood TB and prevent 108,000 child deaths.

1. Dodd PJ, Yuen CM, Becerra MC, Revill P, Jenkins HE, Seddon JA. Potential effect of household contact management on childhood tuberculosis: a mathematical modelling study. The Lancet Global Health 2018; 6(12): e1329-e38.

DTTC Grant Awarded: 2018

Description	Funder	PI
LINKEDiN study (Reducing loss to follow up among TB Patients)	Gates Foundation	Anneke C. Hesselning/ Muhamad Osman
Consultancy for a systematic review of TB mortality in South Africa	TB THINK TANK	Tamaryn Nicholson & Muhammad Osman
Consultancy paediatric MDR-TB National Guidelines	TB THINK TANK	Jennifer Hughes
Protocol Vice Chair Funding	NIH IMPAACT network	Jennifer Hughes
Consultancy for a review of TB preventative therapy implementation in South Africa	TB THINK TANK	Graeme Hoddinott
HPTN 084 site	NIH (HPTN)	Peter Bock
2 nd year extension of postdoctoral fellowship	Ramon Areces Postdoctoral Fellowship	Elisa Lopez
Travel fellowship Prof. Reza Yaesoubi at the Yale School of Public Health, USA	Stellenbosch University Scientific travel grant	Florian Marx
Impact of viral co-infections on lung health in children with TB	SA MRC	Marieke van der Zalm
Travel to the 22 nd International AIDS conference, Amsterdam in July 2018	Stellenbosch University Scientific travel grant	Sue-Ann Meehan & Lario Viljoen
BEAT Paediatric MDR-TB	UNITAID	Tony Garcia-Prats
IMPAACT 2020	IMPAACT NIH	Tony Garcia-Prats
SA MRC SHIP	MRC grant for collateral funding for TB Champ	Anneke Hesselning, James Seddon
Graduate Internship Programme	NRF	Graeme Hoddinott & Anneke Hesselning
Graduate Internship Programme	NRF	Graeme Hoddinott & Anneke Hesselning
Familial management of paediatric co-morbid HIV, TB, and diabetes	Harry Crossley (PhD scholarship)	Dillon Wademan

Travel to the 49th Union World Conference on Lung Health, Amsterdam in October 2018	Stellenbosch University Scientific travel grant	Muhammad Osman
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Awards and Other Recognition

1. Professor Simon Schaaf received his 2nd A-rated NRF award in Port Elizabeth. September 2018.
2. Dr. Sue Purchase received the Discovery Award at the Durban TB Conference for overall “The Best Research Paper”. July 2018
3. Dr. Mareli Claassens was appointed as a Research Fellow for DTTC.
4. Dr. Angela Dramowski was promoted to Associate Professor.
5. Professor Nulda Beyers received the Research Development Award. Prof Beyers mentored four successful PhD Graduates
6. Dr. Jana Winckler secured joint 3rd Place in the Young Scientist Award for podium presentation in the category basic and clinical pharmacology which included lab scientist and clinicians. 08 October 2018.

DTTC Academic meetings

The TB Clinical Forum 2018, hosted by DTTC at the Stellenbosch University FMHS and organized by the City of Cape Town officials was held monthly between February and November 2018 with the objective of creating an interactive platform for academic researchers and government official in health services. Experts from the FMHS and City presented a broad range of relevant scientific research topics. An average of 50 participants attended these lively CPD- accredited interactional meetings on Friday afternoons, facilitating dialogue between service providers for TB and HIV care, and researchers at DTTC and the medical faculty. Four speakers from DTTC presented during 2018.

TB Clinical Forum 2018

DATE	PRESENTER	TOPIC
9 Feb. 2018	Dr. Lenny Naidoo (CCT) Dr. Jennifer Hughes (DTTC)	Highlights from the 48 th Union World Conference on Lung Health, Guadalajara, Mexico
9 Mar. 2018	Prof Marc Nichol – (NHLS/UCT)	Interpreting Ultra- A clinician's guide Rapid diagnostic test & improved diagnosis
13 Apr. 2018	Prof. Helen Cox (UCT)	What do we need to do to eliminate drug-resistant TB???
11 May 2018	Prof. Gary Maartens(UCT)	Update on drug interactions between ARVs and TB drugs
8 Jun. 2018	Prof. A. Diacon (TASK) Dr. Anja Reuter (MSF)	Update on Adult MDR-TB treatment Trials
13 Jul. 2018	ChloëShain (UCT)	The Social Markers of TB
24 Aug. 2018	Prof. Graeme Meintjies(UCT)	TB Lymphadenitis: Clinical management
21 Sept. 2018	Dr. Tony Garcia-Pratts (DTTC) Dr V. Mudalay (MSF) Dr A. Reuter (MSF) Dr J. Te Riele(BCH/WCG)	Ethics/Debate: "Do we really need the injectable for managing DRTB?"
12 Oct.2018	Prof. Anneke Hesselning Dr. Tony Garcia-Pratts (DTTC)	DTTC-Update on Paediatric TB treatment Trials
9 Nov.2018	Dr Natalie Beylis (NHLS)	TB diagnostics, discordant results, Heteroresistance and mixed infections (Natalie)

DTTC Academic Meetings 2018

The DTTC Academic Meetings 2018, held fortnightly at the FMHS targeted academic researchers to engage in ground-breaking research initiatives. Speakers from local and abroad were invited to present their area of research in a broad range of relevant topics.

Date	Presenter	Topic
1 Feb. 2018	Cornè Bosch	Molecular diagnosis of M.TB from paediatric stool samples – practice run for masters oral
8 Feb. 2018	Dr. Theresa Mann	Burden and trends of spinal tuberculosis in the Western Cape
22 Feb. 2018	Dr. Lena Ronge	Open or closed Tuberculosis. “Are infants able to spread TB?” - Findings from the European Childhood tuberculosis Archive
1 Mar. 2018	Prof. Helena Rabie	Paediatric HIV current challenges, future opportunities
22 Mar. 2018	Dr. Muhammad Osman	Paediatric XDR-TB Treatment outcomes – A systematic review and individual patient data meta-analysis.
05 Apr. 2018	Dr. Florian Marx	Former TB patients in the context of TB and HIV epidemics - need for tailored health interventions?
19 Apr. 2018	Dr. Sue-Ann Meehan	The contribution of a community based HIV counseling and testing (HCT) initiative in working towards increasing access to HIV counseling and testing in Cape Town
03 May 2018	Dr. James Seddon	The impact of household contact management on childhood tuberculosis: a mathematical modelling study
24 May 2018	Dillon Wademan & Hanlie Myburgh	Chronic conditions and care: Intergenerational experiences of living with HIV, TB and Diabetes in South Africa (Dillon) ----- Relationships, responsibility and the state: Understanding uptake of antiretroviral treatment in South Africa (Hanlie)
31 May 2018	Dr. Kyla Comins-TASK	Update on MDR – TB treatment trials in adults
28 Jun. 2018	Dr. Florian Marx	Projecting the population-levels effects of tuberculosis control in South Africa – update from the DTTC – WGDAM -Working group Data Analysis and Modeling
05 Jul. 2018	Dillon Wademan Lario Viljoen Laing de Villiers ----- Prof Kelly Dooley	How health workers motivated People living with HIV (PLHIV) to initiate antiretroviral treatment (ART) at high CD4 counts within the HPTN 071 (PopART) trial (Dillon) ----- Public condition/private affliction: Negotiating comorbidity, confidentiality, and

		<p>care in South Africa, a narrative from the HPTN 071 (PopART) study (Lario)</p> <p>-----</p> <p>Stigma, secrecy, social support and HIV service access among transgender and gender-fluid people in South Africa, the HPTN 071 (PopART) study (Laing)</p> <p>-----</p> <p>Update on adult trials of TB/HIV (Kelly)</p>
12 July	Dr. Celeste De Vaal	Raising ethical issues in the dead: An exploration of ethical challenges in Forensic Medicine
02 Aug. 2018	Graeme Hoddinott and Constance Mubekapi-Musadaidzwa	HIV services for young people aged 10-24; priorities, gaps, and opportunities from the PopART for young people (P-ART-Y) study
16 August	Dr Tony Garcia-Prats	<p>1) Results of the Bedaquiline CRUSH study</p> <p>2) Emerging data on linezolid PK and safety in children with MDR-TB- feedback- Adult formulation tested ,tablets dissolve in water.</p>
23 Aug. 2018	Prof Andrew Whitelaw	S.areus epidemiology resistance virulence and diagnosis
20 Sept. 2018	Sociobehavioural science team presenters: Kyla Meyerson, Leletu Busakwe, and Stephanie Jacobs.	<p>1)Acceptability of MDR-TB treatment for children, findings from the MDR PK2 Masterchef.</p> <p>2)Video presentation of early thoughts on a knowledge, adherence, and social support app for children with TB.</p>
04 Oct. 2018	Dr. Amy Slogrove	Evaluating long term child health outcomes following pregnancy exposures in South Africa - using HIV and antiretroviral drugs as a starting point”
18 Oct. 2018	Dr. Elisa Lopez	Pharmacokinetics of antituberculosis drugs at the site of disease in children with complicated intrathoracic tuberculosis
08 Nov. 2018	Dr Marije van Schalkwyk	CTU Academic Meeting: Drug PK in pregnancy, what we know we don't know
29 Nov.2018	Dr. Sue Purchase	Looking through a different lens: TB in Literature and the Arts

Advocacy and Community Engagement

World TB Day is an annual joint initiative between the Stop TB Partnership and the WHO Global TB Programme to raise public awareness about the devastating impact of TB. On Friday 23rd March, DTTC organized a World TB Day lunch time event at the FMHS campus in collaboration with TB Proof and TB Alliance. The program included two interactive presentations: *TB prevention in children in the era of TB elimination* (Prof Anneke Hesselring) and *TB prevention in healthcare workers: Caring for the Carers* (Dr Angela Dramowski). The event concluded with a live interview with an adolescent MDR-TB research participant and her mother, explaining the MDR-TB treatment journey from a family perspective. Academic posters were displayed in the hallway for the duration of the day. DTTC staff and CAB members handed out TB information leaflets to FMHS staff and students during the morning to raise general awareness of TB on campus.



Figure 1 DTTC Staff at World TB day, 2018



The DTTC Community Advisory Board (DTTC CAB)

The establishment of a DTTC-CAB with a TB focus was initiated in June 2015 and was officially launched in November 2015, when the first general meeting was held at the Brooklyn Chest Hospital site. Since then, monthly General Meetings are conducted throughout the year. From 2016, the seven Steering Committee members held additional monthly meetings. DTTC CAB activities for January to December 2018 included:

Meetings: The DTTC CAB participated in General meetings; Steering Committee (SC) meetings for the executive body and SUN-CTU CAB Leadership Group (SCCLG) Meetings (i.e with DTTC, FAMCRU and TASK) and a representative participated in every IMPAACT ICAB bi-monthly teleconference call and HPTN CWG monthly teleconference calls including the HPTN 084 study monthly conference calls.

CAB Annual Recruitment and Retention Drive: 14 April 2018 the DTTC CAB hosted an "Open Day" and 22 prospective CAB members attended. Interviews were conducted during May and July. Subsequently, 4 adults and 10 youth were recruited into the DTTC CAB.

HPTN 084 Protocol Review and Study Updates: In February the CAB reviewed the protocol; and educational and marketing materials for the HPTN 084 study. The CLO met with the 084 Monitor to discuss CAB operations. The CAB and CLO met with 084 study staff to provide input; and were involved in activities relating to the call to pause the study for activation and enrolments and the activation.

IMPAACT & HPTN Protocol Review and Study Updates: On 09 June the Study Coordinator presented updates on P1101 and P1026. 14 June the CLO presented a CAB overview to the HPTN 084 team at the Kuilsriver site office.

Network Training: 04–05 February the CAB attended a training workshop hosted by FHI, “Understanding the Clinical Research Process”. Network webinar training workshop invitations for various topics were disseminated and attended where possible.

CAB Youth Development: To raise the voice of our youth 2 youth members were elected to serve on the DTTC CAB Steering Committee during the 25 August Meeting. The youth group have written, produced and directed a 15 minute skit on HIV and TB incorporating a poem authored by one of the members and a song to illustrate the life of young people affected and infected with HIV and TB in the South African context. The production was presented at the 12th International Child TB Training Course. A 14 year-old youth member of the CAB who survived MDR-TB and her mom also shared their experiences with living with MDR-TB at the 12th International Child TB Training course and interacted with course participants thereafter.

International Network Meetings: 14 – 18 May the CAB Chairperson attended the HPTN Annual Meeting in Washington. No funds were available for community representation at the IMPAACT Annual Meeting in June 2018. A video production, “Two Countries; Two Choices” on TB by *Aids-Free World*, which featured 2 of DTTC adolescent research participants, one a CAB member, was screened at the International Aids Conference in Amsterdam, 23 – 27 July 2019.

The Annual Capacity Building Event & Award Ceremony: The CTU CABs (i.e. DTTC, FAMCRU and TASK) held their Annual Capacity Building Retreat on 18 -19 October 2018 at the Tygerberg Campus. This event culminated in the CAB Gala Dinner & Award Ceremony on Saturday, 20 October 2018 at the Bellville Civic Centre. This year we established an award with a floating trophy in honour of, and called the Katleho Mosimanegape Community Achievement Award, which recognizes outstanding leadership, commitment and dedication within the community forum. This year it was awarded posthumously to Katleho Mosimanegape, himself a TB and HIV survivor, who died in an accident on 27 June 2018. The Award will be held in DTTC for 12 months. Representatives of his family received the award at the Gala Dinner on 20 October 2019 at the Bellville Civic Centre.

