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Enquiries: **Laticia Pienaar/Rozaun Botes**

DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

Annual Report for Tygerberg Hospital and Stellenbosch University 2017

HEAD OF DEPARTMENT Professor Mariana Kruger
REPORT COMPILED BY Editor: Professor Mariana Kruger
Authors: Personnel
Administrative assistance: AE Fourie & S Engelbrecht
Tel: (021) 938-9220/938-4538

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EXECUTIVE SUMMARY – 2017

The year 2017, with regards to service delivery, was a difficulty year, secondary to budget and staff constraints. Staff shortages could be managed effectively due to the active recruitment of supernumerary registrars and senior registrars (16 doctors in total). Bed occupancy rates (BOR) were high for neonatology, especially inborn babies and paediatric oncology, often necessitating admissions of paediatric nephrology patients in other wards outside G3 (shared ward for Paediatric Oncology, Paediatric Immunology and Paediatric Nephrology). There was a significant growth in the admissions to paediatric infectious diseases and paediatric gastro-enterology. Major nursing staff shortages in paediatric critical care resulted in a subsequent low BOR for the paediatric high care facility, since the facility could not be staffed adequately daily due to service pressures in PICU, necessitating professional nurses to be allocated to that service.

Children were often admitted to subspecialist beds due to limited beds for General Paediatrics. There were also still inappropriate referrals by primary care nurses to Subspecialist Paediatrics, bypassing General Paediatrics, especially as there is no dedicated ambulatory care facility for this service. This resulted in high workload for Paediatric Neurology, Neurodevelopmental Paediatrics and Paediatric Pulmonology with an overall increase in highly specialised ambulatory paediatric visits. There were no clinics for high risk infants to down refer these patients for the necessary assessment and screening procedures and therefore was a significant workload in the highly specialised ambulatory paediatric service.

The undergraduate pass rate remained high (99%), which in part was due to the innovative introduction of an improved examination system in 2016. The postgraduates also had a 99% pass rate for Part II and 8 obtained their Masters degrees. A record number of 6 postgraduate students completed their PhD degrees (5 from DTTC). Publication output was again a record of 2 book chapters and 121 peer review articles. The research centres Desmond Tutu TB Centre (DTTC) and Family Clinical Research Unit (FAMCRU) were major contributors, while South-2-South closed after successful completion of a successful integrative capacity-building model for maternal and child HIV/TB care for National Department of Health and due to ending of funding cycle by USAID.

Tygerberg Children's Hospital Trust (TCHT) assisted with the upgrade of the ophthalmology screening service for high risks premature infants, the offices of C3A nursing manager, the paediatric typist and the HOD, as well as the joint staff committee room. Additional equipment to the value of R227 266,21 was also bought for the wards. Several major donations were received from private donors such as 2 PICU beds, equipment for paediatric oncology, as well as renovations by private funding for G3 paediatric oncology isolation rooms.

Professor Mariana Kruger

Part 1

RESOURCES AND OUTPUT

Human Resources

Posts (full-time)	Number	Filled
Professor/Chief Specialists	*2*	*2*
Chief Specialist	*1*	*1*
Principal Specialists	*4*	*4*
Senior Specialists	*25+1(5/8)*	*25+1(5/8)*
Senior Registrars	*10 (5 Supernumeraries)*	*10 (5 Supernumeraries)*
Registrars	*43 (11 Supernumeraries)*	*43 (11 Supernumeraries)*
Medical Officer	*24*	*24*
Posts (sessional – hours per week)		
Specialist	*4 (35 hours)*	*4 (35 hours)*
Number of beds	*268*	*268*

Subspecialist Paediatrics	**2017**	**2016**	**2015**
Inpatients	5885 (4.0%)	5658 (-4.1%)	5902 (-2.7)
Outpatients	13721 (3.7%)	13224 (-1%)	13384 (-1.5%)
Summary of Output General Paediatrics			
Inpatients	9810 (-0.9%)	9906 (-11.8%)	11238 (-1.5%)
Outpatients	12637 (5.4%)	11983 (-18%)	14658 (-1.4%)

Output

SUBSPECIALIST PAEDIATRICS

Total patient admissions 2017 (Clinicom data)

*A9 NICU	A9 PICU	A9 High Care	Trachea Unit	G1	G3	G9	G10	Total
461	698	181	109	989	985	1538	924	**5885**

*A9 NICU includes High-care beds, since Clinicom cannot separate data.

Bed Occupancy Rate 2017(Clinicom data)

*A9 NICU	A9 PICU	A9 High Care	Trachea Unit	G1	G3	G9	G10	Total
81%	84%	#34%	62%	85%	718%	70%	82%	**71%**

*A9 NICU includes High-care beds, since Clinicom cannot separate data.
#BOR low due to nursing staff shortages.

Neonatology

Staff: Prof J Smith, A Bekker, Drs S Holgate, G Kali, JCF du Preez, H Hassan, L Van Wyk, L Lloyd; 3 Senior Registrars (2 supernumerary) – Dr N Paulse, Dr MW Kariuki, Dr A Onwona; 6 Registrars; 7 Medical Officers

A9 Intensive Care Unit

Staff: 1 Consultant (on rotation), 2 Registrars, 1 Medical Officer

Beds *n=8*	***2017***	***2016***	***2015***
Admissions	461	442	506
Average NICU Stay in Days	8	9	7.9
Average Bed Occupancy %	81%	88%	88.4%
% Growth	+4.3%	-12.6%	+7%
Deaths	108 (23.4%)	76 (17.1%)	101 (20%)

- **Referrals from outside TCH** (outborns) (n) = 178; 38.6 % of admissions
- **Top 5 referring hospitals:**
  - KBH 48 (27.0%)
  - HH 43 (24.2%)
  - Paarl 25 (14%)
  - Worcester 22 (12.4%)
  - Stellenbosch 9 (5%)
- **Referrals for therapeutic hypothermia (TH): total 87 (18.9% of admissions); actually cooled 81**
  - Referrals for **TH** from referring hospitals (n) = 47/87(54%); 15 (17.2%) from HH and 12 (13.8%) from KBH (56.7% of outborn referrals from HH & KBH)
  - Inborn babies treated with therapeutic hypothermia (n) = 38 (46.9%)
  - Total subjected to therapeutic hypothermia (n) = 81 (17.6%) of total admissions for 2017
- Cranial ultrasounds: +/-980 (whole service)
- Neonatal echocardiography: +/-180 (whole service)

Ward G1: Neonatal Unit – Babies born outside TBH

Staff: 2 Consultants (on rotation), 2 Registrar, 1 Medical Officers, 1 Intern

Beds n=30	***2017***	***2016***	***2015***
Admissions	989	1115	1152
Average Ward Stay in Days	10	9	9.2
Average Bed Occupancy %	85%	91%	95.3%
% Growth	-11.3%	-3.2%	-1.3%
Deaths	22 (2.2%)	33 (3%)	36

A9 Paediatric Intensive Care Unit

Staff: Prof P Goussard, Drs N Parker, Dr I Appel, 3 Registrars, Medical Officer

Beds *n=10*	***2017***	***2015***	***2016***

Admissions	728	745	661
Average Hospital Stay in Days	4	4	5
Average Bed Occupancy %	84%	81.6%	82%
% Growth	10.1%	4.6%	-11%
Deaths	79 (10.85%)	55 (7.39%)	62

Outcome of all bookings for elective postop or procedure beds in PICU patients

	Admitted n (%)	**Not admitted (NA) – PICU bed cancelled by anaesthetist**	**NA – not required on day n (%)**	**NA – bed cancelled by specialty**	**NA – PICU Bed not avail**	**NA - Bed refused by PICU as not required**	**NA - Bed refused by PICU, referred NICU**	**NA – nursing short-staffed**	**NA – CRE**	**NA – reason not documented**
Thoracic	45 (24%)	2	8 (15%)	6 (21%)	4 (25%)			1		6
General	54 (29%)		23 (42%)	17 (61%)	9 (56%)	3	3			3
ENT	28 (15%)		12 (22%)	2 (7%)	2 (13%)			1	1	2
Orthopaedic	7 (4%)		1 (2%)							1
Spinal	15 (8%)		2 (4%)	2 (7%)	1(6%)					
Plastics	11(6%)		1 (2%)							
Urology	15 (8%)		3 (5%)	1 (4%)			1			
Post CT / MRI bed booked	1 (1%)		4 (7%)							
Ophthalmology			1 (2%)							
Paed/Haem Oncology	1 (1%)									
Neurosurgery	7 (4%)									2
Bronchoscopy	1 (1%)									
Total 310 patients n (%)	**185 (60%)**	**2 (1%)**	**55 (18%)**	**28 (9%)**	**16 (5%)**	**3 (1%)**	**4 (1%)**	**2 (1%)**	**1 (1%)**	**14 (5%)**

NA = not admitted to PICU
CRE = *Colistin resistant Enterobacteriaceae*

A9 Paediatric High Care Unit

Staff as mentioned above.

Beds *n=4*	**2017**	**2016**	**2015**
Admissions	181	108	220
Average Hospital Stay in Days	4	3.2	3
Average Bed Occupancy %	34%*	25%	45.2%
Deaths	2	3	3

* Due to nursing staff shortages

A9 Tracheostomy Unit

Staff as mentioned above:

Beds n=6	**2017**	**2016**	**2015**
Admissions	109	96	91
Average Bed Occupancy %	62%	44%	69%
Deaths	1	0	1*
Decannulation	10	/	/

Ward G9 Paediatric Pulmonology and Allergy*

Staff: Prof P Goussard, Dr J Morrison, 2 Senior Registrars (Dr L Green & Dr Y Mulambia), 2 Registrars, Shared Medical Officer in G9. *Allergy (largely outpatients service) Prof S Kling, Prof E Zöllner, Dr Y Kooblal (4hrs per week)

Pulmonology Beds *n=10*	***2017***	***2016***	***2015***
Admissions Pulmonology	956	977	925
Average Hospital Stay in Days	4.5	5.6	5.7
Average Bed Occupancy %	93%	94%	92%
% Growth	-2%	9%	9%
Deaths	1	2	1

***Theatre* procedures and Other Activities**

- Bronchoscopies: 415
  Thoracic surgery: 63
  Referrals – 90-110 per month
- 6 Outreach clinical teaching sessions and ward rounds to Karl Bremer hospital

Ward G9 Neurology

Staff: Prof R van Toorn, Prof R Solomons, Dr P Springer, 1 Senior Registrar (Dr T Katangwe), Dr A Thomas(8hrs per week), Dr Y Kooblal(4hrs per week) 2 Registrars

Beds *n=10*	***2017***	***2016***	***2015***
Admissions	421	388	425
Average Hospital Stay in Days	6.0	6.1	6.2
Referral other wards	680	550	420
Average Bed Occupancy %	72%	65%	68%
% Growth	10.8%	-8.8%	20%
Deaths	4	5	3 (1.2%)

Other Activities

- Paediatric EEG from Worcester hospital: 120
- Paediatric and neonatal EEG's from TBH reported by the 2 consultants: 470
- 6 Outreach clinics to Paarl hospital (patients seen): 92
- 4 Outreach clinics Worcester hospital (patients seen): 110
- 2 Clinics at Alta du Toit special school (patients seen): 42

- 8 Clinics Paarl School (patients seen): 80
- Autism Diagnostic Observations Schedule (ADOS) (patients): 12
- Griffith Developmental Scales assessments: 20

Ward G9 Paediatric Endocrinology

Staff: Prof E Zöllner, Dr M Grantham (8 hrs per week), Registrar, and shared intern for G9

Beds *n=5*	***2017***	***2016***	***2015***
Patients admitted	120 Diabetic	95	105 Diabetic
	131 Endocrinology	167	131 Endocrinology
Admission Subtotal	251	262	236
Admissions other wards, day cases	10	14	
Admissions total	261	275	
Ward reviews	6	98	
Average Hospital Stay in Days	6	6	6
Average Bed Occupancy %	81% (not counting outliers)	84% (not counting outliers)	80%
% Growth	-5%	17% (not counting ward reviews)	5%
Deaths	0	0	0

Endocrine tests performed; 52

Ward G10 Gastroenterology

Staff: Prof ED Nel, 1 Senior Registrar (Dr LT Radebe), Registrar, and one Intern.

Beds *n=9*	***2017***	***2016***	***2015***
Admissions	254	185	231
Average Hospital Stay in Days	8	11	8 (median 4.5)
Average Bed Occupancy %	82%	75%	96%*
% Growth	37%	-19%	35%
Deaths	4	5 (2,7%)	5 (2%)

*Clinicom data combined for gastroenterology and infectious diseases

Theatre procedures

- Paediatric Endoscopy: 65
- Adult Colonoscopy: 202

Ward G10 Infectious Diseases Unit

Staff: Prof MF Cotton, Prof H Rabie (HIV Clinic), Dr L Frigati/Dr P Rose, Registrar, Shared Medical Officer for G7

Beds *n=14*	***2017***	***2016***	***2015***

Admissions	353	269	317
Average Hospital Stay in Days	9	14	12.7
Average Bed Occupancy %	82%	75%	96%
% Growth	31%	-15%	30%
Deaths	4	2	2

* Clinicom data combined for gastroenterology, cardiology and infectious diseases

- 10 new referrals per week.
- Telephonic referrals: 100 per week (including outside calls)
- Stewardship rounds: 2 per week.

HIV service:

- Total children followed up: 467
- Total New cases initiating and followed up at TBH: 54 children started (32 infants <12 months)
- Transfers out: 34
- Transfers in: 12

G10 Cardiology

Cross Platform Staff:
Tygerberg Hospital (TBH): Prof J Lawrenson, Dr B Fourie, 2 Registrars

Red Cross War Memorial Children's Hospital (RXH): 2 Consultants, 2 Senior Registrar

Beds *n=10 (G3=5, G10=5)*	***2017***	***2016***	***2015***
Admissions	146	171	194
Average Hospital Stay in Days	*	7	*
Average Bed Occupancy %	*	*	*
Inpatient Echocardiography	845	836	854
Inpatient Consultations	882	875	925
Deaths	2	3	2

* Clinicom data combined for gastroenterology, cardiology and infectious diseases

Worcester Clinic: 157 patients
Paarl Clinic: 84 patients

Ward G3 Oncology & Haematology

Staff: Prof M Kruger, Drs A van Zyl, R Uys, 1 Senior Registrar (Dr Lillian Gesami-Steytler), 2 Registrars

Beds *n=9*	***2017***	***2016***	***2015***	***2014***
New patients Haematology	46	43	42	40
New patients Oncology	60	72	73	56
New patients	106	115	114	96

Total				
Admissions	734	759	678	596
% Growth	-3.2%	11.4%	11.9%	
Average Hospital Stay in Days	5.25	6.05	4.9	5.25
Average Bed Occupancy %	120.5%	148.25%	93.8%	74.3%
Total deaths in G3	12	14	9	7
Expected palliative	8			
Sepsis/other	*4			
Referrals	Oncology 65 Haematology 73			
G3 Day Patients (Haem/Onco)	2094	2806	1905	1421
Chemotherapy administrations	2044	2590	1944	
Bone marrow aspirations and biopsies	108	143	122	83
Intra-thecal chemotherapy procedures	396	263	286	269

*1 Patient died within 24 hours after surgery, necessitating a forensic post mortem.