Annual Dissemination Meeting: On 23 November 2018, the CAB members attended the Annual DTTC Dissemination Meeting, held at the Lord Charles Hotel Somerset West.

DAIDS Programme Officer Site Visit: On 04 September 2018, Eileen Pouliot, the DAIDS Programme Officer met with the community members during a joint CTU CAB Overview presentation at Tygerberg, J8 seminar room.

World TB Day: 23 March 2018, the CAB members participated in the World TB Day programme hosted by DTTC at the Tygerberg campus.

Special extramural events: On 9 October 2018 12 members of the CAB attended the 8th International Desmond Tutu Peace Lecture at the Artscape where guest speaker, Cyril Ramaphosa, addressed the audience. On 20 October 2018 the CLO presented a CAB Overview to to US Health Attaché, Steven Smith at the Kuilsriver site office.

The DTTC CAB Budget: In March the CAB SC reviewed the 2018 CAB Budget which was accepted in principle by the DTTC EXCO in April.

The 2019 IMPAACT Budget: The CLOs of DTTC, FAMCRU and TASK met in November 2018 to finalise the 2019 IMPAACT Budget. The final proposal for the R178 000.00 allocation was submitted to the CTU Unit Manager and SU Grants Office on 7 December 2018.

Funding Opportunity - Public engagement Fund: The CAB CLO and two DTTC executive officers met to discuss the funding opportunity with the Wellcome Trust regarding a possible funding opportunity through creative approaches in engaging the public with health research.

Condolences: 27 June 2018, Executive member and Acting-Secretary, Katleho Mosimanegape, passed away in an accident. A vigil was held in the DTTC seminar room on 28 June 2018 and CAB members and DTTC staff visited the family home that evening. CTU CAB members attended the Memorial Service on 3 July 2018. The DTTC CAB and staff participated in a collection of cash and kind for the bereaved family as part of the 18 July 2018 Madiba Day activities.

The HPTN 071 (PopART) CAB

In the HPTN 071 (PopART) trial, each participating clinic had a health Committee that links it with its community. The PopART CAB was established in 2013 with representatives from the 9 sites in which PopART is being conducted. These representatives (2 from each site) were chosen from health committee members and they work as volunteers in making sure that health related issues within their communities and the clinics are addressed properly. The CAB is the link between the communities and the PopART researchers and has a constitution with rules and guidelines as to how to conduct their meetings. The PopART CAB meets once a month where various study related issues are discussed.

The CAB helps the researchers in making sure that community related issues are addressed and that misunderstandings between the community and the researchers are dealt with in a professional way. The CAB takes initiative in setting up these meetings. The CAB also helps in reviewing community related study material like informed consent documents and study questionnaires. In return, DTTC offers trainings for these

members to develop them. The PopART CAB members have received training in the following areas:

- GCP training
- Basic HIV knowledge
- Minute and record keeping
- Basic Counselling
- Cancer screening tips

The PopART CAB, Community Engagement team and the Intervention Managers had a Workshop at the Lord Charles Hotel in preparation for the six events of Disseminating Intervention results planned for June /July 2018. The CAB and the teams worked together to find appropriate ways to communicate study results communities and making sure that closed venues are secured for the six dissemination events. The mobilisers are working closely with the CAB members in making sure that all stakeholders are aware of and invited to these events.

- The CAB members have been taking the lead in the establishment of community committees in preparation for disseminations (Intervention and the upcoming Primary Outcomes Dissemination Meeting).
- All the Nine Primary Outcomes Dissemination meetings will be held in March 2019.
- The role of CAB is to use community platforms to invite the relevant stakeholders
- The CAB meetings are held bi-monthly to review progress about these preparations.
- The last CAB for the year was on the 5th of November 2018 where site reports from all community committees were laid down to ensure the readiness of all sites for the Dissemination meeting.

HPTN 071 (PopART) Community Engagement (CE)

The HPTN 071 (PopART) community engagement team were involved in several activities for the final year of the trial. These include the following:

In 2018, the Intervention District Logistic Managers (DLOs) and the Data Coordinators together with the Community Advisory Board members (CABs) for each site formed community working groups in preparation for the Intervention Dissemination meetings for the six communities involved.

- Out of the six, four dissemination meetings were held in June and the remaining

two in July, 2018.

- At the end of the Population Cohort (PC) Research Assistant's contracts in June 2018, the DLOs and the CAB helped by members of the CE team started preparing for the Primary Outcomes Community Dissemination meetings to be held in March, 2019.
- Community Committees comprising of 2 CAB members, 1 CE member and 1 PC member were established to work on all site logistics for each site.
- The logistics included securing of venues, identifying community stakeholders to be invited and determining the most appropriate means to invite community members in the relevant sites
- The CE team was also consulting with the events office within the City of Cape Town to ensure that all events followed guidelines.

The HPTN 071 (PopART) P-ART-Y Adolescent Community Advisory Board (ACAB)

The Adolescent CAB advised researchers on how best to implement the P-ART-Y evaluation survey and supported the community-level delivery of optimisations of the PopART intervention package for young people. In 2018 the P-ART-Y CAB members were involved in the general and focused meetings in which study processes and CAB issues were discussed.

The PARTY study team and five ACAB members (Luthando Ngwatyu, Nandipha Anta, Jafta Siyavuaya Nonkondlo, Katleho Mosimanengape and Mhlali Ngqawule) attend the Annual DTTC Dissemination Meeting held at Stellenbosch University on the 8 December 2017. This meeting brought together various stakeholders from the Western Cape Department of Health, City of Cape Town, and DTTC Paediatrics and Community Advisory boards. The meeting was themed "With Communities, for Communities", with aim of discussing studies currently underway at the centre and sharing lessons learnt. The ACAB had its first meeting on the 3rd of February 2018, and the meeting commenced with young people giving feedback on the DTTC annual dissemination meeting. The ACAB members then reviewed the dissemination plan and suggested ways of reaching young people. ACAB closeout was discussed and it was recommended that members apply to be part of the DTTC CAB. Since then, 7 P-ART-Y ACAB members have been welcomed into the DTTC CAB and continue to engage in CAB meetings.

Conferences

During 2018, personnel from the DTTC participated in several local and international conferences, including the Union conference in The Hague, the International AIDS conference in Amsterdam, the South African TB conference in Durban, the Stellenbosch University research day and several other academic platforms.

PEPFAR Conference. Pretoria, South Africa. 16 January 2018.

- HPTN 071 (PopART) staff presented study findings and lessons learnt

SACEMA seminar. Stellenbosch, South Africa. 9 March 2018

- Sue-Ann Meehan. Community based HIV testing services: using a case study from Cape Town to provide evidence-based lessons learnt for program implementation.

Annual TB Seminar at the Human Sciences Research Council. Cape Town, South Africa. 28 March 2018

- Boffa J. Is prevention better than cure? Perceptions of isoniazid preventive therapy in KwaZulu-Natal.

Paediatric TB Pre-conference Symposium and Round Table Discussion at the 5th South African TB conference. Durban. 12 June 2018

Convened and chaired by the DTTC: Tuberculosis in children: old problems and new solutions

- James Seddon. The evolving epidemiology of TB in children
- Karen du Preez. Children with TB in South Africa: where are they, who are they, and where do we find more of them.
- Marieke van der Zalm. Paediatric TB within the broader lung health context
- Anneke Hesseling. Therapeutic strategies for drug-susceptible and drug-resistant TB in children

5th South African TB Conference. Durban, South Africa. 12 - 15 June 2018

- Sue Purchase. Acceptability and palatability of a novel paediatric dispersible levofloxacin formulation in children

Oral Presentations:

- Karen du Preez, Simon Schaaf, Rory Dunbar, Elisabetta Walters, Alvera Swartz, Regan Solomons, Anneke Hesseling. Complementary hospital-based surveillance strategies to better characterise the epidemiology of tuberculosis in children.

- Boffa J, Mayan M, Mhlaba T, Ndlovu S, Williamson T, Fisher D. Why agency is important when implementing IPT: Lessons from oMakoti in KwaZulu-Natal, South Africa.
- Boffa J, Mayan M, Ndlovu S, Fisher D, Staples S, Sauve R, Williamson T. Is prevention better than cure? Perceptions of isoniazid preventive therapy in KwaZulu-Natal, South Africa.
- Boffa J, Fisher D, Sauve R, Mayan M, Williamson T. The effectiveness of untargeted 6-month IPT to reduce tuberculosis incidence among people living with HIV with and without antiretroviral therapy in KwaZulu-Natal, South Africa.

Poster presentation

- Boffa J, Mayan M, MacDonald H, Cele N, Dhladhla C, Ndlovu S. Creating culturally-appropriate dissemination products in tuberculosis research.

AIDS 2018 Pre-conference and 4th International Conference on the Social Sciences and Humanities in HIV (ASSHH). Amsterdam, Netherlands. 20 – 23 July 2018.

Oral presentations

- L. Viljoen, L. Reynolds, H. Myburgh, G. Hoddinott, V. Bond, on behalf of the HPTN 071 (PopART) team. Public condition/private affliction: negotiating co-morbidity, confidentiality, and care in South Africa, a case-study from the HPTN 071 (PopART) study .
- N. Peton, C. Mubekapi-Musadaidzwa, D. Wademan, P. Hendricks, G. Carolus, R. Mbaezue, J. Kruger, K. Jennings, C. Gunst, N. Grobbelaar, F. Louis, P. Bock, G. Hoddinott. How health workers motivated People living with HIV (PLHIV) to initiate antiretroviral treatment (ART) at high CD4 counts, the HPTN 071 (PopART) study.
- L de Villiers. L. Reynolds, A. Thomas, L. Busakwe, J. Hargreaves, A. Stangl, V. Bond, P. Bock, G. Hoddinott, on behalf of the HPTN 071 (PopART) study team. Stigma, secrecy, social support and HIV service access among transgender and gender-uid people in South Africa, the HPTN 071 (PopART) study.
- V. Bond, M. Mwamba, N. Vanqa, M. Steinhaus, D. Ziba, D. Milimo, L. Viljoen, T. Mainga, T. Nicholson, H. Ayles, S. Fidler, R. Hayes, P. Bock, J. Hargreaves, G. Hoddinott, J. Seeley and A. Stangl on behalf of the HPTN 071 (PopART) study team. “Self-stigma is the worst kind of stigma”: Internalised stigma and navigating HIV care amongst health workers living with HIV in Zambia and South Africa, the HPTN 071 (PopART) stigma ancillary study.

Oral presentations

- G. Hoddinott on behalf of the HPTN 071 (PopART) study team. Acceptability of a HIV prevention package among young people: HPTN 071 (PopART) for Youth Study.

Poster presentations

- S.-A. Meehan, D. Wademan, G. Hoddinott, R. Holtman, N. Grobbelaar, J. Kruger, M. Leonard, B. Yang, V. Naidoo, P. Bock, C. Gunst. Implementing community-based adherence clubs for stable HIV-infected patients in South Africa. Lessons learned from patient and health worker experiences.
- S.-A. Meehan, D. Wademan, G. Hoddinott, R. Holtman, N. Grobbelaar, J. Kruger, L. Maschilla, B. Yang, V. Naidoo, P. Bock, C. Gunst. Evaluating the impact of community-based adherence clubs on the clinical outcomes amongst ART patients in the Cape Winelands district of Western Cape Province of South Africa.
- S. Fidler, S. Floyd, B. Yang, M. Phiri, D. McLeod, A. Schaap, R. Sloot, K. Shanaube, S. Griffith, P. Bock, N. Beyers, H. Ayles, R. Hayes, on behalf of the HPTN071(PopART) Study Team. Dramatic reductions in time to ART initiation among HIV+ individuals referred to HIV care following home-based testing services: Experiences from the HPTN071(PopART) trial between 2014 and 2017.
- K. Shanaube, D. Macleod, J. Mwate Chaila, G. Hoddinott, A. Schaap, S. Floyd, C. Mackworth-Young, P. Bock, R. Hayes, S. Fidler, H. Ayles, HPTN071 (PopART) Study Team. HIV care cascade among adolescents in a 'test and treat' community based intervention in Zambia and South Africa: HPTN071 (PopART) for Youth study.
- R. Thomas, S. Kanema, L. Mwenge, S. Floyd, P. Bock, H. Ayles, N. Beyers, S. Fidler, R. Hayes, K. Hauck, HPTN 071(PopART) Study Team. Costs of two rounds of home-based HIV testing and counselling in Zambia: Evidence from the HPTN 071(PopART) study.
- R. Thomas, R. Friebel, K. Barker, L. Mwenge, S. Kanema, N. Vanqa, A. Harper, N. Bell-Mandla, P. Smith, S. Floyd, P. Bock, H. Ayles, N. Beyers, S. Fidler, R. Hayes, K. Hauck, HPTN 071(PopART) Study Team. Work and home productivity of HIV-positive and HIV-negative individuals in Zambia and South Africa: A cross-sectional baseline survey of the HPTN071/PopART trial.
- M. Simwinga, J. Mwate, T. Ng'ombe, S. Belemu, N. Makola, C. Mubekapi-Musadaidzwa, G. Hoddinott, R. White, K. Shanaube, V. Bond, T. Mainga. Adolescent and young people's participation and representation in clinical trials: Lessons from a community-wide HIV testing and treatment study, the HPTN 071

(PopART) study. (poster discussion).

- M. Mbewe, C. Mackworth-Young, D. Ziba, R. Ndubani¹, B. Chiti, M. Simuyaba, M. Gondwe, K. Shanaube, G. Hoddinott, V. Bond. 'In their shoes': Limited disclosure amongst young people living with HIV stifles their ability to contact others in the same situation, a qualitative cohort HPTN071 (PopART) study in Zambia.
- D. Macleod, B. Yang, S. Floyd, A. Schaap, S. Griffith⁴, K. Shanaube, M. Phiri, R. Slood, P. Bock, N. Beyers, H. Ayles, S. Fidler, R. Hayes. Retention on ART within the HPTN 071 (PopART) universal testing and treatment programme in Zambia and South Africa.
- J. Hargreaves, A. Stangl, G. Hoddinott, T. Mainga, S. Floyd, K. Sabapathy, H. Jones, L. Viljoen, T. Pliakas, S. Krishnaratne, C. Mubekapi-Musadaidzwa, V. Bond, HPTN (071) PopART Team. The HIV stigma landscape in sub-Saharan Africa: Baseline findings of a mixed-method, comprehensive evaluation nested in the HPTN 071 (PopART) trial.
- R.J. Hayes, S. Floyd, A. Schaap, K. Shanaube, B. Yang, S. Griffith, P. Bock, N. Beyers, H. Ayles, S. Fidler, HPTN 071 (PopART) Study Team. Achieving the first two UNAIDS 90-90-90 targets on completion of a three-year universal testing and treatment (UTT) intervention in the HPTN 071 (PopART) randomised trial in Zambia and South Africa.
- B. Yang, R. Slood, S. Floyd, F. Esau¹, J. Molaolwa¹, D. Awoniyi, Y. Saunders¹, P. Siboto, L. Gqiba-Tunywa, D. Myburgh, B. Cimi, S. Griffith, P. Bock, H. Ayles, S. Fidler, R. Hayes, N. Beyers, HPTN 071 (PopART) Study Team. HIV testing patterns in two community-based approaches to universal test and treat in the HPTN 071 (PopART) intervention in South Africa.
- K. Sabapathy, C. Mulubwa, C. Mubekapi-Musadaidzwa, V. Bond, G. Hoddinott, H. Stockl, S. Floyd, P. Bock, J. Seeley, H. Ayles, S. Fidler, R. Hayes, HPTN 071 (PopART) Study Group. Intimate partner violence and associated factors in HPTN 071 (PopART) study communities - a comparison by HIV status.

Stellenbosch University 6nd Annual Academic Day. Tygerberg Medical Campus. 29 August 2018.

Oral presentations

- Celeste de Waal. Raising ethical issues in the dead: An exploration of ethical challenges in forensic medicine
- Peter Bock on behalf of the HPTN 071 (PopART) team. Baseline CD 4 count as a predictor of clinical outcomes when providing antiretroviral treatment regardless of CD 4 count at government clinics within the HPTN 071 (PopART) trial.

- Lario Viljoen on behalf of the HPTN 071 (PopART) team. Public condition/private affliction: Negotiating comorbidity, confidentiality and care in South Africa, a case study from the HPTN 071 (PopART) study.
- Karen du Preez. Ten years of routine paediatric TB surveillance data in South Africa – high disease burden and poor treatment outcomes

Poster presentations

- Sue-Ann Meehan. Evaluating the impact of adherence clubs on the clinical outcome amongst ART patients in the Cape Winelands District of Western Cape Province, South Africa
- Dillon Wademan. Implementing community-based adherence clubs for stable HIV-Infected patients in South Africa. Lessons learned from patient and health worker experiences.
- Blia Yang. HIV-testing patterns in two community-based approaches to Universal Test and Treat in the HPTN 071 (PopART) intervention in South Africa.
- Mareli Claassens. Mortality amongst HIV-positive female tuberculosis patients in South Africa.
- Constance Mubekapi-Musadaidzwa. Motivating people living with HIV to initiate antiretroviral treatment at high CD 4 counts in three HPTN 071 (PopART) health facilities in the Western Cape, South Africa.
- Kerry Nel. Patterns of facility-based HIV testing service (HTS) at two public health facilities participating in the HPTN 071 (PopART) Universal Test and Treat intervention in Cape Town, South Africa.
- Mark Theart. Using aerial photography in longitudinal community studies
- Jana Winckler. The pharmacokinetics of high dose isoniazid for the prevention or treatment of drug-resistant tuberculosis in HIV-infected and –uninfected children (The SHINE trial)
- Megan Palmer. Use of chest radiographs in a phase 3 randomised controlled efficacy trial for treatment shortening of non-severe drug-susceptible TB in children (The SHINE trial)
- Klassina Zimri. Clinical trial and emotional labour: The role of the research nurse in paediatric MDR-TB studies
- Louwina van der Laan. Pharmacokinetics of intracellular Stavudine-Triphosphate in children after reduced dose: Can we improve Stavudine's safety profile?
- Nomsa Apleni, Gerald J Maarman, Nomtha Mandla, Peter Bock, Nulda Beyers on behalf of the HPTN 071 (PopART) team. Presenter: Kate Fortuin. Roles of nurses in ensuring quality and effectiveness of blood sample collection.

SACEMA Research Conference. Stellenbosch. 10-13 September 2018

Poster presentation

- Muhammad Osman, Alex Welte, Rosemary Brown, Rory Dunbar, Graeme Hoddinott, Anneke C Hesseling, Florian M Marx. Former tuberculosis patients, a high-risk group for tuberculosis-associated morbidity and mortality in Cape Town, South Africa: a pilot study.

12th Annual Early Career Scientist Convention (ECSC). 17-19 October 2018

Abstract published

- Muhammad Osman, Alex Welte, Rosemary Brown, Rory Dunbar, Graeme Hoddinott, Anneke C Hesseling, Florian M Marx. Former tuberculosis patients, a high-risk group for tuberculosis-associated morbidity and mortality in Cape Town, South Africa: a pilot study.

The 49TH Union World Conference on Lung Health. The Hague, Netherlands. 24-27 October 2018.

Symposium organizer and chair

- M. van der Zalm. Paediatric lung function measurements in low-middle income countries with a high burden of TB/ HIV, malnutrition and environmental exposures.

Symposium presentation

- N Suryavanshi, G. Hoddinott High-quality social science to inform the design and interpretation of paediatric tuberculosis treatment trials

Oral presentations

- M. van der Zalm. Speaker at symposium: "Lung function in children presenting with symptoms suggestive of pulmonary tuberculosis".
- Garcia-Prats. Pharmacokinetics and pharmacodynamics in designing clinical trials in children
- Garcia-Prats. The current landscape of paediatric trials for the prevention and treatment of DS- and DR-TB: feeding the pipeline
- Garcia-Prats. Meet the Expert Session: Injectable-free regimens, and the role of

injectable agents, in the treatment of children with DR-TB

- Garcia-Prats. Pharmacokinetics, safety and optimal dosing of linezolid in children with multidrug-resistant tuberculosis
- Garcia-Prats. Pharmacokinetics, safety and dosing of levofloxacin 100 mg dispersible tablets in children exposed to multidrug-resistant tuberculosis
- S. Schaaff. TB prevention in children in high TB burden settings: implementing the child contact management (CCM) care cascade. Introductory & 2nd talk: Preventive treatment considerations for multidrug-resistant tuberculosis
- S. Schaaff. Update on clinical and programmatic management of multidrug- and extensively drug-resistant TB (MDR-/XDR-TB) oral treatment of MDR-TB in children
- M Osman, EP Harausz, A Garcia-Prats, HS Schaaf, JA Seddon, AC Hesselning. Good treatment outcomes in children with extensively drug-resistant tuberculosis: a systematic review and individual patient meta-analysis.
- Megan Palmer Use of existing tools for entry points and end points in paediatric TB trials: how can we better use the chest radiograph?
- Elisabetta Walters, Pamela Nabeta, Padmapriya Banada, Anne-Marie Demers, Corne Bosch, Gary Reubenson, Naazley Pandor and Lesley Scott. Mycobacterium tuberculosis detection from stool in young children using a novel centrifugation-free method with Xpert MTB/RIF.

Short oral abstract

- M. Osman. Mortality amongst HIV-positive female tuberculosis patients in South Africa
- K. Du Preez M. Osman, P. Naidoo, S. Dlamini, A.C. Hesselning. Ten years of routine paediatric TB surveillance data in South Africa - high disease burden and poor treatment outcomes
- F. Solomon-da Costa, K. Joseph, M. Osman, K. du Preez. Burden, characteristics and treatment outcomes of patients treated for Isoniazid mono-resistant TB in Cape Town, South Africa.

Poster presentations

- S. Schaaf. Culture-confirmed tuberculosis in infants less than 3 months of age: clinical presentation and management
- M Osman, K du Preez, R Dunbar, A Welte, P Naidoo, AC Hesselning. Trends in the South African tuberculosis epidemic with scale-up of TB-HIV integration services.

- M Palmer, E Walters, M vd Zalm, HR Draper, HS Schaaf, P Goussard, J Morrison, RP Gie, AC Hesselning. Could 'non-typical' chest radiographic features in children with culture-confirmed tuberculosis reflect early, less severe disease?
- M Palmer, R Mboizi, V Mulenga, A Kinikar, D Baskaran, M Thomason, A Crook, AC Hesselning and the SHINE trial team. Use of chest radiographs in a phase 3 randomised controlled efficacy trial for treatment shortening of non-severe drug-susceptible TB in children (the SHINE Trial)

Scientific Meetings, Workshops and events

January 2018

- GATES meeting: Demo project to address the gaps in TB testing
- National TB Network SA Focus on BRIX Countries for TB trials (Anneke Hesselning)

February 2018

- Academic Writing Workshop (Blia Yang, Nomtha Mandla, Kerry Nel, Constance Mubekapi-Musdaidzwa, Rosa Sloom, Mohammed Osman, Gerald Maarman)
- FHI 360 Workshop: Understanding the Clinical Research Process and Principles of Clinical Research (PopART team)
- HPTN071 (PopART) annual workshop in Cape Town. (PopART team)
- Gates Foundation ILTF meeting
- IMPAACT 2005 Regional Meeting

March 2018

- IMPAACT Smart-kids P2020 protocol writing workshop (Anneke Hesselning, Simon Schaaf, James Seddon, Tony Garcia-Prats)
- PhD Graduation gala event (Peter Bock, Florian Marx, Sue-Ann Meehan and Rory Dunbar)
- CAB General Meeting: planning of open day to recruit additional members (Gwynneth Hendricks; DTTC CAB & prospective members)
- South African Social Science and HIV Programme (SASH) event: What does the future of HIV research look like? (Sociobehavioural science team)
- Department of Health in Winelands workshop: lessons learnt from field staff for transmission into policy - budget concerns (PopART team)
- WHO Meeting in Geneva (Anne-Marie Demers, Anneke Hesselning)

- Stigma meeting: Dissemination meeting on clinical level. Fieldworker (CHiPs) data feedback to healthcare services (Kerry Nel)
- World TB Day Event on Tygerberg Campus (DTTC staff and Tygerberg campus staff)
- Gates Foundation ILTFU meeting in Johannesburg (Anneke Hesseling, Muhammad Osman)
- Paediatric TB Meeting in Lithuania (James Seddon, Tony Garcia-Prats)
- Final P-ART-Y CAB meeting before members integrated into DTTC CAB

April 2018

- Mini ORAP Workshop (facilitated by Muhammad Osman)
- Thoracic Meeting in Johannesburg – presentations on preventative therapy and diagnosis in children (Anneke Hesseling, Muhammad Osman)
- CAB Meeting: Recruitment and Retention Drive
- Various research visits: Florian Marx to Europe; Anne-Marie Demers to Peru; James Seddon to the United Kingdom
- APSA meeting in Johannesburg (Constance Mubekapi-Musdadzwa, Graeme Hoddinott)
- HPTN 071 (PopART) Secondary outcomes meeting with Zambian Colleagues (Sue-Ann Meehan)
- HPTN 084 Lab Audit

May 2018

- AURUM Global Funding Meeting in Johannesburg (Anneke Hesseling)
- HPTN Annual Meeting in Washington, USA. (Sue-Ann Meehan, Peter Bock, Blia Yang, Nomtha Mandla, Redwaan Vermaak, Nozi Makola, Jabulile Mantantana, and 2 CAB Members)
- HPTN Annual Community Working Group Meeting in Washington, USA (Nozi Makola)
- Scientific Advisory Board Meeting in Paris. Workshop: Chest X-Rays in Children (James Seddon)
- Research Day – plenary presentation (Nulda Beyers)
- Pre-conference Union Planning Meeting in the Hague (James Seddon)
- TB Think Tank Meeting (Johannesburg). LTFU – finding the missing cases. Improvement of health info exchange by upgrading the HIE for easier data

reporting (Muhammad Osman)

- Research Day at UKWANDA – Stellenbosch University Worcester Campus. Nulda Beyers presented.
- Scientific Advisory Board Meeting in Paris: 1st TB-Speed symposium (re TB in children)

June 2018

- IMPAACT Annual Meeting in Washington. (Tony Garcia-Prats, Frieda Verheye-Dua, Anne-Marie Demers, Sharon Mbaba, Simon Schaaf, Anneke Hesseling, Anneen van Deventer)
- Community Dissemination of HPTN071 (PopART)
- CAB general meeting: HPTN meeting feedback and study protocol reviews.
- British academy writing retreat at Goedgedacht farm (Malmesbury). Six of the Sociobehavioural Science Team received sponsorships: Graeme Hoddinott, Laing de Villiers, Dionne Jivan, Rozanne Casper, Nosivuyile Vanqa and Angelique Thomas.
- SUN-CTU Meeting chaired by Prof Mark Cotton.
- ACTG Network Meeting in Washington DC (Annemarie Demers).
- Consultation workshop for Scoping review on ART scale-up in South Africa with the PopART sociobehavioural science team in collaboration with HIV programme implementers and managers at provincial, city, and district levels (Hanlie Myburgh).
- GHIT Funding Presentation Tokyo, Japan (Anneke Hesseling).
- Scalabrini – The team addressed and shared information with foreigners on TB and HIV, chronic illnesses, access to clinics and services available if unemployed.