**G3Ward data

Ward G3 Rheumatology & Immunology

Staff: Prof M Esser, Dr D Abraham (15 hrs per week), Registrar Shared with G3, Shared Medical Officer for G3

Beds *n=4 (shared with Nephrology)*	***2017***	***2016***	***2015***
Admissions (Ward attenders)	110 (82)	90	66
Average Hospital Stay in days	2	3	3
Average bed occupancy %	16%		12%
% Growth	22%	36%	
G3 Day Patients (Rheuma&Imm)	6		
Deaths	0	0	0

Ward G3 Nephrology

Staff: Dr CJ du Buisson, Dr JL Shires – part-time, Senior Registrar (Dr S Irusen), Registrar shared with Rheumatology&Immunology, Shared Intern for G3

Beds *n=5(Beds shared with*	***2017***	***2016***	***2015***

Rheumatology and Immunology)			
Admissions	120	134	240
Average Hospital Stay in days	5	5	5
Average bed occupancy %	31% ***	45%	75%
% Growth	-32% ***	-44%	31%
Deaths	0		0
Renal Biopsies*	23	21	24
Acute Dialysis**	11	12	25
Renal patients outside of G3***	384 9% increase	354 26% increase	282
Referrals****	428	345	313

* Done in C4B Theatre under general anaesthesia

** All done in PICU and NICU

*** Most of our patients are not in our ward, due to acute infections and inborn neonates are cared for in neonatal wards, thus neonates diagnosed antenatally. More patients where seen outside due to lack of space within G3 as we share with oncology and our patients are infectious.

**** These are patients on which only advise needed in the acute phase, not continuous care and referred to outpatient service for further treatment

OUTPATIENT COMPLEX

Subspecialist Clinics

	2017	**2016**	**2015**
Clinics	**Total**	**Total**	**Total**
Haematology	285	307	311
Immunology	229	191	156
Oncology	471	361	376
Pulmonology	1130	1063	1015
Gastroenterology	581	563	605
High-risk Babies	2056	2005	2006
Neurology & Developmental paediatrics	2176	2185	2375
Allergy	550	580	583
Premature Follow-up	262	234	228
Nephrology*	1482	1469	1374
Cardiology	1108	1073	1064
Diabetic	720	703	670
Endocrinology	666	689	661
Rheumatology	367	348	351
Infectious diseases	855	890	983
Genetics	529	393	415
Pharmacy prescriptions	254	170	208
Total	**13721**	**13224**	**13384**

*Centre for Referral for Congenital Anomalies of the Kidney and Urinary Tract.

GENERAL SPECIALIST SERVICES

Total Patient Admissions 2017 (Clinicom data)

GG Short Stay	G2	G7	G8	J3	Total
4567	2142	1136	1057	908	**9810**

Bed Occupancy Rate 2017 (Clinicom data)

GG Short Stay	G2	G7	G8	J3	Total
63%	100%	74%	87%	101%	**85%**

Neonatology

Ward G2 Neonatal Unit – Babies born in TBH

Staff: 2 Consultants (on rotation), 1 Registrar, 3 Medical Officers, 1 Intern (if available)

Beds *n=27*	***2017***	***2016***	***2015***
Admissions	2142	2087	2067
Average Ward Stay in Days	5	5	5
Average Bed Occupancy	105%	104%	105.8%
% Growth	+2.6%	0.96%	-5.3%
Deaths	70 (3.3%)	94 (4.5%)	64 (3%)

Ward J3 Neonatal Unit – Babies born in TBH

Staff: 1 Consultant (on rotation), 1 Registrar, 1 Medical Officer, 1 Intern

Beds *n=25*	***2017***	***2016***	***2015***
Admissions	908	972	1007
Average Ward Stay in Days	10	10	10
Average Bed Occupancy	101%	109%	114%
% Growth	-6.6%	-3.4%	5.9%
Deaths	2 (0.2%)	1(0.1%)	2

Ward G8 Low Care Neonates & Kangaroo-mother Care – Step-down Facility

Staff: 1 Consultant (on rotation), 1 Medical Officer, 2 Interns

Beds *n=30*	***2017***	***2016***	***2015***
Admissions	1057	1013	917
Average Ward Stay in Days	9	10	10.8
Average bed occupancy %	87%	88%	85.4%
% Growth	+4.3%	10.4%	-5.5%
Deaths	0 (0%)	3 (0.3%)	4

Postnatal wards (J5, J2, C2A)

Staff: 1 intern from neonatal pool

3640 clinical contacts/year

Short-stay G Ground: <48-hour Admissions

Staff: Prof S Schaaf, Drs E Malek, L Smit, A Redfern, 2 Registrars, (1 Emergency Medicine Registrar), 2 Medical Officers, 2 Interns

Beds n=24	***2017***	***2016***	***2015***
Admissions	4567	4643	5 943
Average Hospital Stay in Days	1	1	1.0
Average Bed Occupancy %	63%	62%	81%
% Growth	-2%	-22%	- 0%
Average Admissions per day	13	17	16
Deaths	7	16	14
HIV-related Mortality	n.a.	0	2
HIV Exposed-related Mortality	n.a.	2	4

Ward G7 General Paediatrics

Staff: Prof S Kling, Dr H Finlayson, 1 Registrar, 2 Medical Officers, 2 Interns

Beds *n=25*	***2017***	***2016***	***2015***
Admissions	1136	1191	1232
Admissions to HCU (July-December)	134		
Average Hospital Stay in Days	6	6	*6.5
Average Bed occupancy	74%	77%	*88.25%
Increase in Admissions	-4.3%	-3.3%	+5%
Deaths	10	17	12(1%)

*Clinicom data

General Paediatrics: Emergency & Clinics

Clinics	***2017***	***2016***	***2015***
OPD 8am-4pm: Emergency & Routine	**8017 (GG total)** 1203 OPD 6814 Emergency	***7661 (GG total)*** 1643 OPD 6018 Emergency	***9766 (GG total)*** 2 790 OPD 6 976 Emergency
Daily average seen	32	31	39
Annual OPD after hours: 4pm-8am &	4620	4322	4892

weekend – Emergency			
Daily average seen after hours (4pm-8am)	13	12	13
OPD after hours: 4pm-8am %	36%	36%	34%
Total	**12637**	**11983**	**14 658**

2017 Morbidity & Mortality

PPIP data from PPIP database 2017

Total inborn births in TCH (TBH): = **7986**

(Stillbirths = 521) (Total live births = 7465)

Inborn mortality rates at TCH:

- Perinatal Mortality Rate (PNMR) (≥500g) = **80.0/1000**
- Perinatal Mortality Rate (PNMR) (≥1000g) = **46.7/1000**
- Early Neonatal Death Rate (ENNDR) (≥500g) = **15.8/1000**
- Early Neonatal Death Rate (ENNDR) (≥1000g) = **10.1/1000**
- Late Neonatal Death Rate (LNNDR) (≥500g) = **3.9 / 1000**
- Late Neonatal Death Rate (LNNDR) (≥1000g) = **2.2 / 1000**

Inborn Survival Rate for babies born alive at TCH:

- Survival Rate (≥500g) = **98.0 %**
- Survival Rate (≥1000g) = **98.8 %**

Inborn mortality of babies born alive per birth weight category:

Total inborn neonatal deaths on PPIP = **147**

Birth Weight	% Mortality 2017	% Mortality 2016	% Mortality 2015
< 1000g	**26.3** (58/220)	27.6	26.6
1000 to 1499g	**6.5** (31/471)	5.6	4.8
1500 to 1999g	**2.5** (18/722)	2.3	1.4
2000 to 2499g	**1.1** (12/1124)	0.9	0.4
≥2500g	**0.56** (28/4928)	0.2	0.5

Mortality % calculated for each weight category as: number of deaths per number of live births in that weight category for 2017.

Causes of death of babies born in TCH (TBH):

Total inborn neonatal deaths on PPIP = 147

(Total deaths with cause coded on PPIP = **124**)

Cause of Death	% of Total 2017	% of Total 2016	% of Total 2015
Prematurity-related Complications	44.4	61.4	50.0
Infection-related	12.9	10.5	15.2

Peripartum Hypoxia	16.9	7.9	14.1
Congenital Anomalies	19.4	14.9	10.9
Other	6.4	5.3	9.8

% calculated from detailed perinatal death forms on PPIP (124 forms available out of 147 deaths).

% Deaths of babies referred to TCH per weight category:
Total neonatal deaths in babies referred to TCH = 51
(Total neonates referred to TCH = unknown)

Birth Weight	% Mortality 2017 (n= 51)	% Mortality 2016 (n=62)	% Mortality 2015 (n= 56)
<1000g	7.8 (4/51)	25	23.2
1000 to 1499g	17.6 (9/51)	35	28.6
1500 to 1999g	17.6 (9/51)	10	5.3
2000 to 2499	7.8 (4/51)	7.5	8.9
≥2500g	49 (25/51)	25	30.4

% calculated as the number of referred (outborn) deaths in each weight category out of all the referred (outborn) neonatal deaths (all weight categories).

Outborn babies mortality (total numbers) according to referral area of origin:

Geographic Service Area	2017 (n= 51)	2016 (n=62)	2015 (n=56)
Metro East	30	26	30
Winelands (Paarl area)	11	14	22
Overberg (Worcester drainage area)	10	5	4
Unknown	0	17	

Geographic distribution of Outborn Neonatal Mortality according to PLACE OF BIRTH:

	≥2500g	2000 - 2499g	1500 - 1999g	1000 - 1499g	<1000g	Total
Helderberg	4	1		1		6
Vredendal			2			2
Macassar	3			2		5
KBH	7			1		8
Symphony				1		1
Stellenbosch	2		1			3
ERH	1				1	2
Delft	1			1		2
Worcester		2		2		4
KDH	1					1
Caledon	1				2	3
Paarl	1		2	1		4
Ceres			1			1
Porterville			1			1

KFT	1		1			2
Robertson	1					1
Elsies	1		1		1	3
BFW	1					1
Piketberg		1				1
TOTAL	**25**	**4**	**9**	**9**	**4**	**51**

CHPIP MORTALITY for all sub-specialist paediatric wards (2017)

Audited deaths CHPIP MORTALITY for all paediatric wards (2017)

CHPIP Mortality	**Total Admissions/ Tally**	**% Total**	**Deaths**	**Hosp Mortality Rate**	**Male**	**Female**
*0-28 days	315	4.7	6	5.0	*4*	*2*
28 days – 1 year	2016	30.5	46	38.6	*18*	*28*
1-5 year	2556	38.7	36	30	*17*	*19*
5-13 years	1427	21.6	24	20	*11*	*13*
13-18 years	290	4.3	6	*5*	*5*	*1*
Unknown			1	0.8		1
Total	**6604**		**119**		**55**	**64**

*Please note: Excluding neonatal deaths reported under the PPIP section

Referral

Referring facility	**Number**	**%**
Not referred/not noted	**43**	
Community clinics		
Delft CHC	7	41
Kraaifontein CHC	6	35
Ruyterwacht CHC	1	5
Site B CHC	1	5
Macassar CHC	1	5
Grabouw CHC	1	5
Bloekombos CHC	1	5
Macassar CHC	1	5
St Josephs Home	1	5
Total	**17**	
Level 1 Metro		
Khayelitsha Hospital	14	36
Helderberg Hospital	12	31
Karl Bremer Hospital	7	18
Eerste River Hospital	5	13
Total	**38**	
Level 1 Outside Metro		
Stellenbosch Hospital	2	33

Robertson Hospital	1	16
Vredendal Hospital	1	16
Caledon Hospital	1	16
Louis Leipoldt Medi-Clinic Private Hospital	1	16
Total	**6**	
Referral from Level 2		
Worcester Hospital	8	61
Paarl Hospital	5	46
Total	**13**	

Main Causes of Death in Children*	**Number**	**%**
Septicaemia, possible serious bacterial infection	18	15.1
Respiratory system	15	12.6
Nervous system	14	11.8
Heart failure, Pulmonary Oedema	11	9.2
Pneumonia, ARI	10	8.4
Tumours	8	6.7
Acute diarrhoea, hypovolaemic shock	6	5
Cirrhosis, Portal hypertension, Liver Failure, Hepatitis	4	3.4
Other cardiology system	4	3.4
Ill-defined/unknown cause of mortality	3	2.5
TB: Meningitis	2	1.7
Genito-urinary system	2	1.7

*Please note: Other co-morbidities not reflected.

HIV - mortality	**Number**	**%**
Negative	87	73.1
Unknown	15	12.6
Exposed status not known	6	5
Infected	5	4.2
Not tested (not indicated)	3	2.5
No result	3	2.5

Mortality according to Weight Category

Weight Category	**Number**	**%**
Normal	76	63.9
UWFA	19	16
Marasmus	12	10.1
Unknown	8	6.7
Marasmic-Kwashiorkor	2	1.7
Over weight for age	1	0.8
Kwashiorkor	1	0.8

Mortality per Ward Audited deaths only (from available CHPIP data)

Ward	**Number**	**%**

Paediatric Intensive Care Unit	76	63
Oncology (G3)	12	10%
Acute Care (GG)	9	7.56
General Paediatrics (G7)	9	7.56
Infectious Diseases (G10)	5	4.2
Gastroenterology (G10)	4	3.36
Neurology (G9)	4	3.36
Neonatology	4	3.36
Cardiology (G10)	1	0.84
Total	**119**	

Mortality in the paediatric wards and of children >29 days of age in the neonatal service

Ward name	**Freq**	**% including neonatal service**	**% excluding neonatal service**
A9 Paediatric High Care & tracheostomy	3	2	2
A9 Paediatric ICU	75	50	60
G10 all firms	12	8	10
G3 Paediatric Oncology	12	5	7
G7 General Paediatrics	10	6	8
G9 Paediatric all firms	5	3	4
GG Paediatric Emergency	7	4	6
Neonatal service older than 29 days died in neonatal service	23	16	
Died outside of paediatrics	5	3	4
Total	**148**		
Total excluding deaths in neonatal service	**125**		

Table of Length of Stay*

Ward	**Mean**
G10 (Combined speciality ward)	8
G3 (Combined speciality ward)	6
G7 General paediatrics	6
G9 (Combined speciality ward)	5
A9 High Care	4
A9 Intensive Care Unit	4
GG Emergency service	1

*Clinicom data

Infrastructure Development

Tygerberg Children's Hospital Trust Contribution to Infrastructure

DATE	SUPPLIER	EQUIPMENT	AMOUNT
10/04/2017	Dräger South Africa (Pty) Ltd	Resuscitaire for Paediatric Ophthalmology	R157 974,08
29/09/2017	Medtronic Africa (Pty) Ltd	Two Bedside Oxygen Saturation Monitors for B5 Eye Clinic	R29 613,23
29/09/2017	AC Flooring Services CC	Supply and installation of flooring for Seminar Room C3A	R29 183,90
18/10/2017	De Klerk Painters & Maintenance	50% payment for painting of C3A and corridors	R10 495,00
TOTAL			R227 266,21

Donations received by Tygerberg Children's Hospital Wards

DATE	SUPPLIER	EQUIPMENT	AMOUNT
Monthly	Dischem	Goods for G3 Oncology	R 7500 per month
28 March 2017	Ms Logandree Gounden (Memory of late father)	Monetary for G3 Oncology	R 10 000
18 May 2017	Dancers with Heart	Monetary for G3 Oncology	R 4000
May 2017	Mrs Elizma Bellingan (ex parent)	Kangaroo chairs for parents x6 for G3 Oncology	Unknown
May 2017	Mrs B Lotz (parent)	Cleaning materials for G3 Oncology	Unknown
2017	Mrs D Erasmus(parent)	Kettle, Toaster for G3 Oncology	Unknown
2017	Mrs Mullins (parent)	Kettle for G3 Oncology	Unknown
28 September 2017	Ilze Noble (Amman, Jordan) Father died of Cancer	Monetary for G3 Oncology	R 5000

September 2017	Rotary Club, Oostenberg District	Upgrade of A9 counselling room	Unknown
Oct, Nov 2017	Auto Armour (Rian Malan)	Tinting Windows for G3 Oncology	Unknown
	Cupcakes of Hope Ms S Cipriano	Monetary for G3 Oncology	R 10 000
October 2017	Aneesa Parker & Friends	2 Paediatric ICU beds	R 80 000
Nov/Dec 2017	Mrs B Lotz (parent)	Pillows for G3 Oncology	Unknown

Part 2

Community Outreach Programmes/Community Service and Interaction & Partnerships

Expert Members

Prof Mariana Kruger

- Member of an Expert Committee of the Medicines Control Council: Clinical Committee since November 2014
- Member of the Executive Committee of the South African Children's Cancer Study Group (SACCSG)
- Member Council of College of Paediatricians since 2014
- Member of the Provincial Clinical Governance Committee (PCGC)
- Member of the Senate Research Ethics Committee of Stellenbosch University
- Member of the Research Ethics Executive Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University

Prof Sharon Kling

- Colleges of Medicine of South Africa (CMSA)
    - President, Council of College of Paediatricians since 2014
    - Senator, CMSA, for the triennium since 2011
    - Member of Financial and General Purposes Committee since 2011
    - Member of Management Committee, Financial and General Purposes Committee, 2013 – date
- Ethics accreditor, CPD Committee, Faculty of Heath Sciences.
- Vice-chair, Undergraduate Research Ethics Committee since 2015
- Member of the Research Ethics Executive Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University
- Member, Clinical Ethics Committee Tygerberg Hospital (2002 – 2004 and 2009 to current).
- Allergy Society of South Africa (ALLSA)
    - Member of Executive Committee since 1998
    - Chairman, Research Subcommittee (2011 to date)

Prof Anneke Hesseling

- NRF SARChi Chair in Paediatric Tuberculosis.