July 2018

- KNCV MDR-TB Training Roll Out of preventative therapy for MDR-TB exposed children – Indonesia (Presenter: Tony Garcia-Prats).
- HPTN 071 (PopART) Stigma working group workshop at London School of Hygiene and Tropical Medicine (Graeme Hoddinott, Lario Viljoen, Constance Mubekapi-Musadaidzwa, Laing de Villiers, Dillon Wademan).

August 2018

- Cluster Randomized Trials for Evaluation of HIV interventions workshop at

FMHS. Facilitated by Prof. Rhoderick Machekano.

- Marieke van der Zalm visited the Wilhelmina Children's Hospital from 22 August to 30 October 2018 for capacity building in Lung Health as part of the HB Thom award received at the end of 2017.
- Graeme Hoddinott and Karen du Preez attended and a multi-stakeholder meeting on behalf of DTTC hosted by TB HIV Care for the South African Assessment of Barriers & Facilitators to TB Services in Johannesburg.

September 2018

- 12th International Child TB Training Course at Goudini ATKV Spa, Rawsonville, Cape.
- SHINE TGM Meeting in Lusaka, Zambia (DTTC Paediatric team)
- Faith Leaders meeting at the Kwazulu Natal Christian Council in Pietermaritzburg (Jody Boffa).
- Basic HIV counselling and testing short course (SETA). US hosted at Ruslamere in Durbanville. Counsellors from DTTC Sociobehavioural science and Paediatric teams CPUT and FAMCRU attended.
- Current TB meeting – Adult TB. Complications after treatment and cure. (James Seddon).
- CHEC Module 1.8 Effective Communication. Devon Valley Hotel (Gwynneth Hendricks).
- TB meeting between Sociobehavioural science and Zambart – Quantitative Data and Qualitative data score and Impact on study outcomes. (Graeme Hoddinott).

October 2018

- SACEMA meeting with Muhammad Osman presenting his paper (Muhammad Osman and Anneke Hesseling).
- British Academic Writing workshop in Goedgeacht, Riebeeck Kasteel (Laing de Villiers; Dionne Jivan; Angelique Thomas, Rozanne Casper, Nosi Vanqa).
- Dr. Karen du Preez was selected to attend a World Health Organization Training Workshop for TB Surveillance: Establishing a Roster of Consultants Providing Technical Assistance for Epidemiological Reviews and Data Analysis and use in The African Region, which was held in Kigali, Rwanda (8 to 12 October 2018).
- CTU-CAB Retreat (FMHS). Two day training program involving TASK, FAMCRU and DTTC. A Gala Dinner was held on Saturday 20th Oct at the Bellville Civic Centre. In honour of Katleho the "Katleho Mosimanegape CAB Achievement

Award” was established.

November 2018

- Discussions with WHO country representative on Operational Research, Surveillance and ETR.net .in Pretoria (Karen Du Preez)
- Paediatrics and Child Health Academic Day of Excellence (Liz Walters presented on Pulmonary TB)
- Desmond Tutu TB Centre Dissemination meeting at the Lord Charles Hotel. Opening guest Speaker is Professor Mark Cotton, FAMCRU, Department of Paediatrics and Child Health and the topic of his talk, “The state of HIV & Prevention studies in South Africa.
- HPTN 071 (PopART) Stigma Working Group writing workshop in Choma, Zambia (Lario Viljoen, Dillon Wademan, Laing de Villiers, Angelique Thomas, Rozanne Casper)
- LINKEDin study site visits to Gauteng and KwaZulu Natal (Sue-Ann Meehan and Muhammad Osman). Visited NICD, spent time with implementing study partners (Right to Care and IRD), visiting hospitals and a selection of primary healthcare facilities in the Johannesburg Metro and the Ugu district, where the study will be implemented.
- WHO GIC Implementation Guidelines. Dr. James Seddon presented on Implementation of WHO guidelines for the treatment of MDR treatment in children.
- TB Innovations Consortium Meeting in Johannesburg (Anneke Hesseling; Sue-Ann Meehan; Muhammad Osman)

December 2018

- HPTN 071 (PopART) results “unblinding” meeting in Seattle, United States of America (Peter Bock)

Ongoing 2018

- Joint SUN-CTU CAB Leadership Group Meetings (DTTC CAB EXCO; TASK CAB EXCO; FAMCRU EXCO). Meetings held throughout the year.
- Working Group for Data Analysis & Modeling (WGDAM). WGDAM is a working group that aims to produce research output (such as our publication in SAMJ August 2018). They are currently working on a paper led by Muhammad Osman and Florian Marx, which aims to assess the impact of antiretroviral therapy on tuberculosis incidence and mortality in nine South African Provinces using a

mathematical model. The group met on a regular basis throughout the year.

Visitors at the DTTC during 2018

Date	Visitor	Reason
29 Jan. 2018	Yael Hirsh-Moverman - Assistant Professor in Epidemiology (In ICAP) at the Columbia University Medical Center, Mailman School of Public Health, Columbia University.	Dr Yael Hirsch-Moverman visited the paediatric team to discuss ongoing collaboration and a joint NIH R01 grant application that was submitted in June 2018.
5-9 Feb. 2018	Dr Virginia Bond – Social Scientist at ZAMBART in Zambia	Discussion with Sociobehavioural Science Team
12 Feb. 2018	Vundli Ramokolo – Senior Scientist DOH Systems Research Unit, SA MRC	Discussion with Anneke Hesselning regarding potential post-doc with DTTC
12-15 Feb. 2018	Lily Telisinghe - London School of Hygiene & Tropical Medicine	Visiting PopART, to work on TB case notification data from PopART.
19-23 Feb. 2018	Georgia White – AIDS Free World	Discusison with Anneke regarding filming in SA for TB/HIV advocacy
Feb. 2018	Carl Swenson – UPSALLA Pharmacokinetics	Discussion regarding TB dosing
Mar. 2018	Dr Rafael Saulter and Dr William Probert, Researchers in Infectious Disease Modelling Big Data Institute, Ki La Shing Centre for Health Information and Discovery, Oxford University	IMPAACT Smart-kids P2020 protocol writing workshop
Mar. 2018	Pauline Howell – Senior Medical Officer at Sizwe Tropical Disease Hospital Katie McCarthy - IMPAACT Operations Centre, Science Facilitation FHI360) Leavitt Morrison, Soyeon Kim – Harvard University	IMPAACT Smart-kids P2020 protocol writing workshop
16 Mar. 2018	Jeff Haskins – Otsuka	Meetings with Tony Garcia-Prats and Anneke Hesselning

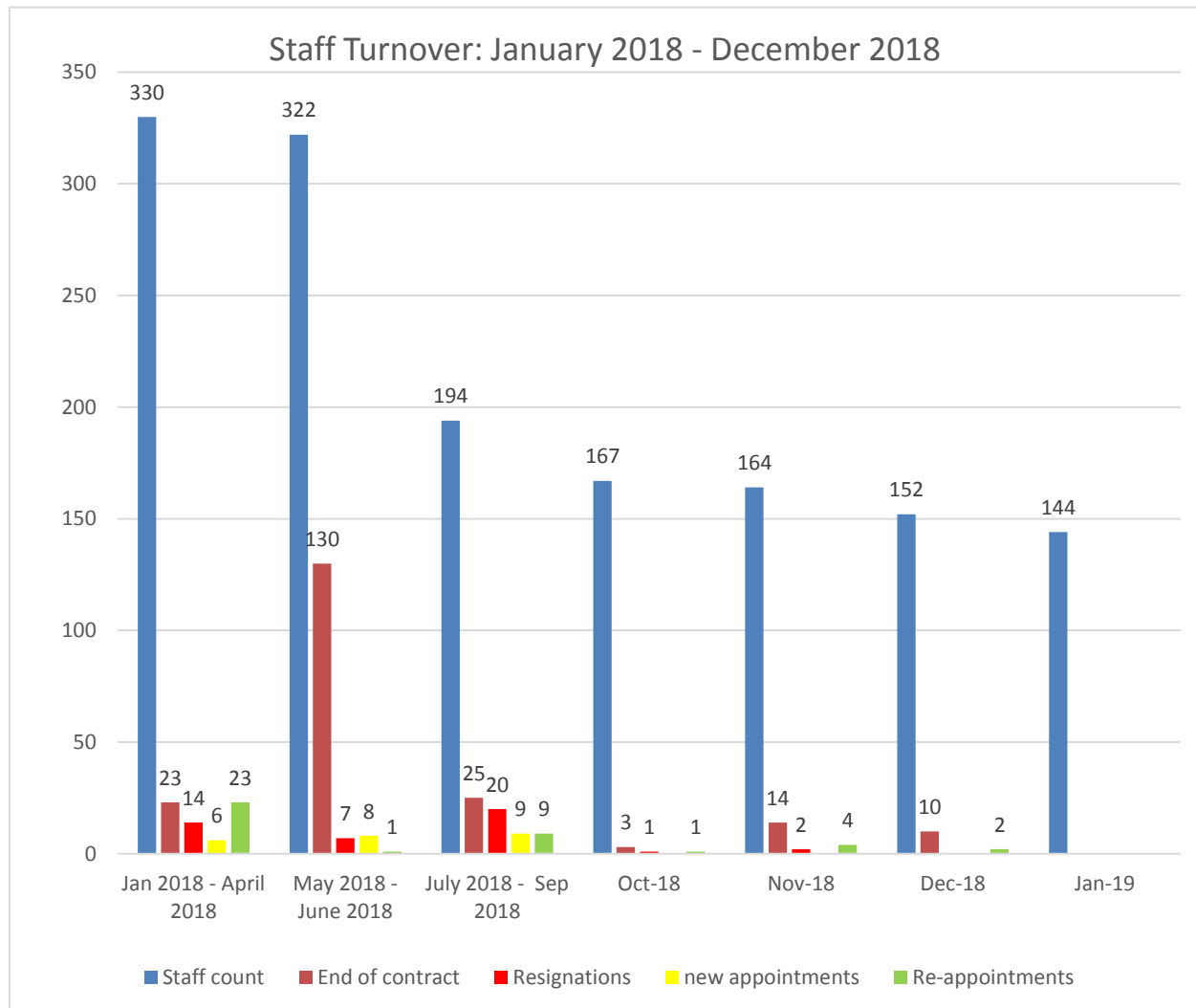
26-29 Mar. 2018	Yael Hirsch – Assistant Professor Epidemiology, Columbia University Medical Centre	Meeting with Paediatric team
9-13 Apr.2018	Ben Daniels – McGill University’s Standardized Patients Project	Assisted Jody Bofta to set up a Quantitative Data Base
17-18 Apr.2018	Ms Mwelwa Phiri and Ms Ramya Kumar	HPTN 071 (PopART) visit
Jun.- Aug. 2018	Rachel Morse – student at Kings College London	Exchange program through partnership between faculty and Department of Social Health and Medicine
06-13 Jul. 2018	Kelly Dooley - John Hopkins University and extraordinary professor at DTTC (Department of Paediatrics)	Pharmacokinetic research meetings / Goudini TB Workshop
06-21 Jul. 2018	Ava Archery (student)	Intern on SHINE study
06-13 Jul. 2018	Sebastian Goodwin-Groen (student)	Intern
03-07 Sept. 2018	Oladapo Alli is PAB senior protocol pharmacist at the Division of AIDS.	DAIDS site visit
03-07 Sept. 2018	Eileen Pouliot - Branch Chief for the Africa and Domestic Partners Branch in the Office of Clinical Site Oversight (OCSO)	DAIDS site visit / CTU visit
17-19 Sept. 2018	Erin Sizemore ; Rosanna Boyd TB Trials Consortium (TBTC)	Site Visit and training
28 Sept. 2018	Teja Stojiljkovic, BARC	Site Visit
03-06 Sept. 2018	Lebogang Tshehla	Regulatory monitoring visit
03-06 Sept. 2018	PPD (IMPAACT)	External monitoring visit
22-26 Oct. 2018	Representatives of Consul General USA, Steven Smit (Health Attaché)	Visiting Kuils River Site office
30-31 Oct. 2018	Cathy Tupman, Global Health Manager and Aimi Vanden-Oever Section Manager	Meetings with key academics and the Grants office; DTTC, Tygerberg

	for Global Health Imperial College, London- James Seddon	Hospital, Brooklynn Chest Hospital
28-30 Nov. 2018	PPD Monitor	Monitoring visits at Kuils River and the DTTC
28-30 Nov. 2018	Dessislava Tarlton (UNITAID) & Ekaterina Rykovanova (WHO)	Evaluation of the Centre and a walk through
31 Nov. 2018	Representatives of Consul General USA, Steven Smit (Health Attaché) and Virginia Blaser	Visited the PopART team to assess project progress on the
28-30 Nov. 2018	WHO-Unitaid (Led by Tony Garcia-Prats)	Visit to PK unit and Faculty doing an evaluation of facility, resources and staff. In depth assessment of all activities.

Employees

During 2018 a total of (205) employee contracts ended. The exit of staff included the final annual round of the PC Field remunerators in June 2018. Between July and September, a high number of employees (20) resigned, seeking permanent employment elsewhere. The Centre also employed total of (23) new staff members on different studies, linked to different post levels. Total of (40) staff members could be re-employed, which relates our current HR retention strategy.

Month	Staff count	End of contract	Resignations	New appoint.	Re-appoint.
Jan – Apr. 2018	330	23	14	6	23
May - Jun. 2018	322	130	7	8	1
Jul. - Sept. 2018	194	25	20	9	9
Oct. 2018	167	3	1	-	1
Nov. 2018	164	14	2	-	4
Dec. 2018	152	10	-	-	2
Jan. 2019	144	-	-	-	-



DTTC Governance

DTTC Executive Committee (ExCo)

The DTTC is led by the Director, Distinguished Professor Anneke Hesseling, who is assisted by an Executive Committee (EXCO) of 12 senior scientific and core support DTTC staff members. The Director, who chairs the EXCO, reports to the Executive Head of the Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences 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.

The DTTC ExCo meets once a month. In addition, there is a dedicated scientific strategy meeting convened once a month for the ExCo and additional *ad hoc* member to discuss and plan ongoing and future research priorities and strategies.

Primary focus areas for 2019 will include applying to remain within the DAIDS and TBTC networks which offer core and study specific funding over a 7 year period. In addition DTTC is actively applying for research opportunities to strengthen core funding to support studies being conducted across the DTTC platform.

DTTC Executive Committee Roles and Responsibilities

Name	Role
Prof Anneke Hesseling	DTTC Director and chair of DTTC ExCo
Dr Tony Garcia- Pratts	Medical director of the Desmond Tutu TB Centre Brooklyn Chest Hospital Paediatric Pharmacokinetics Unit
Dr Marieke van der Zalm	Clinical lead: Paediatric lung health studies
Dr Frieda Verheye-Dua	Regulatory Manager
Prof Simon Schaaf	Lead investigator Paediatric MDR-TB studies
Dr Sue-Ann Meehan	Project Manager and co-investigator
Dr Peter Bock	Lead HIV Prevention research
Dr Muhammad Osman	Lead: Implementation Research
Mr Graeme Hoddinott	Lead Sociobehavioural Scientist
Mrs Sterna Brand	Human Resources Manager
Mr Theo Smith	Logistics /Operations Manager
Dr Rory Dunbar	Data centre manager
Dr AnneMarie Demers	Laboratory Director

Risk Management

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 DTTC in our aim to deliver high quality reputable research outputs. DTTC will continue to support staff training in good clinical practice (GCP) and research confidentiality prior

to any study commencement. Through constant data monitoring by dedicated data centre staff, dual entry of any research information as well as GCP training, 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.

Poor marketing and communication to external stakeholders, has resulted in low exposure to the scientific community and funding agencies. DTTC is actively working on a development plan to improve their marketing and communication efforts in order to improve our local and global footprint and develop strategic relationships with new and current external stakeholders.

Accessibility to communities for recruitment and retention of study participants is still a potential risk. DTTC Field offices have been established in various communities and the development of community advisory boards to strengthen the support for DTTC in communities has been implemented to improve accessibility. Strong line management in field offices mitigates against any HR irregularities (attendance, working hours) that may arise.

Sustainability of core support staff is an ongoing risk due to a lack of core funding. Ongoing efforts to obtain core funding is being implemented. Human resource risks relating to the safety of staff training, staff contracts to retain core staff and staff diversity has been reduced.

Political instability and violence or unrest in study communities places staff and patient safety at risk. DTTC has implemented many safety measures but have also identified various other measures to provide safe working conditions for staff. In the first quarter of 2019 all DTTC drivers will be trained and retrained in defensive driving, including highjack prevention and evaluation. The high burden of TB disease and HIV infection among the population served, poses a health risk to DTTC staff. DTTC has taken many infection control measures through modification of vehicles and offices. Infection prevention control (IPC) training has been scheduled to start in February 2019, the aim is to train all DTTC staff in Infection prevention Control measurements. A Baseline Hep B testing campaign for all staff was launched in November 2018. Staff will be tested and vaccinated in line with national guidelines.

To mitigate the risks of temporary staff contracts leading to insecurity, demotivation and often to early exit, the DTTC has adapted all adverts to two year contracts with benefits, unless the appointment is for a specific intervention linked to a shorter term...

DTTC is committed to adhere to SU diversity policies during their recruitment processes. Staff has been identified from disadvantaged backgrounds to be promoted to levels that are more senior.

Enrolment of Principle investigators in formal supervision programs has been implemented to support Master's and PhD students.

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 loss

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International Collaborators | Funders | Partners



Radboud Universiteit





South African Collaborators | Funders | Partners



CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD



SARChI Chair in Paediatric TB (Hesseling)



Department
for International
Development



WITS REPRODUCTIVE HEALTH & HIV INSTITUTE



SACEMA
DST-NRF Centre of Excellence in Epidemiological Modelling and Analysis



science
& technology

Department:
Science and Technology
REPUBLIC OF SOUTH AFRICA



National
Research
Foundation



BETTER TOGETHER.



Funded by Evidence for HIV Prevention in
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Appendix I. Research outputs - publications

DTTC Publications January 2018 – December 2018

1. Allwood BW, **Maarman GJ**, Kyriakakis CG, Doubell, AF. Post-pulmonary tuberculosis complications in South Africa and a potential link with pulmonary hypertension: Premise for clinical and scientific investigations. *S Afr Med J*. 2018 Jun. 26;108(7):12339. doi: 10.7196/SAMJ.2018.v108i7.13359. PubMed PMID: 30004336.
2. Basu-Roy R, Whittaker E, **Seddon JA**, Kampmann B. Tuberculosis susceptibility and protection in children. *Lancet Infect Dis*. 2018 Oct 12. pii: S1473-3099(18)30157-9. doi: 10.1016/S1473-3099(18)30157-9. Epub ahead of print. PubMed PMID: 30322790.
3. **Bock P**, Fatti G, Ford N, Jennings K, Kruger J, Gunst C, Louis F, Grobbelaar N, Shanaube K, Floyd S, Grimwood A, Hayes R, Ayles H, Fidler S, **Beyers N**; HPTN 071 (PopART) trial team. Attrition when providing antiretroviral treatment at CD4 counts >500cells/ μ L at three government clinics included in the HPTN 071 (PopART) trial in South Africa. *PLoS One*. 2018 Apr 19;13(4):e0195127. doi: 10.1371/journal.pone.0195127. PubMed PMID: 29663952.
4. **Bock P**, Jennings K, Vermaak R, Cox H, Meintjes G, Fatti G, Kruger J, De Azevedo V, Maschilla L, Louis F, Gunst C, Grobbelaar N, **Dunbar R**, Limbada M, Floyd S, Grimwood A, Ayles H, Hayes R, Fidler S, **Beyers N**. Incidence of Tuberculosis among HIV-positive individuals initiating antiretroviral treatment at higher CD4 counts in the HPTN 071 (PopART) trial in South Africa. *J Acquir Immune Defic Syndr*. 2018 Jan 1;77(1):93-101. doi: 10.1097/QAI.0000000000001560. PubMed PMID: 29016524.
5. Bond, V, Ngwenya F, **Thomas A**, Simuyaba M, **Hoddinott G**, Fidler S, Hayes R, Ayles H, Seeley, J; HPTN 071 (PopART) study team. Spinning plates: livelihood mobility, household responsibility and anti-retroviral treatment in an urban Zambian community during the HPTN 071 (PopART) study. *J Int AIDS Soc*. 2018 Jul;21 Suppl 4:e25117. doi.org/10.1002/jia2.25117. PubMed PMID: 30027643.
6. Bond V, Nomsenge S, Mwamba M, Ziba D, Birch A, **Mubekapi-Musadaidzwa C**, **Vanqa N**, **Viljoen L**, Pliakas T, Ayles H, Hargreaves J, **Hoddinott G**, Stangl A, Seeley J; HPTN 071 (PopART) study team. "Being seen" at the clinic: Zambian and South African health worker reflections on the relationship between health facility spatial organisation and items and HIV stigma in 21 health facilities, the HPTN 071 (PopART) study. *Health Place*. 2018 Dec 7. pii: S1353-8292(18)30608-7. doi: 10.1016/j.healthplace.2018.11.006. [Epub ahead of print]. PubMed PMID: 30528346.
7. Bond V, Ngwenya F, Murray E, Ngwenya N, **Viljoen L**, Gumede D, Bwalya C, **Mantantana J**, **Hoddinott G**, Dodd PJ, Ayles H, Simwinga M, Wallman S, Seeley J. Value and Limitations of Broad Brush Surveys Used in Community-Randomized Trials in Southern Africa. *Qual Health Res*. 2018 Dec 17:1049732318809940. doi: 10.1177/1049732318809940. [Epub ahead of print]. PubMed PMID: 30556470.
8. Bradley J, Floyd S, Piwovar-Manning E, Laeyendecker O, Young A, **Bell-Mandla N**, Bwalya J, **Bock P**, Fidler S, Ayles H, Hayes, RJ; HPTN 071(PopART) Study Team. Sexually transmitted bedfellows: exquisite association between HIV and Herpes

- Simplex Virus Type 2 in 21 Communities in Southern Africa in the HIV Prevention Trials Network 071 (PopART) study. *J Infect Dis.* 2018 Jul 2;218(3):443-452. doi: 10.1093/infdis/jiy178. PubMed PMID: 29659909.
9. Byamungu LN, **du Preez K, Walters E, Nachega JB, Schaaf HS.** Timing of HIV diagnosis in children with tuberculosis managed at a referral hospital in Cape Town, South Africa. *Int J Tuberc Lung Dis.* 2018 May 1;22(5):488-495. doi: 10.5588/ijtld.17.0613. PubMed PMID: 29663952.
 10. Chabala C, Turkova A, Thomason MJ, Wobudeya E, Hissar S, Mave V, **van der Zalm M, Palmer M, Kapasa M, Bhavani PK, Balaji S, Raichur PA, Demers AM, Hoddinott G, Owen-Powell E, Kinikar A, Musoke P, Mulenga V, Aarnoutse R, McIlleron H, Hesselning A, Crook AM, Cotton M, Gibb DM; SHINE trial team.** Shorter treatment for minimal tuberculosis (TB) in children (SHINE): a study protocol for a randomised controlled trial. *Trials.* 2018 Apr 19;19(1):237. doi: 10.1186/s13063-018-2608-5. PubMed PMID: 29673395.
 11. Cranmer LM, **Draper HR, Mandalakas AM, Kim S, McSherry G, Krezinski E, Coetzee J, Mitchell C, Nachman S, van der Linde M, Cotton MF, Hesselning AC; IMPAACT P1041 Team.** High incidence of tuberculosis infection in HIV-exposed children exiting an Isoniazid preventive therapy trial. *Pediatr Infect Dis J.* 2018 Oct;37(10):e254-e256. doi: 10.1097/INF.0000000000001946. PubMed PMID: 29462104.
 12. Cruz AT, **Garcia-Prats AJ, Furin J, Seddon JA.** Treatment of Multidrug-Resistant Tuberculosis Infection in Children. *Pediatr Infect Dis J.* 2018 Oct;37(10):1061-1064. doi: 10.1097/INF.0000000000002135. No abstract available. PubMed PMID: 30216296.
 13. Denti P, **Garcia-Prats AJ, Draper HR, Wiesner L, Winckler J, Thee S, Dooley KE, Savic RM, McIlleron HM, Schaaf HS, Hesselning AC.** Levofloxacin population pharmacokinetics in South African children treated for multidrug-resistant tuberculosis. *Antimicrob Agents Chemother.* 2018 Jan 25;62(2). pii: e01521-17. doi: 10.1128/AAC.01521-17. PubMed PMID: 29133560.
 14. Dodd PJ, Yuen CM, Becerra MC, Revill P, Jenkins HE, **Seddon JA.** Potential effect of household contact management on childhood tuberculosis: a mathematical modelling study. *Lancet Glob Health.* 2018 Dec;6(12):e1329-e1338. doi: 10.1016/S2214-109X(18)30401-7. PubMed PMID: 30266570.
 15. **Donald PR, Diacon AH, Lange C, Demers AM, von Groote-Biddlingmeier F, Nardell E.** Droplets, dust and guinea pigs: an historical review of tuberculosis transmission research. 1878–1940. *Int J Tuberc Lung Dis.* 2018 Sep 1;22(9):972-982. doi: 10.5588/ijtld.18.0173. PubMed PMID: 30092861.
 16. **du Preez K, Schaaf HS, Dunbar R, Walters E, Swartz A, Solomons R, Hesselning AC.** Complementary surveillance strategies are needed to better characterise the epidemiology, care pathways and treatment outcomes of tuberculosis in children. *BMC Public Health.* 2018 Mar 23;18(1):397. doi: 10.1186/s12889-018-5252-9. PubMed PMID: 29566651.
 17. **du Preez K, du Plessis L, O'Connell N, Hesselning AC.** Burden, spectrum and outcomes of children with tuberculosis diagnosed at a district-level hospital in South Africa. *The International Journal of Tuberculosis and Lung Disease.* 2018 Sep 1;22(9):1037-1043. doi: 10.5588/ijtld.17.0893. PubMed PMID: 30092869.