Prof Cotton

- Member of the Clinical Guideline Development Group (GDG) to support the update of the World Health Organization Consolidated Guidelines on the use of antiretroviral drugs for treating and preventing HIV infection
- WHO HIV/TB Task Force Advisor

Prof Beyers

- National Department of Health
- POPART Zambia & RSA

Prof HS Schaaf

- Board of Directors and Chairperson of Adult and Child Lung Health section, The Union (International Union Against Tuberculosis and Lung Disease)
- Expert on ATS/CDC committee for new TB guidelines
- MDR-TB Review Board Western Cape
- Member of the Subcommittee C of the Research Committee, Faculty of Medicine and Health Sciences

Dr Barend Fourie

- Safety representative on Health and Safety Committee, Faculty of Medicine and Health Sciences

Profs A Bekker & P Goussard

- Health Research Ethics Committee, Faculty of Medicine and Health Sciences

Prof A Bekker

- International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) P1106 vice-chair
- CDC: Tuberculosis Trials Consortium (TBTC) Tuberculosis and Pregnancy Working Group - membership

Drs GTJ Kali& & S Holgate

- USANA executive committee members – organiser and treasurer respectively

Prof R van Toorn

- PANDA executive committee member –treasurer

Outreach

International

- Profs PB Hesseling & M Kruger – Childhood cancer Cameroon

Regional and District

- Worcester – Profs R van Toorn, R Solomons, J Lawrenson & dr C du Buisson
- Paarl – Profs P Goussard, H Rabie, R van Toorn, R Solomons, HIV outreach, Dr Frigati
- Delft - Drs L Smit, R Gioio (HIV outreach)
- Helderberg – Dr T Wessels; Perinatal – Dr H Hassan, Dr Frigati, (HIV outreach)
- Khayalitsha district hospital – Prof H Rabie
- Eersterivier – Drs H Finlayson (HIV outreach), M du Preez
- Ikwezi clinic HIV outreach
- Bishop Lavis clinic, HIV outreach
- Grabouw CHC HIV outreach
- Kraaifontein CHC HIV outreach
- City of Cape Town - DTTC
- DTTC - skills development in the community
- Karl Bremer Hospital, Haemophilia, Childhood Cancer - Dr A van Zyl; Perinatal – Dr H Hassan, Prof S Kling (General Paediatrics) and Dr H Finlayson (Antibiotic Stewardship)

- George – Dr B Fourie, Prof J Lawrenson
- East London – Prof J Lawrenson
- Brooklyn Chest Hospital – Prof HS Schaaf, Dr H Finlayson
- Paarl School for Children with Cerebral Palsy, Brackenfell---Dr Cilla Springer

Media Exposure

TV/Radio Interviews:

- Prof Mariana Kruger: RSG – Gesondheid: Invited speaker – Leukemia, 13 February 2017

Articles:

Name of publication: Spiegel Online
Name of article: Ein rätselhafter Patient: Verschluckt (Prof Pierre Goussard)
Date: 16 April 2017

Name of publication: Stellenbosch University Webpage
Name of article: Paediatricians share skills with colleagues in Eastern Cape (Drs Gugu Kali, Lunga Mfingwana & Julie Morrison)
Date: 5 July 2017

Name of publication: FMHS Media Review
Name of article: SA boy's HIV in remission for over 8 years after antiretroviral treatment ended (Prof Mark Cotton)
Date: 24 July 2018

Name of publication: The Washington Post
Name of article: New hope for HIV cure as child remains virus-free years after final treatment (Prof Mark Cotton)
Date: 24 July 2017

Name of publication: Netwerk24
Name of article: Operasie om vroeggebore baba se long te red 'n eerste in SA (Prof Pierre Goussard)
Date: 27 July 2017

Name of publication: Tygerburger
Name of article: Cake auction raises R48 325 (Tygerberg Children's Hospital Trust)
Date: 30 August 2017

Name of publication: Stellenbosch University Webpage
Name of article: PhD research aided by DoH scholarships (Drs Lisa Frigati & Muhammad Osman)
Date: 20 September 2017

International visitors:

Prof Kevan Jacobson, Head, Division of Paediatric Gastroenterology, Hepatology & Nutrition at the University of British Columbia 25 January – 10 February 2017):

- To develop closer ties on a clinical, educational and research level between Stellenbosch University and the University of Columbia

Prof Paul Rogers, Clinical Professor, University of British Columbia & BC Children's Hospital (29 March – 19 April 2017):

- Provided expert advice as co-supervisor towards the planning of the PhD of Dr Anel van Zyl titled: 'Long-term follow-up and care of childhood cancer survivors in South Africa', under my supervision.
- Discussed the planned PhD of Dr Judy Schoeman titled: 'Nutritional interventions in children with cancer.'
- Led training rounds in Tygerberg Hospital for our Paediatric registrars.
- Led training rounds in Tygerberg Hospital for our senior registrars in Paediatric Oncology

Dr Paula Mahon, Clinical Assistant Professor, Department of Nursing, University of British Columbia (19 April 2017):

- Led two discussion groups in Paediatric Intensive Care and Neonatal Intensive Care at Tygerberg Hospital respectively towards understanding and exploration of nursing issues.

Prof Christiane de Boeck – Professor, Kinderziekenhuis, UZ Leuven (21 August 2017)

- Discussions with Prof M Kruger regarding under- and postgraduate exchange programmes.

Prof Mirjam M van Weissenbruch, Professor of Neonatology, Department of Pediatrics, subdivision IC neonatology, VU University Medical Center, Amsterdam, Netherlands (19 September 2017)

- NRF-Nuffic PhD scholarship collaboration with Prof Adrie Bekker, Dr Lizel Lloyd and Dr Angela Dramowski

Prof Marceline Tutu-Van Furth & Dr Martijn van der Kuip: Department of Pediatric Infectious Diseases-Immunology, VU Medical Center, Amsterdam, The Netherlands (9 October 2017)

- Joint Stellenbosch University and VU University Amsterdam – NRF Desmond Tutu Doctoral Programme for PhD candidates, Drs Yajna Kooblal and Dan Zahari.

Prof Mary Rutherford – Professor in Perinatal Imaging, Imperial College of Science, Technology and Medicine, Hammersmith Campus

- PhD supervision of Dr Gugu Kali

Part 3

Teaching & Training

Education-related Activities

Postgraduate Students

Successful PhD Candidates

- **Dr P Bock:** Title: Impact of a Universal Test and Treat strategy on clinical outcomes amongst HIV - infected adults in South Africa: Supervisor: Prof N Beyers, Dr S Fidler
- **Dr A Dramowski:** Title: Determinants Of Healthcare-Associated Infections Among Hospitalised Children. Supervisors: Proff MF Cotton, A Whitelaw
- **Mr R Dunbar:** Title: How can virtual implementation modelling inform the scale-up of new molecular diagnostic tools for tuberculosis? Supervisor: Prof N Beyers, Mr I Langley
- **Dr F Marx**: Title: Mathematical modelling to project the impact of interventions targeted to previously treated individuals on the trajectory of the tuberculosis epidemic in high tuberculosis prevalence settings Supervisors: Prof N Beyers, Prof T Cohen
- **Dr S-A Meehan**: Title: The contribution of a community based HIV counselling and testing (HCT) initiative in working towards increasing access to HIV counselling and testing in Cape Town, South Africa. Supervisors: Proff N Beyers, R Burger
- **Dr P Naidoo**: Title: Evaluating the Impact of an Xpert® MTB/RIF- based TB Diagnostic Algorithm in a Routine Operational Setting in Cape Town. Supervisors: Prof N Beyers, Dr C Lombard

Enrolled PhD students

- **Dr K du Preez**: Title: Complementary surveillance strategies and interventions to inform a tuberculosis care cascade for children. Supervisors: Proff AC Hesseling, HS Schaaf and Dr P Naidoo
- **Dr AJ Garcia-Prats**: Title: Addressing critical knowledge gaps to improve and shorten MDR-TB treatment regimens in children. Supervisors: Profs Anneke Hesseling and Simon Schaaf
- **Dr GTJ Kali**: Title: A comparative study of neuroprotective strategies in neonatal hypoxic ischaemic encephalopathy. Supervisors: Prof J Smith, M Rutherford
- **Dr Y Kooblal:** Title: The relationship of body composition on nutritional and immunological status in childhood tuberculosis. Supervisors: Prof Ronald van Toorn, Dr Martijn van der Kuip and prof Marceline Tutu van Furth

- **Dr B Laughton:** Title: The effects of early versus delayed antiretroviral treatment on the short and long term neurodevelopmental outcome of children who are HIV positive. Supervisor: Prof MF Cotton, Prof M Kruger
- **Dr M Osman:** Title: TB-associated mortality in South Africa: longitudinal trends and the impact of health system interventions. Supervisors: Prof AC Hesseling and Dr P Naidoo
- **Dr H Rabie**: Title: Pharmacokinetics and therapeutic outcomes of children with tuberculosis/HIV co-infection treated with lopinavir/ritonavir and a rifampicin-containing anti-tuberculosis regimen. Supervisors: Proff MF Cotton, HS Schaaf, RP Gie
- **Me J Schoeman:** Title: Nutritional status of children at cancer diagnosis and during treatment, with a focus on the association with their clinical outcome . Supervisors: Profs M Kruger, Elena J. Ladas and Paul Rogers.
- **Dr P Springer:** Neurodevelopmental Outcome of the HIV exposed but uninfected Infant and evaluation of a developmental screening tool. Supervisors: Prof Mariana Kruger, Prof Christopher Molteno
- **Dr J van Heerden**: Title: Neuroblastoma In Low And Middle Income Countries. Supervisors: Prof M Kruger
- **Dr L van Wyk:** Title: Non-invasive cardiac output monitoring in preterm infants . Supervisors: Prof Johan Smith, Dr John Lawrenson and Prof Willem-Pieter de Boeck
- **Dr A van Zyl:** Title: Long-term follow-up and care of childhood cancer survivors in South Africa. : Supervisors: Profs M Kruger and P Rogers
- **Dr E Walters**: Title: Novel diagnostic strategies and markers of treatment response for paediatric pulmonary tuberculosis. Supervisors: Proff AC Hesseling, RP Gie
- **Dr D Zahari:** Title: New insights in the pathogenesis of central nervous system (CNS) granulomatous inflammation in tuberculous meningitis**.** Supervisors: Prof M Kruger, Dr Martijn van der Kuip and prof Marceline Tutu van Furth.

Successful MMed(Paed) Candidates

- **Dr C Jacobs:** Title: Necrotising Pneumonia: Retrospective review. Supervisors: Proff P Goussard, RP Gie
- **Dr FP van der Westhuizen**: Title: The identification of risk factors for adverse clinical outcome in patients aged three months to five years, admitted to Worcester Hospital with acute gastroenteritis. Supervisors: Dr A Slogrove, Prof M Kruger
- **Dr K Carceek:** Title: Outcomes of children admitted to TBH with Myocarditis and dilated cardiomyopathy between 1 January 2008 and 30 May 2014. Supervisors: Profs H Rabie & J Lawrenson
- **Dr S Irusen**: Title: Paediatric bacterial urinary tract infections in the South African context. Supervisors: Dr C Du Buisson & Prof H Rabie

- **Dr A Lakhan**: Title: The role of cytomegalovirus in children with hypoxic pneumonia admitted to a paediatric intenstive care unit. Supervisors: Prof P Goussard & Dr N Parker
- **Dr M Roos**: Title: Childhood tuberculosis meningitis: A thirty year review of clinical and cerebrospinal fluid factors associated with bacteriological confirmation. Supervisors: Profs R Van Toorn & R Solomons
- **Dr C Smit**: Title: Incidence and outcomes of Primary Malignant Thoracic Neoplasms – A 31-year review at Tygerberg Children's Hospital, South Africa, 1983-2014. Supervisors: Prof P Goussard & Dr A Van Zyl
- **Dr A van Eck**. Title: A Retrospective Review of the Outcomes of Gastroschisis at a Tertiary Hospital in Cape Town. Supervisors: Dr S Holgate & Prof E Nel

Colleges of Medicine of South Africa (CMSA)

- **Certificate in Developmental Paediatrics**
  - Dr Angeline Thomas
- **Certificate in Medical Oncology**
  - Dr Elly Madzia
- **Certificate in Paediatric Cardiology**
  - Dr Lenise Swanson
- **Certificate in Paediatric Gastroenterology**
  - Drs Joahnah Ikobah, Simone Maclou
- **Certificate in Paediatric Endocrinology**
  - Dr Michele Grantham
- **FC Paed (SA) Part II**
  - Drs Elri du Plooy, Carine Smit, Ilhaam Abraham, Michelle Roos, Brad Wentzel

Undergraduate Students

99% pass rate (2016 = 99%)

Education-related Activities

- The Education Committees of the Department comprised as follows:
  - Undergraduate: Dr L Smit (Chairperson), Dr A Redfern (secunde)
    - MBChB II: Drs R Uys, E Malek, S Holgate, L LLoyd
    - Early rotation: Drs I Appel, L Frigati, prof H Rabie, H Hassan, Drs B Makongwana, A Thomas, M Morkel, Sr L Yzelle
    - Middle rotation: Drs N Parker, B Fourie, C du Buisson, H Finlayson, G Kali, A Bekker