18. Floyd S, Schaap A, Shanaube K, Macleod D, Phiri M, Griffith S, **Bock P, Beyers N**, Fidler S, Hayes R, on behalf of the HPTN 071 (PopART) study team. Towards 90-90: Findings after two years of the HPTN071 (PopART) universal testing-and-treatment intervention in Zambia. *PLoS One*. 2018; 13(8): e0197904. PubMed PMID: 30096139.
19. Fregonese F, Ahuja SD, Akkerman OW, Arakaki-Sanchez D, Ayakaka I, Baghaei P, Bang D, Bastos M, Benedetti A, Bonnet M, Cattamanchi A, Cegielski P, Chien JY, Cox H, Dedicoat M, Erkens C, Escalante P, Falzon D, **Garcia-Prats AJ**, Gegia M, Gillespie SH, Glynn JR, Goldberg S, Griffith D, Jacobson KR, Johnston JC, Jones-López EC, Khan A, Koh WJ, Kritski A, Lan ZY, Lee JH, Li PZ, Maciel EL, Galliez RM, Merle CSC, Munang M, Narendran G, Nguyen VN, Nunn A, Ohkado A, Park JS, Phillips PPJ, Ponnuraja C, Reves R, Romanowski K, Seung K, **Schaaf HS**, Skrahina A, Soolingen DV, Tabarsi P, Trajman A, Trieu L, Banurekha VV, Viiklepp P, Wang JY, Yoshiyama T, Menzies D. Comparison of different treatments for isoniazid-resistant tuberculosis: an individual patient data meta-analysis. *Lancet Respir Med*. 2018 Apr;6(4):265-275. doi: 10.1016/S2213-2600(18)30078-X. PubMed PMID: 29595509.
20. Frigati L, Bekker A, Stroebele S, Goussard P, and **Schaaf HS**. Culture-Confirmed Tuberculosis in South African Infants Younger Than 3 Months of Age: Clinical Presentation and Management of Respiratory Complications. *The Pediatric infectious disease journal*. 2018 Aug 27. doi: 10.1097/INF.0000000000002163. PubMed PMID: 30153235.
21. Furin J, Tommasi M, **Garcia-Prats AJ**. Drug-resistant tuberculosis: will grand promises fail children and adolescents? *Lancet Child Adolesc Health*. 2018 Apr;2(4):237-238. doi: 10.1016/S2352-4642(18)30068-3. Epub 2018 Mar 13. No abstract available. PubMed PMID: 30169295
22. **Garcia-Prats AJ, Draper HR**, Finlayson H, **Winckler J**, Burger A, Fourie B, Thee S, **Hesseling AC, Schaaf HS**. Clinical and cardiac safety of long-term levofloxacin in children treated for multidrug-resistant tuberculosis. *Clin Infect Dis*. 2018 Nov 13;67(11):1777-1780. doi: 10.1093/cid/ciy416. PubMed PMID: 29788331.
23. **Garcia-Prats AJ, Rose PC, Draper HR, Seddon JA**, Norman J, McIlleron HM, **Hesseling AC, Schaaf HS**. Effect of co-administration of Lidocaine on the pain and pharmacokinetics of intramuscular Amikacin in children with multidrug-resistant tuberculosis: a randomized crossover trial. *Pediatr Infect Dis J*. 2018 Dec;37(12):1199-1203. doi: 10.1097/INF.0000000000001983. PubMed PMID: 29561515.
24. **Garcia-Prats AJ**, Svensson EM, Weld ED, **Schaaf HS, Hesseling, AC**. Current status of pharmacokinetic and safety studies of multidrug-resistant tuberculosis treatment in children. *Int J Tuberc Lung Dis*. 2018 May 1;22(5):15-23. doi: 10.5588/ijtld.17.0355. PubMed PMID: 29665949.
25. García-Basteiro AL, **Schaaf HS**, Diel R, Migliori GB. Adolescents and young adults: a neglected population group for tuberculosis surveillance. *Eur Respir J*. 2018 Feb 21;51(2). pii: 1800176. doi: 10.1183/13993003.00176-2018. PubMed PMID: 29467211.
26. Goussard P, **Gie RP**, Janson J. Lethal fibrosing mediastinitis in a child possibly due to *Mycobacterium tuberculosis*. PMID: 29635837 *Pediatr Pulmonol*. 2018 Jun;53(6):E18-E20. doi: 10.1002/ppul.24012. Epub 2018 Apr 10. DOI: 10.1002/ppul.24012.

27. **Harausz EP, Garcia-Prats AJ, Law S, Schaaf HS, Kredo T, Seddon JA, Menzies D, Turkova A, Achar J, Amanullah F, Barry P, Becerra M, Chan ED, Chan PC, Ioana Chiotan D, Crossa A, Drobac PC, Fairlie L, Falzon D, Flood J, Gegia M, Hicks RM, Isaakidis P, Kadri SM, Kampmann B, Madhi SA, Marais E, Mariandyshev A, Méndez-Echevarría A, Moore BK, Nargiza P, Ozere I, Padayatchi N, Ur-Rehman S, Rybak N, Santiago-Garcia B, Shah NS, Sharma S, Shim TS, Skrahina A, Soriano-Arandes A, van den Boom M, van der Werf MJ, van der Werf TS, Williams B, Yablokova E, Yim JJ, Furin J, Hesselning AC;** Collaborative Group for Meta-Analysis of Paediatric Individual Patient Data in MDR-TB. Treatment and outcomes in children with multidrug-resistant tuberculosis: A systematic review and individual patient data meta-analysis. *PLoS Med.* 2018 Jul 11;15(7):e1002591. doi: 10.1371/journal.pmed.1002591. PubMed PMID: 29995958.
28. Hargreaves JR, Krishnaratne S, **Mathema H**, Lilleston PS, Sievwright K, **Mandla N**, Mainga T, **Vermaak R**, Piwovar-Manning E, Schaap A, Donnell D, Ayles H, Hayes RJ, **Hoddinott G**, Bond V, Stangl A; HPTN 071 (PopART) Study Team. Individual and community-level risk factors for HIV stigma in 21 Zambian and South African communities: analysis of data from the HPTN071 (PopART) study. *AIDS.* 2018 Mar 27;32(6):783-793. doi: 10.1097/QAD.0000000000001757. PubMed PMID: 29369164.
29. Hirsch-Moverman Y, Mantell JE, Lebelo L, Wynn C, **Hesselning AC**, Howard AA, Nachman S, Frederix K, Maama LB, El-Sadr WM. Tuberculosis preventive treatment preferences among care givers of children in Lesotho: a pilot study. *Int J Tuberc Lung Dis.* 2018 Aug 1;22(8):858-862. doi: 10.5588/ijtld.17.0809. PubMed PMID: 29991393.
30. **Hoddinott G, Hesselning AC.** Sociobehavioural science is needed to understand the impact of paediatric MDR-TB treatment on children and their families. *Int J Tuberc Lung Dis.* 2018 Jan 1;22(1):4. doi: 10.5588/ijtld.17.0814. PubMed PMID: 29297419.
31. **Hoddinott G, Myburgh H, de Villiers L**, Ndubani R, **Mantantana J, Thomas A**, Mbewe M, Ayles H, **Bock P**, Seeley J, Shanaube K, Hargreaves J, Bond V, Reynolds L; HPTN 071 (PopART) Study Team. Households, fluidity, and HIV service delivery in Zambia and South Africa - an exploratory analysis of longitudinal qualitative data from the HPTN 071 (PopART) trial. *J Int AIDS Soc.* 2018 Jul;21 Suppl 4:e25135. doi: 10.1002/jia2.25135. PubMed PMID: 30027687.
32. **Hoddinott G**, Staples S, **Brown R**, Simwinga M, **Mubekapi-Musadaidzwa C**, **Hesselning AC, Hendricks G, De Koker P**, McKenna L. Community engagement for paediatric MDR-TB clinical trials: principles to support ethical trial implementation. *Int J Tuberc Lung Dis.* 2018 May 1;22(5):40-45. doi: 10.5588/ijtld.17.0356. PubMed PMID: 29665952.
33. Innes S, **van der Laan L**, Anderson PL, **Cotton M**, Denti P. Can we improve Stavudine's safety profile in children? Pharmacokinetics of intracellular Stavudine Triphosphate with reduced dosing. *Antimicrob Agents Chemother.* 2018 Oct 24;62(11). pii: e00761-18. doi: 10.1128/AAC.00761-18. PubMed PMID: 30104267.
34. Jacobs C, Goussard P, **Gie RP.** Mycobacterium tuberculosis, a cause of necrotising pneumonia in childhood: a case series. *Int J Tuberc Lung Dis.* 2018 Jun 1;22 (6):614-616. doi: 10.5588/ijtld.17.0570. Epub 2018 Mar 22. PMID: 29566781 DOI: 10.5588/ijtld.17.0570

35. Kampmann B, **Seddon JA**, Paton J, Nademi Z, Keane D, Williams B, Williams A, Liebeschutz S, Riddell A8, Bernatoniene J, Patel S, Martinez N, McMaster P, Basu-Roy R, Welch SB. Evaluating UK national guidance for screening of children for tuberculosis. A prospective multicenter study. *Am J Respir Crit Care Med*. 2018 Apr 15;197(8):1058-1064. doi: 10.1164/rccm.201707-1487OC. PubMed PMID: 29190430.
36. Kay A, **Garcia-Prats AJ**, Mandalakas A M. HIV-associated pediatric tuberculosis: prevention, diagnosis and treatment. *Curr Opin HIV AIDS*. 2018 Nov;13(6):501-506. doi: 10.1097/COH.0000000000000500. PubMed PMID: 30286040.
37. Keshavjee S, Amanullah F, Cattamanchi A, Chaisson R, Dobos KM, Fox GJ, Gendelman HE, Gordon R, **Hesseling A**, Hoi LV, Kampmann B, Kana B, Khuller G, Lewinsohn DM, Lewinsohn DA, Lin PL, Lu LL, Maartens G, Owen A, Protopopova M, Rengarajan J, Rubin E, Salgame P, Schurr E, **Seddon JA**, Swindells S, Tobin DM, Udwadia Z, Walzl G, Srinivasan S, Rustomjee R, Nahid P. Moving toward tuberculosis elimination: critical issues for research in diagnostics and therapeutics for tuberculosis infection. *Am J Respir Crit Care Med*. 2018 Oct 18. doi: 10.1164/rccm.201806-1053PP. [Epub ahead of print] PubMed PMID: 30335466.
38. Khan PY, Yates TA, **Osman M**, Warren RM, van der Heijden Y, Padayatchi N, Nardell EA, Moore D, Mathema B, Gandhi N, Eldholm V, Dheda K, **Hesseling AC**, Mizrahi V, Rustomjee R, Pym A. Transmission of drug-resistant tuberculosis in HIV-endemic settings. *Lancet Infect Dis*. 2018 Dec 13. pii: S1473-3099(18)30537-1. doi: 10.1016/S1473-3099(18)30537-1. [Epub ahead of print] Review. PubMed PMID: 30554996.
39. Kim S, **Seddon JA**, **Garcia-Prats AJ**, Montepiedra G. Statistical considerations for pediatric multidrug-resistant tuberculosis efficacy trials. *Int J Tuberc Lung Dis*. 2018 May 1;22(5):34-39. doi: 10.5588/ijtld.17.0358. PubMed PMID: 29665951.
40. Liu C, Lyon CJ, Bu Y, Deng Z, **Walters E**, Li Y, Zhang L, **Hesseling AC**, Graviss EA, Hu Y. Clinical evaluation of a blood assay to diagnose Paucibacillary tuberculosis via bacterial antigens. *Clin Chem*. 2018 May;64(5):791-800. doi: 10.1373/clinchem.2017.273698. PubMed PMID: 29348166.
41. **Maarman GJ**. Pulmonary arterial hypertension and the potential roles of metallothioneins: A focused review. *Life Sci*. 2018 Dec 1;214:77-83. doi: 10.1016/j.lfs.2018.10.039. Epub 2018 Oct 22. PubMed PMID: 30355531
42. Mann TN, **Schaaf HS**, Dunn RN, Dix-Peek S, **du Preez K**, Lamberts RP, du Toit J, Davis JH. Child and adult spinal tuberculosis at tertiary hospitals in the Western Cape, South Africa: 4-year burden and trend. *Epidemiol Infect*. 2018 Dec;146(16):2107-2115. doi: 10.1017/S0950268818002649. Epub 2018 Sep 28. PubMed PMID: 30264687.
43. **Marx FM**, Yaesoubi R, Menzies NA, Salomon JA, Bilinski A, **Beyers N**, Cohen T. Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: a modelling study. *Lancet Glob Health*. 2018 Apr;6(4):e426-e435. doi: 10.1016/S2214-109X(18)30022-6. PubMed PMID: 29472018.
44. **Meehan SA**, **Sloot R**, **Draper HR**, Naidoo P, Burger R, **Beyers N**. Factors associated with linkage to HIV care and TB treatment at community-based HIV testing services in Cape Town, South Africa. *PLoS One*. 2018 Apr 2;13(4):e0195208. doi: 10.1371/journal.pone.0195208. eCollection 2018. PubMed PMID: 29608616.