        - SI: Prof R Solomons, Drs M du Preez, L Smit, A van Zyl, S Holgate, C Springer, Prof E Zöllner, Drs M Morkel
        - Remedial: Dr M Morkel, Sr L Yzelle
        - Elective students: Drs H Finlayson, I Appel, Prof M Kruger
    - Postgraduate: Proff R van Toorn (chairperson), A Bekker, M Kruger, ED Nel, H Rabie, P Goussard, HS Schaaf, Dr G Kali
    - PhD: Proff M Kruger (Chairperson), MF Cotton, AC Hesseling, HS Schaaf, J Smith
- All consultants are involved with under- and postgraduate teaching on a daily basis. Additional education activities included:
- External examiners at universities in South Africa:
    - Undergraduate:
        - Dr FCP du Preez, B Fourie: University of the Free State
        - Prof R Solomons: University of Kwazulu-Natal
        - Dr A Redfern: MEDUNSA
- Senior registrars in training:
    - Neonatology: Drs N Paulse, Dr M Kariuki (Supernumerary from Kenya), Dr K Onwona-Agyeman (Supernumerary from Ghana)
    - Paediatric Oncology: Drs EI Madzia (supernumerary from Gauteng Department of Health), F Tchintseme Kouya (Supernumerary from Cameroon), L Gesami-Steytler (Supernumerary from Namibia)
    - Paediatric Cardiology: Dr L Swanson
    - Developmental Paediatric: Dr A Thomas, with Life Healthcare Scholarship
    - Paediatric Rheumatology: Dr Abraham
    - Paediatric Endocrinology: Dr M Grantham
    - Paediatric Pulmonology: Drs Y Mulambia, L-L Green
    - Paediatric Neurology: Dr T Katangwe
    - Paediatric Gastroenterology: Dr JM Ikobah, sponsored by a Nestle Nutrition Institute Fellowship endorsed by the European Society of Paediatric Gastroenterology
- Lectures at courses
    - Dr C du Buisson
        - Active 3 day workshop, Queens Hospital, Blantyre. Taught general medical officers and pediatricians (as well as adult physicians), nurses how to assess, manage children with acute and chronic kidney disease. When to intervene with dialysis, how to insert the catheters (using a make shift model) and start and continue dialysis.
        - Active 5 day workshop where Doctor (mostly paediatrician and some adult nephrologists) together with a nurse, from all over Africa. Ivory coast to Namibia. They are first taught how to recognize then manage renal disease. Then after the first day its hands on.
- South African Research Ethics Training Initiative (SARETI) UKZN, funded by Fogarty International Fogarty International Center (FIC) of the National Institutes of Health (NIH), grant number 6R25TW001599-13: Prof M Kruger (Co-principal Director)

Part 4

Achievements and Highlights

Prof Mariana Kruger appointed as Honorary Professor in the School of Applied Human Sciences (Discipline of Psychology), University of KwaZulu-Natal from 1 March 2017.

Prof John Lawrenson appointed as Associate Professor from 1 April 2017.

Professor Adrie Bekker and **Steve Innes** were appointed to associate professors from 1 July 2017.

NRF ratings:
New:

- Prof AC Hesseling B1

Existing:

- Prof MF Cotton A2
- Prof PR Donald A2
- Dr A Dramowski C3
- Prof HS Schaaf A2
- Prof EWA Zöllner C3
- Dr A Bekker C3
- Prof J Smith C2
- Prof R Van Toorn C2
- Prof P Goussard C2
- Prof PB Hesseling C2
- Dr H Rabie C3
- Dr S Innes Y2
- Prof R Solomons Y2

The **sixth annual Here by Lungs Congress,** organised by Profs P Goussard and J Smith, was held on 16-17 March 2017 at Lanserac, Stellenbosch. It included invited overseas speakers: Prof Andy Bush (Professor of Paediatrics and Head of Section (Paediatrics, Imperial College London), Prof Adnan Custovic (Clinical Professor of Paediatric Allergy at Imperial College London), Prof Christian Speer (Chairman and Director of the University Children's Hospital in Würzburg, Germany), and Prof Hartmut Grasemann (Professor at The Hospital for Sick Children, Essen, Germany).

The **fourth annual PhD Lectures** was held on Wednesday 30 August 2017 in the Faculty with Dr Pren Naidoo, Prof Adrie Bekker and Dr Angela Dramowski presenting.

The **third Annual Paediatric Registrar Research Day** was held on Wednesday 30 October 2017here in the Faculty where 6 registrars presented their research. The prize for best research was awarded to Dr Madelein Grobbelaar and Mia van Velden.

The **seventh annual Paediatric Academic Day of Excellence** was held on Friday 1 November 2017 in the Faculty.

Grants:

Dr Lisa Frigati

South African Medical Research Council (SAMRC) Scholarship of R627 568 towards her PhD entitled: '*HIV-infected Adolescent Health: Spectrum of disease and progression over time in adolescents on ART*' under the supervision of Proff Mark Cotton, Heather Zar and Landon Myer.

Prof Adrie Bekker

The Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) Growing the Leaders of Tomorrow Fellowship Programme of the International AIDS Society (IAS) awarded funding of a total amount of US $70,000.00 to Dr Bekker for the research project entitled "Pharmacokinetic and safety characteristics of nevirapine and lopinavir/ritonavir in HIV-exposed and infected low birth weight infants".

Dr Amy Slogrove

The Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) Grant Programme of the International AIDS Society (IAS) awarded funding of a total amount of US$149,998.89 for the research project entitled "Does initiation of antiretroviral therapy prior to immune suppression protect against maternal hypertensive disorders in pregnancy and associated adverse birth outcomes in HIV-infected women?"

Fogarty International Center of the National Institutes of Health under Award Number K43TW010683 for research project entitled: The effect of hypertensive disorders in pregnancy and HIV-infection on maternal, birth and infant outcomes in South Africa of an amount of $112 530 per annum over 5 years.

Dr Angela Dramowski

Fogarty International Center of the National Institutes of Health under Award Number K43TW010683 for research project entitled: Developing a care bundle for neonatal sepsis prevention in low-resource settings of an amount of $112 530 per annum over 5 years.

Prof Ekkehard Zöllner

Astra Zeneca Award from the SA Thoracic Society to partially fund the project entitled "Genetic predictors of hypothalamic-pituitary-adrenal suppression in school age children treated with corticosteroids at the allergy clinics of the Cape Peninsula." Value: R 100 000.00.

Publications

Journal Articles (subsidised)

1. AFUNGCHWI GM, HESSELING PB, LADAS EJ. The role of traditional healers in the diagnosis and management of Burkitt lymphoma in Cameroon: understanding the challenges and moving forward. *BMC Complementary and Alternative Medicine* 2017; **17**:209.
2. ALLWOOD BW, GILLESPIE R, GALPERIN-AIZENBERG M, BATEMAN M, OLCKERS H, TABORDA-BARATA L, CALLIGARO G, SAID-HARTLEY Q, VAN ZYL-SMIT R, COOPER CB, VAN RIKXOORT E, GOLDIN J, BEYERS N, BATEMAN ED. Obstructive pulmonary disease in patients with previous tuberculosis: Pathophysiology of a community-based cohort. *SAMJ SOUTH AFRICAN MEDICAL JOURNAL* 2017; **107**(5):440-445.
3. ANDRONIKOU S, GOUSSARD P, SORANTIN E. Computed tomography in children with community-acquired pneumonia. *PEDIATRIC RADIOLOGY* 2017; **47**(11):1431-1440.
4. Araujo da Silva AR, Albernaz de Almeida Dias DC, Marques AF, Biscaia di Biase C, Murni IK, Dramowski A, Sharland M, Huebner J, Zingg W. The role of antimicrobial stewardship programmes in children: a systematic review. J Hosp Infect. 2017; pii: S0195-6701(17)30447-4.
5. BOCK PA, COX HS. Acute care – an important component of the continuum of care for HIV and tuberculosis in developing countries. *ANAESTHESIA* 2017; **72**:147-150.
6. BOCK PA, PHIRI C, PIWOWAR-MANNING E, KOSLOFF B, MANDLA N, YOUNG A, JAMES A, SCHAAP AB, SCHEEPERS M, DONNELL D, GRIFFITH S, EL-SADR W, SHANAUBE K, BEYERS N, HAYES R, FIDLER S, AYLES H. Understanding low sensitivity of community-based HIV rapid testing: experiences from the HPTN 071 (PopART) trial in Zambia and South Africa. *Journal of the International AIDS Society* 2017; **20**(Suppl6):21780.
7. BOND V, FLOYD S, FENTY J, SCHAAP AB, GODFREY-FAUSSETT P, CLAASSENS MM, SHANAUBE K, AYLES H, HARGREAVES JR. Secondary analysis of tuberculosis stigma data from a cluster randomised trial in Zambia and South Africa (ZAMSTAR). *INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE* 2017; **21**(11):S49-S59.
8. BULABULA ANH, DRAMOWSKI A, MEHTAR S. Maternal colonization or infection with extended-spectrum beta-lactamase-producing Enterobacteriaceae in Africa: A systematic review and meta-analysis. *INTERNATIONAL JOURNAL OF INFECTIOUS DISEASES* 2017; **64**:58-66.
9. CLAASSENS MM, DUNBAR R, YANG B, LOMBARD C. Scanty smears associated with initial loss to follow-up in South African tuberculosis patients. *INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE* 2017; **21**(2):196-201.
10. CLAASSENS MM, VAN SCHALKWYK C, FLOYD S, AYLES H, BEYERS N. Symptom screening rules to identify active pulmonary tuberculosis: Findings from the Zambian South African Tuberculosis and HIV/AIDS Reduction (ZAMSTAR) trial prevalence surveys. *PLoS One* 2017; **12**(3):e0172881.
11. COHEN C, VON MOLLENDORF C, DE GOUVEIA L, LENGANA S, MEIRING S, QUAN V, NGUWENEZA A, MOORE DP, REUBENSON G, MOSHE M, MADHI SA, ELEY B, HALBAUER U, FINLAYSON H, ET AL . Effectiveness of the 13-valent pneumococcal conjugate vaccine against invasive pneumococcal disease in South African children: a case-control study. *Lancet Global Health* 2017; **5**:e359-69.

12. CORDES JL, STANGL A, KRISHNARATNE S, HODDINOTT G, MATHEMA HT, BOND V, SEELEY J, HARGREAVES JR. Trends in responses to DHS questions should not be interpreted as reflecting an increase in anticipated stigma in Africa. *Journal of Acquired Immune Deficiency Syndromes* 2017; **75**(1):e22-e23.
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1. ABRAHAM DR. A portrait of my life with Lupus. Joint Ability 2017; 1:4-5.
2. DU PLESSIS L, DETJEN AK, HESSELING AC, DU PREEZ K. Operational implementation and impact of the Union's online childhood TB training course in South Africa. Public Health Action 2017; 7(2):175-177.
3. GIE RP. Reading chest radiographs in children suspected of having pulmonary tuberculosis. Residência Pediatrica 2017; 7(suppl 1):20-26.
4. MEEHAN S, DRAPER HR, BURGER R, BEYERS N. What drives 'first-time testers' to test for HIV at community-based HIV testing services?. Public Health Action 2017; 7(4):304-306.
5. MEEHAN S, ROSSOUW L, SLOOT R, BURGER R, BEYERS N. Access to human immunodeficiency virus testing services in Cape Town, South Africa: a user perspective. Public Health Action 2017; 7(4):251-257.
6. SMIT EJ, MEYER R, CRAFFORD I, PARRIS DL. Exploring the experience of postgraduate students in their transition from a health science to an educational scholarship in an African university setting. SOTL in the South 2017; 1(1):78-90.
7. VANKER A, BARNETT W, WORKMAN L, NDURU PM, SLY PD, GIE RP, ZAR H. Early-life exposure to indoor air pollution or tobacco smoke and lower respiratory tract illness and wheezing in African infants: a longitudinal birth cohort study. Lancet Planet Health 2017; 1:e328-36.

Chapters in Books

1. KLING S, KRUGER M. Paediatric ethics. In: MOODLEY K (ed.) Medical ethics, law and human rights, Van Schaik Publishers, Pretoria, South Africa, 2017: 215-235.
2. MOODLEY K, MOOSA MR, KLING S. Justice. In: MOODLEY K (ed.) Medical ethics, law and human rights, Van Schaik Publishers, Pretoria, South Africa, 2017: 91-104.

Courses & Conferences Attended and/or Participated

NAME	COURSES/CONFERENCES ATTENDED	DATES	TYPE OF TRAINING	LEVEL	PROVIDER
Appel,I	1. INPAT Course, Italy	1. 4- 7 Apr 2017	1. Course	1. Advanced	1. INPAT
Bekker,A	1. ADA Summer school 2. 61st Annual Academic Day 3.USANA Conference 2017 4. Fetal MRI Symposium 2017	1. 9- 13 Jan 2017 2. 30 Aug 2017 3. 14 - 17 Sept 2017 4.17 Nov 2017	1. Course 2. Course 3. Conference 4. Symposium	1. Advanced 2. Level 1 3. Level 1 4. Level 1 & 2	1.SU - African Doctoral Academy 2. US 3.MYCPD Discovery 4. Med clinic Panorama
Cotton,M	1. Paeds HIV Workshop & IAS,Paris 2. WSPID 2017,Shenzen,China	1. 19 - 28 July 2017 2. 27 Nov - 01 Dec2017	1. Workshop 2. Conference	1. Advanced 2. Advanced	1. Paeds HIV & IAS 2. WSPID 2017
Donald, PR	Keynote speaker (A brief history of tuberculosis transmission research between 1880 and 1940: yesterday, today and tomorrow) at the Halting TB transmission in HIV endemic settings Conference, Vineyard Hotel, Newlands 48TH Union World Conference on Lung Health, Guadalajara, Mexico	1-2 June 2017 11 October 2017			
Du Preez,J	1. GCP Course	1.26 - 27 Jan 2017	1. Congress	1. Advanced	1. US
Finlayson, H	1. FIDDSA Conference, Cape Town	1. 09 - 10 Nov 2017	1. Conference	1. Advanced	1. FIDDSA
Fourie,B	1. Attending a Conference in Kenia	1. 30 Nov - 01 Dec 2017	1. Conference	1. Advanced	1. .....
Gesami-Steytler,L	1. SACCGS Working group,STIAS,Stellenbosch	1. 19 May 2017	1. Workshop	1. Advanced	1. US
Holgate.,S	1. USANA Conference,JHB	1. 14 - 15 Sept 2017	1. Congress	1. Advanced	1. USANA
Kali,G	1. USANA Conference,JHB	1. 14 - 15 Sept 2017	1. Congress	1. Advanced	1. USANA
Kling,S	1. Child`s rights and Child Law short Course 2. ALLSA Congress,PE 3. College of Paediatric	1. 2. 14 - 15 Sept 2017 3. 10 Nov	1. Short Course 2. Congress 3. Workshop	1. Advanced 2. Advanced	1. UCT 2. ALLSA 3. College of Paediatric FCPaed