45. Mohiyuddin T, **Seddon JA**, Thomas HL, Lalor MK. The changing landscape of childhood Tuberculosis in the United Kingdom: A retrospective cohort (2000 to 2015). *Pediatr Infect Dis J*. 2018 Sep 25. doi: 10.1097/INF.0000000000002200. PubMed PMID: 30256311.
46. **Myburgh H**, Calitz E, Railton JP, Maluleke C, Mashao E, Ketelo P, Jobson G, Grobbelaar CJ, Struthers HE, Peters RPH. Breaking down barriers to tell: A mixed methods study of health worker involvement in disclosing to children that they are living with HIV in rural South Africa. *J Assoc Nurses AIDS Care*. 2018 Nov - Dec;29(6):902-913. doi: 10.1016/j.jana.2018.04.009. Epub 2018 Apr 25. PubMed PMID: 29784521.
47. Nemes E, **Hesseling AC**, Tameris M, Mauff K, Downing K, Mulenga H, Rose P, **van der Zalm M**, Mbaba S, Van As D, Hanekom WA, Walzl G, Scriba TJ, McShane H, Hatherill M; MVA029 Study Team. Safety and immunogenicity of newborn MVA85A vaccination and selective, delayed Bacille Calmette-Guerin for Infants of Human Immunodeficiency Virus-Infected mothers: a phase 2 randomized, controlled trial. *Clin Infect Dis*. 2018 Feb 1;66(4):554-563. doi: 10.1093/cid/cix834. PubMed PMID: 29028973.
48. Obihara NJ, **Walters E**, Lawrenson J, **Garcia-Prats AJ**, **Hesseling AC**, **Schaaf HS**. Tuberculous Pericardial Effusions in Children. *J Pediatric Infect Dis Soc*. 2018 Dec 3;7(4):346-349. doi: 10.1093/jpids/pix087. PubMed PMID: 29096017
49. Opollo VS, Wu X, Hughes MD, Swindells S, Gupta, A, **Hesseling A**, Churchyard G, Kim S, Lando R, Dawson R, Mave V, Mendoza A, Gonzales P, Kumarasamy N, von Groote-Bidlingmaier F, Conradie F, Shenje J, Fontain SN, **Garcia-Prats A**, Asmelash, A, Nedsuwan S, Mohapi L, Mngqibisa R, Garcia Ferreira AC, Okeyo E, Naini L, Jones L, Smith B, Shah NS. HIV testing uptake among the household contacts of multidrug-resistant tuberculosis index cases in eight countries. *Int J Tuberc Lung Dis*. 2018 Dec 1;22(12):1443-1449. doi: 10.5588/ijtld.18.0108. PubMed PMID: 30606316.
50. **Purchase SE**, **Garcia-Prats AJ**, **De Koker P**, **Draper HR**, **Osman M**, **Seddon JA**, **Schaaf HS**, **Hesseling AC**. Acceptability of a Novel Levofloxacin Dispersible Tablet Formulation in Young Children Exposed to Multidrug-Resistant Tuberculosis. *Pediatr Infect Dis J*. 2018 Dec 13. doi: 10.1097/INF.0000000000002268. [Epub ahead of print] PubMed PMID: 30550511.
51. Rosser A, **Marx FM**, Pareek M. Recurrent tuberculosis in the pre-elimination era. *Int J Tuberc Lung Dis*. 2018 Feb 1;22(2):139-150. doi: 10.5588/ijtld.17.0590. PubMed PMID: 29506610.
52. Basu-Roy R, Whittaker, E, **Seddon JA**, Kampmann B. Tuberculosis susceptibility and protection in children. *Lancet Infect Dis*. 2018 Oct 12. pii: S1473-3099(18)30157-9. doi: 10.1016/S1473-3099(18)30157-9. PubMed PMID: 30322790.
53. Sabapathy K, Mulubwa C, **Mathema H**, **Mubekapi-Musadaidzwa C**, Schaap A, **Hoddinott G**, Hargreaves J, Floyd S, Ayles H, Hayes R; HPTN 071 (PopART) Study Team. Is home-based HIV testing universally acceptable? Findings from a case-control study nested within the HPTN 071 (Pop ART) trial. *Trop Med Int Health*. 2018 Jun;23(6):678-690. doi: 10.1111/tmi.13055. Epub 2018 Apr 16. PubMed PMID: 29608231.
54. **Schaaf HS**, **Garcia-Prats AJ**, McKenna L, **Seddon JA**. Challenges of using new and repurposed drugs for the treatment of multidrug-resistant tuberculosis in children.

- Expert Rev Clin Pharmacol. 2018 Mar;11(3):233-244. doi: 10.1080/17512433.2018.1421067. PubMed PMID: 29280409.
55. **Seddon JA**, Weld ED, **Schaaf HS**, **Garcia-Prats AJ**, Kim S, **Hesseling AC**. Conducting efficacy trials in children with MDR-TB: what is the rationale and how should they be done? *The Int J Tuberc Lung Dis*. 2018 May 1;22(5):24-33. doi: 10.5588/ijtld.17.0359. PubMed PMID: 29665950.
 56. **Seddon JA**, **Garcia-Prats AJ**, **Purchase SE**, **Osman M**, Demers AM, **Hoddinott G**, Crook AM, Owen-Powell E, Thomason MJ, Turkova A, Gibb DM, Fairlie L, Martinson N, **Schaaf HS**, **Hesseling AC**. Levofloxacin versus placebo for the prevention of tuberculosis disease in child contacts of multidrug-resistant tuberculosis: study protocol for a phase III cluster randomised controlled trial (TB-CHAMP). *Trials*. 2018 Dec 20;19(1):693. doi: 10.1186/s13063-018-3070-0. PubMed PMID: 30572905; PubMed Central PMCID: PMC6302301.
 57. **Seddon JA**, **Schaaf HS**, Marais BJ, McKenna L, **Garcia-Prats AJ**, **Hesseling AC**, Hughes J, Howell P, Detjen A, Amanullah F, Singh U, Master I, Perez-Velez CM, Misra N, Becerra MC, Furin. Time to act on injectable-free regimens for children with multidrug-resistant tuberculosis. *Lancet Respir Med*. 2018 Sep;6(9):662-664. doi: 10.1016/S2213-2600(18)30329-1. PubMed PMID: 30191832
 58. **Seddon JA**, Chiang SS, Esmail H, Coussens AK. The Wonder Years: What Can Primary School Children Teach Us About Immunity to Mycobacterium tuberculosis? *Front Immunol*. 2018 Dec 13;9:2946. doi: 10.3389/fimmu.2018.02946. eCollection 2018. PubMed PMID: 30619306.
 59. Seeley J, Bond V, **Yang B**, Floyd S, MacLeod D, **Viljoen L**, Phiri M, Simuyaba M, **Hoddinott G**, Shanaube K, Bwalya C, **de Villiers L**, Jennings K, Mwanza M, Schaap A, **Dunbar R**, Sabapathy K, Ayles H, **Bock P**, Hayes R, Fidler S; HPTN 071 (PopART) study team. Understanding the Time Needed to Link to Care and Start ART in Seven HPTN 071 (PopART) Study Communities in Zambia and South Africa. *AIDS Behav*. 2018 Nov 10. doi: 10.1007/s10461-018-2335-7. [Epub ahead of print]. PubMed PMID: 30415432.
 60. **Sloot R**, **Maarman GJ**, **Osman M**, **Marx F**. On Behalf Of The Desmond Tutu Tb Centre-Working Group Data Analysis And Modelling FM. Variation in HIV prevalence and the population-level effects of antiretroviral therapy in reducing tuberculosis incidence in South Africa. *S Afr Med J*. 2018 Jul 25;108(8):12370. doi: 10.7196/SAMJ.2018.v108i8.13394. PubMed PMID: 30182871.
 61. Svensson EM, du Bois J, Kitshoff R, de Jager VR, Wiesner L, Norman J, Nachman S, Smith B, Diacon AH, **Hesseling AC**, **Garcia-Prats AJ**. Relative bioavailability of bedaquiline tablets suspended in water: implications for dosing in children. *Br J Clin Pharmacol*. 2018 Jun 27. doi: 10.1111/bcp.13696. [Epub ahead of print] PubMed PMID: 29952141.
 62. Swindells S, Gupta A, Kim S, Hughes MD, Sanchez J, Mave V, Dawson R, Kumarasamy N, Comins K, Smith B, Rustomjee R, Naini L, Shah NS, **Hesseling A**, Churchyard G. Resource utilization for multidrug-resistant tuberculosis household contact investigations (A5300/I2003). *Int J Tuberc Lung Dis*. 2018 Sep 1;22(9):1016-1022. doi: 10.5588/ijtld.18.0163. PubMed PMID: 30092866; PubMed Central PMCID: PMC6104641.

63. Thuboy B, Kellermann T, Castel S, Norman J, Joubert A, **Garcia-Prats AJ, Hesselning AC**, Wiesner L. The determination of capreomycin in human plasma by LC-MS/MS using ion-pairing chromatography and solid-phase extraction. *Biomed Chromatogr*. 2018 May 3:e4269. doi: 10.1002/bmc.4269. PubMed PMID: 29726023.
64. Vanker A, **van der Laan LE, Garcia-Prats AJ, Schaaf HS**, Tikiso T, Wiesner L, de Kock M, **Winckler J**, Norman J, McIlleron H, Denti P, **Hesselning AC**. Pharmacokinetics and drug-drug interactions of Lopinavir-Ritonavir administered with first- and second-line antituberculosis drugs in HIV-Infected children treated for multidrug-resistant tuberculosis. *Antimicrob Agents Chemother*. 2018 Jan 25;62(2). pii: e00420-17. doi: 10.1128/AAC.00420-17. PubMed PMID: 29133558.
65. Van Elsland SL, Van Dongen SI, Bosmans JE, **Schaaf HS**, Van Toorn R, Van Furth AM. Cost-effectiveness of home-based vs. in-hospital treatment of paediatric tuberculous meningitis. *Int J Tuberc Lung Dis*. 2018 Oct 1;22(10):1188-1195. doi: 10.5588/ijtld.18.0236. PubMed PMID: 30236187.
66. Vanker A, **Gie RP**, Zar HJ. Early life exposures to environmental tobacco smoke and indoor air pollution in the Drakenstein Child Health Study: Impact on child health. *S Afr Med J*. 2018 Feb 1;108(2):71-72. doi: 10.7196/SAMJ.2017.v108i2.13088. PMID: 29429431 DOI: 10.7196/SAMJ.2017.v108i2.13088.
67. **Walters E, Demers AM, van der Zalm M**, Whitelaw A, **Palmer M, Bosch C, Draper HR, Gie RP, Hesselning AC**. Reply to Drancourt, "Culturing Stools To Detect Mycobacterium tuberculosis". *J Clin Microbiol*. 2018 Apr 25;56(5). pii: e00056-18. doi: 10.1128/JCM.00056-18. PubMed PMID: 29695539.
68. **Walters E, van der Zalm MM, Demers AM**, Whitelaw A, **Palmer M, Bosch C, Draper HR, Schaaf HS**, Goussard P, Lombard CJ, **Gie RP, Hesselning AC**. Specimen Pooling as a Diagnostic Strategy for Microbiologic Confirmation in Children With Intrathoracic Tuberculosis. *Pediatr Infect Dis J*. 2018 Nov 9. doi:10.1097/INF.0000000000002240. [Epub ahead of print] PubMed PMID: 30418355.
69. **Walters E**, Scott L, Nabeta P, Demers AM, Reubenson G, Bosch C, David A, **van der Zalm M**, Havumaki J, **Palmer M, Hesselning AC**, Ncayiyana J, Stevens W, Alland D, Denkinger C, Banada P. Molecular Detection of Mycobacterium tuberculosis from Stools in Young Children by Use of a Novel Centrifugation-Free Processing Method. *J Clin Microbiol*. 2018 Aug 27;56(9). pii: e00781-18. doi: 10.1128/JCM.00781-18. Print 2018 Sep. PubMed PMID: 29997199; PubMed Central PMCID: PMC6113478.
70. **Walters E**, Scott L, Nabeta P, **Demers AM**, Reubenson G, **Bosch C**, David A, **van der Zalm M**, Havumaki J, **Palmer M, Hesselning AC**, Ncayiyana J, Stevens W, Alland D, Denkinger C, Banada P. Molecular detection of Mycobacterium tuberculosis from stool in young children using a novel centrifugation-free processing method. *J Clin Microbiol*. 2018 Aug 27;56(9). pii: e00781-18. doi: 10.1128/JCM.00781-18. PubMed PMID: 29997199.
71. Wood LF, Brown BP, Lennard K, Karaoz U, Havyarimana E, Passmore J, **Hesselning AC**, Edlefsen PT, Kuhn L, Mulder N, Brodie EL, Sodora DL, Jaspan HB. Feeding-related gut microbial composition associates with peripheral T cell activation and mucosal gene expression in African infants. *Clin Infect Dis*. 2018 Sep 28;67(8):1237-1246. doi: 10.1093/cid/ciy265. PubMed PMID: 29659737.
72. Yates TA, Ayles H, Leacy FP, Schaap A, Boccia D, **Beyers N**, Godfrey-Faussett P, Floyd S. Socio-economic gradients in prevalent tuberculosis in Zambia and the Western

Cape of South Africa. Trop Med Int Health. 2018 Apr;23(4):375-390. doi: 10.1111/tmi.13038. PubMed PMID: 29432669.