	FCPaed MCQ Workshop,JHB	2017		3. Advanced	MCQ
Kruger,M	1. SIOP Africa 2017,Morocco 2. PHD Supervision, Belgium 3.Haematology Oncology Symposium,Newlands 4. SACCGS Workshop,STIAS,Stellenbosch 5. DMT & EHod Bosberaad,STIAS Stellenbosch 6. Oxford Education Research Symposium,UK 7. South African Research Ethics Training Initiative(SARETI) Lecture Series, Pietermaritzburg 8.IMPAACT P1115 TRAIL`s,Washington,USA 9. Childhood Cancer Awareness Indaba,MRC,Auditorium 10. SIOP Congress Satellite Symposium on the Impact of Hearing Loss in Children,Washington,USA 11. College of Paediatric FCPaed MCQ Workshop,JHB	1. 5 - 7 Apr 2017 2. 5 - Apr 2017 3. 26 May 2017 4.19 May 2017 5. 30 May 2017 6. 31Jul - 1 Aug 2017 7. 14 - 15 Aug 2017 8. 12 Sept - 15 Sept 2017 9. 20 Sept 2017 10. 12 Oct - 13 Oct 2017 11. 10 Nov 2017	1. Congress 2. Congress 3. Symposium 4. Workshop 5. Symposium 6. Symposium 7. Course 8. Trail 9. Congress 10. Congress 11. Workshop	1. Advanced 2. Advanced 3. Advanced 4. Advanced 5. Advanced 6. Advanced 7. Advanced 8. Trail 9. Advanced 10.Advanced 11. Advanced	1.SIOP 2. SIOP 3. Haematology Oncology Symposium, CT 4.US 5. DMT & EHod Bosberaad,STIAS 6. St John`s College,Oxford,UK 7. (SARETI) 8. IMPAACT 9. Childhood Cancer Awareness Indaba,MRC,Auditorium 10. SIOP 11. College of Paediatric FCPaed MCQ
Malek,E	1.Midwivery Symposium,RCCH 2. FTF workshop Branding & Comms 3. Child & Family studies and parenting in African (PAN) Conference, Cape Town 4. Breastfeeding Seminar, Cape town 5. Childhood Cancer Awareness Indaba,MRC,Auditorium 6. Priorities Congress, Pretoria	1. 31 Mar 2017 2. 12 Apr 2017 3. 16 - 17 May 2017 4. 4 Aug 2017 5. 20 Sept 2017 6. 01 Dec 2017	1.Symposium 2. Worksop 3. Conference 4. Seminar 5. Congress 6. Congress	1. Advanced 2. Advanced 3. Conference 4. Advanced 5. Advanced 6. Advanced	1. Midwifery Symposium,RCCH 2. FTF 3. UCT 4. UWC 5. Childhood Cancer Awareness Indaba,MRC,Auditorium 6. Priorities Congress, Pretoria
Nel,E	1. Gastroenterology Course 2. Gastroenterology Course	1. 27 Jan 2017 2. 24 Nov2017	1. Course 2. Course	1. Advanced 2. Advanced	1. SU 2. Groote Schuur Hospital

Parker,N	1. SPRINTT PROGRAM	1. 23 August 2017	1. Course	1. Advanced	1. RED CROSS SKILLS LAB
Rabie,H	1. Invited speaker at FIDDSA Conference, Cape Town	1. 09 - 10 Nov 2017	1. Conference	1. Advanced	1. FIDDSA
Redfern,A	1. Stellmed BLS Course 2. Instructing on APLS 3. Medical video workshop 4. Global leadership summit Conference 5. Faculty on Paediatric Emergency Medicine Course at Red Cross Skills Lab	1. 19 - 20 Jan 2017 2. 14 - 15 Sept 2017 3. 29 Sept 2017 4. 18 Oct 2017 5. 29,30 Nov - 01 Dec 2017	1. Course 2. Course 3. Workshop 4. Conference 5. Course	1. Advanced 2. Instructor 3. Advanced 4. Advanced 5. Advanced	1. SU- Stellmed 2. APLS 3. US 4. Global Leadership Summit 5. UCT
Schaaf.S	1. SATS Congress, Century City Congress Centre 2. Child TB training Course,Goudini 3. Phoenix Study training,JHB	1. 22 Aug 2017 2. 11 - 14 Sept 2017 3. 06 Nov 2017	1. Congress 2. Course 3. Training	1. Advanced 2. Advanced 3. Advanced	1. SATS 2. US 3. Phoenix Study training,JHB
Smit,L	1. MBCHb Workshop 2. Writing Workshop,Stellenbosch 3. SAAHE Congress,Potchefstroom 4. MBCHb Curriculum Renewal Workshop,Houwhoek	1. 17 - May 2017 2. 29May - 31 May 2017 3. 4 -7 July 2017 4. 10 - 11 Aug 2017	1. Workshop 2. Workshop 3. Congress 4. workshop	1. Project 2. Advanced 3. Advanced 4. Advanced	1. US 2. US 3. SAAHE 4. US
Solomons, R	1. Paediatric Epilepsy Training (PET) Course,JHB	1. 03 Nov 2017	1. Course	1. Advanced	1. Paediatric Epilepsy Training (PET)
Springer,P	1. ADA Summer school 2. Presenting at GCP Congress 3. MSc thesis Presentation, Stellenbosch	1. 16 - 20 Jan 2017 2. 23 May 2017 3. 02 Nov 2017	1. Course 2. Conference 3. Presentation	1.Advanced 2. Advanced 3. Advanced	1. SU 2. GCP Congress 3. US
Uys,R	1. Speaker at Cancer Awareness Symposium	1 Aug 2017	1. Symposium	1. Advanced	1. Cancer Awareness Symposium
Van Zyl,A	1. SACCGS Workshop,STIAS,Stellenbosch	1. 19 May 2017	1. Workshop	1. Advanced	1. US
Van Toorn,R	1. Invited Speaker congenital brain malformations and outcome (Fetal medicine symposium Panorama	1. 03 Nov 2017 2. 10 Nov 2017	1. Symposium 2. Workshop	1. Advanced 2. Advanced	1. Panorama Hospital 2. College of Paediatric FCPaed MCQ

	Hospital 2. College of Paediatric FCPaed MCQ Workshop,JHB				
Zöllner, EWA	1. Insulin pump training 2. SATS Congress 3. Poster at SEMDSA Congress 4. Poster at SAPA Congress	1. 20-23 Jan 2017 2. 23-25 Aug 2017 3. May 2017 4. Aug 2017	1. Course 2. Congress 3. Congress 4. Congress	1. Advanced 2. Advanced 3. Advanced 4. Advanced	1.Auf der Bult Kinder-und Jugend-Krankenhaus, Hannover 2. Century City Conference Centre 3. Wanderers Club, Johannesburg 4. Johannesburg

Financial support by Department of Paediatrics and Child Health for current and potential postgraduate students

NAME	Programme	DESCRIPTION	DATE	AMOUNT
Dr JCF du Preez	PhD	GCP Course	26 & 27 January 2017	R3 600,00
Dr P Springer	PhD	ADA Summer School	16 - 20 Jan 2017	R 8 000,00
Prof H Rabie	PhD	Salary support during Sabbatical Leave	February-March 2017	R65 661,12
Drs S Irusen & Dr L van Heerden	MMed(Paed)	Translation services by Languate Centre for MMed(Paed) dissertations	June/July 2017	R 1217,72
Dr A Lakhan	MMed(Paed)	Statistical consultation by Centre for Statistical Consultantion for MMed(Paed) dissertations	August/December 2017	R 540,00
Dr S Gericke	MMed(Paed)	Attendance of USANA Congress	13-17 September 2017	R10 836,20
Dr K Oppel	MMed(Paed)	Attendance of FIDSSA Congress	9-11 November 2017	R4 400,00
Dr S Irusen	CMSA Certificate in Paediatric Nephrology	Attendance of IPNA Master Class	16-17 November 2017	R10 149,29
Dr G Kali	PhD	Salary support during Sabbatical Leave	December-November 2017	R 81668,72
Total				**R186 073.05**

CENTRES

THE FAMILY CLINICAL RESEARCH UNIT (FAMCRU)

Director: Prof MF Cotton

SECTION 1. ACCOMPLISHMENTS

Q1.2 What was accomplished?

CTU and CRS meetings

FAMCRU has monthly unit meetings for all staff on the first Monday of every month.

The 4 teams within FAMCRU meet monthly and on an ad hoc basis.

Since June 2017 FAMCRU's management team meet regularly to discuss policies, procedures current and new studies. This consists of:

- Prof Cotton – PI
- Unit manager – G Fourie
- Project managers: M Hendricks, A Janse v Rensburg, J Louw, J Coetzee
- Study co-ordinator – L Ganger
- Data manager – C Cilliers
- Lab manager – K Smith
- Pharmacy manager – M Smuts
- Quality assurance manager – J Crisp

Paediatricians – S Fry, S Barnabas

Academic meetings

Shaun Barnabas and Samantha represent FAMCRU at the weekly Paediatric Infectious Diseases meeting at Tygerberg.

Monthly CTU academic meetings are held by DTTC

Community engagement

Outreach activities

Discovery Foundation Rural Distinguished Visitor Award – Outreach visits are conducted by Prof Theron and his team to St Elizabeth's Hospital in Lusikisiki in rural Eastern Cape Province.

The Community Advisory Board forum is active within FAMCRU. There are currently 2 CAB groups: an adult and an adolescent group. This age disaggregated approach to our community involvement allows for a more direct community engagement and provides an opportunity for age specific issues to be discussed and information to be shared.

ADULT CAB

- Monthly meetings held.
- 60 - 80% attendance for CAB meetings
- 5 New members recruited.
- 3 Members awarded the Bridgette Murtach Award for continuous dedication to the CAB in June 2017.

- Currently there are 8 members with >10 years membership who use their knowledge for voluntary work in the community. (talks to youth groups, people in the clinics and adolescents in the communities)
- Some of our CAB members are also doing voluntary work with mental health patients in their communities.
- Marie Theunissen received an award at the 2017 IMPAACT meeting in June 2017, Washington DC, for successfully completing her 3-year term as ICAB chairperson.

ADOLESCENT CAB

- Currently consists of 40 active members who meet monthly
- 100 % attendance for the reported time period
- Regular workshops and discussions surrounding social, sexual, mental and physical health issues that impact adolescents today
- Regular excursions with emphasis on self-improvement and environmental awareness
- Volunteer involvement at Tygerberg Hospital at ward G7 to celebrate Youth Day
- Guest adolescent motivational speaker, Gavin Fortuin, was invited to speak on “Identifying Your Worth”.
- Collaboration and outreach with other adolescent CABS and community peers to share knowledge and awareness and increase membership for the future.
- Empowerment for transition from adolescence to young adulthood in a personal capacity and for their health care.
- Evaluation of the past year’s activities and progress will accompany a planning session for the 2018 program to be held in October

Communications

Resource sharing and collaboration

FAM-CRU, in cooperation with the SU Immunology Research Group (IRG) share resources for the ACTG 5349 TB treatment shortening trial. Source information is collected by the SUN IRG and the CRF files are completed and captured into the TBTC database at FAMCRU. FAM-CRU gives pharmacy resources and support and the IRG team recruit patients and follow adults with TB – a new target population for FAMCRU. The pharmacy also provided clinical trial support to the IRG for two large Bill and Melinda Gates Foundation-funded TB trials

The FAMCRU provides the pharmacist of record for DTTC for IMPPACT studies and also for the HPTN084. FAMCRU pharmacy provides the pharmacist of record responsibilities for DTTC (CRS number 31790) by providing the investigational product for P1078, P1101, P1108 and HPTN084. The FAMCRU pharmacy is also monitored for these by PPD during study specific study visits

Steve Innes has established new collaborations with:

- University of California San Diego (UCSD) Wirelessly Observed Therapy research group
- UCSD-Moçambique Ministry of Health Partnership - One successful funding application (UCSD CFAR)

CABS (FAMCRU, DTTC, TASK, ACI AND IRG) share resources with combining retreats and sharing expertise.

FAMCRU-CAB was used to train and mentor the other CABS including:

the Biobank CAB at Tygerberg Hospital

the DTTC CAB

the Cancer Consortium CAB

Mentored investigators

Marije Van Schalkwyk is mentored by Prof Gerhard Theron and Prof Adrie Bekker in her activities for the P1026s protocol and aims to include a PhD on TB and ARV pharmacokinetics in pregnancy.

Dr. Marije van Schalkwyk and the FAMCRU team provided mentorship for the following investigators:

- Dr. A. Hiemstra, who is an experienced family physician, but only recently started work as a trial investigator.
- Dr. P. Ahlers, an experienced medical officer, recently started work as trial investigator.
- Dr Mpho Tlali and Dr Justine Khoury

Study Coordinators Ciska Botha and Lindee Saayman mentored:

- Charmaine Abrahams, a research nurse with years of experienced in observational studies. Her work on the A5349 is her first work on a clinical trial.
- Susanne Tonsing, an experienced coordinator of social studies, new to clinical trial coordination.

Infrastructure development

Upgrading of the continuous temperature monitoring system in the FAMCRU pharmacy

The Immunology Research Group established a dedicated TB clinical trial facility on the university site with support from FAMCRU.

Site monitoring

FAMCRU has quarterly monitoring visits from PPD for IMPAACT and ACTG. These visits are combined to include studies from both networks, which can increase the number of studies monitored at each visit to up to six. Accommodating all the monitors involved for each visit has posed a challenge, however, FAMCRU has successfully completed all monitoring visits during the past reporting period.

A slight increase in error rates was identified during the recent site monitoring visits. This is largely due to the appointment of new staff to replace experienced staff who resigned. To overcome this, FAMCRU has increased and improved the in-house training and support program for all staff, especially those who are gaining experience in ongoing studies. The current quality assurance processes and procedures are also being assessed and evaluated to ensure that the highest standard of research is maintained and the utmost care to protect the participants is taken. A real-time quality control system is currently being implemented. A consolidated and standardized approach to documentation and procedures across the different teams is underway to improve quality assurance and control. Some of these improved procedures have already been implemented successfully within the unit.

The general outcome of FAMCRU monitoring visits has been positive. Despite the challenges of turnover of staff, the implementation of Medidata RAVE electronic capturing system and the need for improved training, FAMCRU is committed to maintain its high standard of scientific research.

The quarterly monitoring reports highlighted some minor findings in the pharmacy, all of which were resolved.

Leadership and other network contributions

Marlize Smuts elected as co-leader of the Pharmacy Working Group of the Protocol Development and Implementation sub-committee of the SMCCC, ACTG in March 2017.

Professor Gerhard Theron currently serves as:

1. Protocol Vice Chair for the IMPAACT P1078 study (A randomized double-blind placebo controlled trial to evaluate the safely of immediate versus delayed INH preventative therapy among HIV infected women in high TB incidence settings)
2. Secondary end point review committee member of IMPAACT P1078 (A randomized double-blind placebo controlled trial to evaluate the safely of immediate versus delayed INH preventative therapy among HIV infected women in high TB incidence settings)
4. Writing committee chair for proposed PROMISE publications: Subsequent pregnancies in 1077BF/1077FF (Writing committee chair) Member of the safe Motherhood and Newborn Health committee (term 2015 – 2018) of the International Federation of Obstetrics and Gynecologists (FIGO).

Steve Innes is a voting member of International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) Complications Scientific Committee since December 2016.

Mark Cotton

1. On IMPAACT Cure Committee
2. Vice chair P1115

Joan Coetzee:

1. Protocol Development and Implementation Sub-committee (PDISC) – Co-chair
2. Scientific Agenda Steering Committee (SASC) – SMCCC representative
3. Site Management Clinical Care Committee (SMCCC) – member
4. Field Representative Working Group (FRWG) – member
5. Site Operations Sub-committee (SOS) – member
6. Field Representative – A5362 and P1106
7. CAB-Liaison for IMPAACT and ACTG CABs

Protocol Specific activities

IMPAACT

FAMCRU started enrolling participants in P1110 within this reporting period.

ACTG

FAMCRU was approved for and started enrolling participants on the following studies: A5263, A5278s/AMCO74, A5243, A5332, A5349. A5354 is currently pending approval.