Other Publications

1. **Schaaf HS**, Marais BJ, Carvalho I, **Seddon JA**. Challenges in childhood tuberculosis. In: ERS Monograph: *Tuberculosis*. Eds. Migliori GB, Bothamley G, Duarte R, Rendon A. European Respiratory Society, Sheffield, UK. 2018:234-262 .
2. Statement on injectable-free regimens for children under the age of 12 years with rifampicin-resistant tuberculosis <http://sentinel-project.org/wp-content/uploads/2018/07/Recommendations-for-Injectable-Free-Regimens-in-Children-with-Rif-Resistant-TB.pdf>
3. Research Priorities for Paediatric Tuberculosis. World Health Organization. https://www.finddx.org/wp-content/uploads/2018/09/Paediatric_TB_ResearchPriorities_FINAL_Web.pdf
4. Roadmap towards ending TB in children and adolescents. World Health Organization <http://apps.who.int/iris/bitstream/handle/10665/275422/9789241514798-eng.pdf>
5. Best Practices in Child and Adolescent TB Care. World Health Organization <https://www.finddx.org/wp-content/uploads/2018/09/Best-Practices-Child-Adolescent-TB-Care.pdf>

Appendix II: Students – Masters, PhD and Postdoctoral

The following PhD students graduated in 2018:

Dr. Anthony Garcia-Prats

Supervisor: Anneke Hesseling; Simon Schaaf

Dissertation: Optimizing and operationalizing MDR-TB treatment in children

Dr. Elisabetta Walters

Supervisors: Anneke Hesseling; Robert Gie

Dissertation: Novel approaches to diagnosis of TB in children

Dr. Peter Bock

Supervisors: Nulda Beyers, Sarah Fidler (Imperial College)

Dissertation: The impact of POPART intervention on the mortality and AIDS related morbidity amongst HIV positive adults in South Africa

Dr. Florian Marx

Supervisors: Nulda Beyers; Ted Cohen

Dissertations: Mathematical modelling to project the impact of interventions targeted to individuals previously treated for tuberculosis on the trajectory of the tuberculosis epidemic in high-burden settings

Sue-Ann Meehan

Supervisors: Nulda Beyers; Ronelle Burger

Dissertation: The contribution of a community based HIV counseling and testing initiative in working towards increasing access to HIV counseling and testing in Cape Town, South Africa.

Rory Dunbar

Supervisors: Nulda Beyers; Ivor Langley; Pren Naidoo

Dissertation: How can virtual implementation modelling inform the scale-up of new

molecular diagnostic tools for tuberculosis?

The following PhD student submitted their dissertations in 2018:

Graeme Hoddinott

Supervisor: Mary van der Riet

Dissertation: Toward a conceptual model of 'the act'; an exercise in theory-generation in the problematic space of school-based HIV prevention through behavior change interventio

DTTC or DTTC-supported students currently registered (2018)

Currently Registered Trainees: Master's Degree				
Name of trainee	Current position	Degree	Supervisor	Research Topic
Jabulile Mantantana, BPsych	Community Engagement, Recruitment, and Retention Officer	MPhil Transdisciplinary Public health and development studies (SU)	Graeme Hoddinott	Continuity of ART for people who experience incarceration
Christopher Mahwire, MD	Medical Officer, DOH	MSc Epid (SU)	Pren Naidoo	Has the use of Xpert [®] 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?"
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)
Lena Ronge, MD	Research Medical Officer Consultant	MSc Epid (SU)	Anneke Hesseling	Operational implementation of treatment of MDR-TB prevention in a community based clinical trial
Nosivuyile Vanga	Social Science Research Officer	MPhil Transdisciplinary Public health and development studies (SU)	Lindsey Reynolds	Utility of Interferon-gamma release assays in predicting incident TB in children.
Dionne Jivan	Social Science Research Intern	MPhil Transdisciplinary Public health and development studies (SU)	Lindsey Reynolds	People who use drugs access to TB and HIV-related care

Melissa Nel	Social Science Research Apprentice	MPhil Transdisciplinary Public health and development studies (SU)	Graeme Hoddinott	A scale for rapidly ascribing socio-economic status estimates to neighbourhoods using observational and participatory research techniques.
Nelis Grobbelaar	Programme Director (ANOVA Health)	MPhil Transdisciplinary Public health and development studies (SU)	Graeme Hoddinott	Integrating change to universal HIV-testing and ART regardless of CD4 -count into routine health services
Dianne van Aswegen	Social Science Research Intern	MA Anthropology (SU)	Shaheed Tayob	Trauma, care and evidence, from the Mosaic centre to the courtroom, gender-based violence and the state in Cape Town, South Africa
Kyla Meyerson	Social Science Research Intern	MA Psychology (SU)	Mark Tomlinson Graeme Hoddinott	The experiences of paediatric MDR-TB patients' (0-5 years old) hospitalised for treatment in terms of separation and attachment
Leletu Busakwe	Social Science Research Intern	MA Anthropology (UWC)	Sakhumzi Mfecane	The experiences of paediatric MDR-TB patients' (14-17 years old) hospitalised for treatment in terms of adolescent social and biological development
Vuyokazi Myoli	Social Science Research Intern	MPhil Transdisciplinary Public health and development studies (SU)	Lindsey Reynolds	Young women's talk about reproductive health service access
Khanya Mama		MCom (SU)	Ronelle Burger Graeme Hoddinott	TB patients with confirmed diagnoses who decline/delay taking up treatment – exploring why
Rene Raad	Social Science Research Intern	MA Anthropology	Thomas Cousins	Termination of pregnancy providers' experiences of stigma and care
Bianca Hamman	Medical microbiology	MSc (SU)	Mae Newton-Foot Marieke vd Zalm	The role of respiratory co-infections and the microbiome in the clinical presentation and response to treatment in South African children with suspected TB

Currently registered PhDs				
Name of trainee	Current position	Degree	Supervisor	Research Topic
Nomtha Mandla, Physio	Project Manager: PopArt	PHD (SU)	Lungiswa Nkonki Peter Bock	Recruitment, participation and retention of research participants in the HPTN 071 Population Cohort, South Africa.
Graeme Hoddinott, MSocSc	Lead Social Scientist	PhD , (UKZN)	Mary Van Der Riet	Toward a conceptual model of 'the act'; an exercise in theory-generation in the problematic space of school-based HIV prevention through behavior change intervention
Martina Mchenga, MPhil	PhD student	PhD (SU)	Ronelle Burger	Vulnerable households and health: evidence from surveys in South Africa and Malawi"
Lario Viljoen, MA	Social Science Researcher	PhD (SU)	Lindsey Reynolds	Young women's sexual decision-making in the context of earlier ART-access
Karen du Preez, MD, MSc	Research Medical Officer	PhD (SU)	Anneke Hesseling Simon Schaaf Pren Naidoo	Complementary surveillance strategies and interventions to inform a tuberculosis care cascade for children
Anne-Marie Demers, MD	Medical Microbiologist	PhD (SU)	Anneke Hesseling Andrew Whitelaw (NHLS)	Use of routine microbiology data in paediatric TB trials
Muhammad Osman, MD, Msc	Research Medical Officer	PhD (SU)	Anneke Hesseling Pren Naidoo Alex Welte	TB-associated mortality in South Africa: longitudinal trends and the impact of health system interventions
Tamaryn Jane Nicholson	Social Science Researcher	PhD (UKZN)	Mike Quayle Mary van der Riet Orla Muldoon	HIV stigma and mass media communication messaging
Louvina van der Laan, MD	Research Medical Officer	PhD (UCT)	Paolo Denti Anthony Garcia-Prats	Pharmacometric modelling as a tool to optimise TB Treatment in children

Post docs current				
Name of trainee		Degree	Supervisor	Research Topic
Marieke van der Zalm	Paediatrician	Postdoc (SU)	Anneke Hesseling	Lung function and respiratory pathogens in children with suspected TB
Rosa Sloot	Biostatistician	Postdoc (SU)	Pren Naidoo	Epidemiology- HPTN071 (PopART)

Graduates 2018				
Name of trainee	Current position	Degree	Supervisor	Research Topic
Heidi van Deventer, MD	Research Medical Officer	MSc Clin Epid (SU)	Anneke Hesseling	Effect of TB on risk of atopy in children
Celeste de Vaal, MD, DCH	Research Medical Officer	MPhil Bioethics (SU)	Lyn Horn	Ethics of post-mortem studies and notifiable diseases including TB
Catherine Wiseman, MD	Research Medical Officer	MPH (UCT)	Anneke Hesseling	Effect of HIV exposure on risk of TB infection in infants in high-burden communities
Anelet James, MSc Microbiology	DTTC Operations Manager	MBA (USB)	Jako Volschenk	Comparing patient costs for MDR TB and HIV co-infected patients under LPA and Xpert diagnostic algorithms
Anthony Garcia-Prats, MD, Msc	Paediatric PI BCH PK Unit Medical Director	PhD (SU)	Anneke Hesseling Simon Schaaf	Optimizing and operationalizing MDR-TB treatment in children
Elisabetta Walters, MD, MMed	Research Pediatrician	PhD (SU)	Anneke Hesseling Robert Gie	Novel approaches to diagnosis of TB in children
Peter Bock, MBChB (UCT), MRCP (UK), MRCP (UK) MPH (UCT)	Specialist Family Physician Co-PI: PopArt	PhD (SU)	Nulda Beyers, Sarah Fidler (Imperial College)	The impact of POPART intervention on the mortality and AIDS related morbidity amongst HIV positive adults in South Africa
Florian Marx, MD*	Research Fellow	PhD (SU)	Nulda Beyers Ted Cohen	Mathematical modelling to project the impact of interventions targeted to individuals previously treated for tuberculosis on the trajectory of the tuberculosis epidemic in high-burden settings"
Sue-Ann Meehan, MA (Research Psychology)	Senior Researcher, LINKED-in Project Manager	PhD (SU)	Nulda Beyers Ronelle Burger	The contribution of a community based HIV counseling and testing initiative in working towards increasing access to HIV counseling and testing in Cape Town, South Africa.

Registering for PhDs to start in 2019				
Name of trainee	Current position	Degree	Supervisor	Research Topic
Hanlie Myburgh, MA	Social Science Researcher	PhD (UVA)	Ria Reis Lindsey Reynolds	The state and the citizen in the scale-up of HIV services in South Africa
Constance Mubekapi-Musadaidzwa	Social Science Researcher	PHD (SU)	Elena Toska Graeme Hoddinott	HIV interventions for young people in southern Africa
Dillon Wademan	Social Science Research Officer	PhD (SU)	Graeme Hoddinott Lindsey Reynolds	Family chronicity and intergenerational syndemics in the chronic management of TB, HIV, and diabetes
Laing de Villiers	Social Science Research Officer	PhD (SU)	Leslie Swartz Graeme Hoddinott	Identity fluidity on the margins of Cape Winelands communities
Rozanne Casper	Social Science Research Officer	PhD (RU)	Catriona Macleod Graeme Hoddinott	Young women's negotiation of gender identity in South Africa
Angelique Thomas	Social Science Research Officer	PhD (UCT)	Lindsey Reynolds Graeme Hoddinott	Maintaining intimacy and boundaries by women who sell sex in the Western cape
Isabelle de Wandel, MD	Medical Officer	PhD (SU)	Anneke Hesseling Marieke Van der Zalm	TB and Lung Health
Megan Palmer, MD, FCP	Paediatrician	PhD (SU)	Anneke Hesseling Pierre Goussard James Seddon	Validity of chest radiographic reading methods in children with suspected tuberculosis
Jennifer Hughes	Research Medical Officer	PhD (SU)	Anthony Garcia-Prats Anneke Hesseling	MDR-TB treatment strategies in adults and children

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

The DTTC has been active in media, both in printed and radio. The centre was represented in a video screening at the 22nd International AIDS conference in Amsterdam, 2 printed news articles and three radio interviews.

Video screening:

- “Two Countries, Two Choices”: a 30 minute documentary film on TB in which two DTTC research child participants are featured was released by the organisation, AidsFree World, at the 22nd International AIDS Conference in Amsterdam. 27 July 2018. Ref: <https://vimeo.com/280906730>.

Newspaper articles:

- “Weerstandige TB: So slag terapie vir kinders”, Elsabie Brits, Die Burger. 18 August 2018.
- Latoya – Independent Newspaper. Interview related to an article on TB. Anneke Hesseling. 21 August 2018.

Radio:

- Elliot Sylvester and Nicola Brand – CapeTalk. Interview with Anneke Hesseling. 22 August 2018.
- Treating MDR-TB in children. Radio Sonder Grense – Mari Hudson. Interview with Anneke Hesseling. 29 August 2018.
- Improvements in TB, SA leading the way globally. Cape Talk. Interview with James Seddon, DTTC. 27 September 2018.