Marije Van Schalkwyk is site PI on P1026, A5288, A5332, A5278s and A5243, and on A5354 pending IRB approval. She is sub-investigator on A5263 and A5349 and on A5302 pending IRB approval.

Adrie Bekker is vice chair for the P1106 protocol team

Training and courses for FAM-CRU Pharmacy Staff

Clinical Pharmacology Quality Assurance and Quality Control course attended by:

- Joan Coetzee
- Lindee Gander
- Kurt Smit
- Mornay Isaacs

Dangerous Goods Regulation course attended by:

- Carlos Moffat
- Anthony Agulhas

Webinar training for IMPAACT 2010 attended by:

- L Rossouw
- M Rossouw
- J Louw
- J Crisp
- S Schnell
- P Ganjana
- N Bonani

L Coetzee attended AMC training in Johannesburg in February 2017

Q1.4 Results disseminated to communities of interest?

Marije Van Schalkwyk presented the P1026s preliminary data from the TB arms to the HIV/TB provincial managers at their Research Day, at the Rural Research Day and to her fellow sub-district HIV clinicians at the regular HIV/AIDS/TB/STI management meeting and the TB clinical forum.

For A5349: Patient specific reports of results and outcomes after treatment completion is provided to the local primary healthcare clinics by the team. Quarterly feedback sessions are also shared with the managers of these PHC's.

A large-scale community outreach day at a local community centre (Adriaanse in Cape Town) was organized, where sponsored meals, music and activities for children was provided, as well as a presentation of talks and facilitated discussions to improve knowledge and awareness of TB and HIV.

Q1.5 Plans for next interim reporting period?

Implement studies A5354, A5302, A5324 and A5362.

FAMCRU is establishing a satellite site at SU's rural school, Ukwanda, in Worcester, 120 km away. The site will be led by Dr Amy Slogrove, a post-doctoral researcher who this year, was awarded the CIPHER award to further develop her research in paediatric HIV.

FAMCRU is currently developing an in-house HIV and research training program that will be aimed at all staff, with a particular focus on the counsellors and their professional development needs. This program will cover topics including: HIV basic sciences, prevention and treatment of HIV, HIV related diseases and STI's, HIV testing and HIV counselling. A continuous refresher in research ethics and principles will be included in the training program and protocol specific requirements will be addressed as necessary.

Q2.2

Website or other internet sites

FAMCRU's website is updated on an ad hoc basis with news about the unit and study related information to the public. The URL is: www.kidcru.org.za

Q2.3 Other products and resources sharing

Marije Van Schalkwyk presented the P1026s preliminary data on the TB arms as a poster at IAS2017 in Paris 23-26 July 2017, at the Annual Academic Day of the Medical Faculty of Stellenbosch University on 30 Aug 2017 as an oral presentation and will present the data as a poster again at the 7th FIDSSA Congress 2017 9-11 Nov 2017. She is sub-investigator on the P1026s site study team.

Lindee Ganger presented A5349 data: Direct Observed Treatment Support (DOTS) at the annual ACTG meeting in June 2017.

Other grants

MRC Research Grant to do a case series of patients with postpartum haemorrhage due to atonic uteruses managed by using the Sinapi uterine balloon tamponade was awarded.

Steve Innes has also received a renewal of the following grant awarded:

Ref #: 1R01HD083042-03 PI: Innes S Date: 03/2015 – 02/2020
Funding Agency: Eunice Kennedy Shriver National Institute of Child Health & Human Development
Title: Screening for atherosclerotic vascular disease in HIV-infected children
Goals: (1) To quantify excess AVD risk; and (2) To generate and validate a diagnostic screening algorithm to identify asymptomatic increased AVD risk in HIV-infected children using low-tech input variables that can be routinely collected during primary care follow-up.
Role: Principal investigator

IMPAACT studies presented by Prof Theron at national congresses in South Africa

March 2017 35th Conference on Priorities in Perinatal Care in Southern Africa.
Title: Comparing Maternal Triple Antiretroviral and Infant Nevirapine Prophylaxis for the Prevention of Mother-to-Child Transmission of HIV during Breastfeeding – the IMPAACT PROMISE trial (1077).

IMPAACT studies published by Prof Theron as Congress abstracts

Abstract and Proceedings of the 35th Conference on Priorities in Perinatal Care in Southern Africa. Title: Comparing Maternal Triple Antiretroviral and Infant Nevirapine Prophylaxis for the Prevention of Mother-to-Child Transmission of HIV during Breastfeeding – the IMPAACT PROMISE trial (1077).

Barbara Laughton (with Mark Cotton)

- Poster at CROI 2017: Neuropsychological outcomes in 2 year African-based pediatric observational study

Mark Cotton

- Oral presentation at 9th HIV Pediatric workshop, Paris July 2017. Asymptomatic Hematologic Toxicity with Very Early Combination Antiretroviral Therapy in In Utero HIV-infected Infants. E Chadwick, A Tierney, A Coletti, MF Cotton et al

SECTION 3 – PARTICIPANTS

Q3.2 New senior/key personnel (submit biosketches)

Shaun Barnabas joined FAMCRU as a Paediatric Infectious Diseases Specialist in January 2017.

Q3.5 New GCP and HSP training

GCP and HSP 19 May 2017
Hosted by Transcendence Solution CC

1. Adendorf, Wendy
2. Andrea, Catherine
3. Bagus, Desmien
4. Barnabas, Shaun
5. Bonani, Nokuza
6. De Freitas, Naomi
7. Dobbels, Els
8. Dyan, Shiela
9. Ellis, Coreen
10. Fourie, George
11. Ganger, Lindee
12. Ganjana, Phoebe
13. Groenewald, Marisa
14. Groepies, Leonie
15. Hamana, Thandiwe
16. Hendricks, Marchalaine
17. Hoorn, Lilly
18. Innes, Steve
19. Laughton, Barbara
20. Lindani, Filicity
21. Louw, Jeanne
22. Makola, Candice
23. Martin, Jackie
24. Matrons, veronica
25. Mboto, Bongiwe
26. Moffat, Carlos
27. Nduna, Nwabisa
28. Neal, Caroldine
29. Nel, Unine
30. Ngwayi, Nosipho
31. Pieterse, Sylvia
32. Reid, Maylene
33. Rossouw, Lindie
34. Slade, Gretchen
35. Smith, Kurt
36. Smuts, Marlize
37. Summers, Gwendoline
38. Sylvester, Sharifah
39. Theunissen, Marie
40. Van Schalkwyk, Marije
41. Welem, Hombaka

1. Arendze, Ronelle
2. Bester, Marietjie
3. Boyana, Tembela
4. Cilliers,Charise
5. Coetzee, Joan
6. Cotton, Mark
7. Crisp, Jacqueline
8. Cweya Aviwe
9. Hugo, Susan
10. Isaacs, Mornay
11. Ismail, Zahiera
12. Janse van Rensburg, Anita
13. Magogotya, Zukiswa
14. Mtshangi, Mandisa
15. Nkani, Nomvuyo
16. Orange, Wilma
17. Rabie,Helena
18. Rossouw, Magdel
19. Sadie, Rolene
20. Samuels, Natasha
21. Van Hyssteen, Hestie-Mari
22. Van Turha, Moschelle
23. Van Whyhe, Kaylee
24. Zimri, Warren
25. Zuidewind, Peter

SECTION 4 - IMPACT

Q4.1 Impact on physical, institutional, or information resources that form infrastructure

ACTG room

Air extraction fans replaced in all rooms FAM-CRU during September 2017

Wifi for monitors was installed in February 2017

SECTION 5 - CHANGES

Q5.1 Actual anticipated challenges or delays and actions or plans to resolve them

Challenges with P1101:

1. Recruitment: enrolment of participants prior to initiation of ARV's proved difficult as HIV testing and initiation of ARV's occurred at first presentation at the TB clinic
2. The caregiver is often not the legal guardian (e.g. the grandmother) and contacting the mother can be difficult.
3. A delay in enrolment occurred due to cohorts being on hold or closed for extended periods of time. This often caused a loss of momentum in enrolment.

However, once participants were enrolled on the study, retention was maintained. This is largely due to dedicated staff who established good interpersonal relationships with the participants. Social issues that were

identified during the study were addressed by the on-site social worker. Other strengths within the unit that aided in the success of the study include: experience with pharmacokinetic studies, excellent phlebotomists and pharmacy services.

Challenges with P1115:

1. Very small time window in which to begin the study specific ARV regimen – which is different to current PMTCT practices
2. Recruitment at primary site was slow due to good uptake of PMTCT and viral suppression in pregnancy
3. Due to current laboratory practices, the birth PCR is usually only available post 48 hours of life

To overcome these challenges, recruitment was extended to district level clinics and hospitals with a lower uptake of antenatal care and PMTCT. Good communication between FAMCRU and these facilities allowed for study specific regimen to be initiated prior to 48 hours of life and once the PCR result was available, a decision was made with regards to eligibility for enrolment. This approach has allowed for effective recruitment but also improved the healthcare facilities' follow up of these high risk newborns, especially those not eligible to enroll.

Delay in sample shipping and protocol activation due to outstanding material transfer agreements (MTA).

During the reporting period, it has become challenging to ship study samples overseas. The South African Department of Health instituted new policies requiring all study sites to have study specific MTA's in place, signed by the legal authority of the Provider Site and the Recipient site, the intermediary shipping labs, and endorsed by the local IRB, before export permits can be applied for. However, no clear guideline on what the MTA must contain and what signatories are required was provided. There was no clarity from the ACTG leadership on the position of the biobanks as legal entities and ownership of the samples. Study A5349 was the first affected and required 4 separate MTA's with all different sample destinations. As this study is jointly implemented with the CDC network, specific MTA templates were provided that needed legal approval from all stakeholders. SU Legal Office provided guidance that required negotiation with the ACTG Leadership and the Recipient Laboratories for final approval of the legal content of the documents. It took 12 months between the first drafts and the final execution of these MTA's before export permits were approved causing significant delay in samples leaving South Africa for all South African sites involved. However, since the A5349 MTA's were accepted by the Department of Health, many more MTAs were submitted using the same standard template approved by all parties. Studies A5263, A5278s, A5332, A5243 were affected by the MTA difficulties, but are now finalized with export applications largely approved. There should not be any further delay in shipment of samples as new studies will use the same template. However, study A5243 implementation was also delayed in ACTG site activation due to an outstanding MTA, as the ACTG leadership implemented its new policy requiring an executed MTA before site activation can be approved.

Interruption in HREC activities.

Our Ethical Committee (IRB) changed to online research ethics application and management processes. This has resulted in the IRB office not accepting any new submissions, except for SAEs (Serious Adverse Events) and requests of similar urgency that may impact on participant safety, after 17 May 2017 and until the new online system is in effect. The 31 May 2017 deadline and the corresponding 21 June IRB meeting have therefore been cancelled. The new system opened on 5 July for new applications only. Communication on existing studies has been following the old submission route since. This interruption in document acceptance affected A5354 and A5302 approval timelines.

Delay in registration of new investigators at MCC.

For A5349: Challenge of the MB forms. The fact that the original MB forms must be completed at 2 locations at 3 different time-points (sample collection at the site, final report at the lab and before submission at the site, posed a constant challenge to submit this form of CRF in the expected time. The form is not standard for the reference lab, and makes it prone to transcription errors. We would suggest that the site investigators be allowed to complete the MB forms, using the standard final report from the reference laboratory as source document.

DOTS (Direct Observed Therapy Support) is new to this team and is often challenging. We worked hard with the protocol team to remain flexible, but still adhere to the protocol when a participant's availability for DOTS visits were impeded for any reason.

SECTION 6 – REPORTING STUDIES

Q6.1 Updates on studies

Current IMPAACT studies:

				Status approval (ref & date)			
Study # and short title	**Clinical Trials. gov #**	**Year commenced, screening,**	**Obstacles & solutions**	**HREC**	**MCC**	**NHREC**	**DOH and CITY**
P1060: Comparison of NNRTI based vs PI based ARV therapy in HIV infected infants in ARV naive infants with no prior PMTCT. A phase II		Commenced in 2005 Screened: 130 Total enrolled: 88 PIDs in FU: 0	Follow-up completed.				
P1104s: Neurocognitive study for P1060 and HIV uninfected children		Commenced in 2013 Screened: 160 Total enrolled:142	Follow-up completed.				
P1066: Safety, tolerability pharmacokinetic and antiretroviral activity of Raltegravir in HIV-1 infected children and adolescents. A phase I/II		Commenced in 2010 Screened: 5 Total enrolled: 2 PIDs in FU: 0	Follow-up completed.				
P1113: Safety and immunogenicity study of a recombinant protein tuberculosis vaccine (AERAS		Commenced in 2013 Screened: 79 Total enrolled: 46 PIDs in FU: 5	Obstacles: Low birthweight, TB contact, Positive Quanti-Feron	11/2012	03/2013	07/2013 DOH 27-071304266	TBH: 05/2013
P1106: Pharmacokinetics of ARVs and anti-TB therapy in low birth weight infants		Commenced Nov 2015. Screened: 96 Total enrolled: 56 PIDs in FU:	A very complicated study which is very labor intensive but going well.	M13/08/037 Appr:02/10/13	20130507 Appr: 09/01/14	23/07/2015	DOH: 07/2016 TBH: 03/2016

P1093 Pharmacokinetic, Safety, Tolerability and Antiviral Activity of GSK1349572, a Novel Integrase Inhibitor, in Combination Regimens in HIV-1 Infected Infants, Children and	NCTO 1302847	Commenced 2014 Screened: 9 Enrolled: 3 PIDs in FU: 3	Obstacles: Difficult to recruit as most of the naive patients in the 12-18 age range did not receive PMC TC	05/2011	09/2012	09/2014	TBH 09/2014
P1115: Very early Intensive treatment of HIV-infected infants for remission. Phase I/II proof of concept study		Commenced Aug 2015 Screened: 87 Total enrolled: 17 PIDs in FU: 12	This is a difficult study to enroll on as we don't usually obtain the HIV PCR result within the first 48 hours. We are currently	M14/06/26 Appr:30/07/14	20140721 Appr:02/10/15	12/07/2016	20/05/2015
P1101: Safety, tolerance and pharmacokinetic study of Raltegravir in ART-naïve TB co-infected		Commenced Oct 14 Screened: 9 Total enrolled: 8 PIDs in FU: 4		M13/07/031 Appr:04/09/13	20130507 Appr:09/01/14	03/07/2014	12/07/2016
P1110: Evaluate the safety and pharmacokinetics of Raltegravir in HIV-1-exposed neonates at high risk of		Commenced: 13 Nov 2015 Screened: 1 pair Total enrolled: 2 PIDs in FU: 2	Very difficult to enroll into this study as mothers need to be taking Raltegravir. Raltegravir is a 3rd line agent and so there are very few	M14/10/049 Appr:19/11/14	20141032 Appr:13/01/15		12/11/2015
P1026s Pharmacokinetic properties of ARV and related drugs during pregnancy	NCT00042289	Commenced July 2014 Screened: 20 mothers Total enrolled: 39 PIDs in FU:	Obstacles: The study staff had to depend on the resident staff to refer	Initial HREC approval: 20/03/2013	N/A	N/A	Tygerberg Hospital approval: 6/092013

P1090 Etravirine (ETR) in ARV Experienced HIV-1 Infected Children, Aged ≥ 2 Months		Commenced: 23 February 2016 Screened: 1 Enrolled: 0 PIDs in FU: 0	Very difficult to find eligible participants. Obstacles: The study is dependent on resident staff to refer	M14/04/16 Appr:27/06/16 Version 5 Appr: 27/06/2016	20120543 Version 5: 11/07/2016		23/02/2016
P1078 – Evaluate the safety of immediate VS deferred Isoniazid preventative therapy among HIV women in high TB incidence		Commenced Jan 2015 Screened: 127 mothers Total enrolled: 74 pairs – 149 total PIDs in FU: 0	Follow-up completed	Initial HREC approval 20 June 2012	Initial MCC approval: 5/08/2013	DOH-27-0813-4064	Tygerberg Hospital approval: 1/10/2013 DOH approval: 20/03/2014
P1112 – Safety and pharmacokinetic parameters of subcutaneous (SC) VRC01, a potent anti-HIV neutralizing monoclonal antibody, in HIV-1 exposed infants. An open-label dose escalating phase 1 study	NCT02256631	Commenced Jan 2016 Screened: 16 Enrolled: 16 pairs – 32 total PIDs in FU: 13 Protocol version 3.0 (dose group 4, cohorts 1 & 2) to start recruiting on 14 September 2017.	Obstacles: The population we are recruiting from is a largely breastfeeding population. Tygerberg Hospital is a "baby friendly" hospital and promotes exclusive breastfeeding for all women. Dose group 4	Initial HREC approval: 15/10/2014	Initial MCC approval: 13/012015	DOH-27-0515-4861	Tygerberg Hospital approval: 10/04/2015
IMPAACT 2010	NCT03048422	Commenced: Screened: N/A Enrolled: N/A PIDs in FU: N/A	Study to open in November 2017.	Initial HREC approval: 1/02/2017	Initial MCC approval: 6/07/2017	Pending	Tygerberg Hospital approval: pending DOH approval

IMPAACT 2008 Evaluate the safety and antiviral activity of VCR01 administered in combination ARV therapy to HIV-1		Commenced: Screened: N/A Enrolled: N/A PIDs in FU: N/A					

ACTG

ACTG studies in FAM-CRU:

				Status approval (ref & date)			
Study # and short title	**Clinical Trials.gov #**	**Year commenced, screening, accrual**	**Obstacles & solutions**	**HREC**	**MCC**	**NHREC**	**DOH and CITY**
A5288 Management using the latest technologies in resource-limited settings to optimize combination therapy after viral failure (MULTI-OCTAVE)		Commenced: May 2015 Screened: 27 Enrolled: 20 PIDs in FU: 0	Fully accrued. Follow-up completed.	M14/04/015 Appr:28/10/14	20120150 Appr:29/10/14		Appr: 8/12/2014
A5263 Comparison of three regimens of chemotherapy with compatible ARV therapy for the treatment of advanced AIDS-KS in		Commenced: May 2017 Screened: 2 Enrolled: 1 PIDs in FU: 1		M15/10/048 Appr:9/12/15	20140743 Appr: 5/04/17		Appr26/07/16
A5278s/AMCO 74 Pharmacological sub-studies of A5263 and A5264 – to investigate the potential for drug interactions		Commenced: May 2017 Screened: 1 Enrolled: 1 PIDs in FU: 1		M16/04/016 Appr: 7/06/16	MCC REF: N/A App Date: N/A		Appr:21/6/16

A5243 Plan for obtaining human biological		Commenced: Screened: N/A Enrolled:		N15/07/060A Appr:26/09/16	MCC REF:N/A Appr Date: N/A		Appr: 20/03/17
A5332 Prevent vascular events in HIV – REPRIEVE. A prospective		Commenced: Nov 2016 Screened: 92 Enrolled: 67 PIDs in FU:		M16/03/13 Appr :28/6/16	20160507 Appr: 4/7/16		Appr:: 16/08/16
A5349 Rifapentine containing treatment shortening regimens for pulmonary tuberculosis. A phase III randomized controlled open-label study		Commenced: Nov 2016 Screened: 19 Enrolled: 18 PIDs in FU: 18		M16/04/018 Appr:28/6/16	20150511 **Appr**: 16/05/16 **DOH**:1/08/16 **City**: Bishop Lavis-8/8/16 Northern Sub District and Tygerberg Sub District-22/7/2016		Approvals **DOH**:1/08/16 **City**: Bishop Lavis-8/8/16 Northern Sub District and Tygerberg Sub District-22/7/2016
A5354 Effect of ARV treatment initiated during acute HIV-1 infection on measures of HIV-1 persistence and on HIV-1		Commenced: Screened: N/A Enrolled: N/A PIDs in FU: N/A					

DESMOND TUTU TB CENTRE (DTTC)

Director: Prof AC Hesseling

DESMOND TUTU TB CENTRE ANNUAL REPORT: 2017

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Every breath counts

CONTENTS

Letter from the Director

The past year at the Desmond Tutu TB Centre (DTTC) has been characterized by wonderful growth, renewed focus, rich new collaborations and opportunities. Major trials like HPTN 071 (PopArt) are ending, while exciting new TB and HIV studies have been initiated.

Internal restructuring, the strengthening of our leadership core and ExCo, standardization, restructuring of core support functions (regulatory, laboratory, data, information technology, administrative support, logistics, communications, and finances) have been completed and a DTTC institutional Community Advisory Board (CAB) was established. Resulting from a deliberate strategy, increased internal collaboration has been established between our three main focus areas (paediatric TB, operational research and HIV prevention research), underpinned by other key competency areas. New internal and external collaborations have been established and a strong emphasis has been placed on transformation of our researcher profile.

An exciting development has been partnering with South African institutions outside of the Western Cape Province, with four new investigator-initiated clinical trials led by the DTTC, which will be implemented in collaboration with national partners. The DTTC has also joined a seminal HIV prevention trial in at-risk young women through the HPTN network, HPTN 084.

We have enormous human capital potential at DTTC, which is our main asset. As evidenced by the substantial number of South African, African and international postgraduate researchers, there is significant potential to train and retain a new generation of clinical and other researchers who will be able to impact on the tuberculosis and HIV epidemics in the Western Cape, in South Africa and beyond. In March 2018 alone, 4 PhD and 4 Masters degree students graduated from DTTC. A unique aspect to our centre is the large proportion of international investigators we attract, with several international funded clinicians based at DTTC long-term.

A highlight of 2017 was the appointment of 3 international colleagues in an extraordinary capacity at DTTC, including Dr. James Seddon, Senior Lecturer, Imperial College London, as Extraordinary Senior Lecturer at DTTC, and the appointment of Professor Kelly Dooley, Johns Hopkins University, as Associate Professor, and Professor Amita Gupta, as Professor. Professor Dooley visited during 2017 and Dr. Seddon has joined DTTC for a 5-year funded period through a BMRC fellowship.

The South African National Research Foundation SaRCHI Chair in Paediatric Tuberculosis, currently held by the director, offers a strategic and sustainable platform to support our vision to address the challenges and improve the control of paediatric TB. Ongoing participation in NIH- and CDC-funded international trial networks including the IMPAACT, HPTN and TBTC (CDC) trial consortia have enhanced long-term collaborations and sustainability of our research program.

Looking ahead, we aim to continue and expand with our strong collaboration with government partners at local and national level, and to design and implement research which will truly impact on the tuberculosis and HIV epidemic in our setting, and globally. We will seek to further transform and diversify our researcher portfolio, engage in strategic new partnerships, seek long-term core funding for ongoing centre support, diversify our funding portfolio, and develop a strategy to anticipate and address expected and unexpected risks. We have undertaken a strategic plan to support communication and dissemination.

Professor Anneke C. Hesseling

Distinguished Professor in Paediatrics and Child Health
Director: Desmond Tutu TB Centre

SARcHi Chair in Paediatric Tuberculosis
March 21, 2018

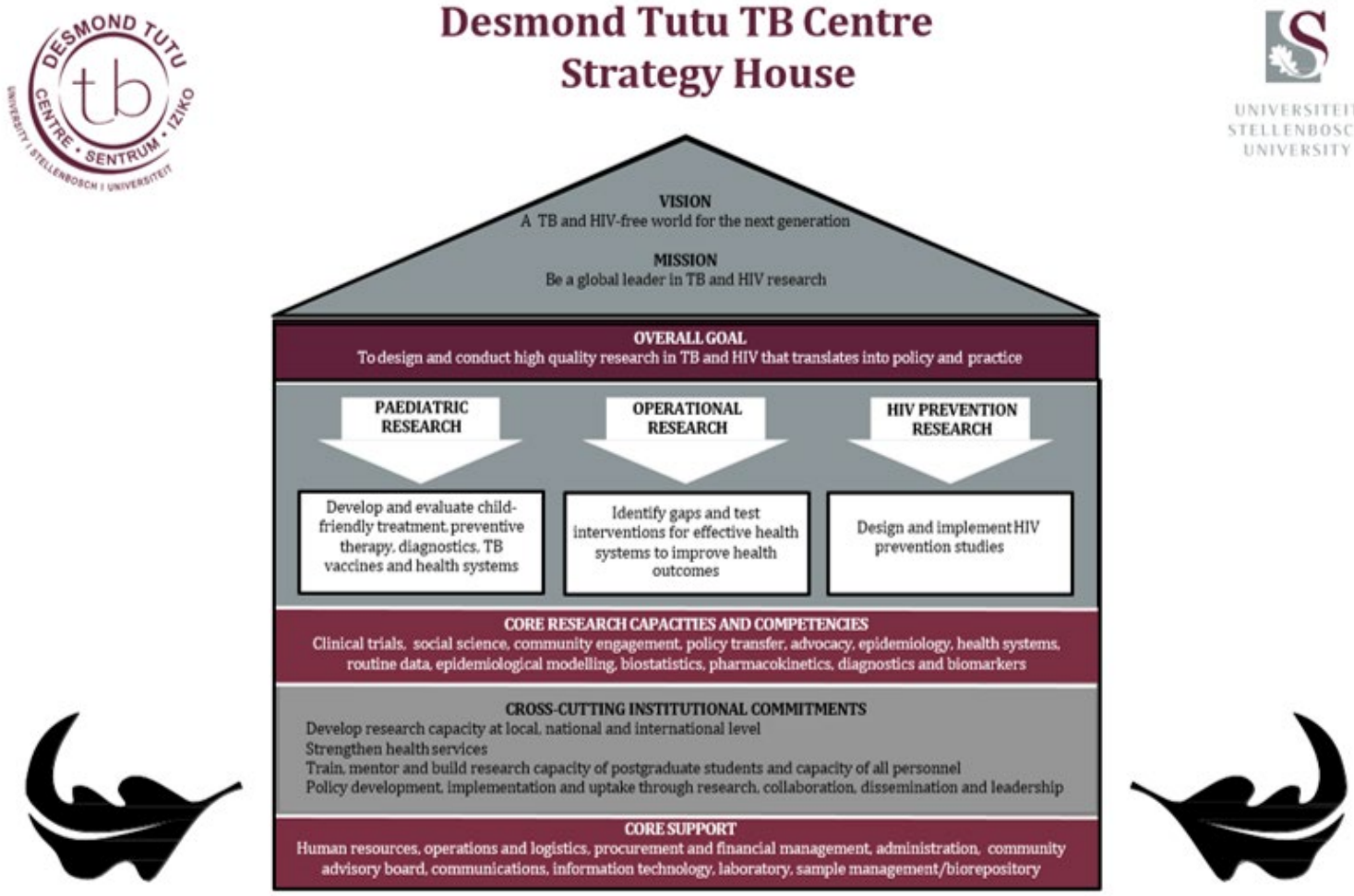


Figure 2. DTTC Strategy House

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
CEBHC	Centre for Evidence based Health Care
CFP-10	Culture Filtrate Protein 10-kDa
CFU	Colony-forming units
CHIP	Community HIV Care Providers
CM	Clarification Memo
COMAPP	Community AIDS Prevention Project
CRS	Clinical Research Site
CTU	Clinical Trials Unit
CXR	Chest X-ray
DAERS	DAIDS Adverse Experience Reporting System
DAIDS	Division of AIDS, NIAID
DFID	Department for International Development
DMC	Data Management Center
DOT	Directly Observed Therapy
DR-TB	Drug-Resistant Tuberculosis
DS-TB	Drug-Susceptible Tuberculosis/Drug-Sensitive Tuberculosis
DSMB	Data and Safety Monitoring Board
DST	Drug Susceptibility Testing
EC	Ethics Committee
DTTC	Desmond Tutu TB Centre
ECG	Electrocardiogram
ERS/ATS	European Respiratory Society/American Thoracic Society
ESAT-6	Mycobacterium tuberculosis early secreted Antigen 6 kDa
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 Development
FMHS	Faculty of Medicines and Health Science
FSTR	Frontier Science & Technology Research Foundation
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
HR	Human Resources
HTS	HIV Testing Services
IMPAACT	International Maternal Pediatric Adolescent AIDS Clinical Trials Group
INH	Isoniazid
IRB	Institutional Review Board/ethics committee
IT	Information Technology

LAB	Laboratory
LFMi	Lung Function Measurement instrument
LPV	Lopinavir
LPV/r	Lopinavir/ritonavir
MA	Master of Arts
MCC	Medicines Control Council
MDR-TB	Multidrug-Resistant Tuberculosis
MIC	Minimum Inhibitory Concentration
MPH	Master of Public Health
MRC	Medical Research Council
MS	Mass Spectrometry
MSF	Médecins sans Frontières
M.tb	*Mycobacterium tuberculosis*
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
NSP	National Strategic Plan
NTP	National TB Program
OR	Operational Research
ORAP	Operational Research Assistance Project
OGAC	Office of the U.S. Global AIDS
PC	Population Cohort
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary Health Care
PI	Principal Investigator
PK	Pharmacokinetics
PID	Patient Identification Number
SID	Study Identification Number
PMTCT	Prevention of Mother To Child Transmission
PTB	Pulmonary Tuberculosis
RIF	Rifampicin
QA	Quality Assurance
QGIT	QuantiFERON Gold-In Tube (QGIT)
RSC	Regulatory Support Center
SACEMA	South African Centre for Epidemiological Modelling & Analysis
SADR	Suspected Adverse Drug Reaction
SANTP	South African National TB Program
STI	Sexually transmitted infections
STINT	Swedish Foundation for International Cooperation in Research and Higher education
SU	Stellenbosch University
TBTC	TB Trials Consortium
UCL	University College London
VMMC	Voluntary Male Medical Circumcision
ZAR	South African Rand (currency)

SCIENTIFIC FOCUS AREAS

DTTC DIRECTOR: PROF AC HESSELING

Paediatric Research

Investigators

Prof Anneke Hesseling
Prof Simon Schaaf
Prof Peter Donald
Dr Anthony Garcia-Pratts
Dr Jana Winckler
Dr Louvina van der Laan
Dr Elisabetta Walters
Dr Anne-Marie Demers
Dr Marieke van der Zalm
Dr Megan Palmer
Dr Sue Purchase
Prof Adrie Bekker
Dr Celeste de Vaal
Dr Heidi van Deventer
Dr Jennifer Hughes
Dr Rolanda Croucamp
Dr James Seddon
Dr Elisa Lopez

Study Coordinators

Petra de Koker
Jessica Workman
Sharon Mbaba
Margaret vanNiekerk
Adelaide Carelse
Elise Batist
Nicola James

Researchers
Nurses
Research Counsellors/ DOT workers

Staff component including support staff – n=89

Operational Research

Investigators

Dr Karen du Preez

Dr Muhammad Osman

Dr Sue - Ann Meehan

Dr Florian Marx

Staff component including support staff – n=4

HIV Prevention Research

Investigators

Prof Nulda Beyers,
Dr Peter Bock

Project Managers/Clinician

Dr Kerry Joubert
Blia Yang
Nomtha Mandla

Junior Project/District Managers/Study Coordinator

Noluvo Rhode
Vikesh Naidoo
Francionette Esau
Jerry Molaolwa
Jacky Hlalukana
Dr Dalapo Awoniyi
Dr Gerald Maarman
Yvonne Saunders
Charise Pedro
Nosi Makola

District Logistic Officers
Nurses
Counsellors
Data Coordinators
Fieldworkers

Staff component including support staff –n=205

Social Sciences Research

Investigator

Graeme Hoddinott

Research Coordinators

Lario Viljoen
Tamaryn Nicholson
Constance Mubekapi-Musadaidzwa
Hanlie Myburgh

Project Coordinators

Jabulile Baleni
Nosivuyile Vanqa
Rosemary Brown
Angeligue Thomas
Laing de Villiers
Dillon Wademan
Rozanne Casper

Graduate Research Assistants

Research Interns

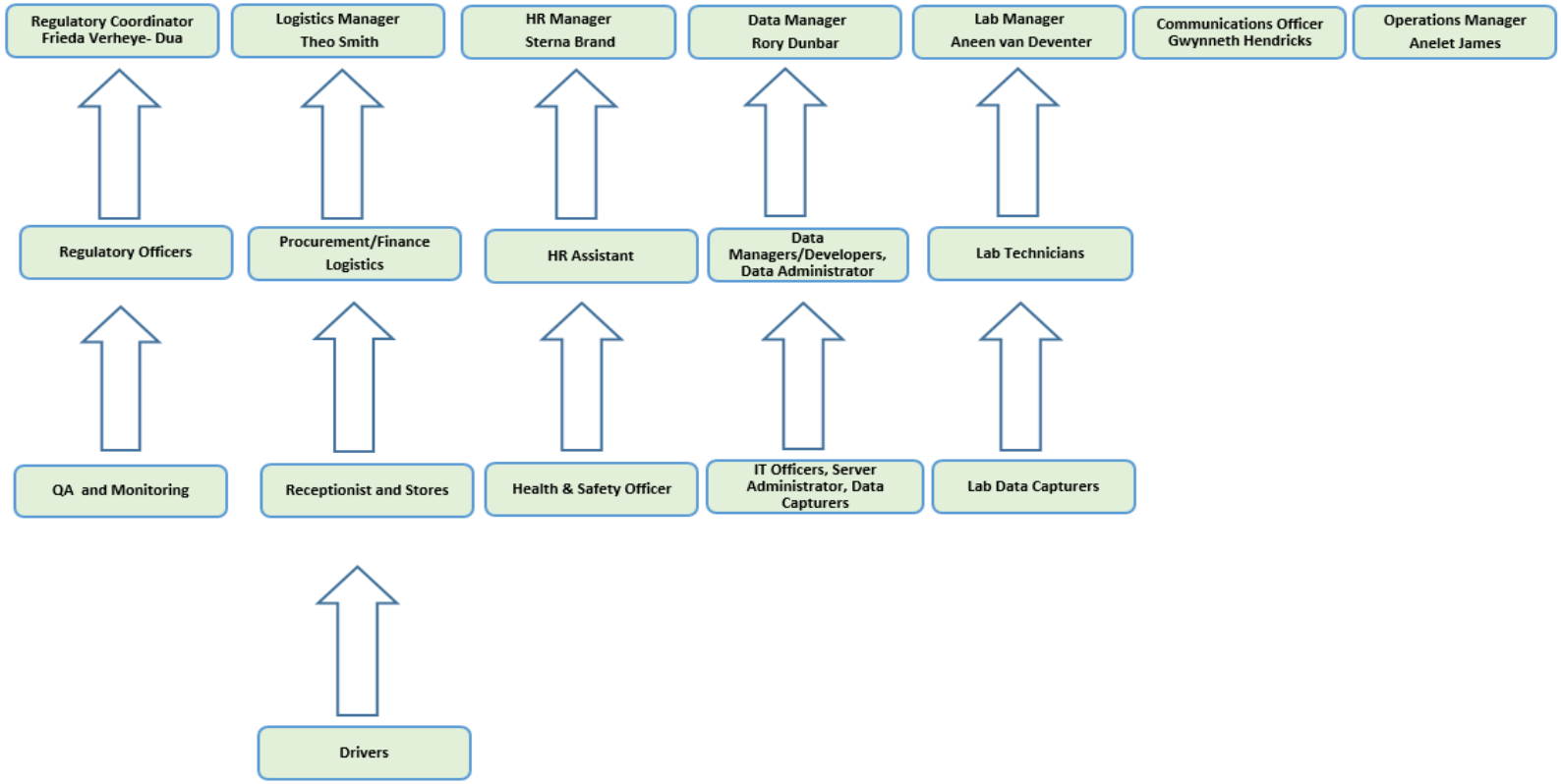
Data Quality Assistants

Research Apprentices

Research Auxiliaries

Staff component including support staff – n=32

SUPPORT COMPONENT



DTTC TOTAL STAFF COMPONENT- 330

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 progam 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 DS and DR-TB in children (leads; Anthony Garcia-Prats, Marieke van der Zalm and Megan Palmer), 2) preventive trial for TB in children (lead: Anneke Hesseling, 3) novel diagnostics and biomarkers for TB diagnosis in children (lead: Elisabetta Walters, Anne-Marie Demers), 4) TB vaccine trials (lead: Heidi van Deventer), and 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 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, bedaquiline) currently ongoing.

During 2017, the paediatric group (n=70 personnel including 19 clinicians) has specifically actively pursued linking and collaborating with the social science group at DTTC (social science 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. 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 group has been highly productive during 2017, resulting in 49 publications in international peer-reviewed journals (Appendix I), participation in several national and international TB treatment guideline meetings, significant numbers grants awarded, 2 new PhD students registered, strategic new South African and international collaborations, several national and international conference presentations and the graduation and ongoing support of several postgraduate students (Appendix II)

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. 12 women were enrolled and follow-up has been completed July 2017. The overall trial was closed to accrual in 2016 and follow-up (740 maternal-infant pairs).was completed in September 2017

TBTC Study 35*:* This multisite study, funded by the CDC TBTC (PIs: Anneke Hesseling, Deron Burton, Kelly Dooley) 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 MCC and local ethics committees. A novel fixed dose score paediatric formulation has been developed for the trial. The database is in development and the trial is expected to open in Q3 of 2018 under an FDA IND.

Therapeutic trials: treatment of drug-susceptible TB (DS-TB)

SHINE: (Site PI: Anneke Hesseling) treatment shortening for non-severe pulmonary TB in children: This multi-site open-label international trial (funder: BMRC/Wellcome Trust, DFID), is the first trial 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. SHINE aims to enrol 1200 children in South Africa, Zambia, Uganda and India by end June 2018. The trial PI and sponsor is the MRC CTU at UCL (PI: Di Gibb). DTTC opened to accrual to July 2016; to date, 220 participants have been enrolled at DTTC. Nested PK sampling has been completed in 17 children to date. 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 (findings presented at the 2016 WHO Childhood TB Subgroup meeting in Liverpool). DTTC is also coordinating the process for central expert review of the CXRs 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.

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*:* this phase I/II trial (PI Hesseling), funded by TB Alliance, will evaluate the optimal and safe dose of rifampicin in HIV-uninfected children treated for TB. The study utilizes a dose escalation approach in a maximum of 5 dosing cohorts of 20 children aged 0-12 years in each cohort. Dosing cohort 1 was successfully enrolled during 2017 and the trial steering committee recommended in January 2018 that dosing cohort 2 be opened using a dose if 35 mg/kg over 14 days. Dosing cohort 2 has opened and it is expected that 3 dosing cohorts will be required. The PK target is determined by recent adult studies using high dose rifampicin (35-40 mg/kg per day), which was well tolerated. 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. Dissemination of initial results is planned during 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.

Therapeutic trials: prevention of MDR-TB

TB-CHAMP: MDR-TB preventive therapy trial: 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 includes approximately 1500 children 0-5 years of age. The trial, led by DTTC (PI: Hesseling, Schaaf, Seddon) 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. Formative social science work preceded the trial opening. The evaluation included a range of mixed data sources: (i) review of routine summary statistics on demography, epidemiology, and health service delivery at each health facility, (ii) day long semi-structured *in situ* observations – completed in 10 of 16 health facilities and surrounding catchment areas, (iii) in-depth interviews with different cadres of health workers including nurses, counsellors, and community-based support staff – n = 14, (iv) group discussions with grassroots community advisory structures – n = 13, and (v) ethnographic interviews with 7 current MDR TB patients and their families – only at the THINK site. These data were collected between May and July 2016. The evaluation was instrumental in characterising the capacity, community acceptability, and operational platforms for delivering the trial at these two sites. It further served to characterise key issues in patient perceptions, understandings, motivations, and anxieties about participation. These insights have been summarised into 16 clinic-community narrative reports and one summary report for the study implementation team.

A formal PK lead-in study was completed in 2017 with the target of enrolling the bio-availability of a novel scored dispersible levofloxacin formulation, to be used in the trial, in 24 children (open-label) showing that the novel paediatric levofloxacin formulation was well tolerated, safe, and had adequate exposers in children < 5 years of age Data have been submitted for publications. The trial opened to accrual in Q4 2017 at DTTC, and in Q1 2018 at the other 2 sites. Additional grant funding has been requested from the 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 multidrug-resistant (MDR) TB (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 trial, Groups 1 (ages 12-18 years) and 2 (ages 6-12 years) have fully enrolled, and data from these groups informed WHO guidance in 2016 for the use of delamanid in children 6-17 years of age with MDR-TB. Group 3 (ages 3-6 years) completed enrolment in 2016 with long-term follow-up now complete. Group 4 (ages 0-2 years) completed enrolment in 2017 for 232, with long-term follow-up in 233 ongoing for this group. The 232 study is now closed with final data analysis 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 antiTB 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 will be reported separately. 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 masters degree students, to date.

MDR PK 2: PI Anthony Garcia-Prats. Building on the data, experience, and clinical platform of MDRPK1, this NIH-funded (R01 grant) seeks to evaluate the pharmacokinetics and safety of model-optimized doses of the key second-line antiTB 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, 56 children have been enrolled. An interim analysis presented in October 2016 provided the first data on both moxifloxacin pharmacokinetics in children <7 years of age and on linezolid pharmacokinetics in children with TB. Analysis of linezolid pharmacokinetics and safety is ongoing, with results anticipated in 2018 that are expected to inform international dosing guidance.

IMPAACT P1108: PIs Anneke Hesseling and 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 21st September 2017. The first 9 children have been enrolled and interim analysis is ongoing.

Bedaquiline CRUSH Study (TASK-002): Protocol Co-Chair – Garcia-Prats. This study, funded by 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. 24 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, Upssala University). Results, which showed that bedaquiline administered dissolved in water was bioequivalent to whole tablets, was presented at multiple international meetings.

TB vaccine trials (PIs: Hesseling, du Preez)

Vaccine Project Management (VPM): PI: A. Hesseling , project lead: Heidi van Deventer. This phase 2 multicentre trial evaluated the safety and immunogenicity of a novel recombinant BCG vaccine in HIV-exposed and unexposed infants, in four South Africa sites (overall PI: Mark Cotton). DTTC enrolled 40 infants in Khayelitsha during 2016 and the trial was closed to accrual during Q4 2016. Clinical follow-up ended October 2017. Based on interim data analysis, no concerning safety signals have been detected. Data analysis is in progress. This novel TB vaccine candidate is moving forward into phase 3 trials in both infants and also in adults.

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.

We are evaluating different diagnostic approaches using samples that are minimally invasive and easy to collect, such as stool, urine and blood. Children who present to Tygerberg and Karl Bremer Hospitals with possible intrathoracic (pulmonary) TB are enrolled and thoroughly investigated clinically and bacteriologically. Novel diagnostic strategies are compared to a rigorous clinical and bacteriological reference standard which includes multiple respiratory samples analysed by smear microscopy, Xpert MTB/RIF and culture. The platform also includes a well-characterized bio-repository of blood and urine samples for evaluation of promising new biomarkers for TB diagnosis and treatment response. Children are followed to 6 months regardless of TB diagnosis. The 1st large study nestled in this platform completed recruitment and follow-up in November 2017, having enrolled over 600 children. This study has resulted in the publication of a number of research articles reporting on the utility of stool specimens for TB diagnosis in children. In addition, it has generated preliminary data on serum and urine-based biomarker signatures, which has resulted in successful funding applications to support ongoing work in these fields. Sub-studies evaluating respiratory co-pathogens and lung function testing in children with suspected TB have also been supported on this platform, and have resulted in successful funding applications.

New study title: Intra-thoracic tuberculosis in children: moving towards better diagnosis and improved lung health (UMOYA "breathe")

A new diagnostic cohort study – UMOYA- opened for recruitment in November 2017. The UMOYA study builds on the pilot data generated in the recently completed study, and has leveraged funding from NIH, Thrasher Foundation, EDCTP and South African MRC. UMOYA will enrol 300 children with suspected TB and 100 healthy sibling controls. 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.

Utility of stool samples for the diagnosis of TB in children:

Xpert MTB/RIF on stool specimens: We have published data demonstrating that the Xpert MTB/RIF assay on stool samples collected from young children who present to hospital with severe pulmonary disease can rapidly detect 1 in 4 children who will be treated on clinical grounds, and 1 in 2 who will be confirmed on respiratory samples collected using invasive procedures.

Liquid mycobacterial culture on stool specimens: We evaluated stool culture as an alternative to respiratory specimens for the diagnosis of suspected intrathoracic TB in 188 children (median age 14.4 months; 15.4% HIV-infected). Stool culture was compared to Xpert and culture of up to 4 respiratory specimens.. Decontamination/digestion with NALC/NaOH 1.25% was completed for stool and respiratory specimens, followed by concentrated fluorescent smear microscopy, Xpert MTB/RIF and liquid culture. Stool cultures were contaminated in 78/188 (41.5%) stool specimens. Of the 110 children with evaluable results, stool culture detected 7/38 (18.4%) children with confirmed TB, and 7/90 (7.8%) children initiating TB treatment. The sensitivity and specificity of stool culture vs. culture and Xpert of 4 respiratory specimens were 28.6% (95% CI 11.3-52.2%), and 98.9% (95% CI 93.9-100.0), respectively. In conclusion, we could not recommend stool culture to replace respiratory specimens, for the diagnosis of intrathoracic TB in children and we advocate for the development and evaluation of improved laboratory protocols to reduce contamination and increase sensitivity.

Evaluation of novel TB biomarkers in children

1. ***Urine Proteomics:*** In collaboration with Boston Children's Hospital (Harvard University; PI Professor R. Husson), our group was awarded a Thrasher Foundation Research grant to evaluate the diagnostic potential of host-based urine proteomic signatures for the diagnosis of TB in children. Preliminary data using urine samples collected from our cohort suggest that the urine proteome of children with TB differs significantly from that of children who do not have active TB. The project will span 2016-2018. Samples collected from South African, Kenyan and Peruvian children will be analysed in the US laboratory.

2. ***Serum bio-signatures:***

a) In collaboration with Arizona State University (PI Tony Hu; South African PI E Walters) and SACEMA (A Welte, E Grebe), we are jointly evaluating NanoShell-MS profiling (to detect *M.tb* antigens CFP-10 and ESAT-6, and the TB-associated host marker IP-10) to develop a quantitative prediction model for active TB diagnosis and for evaluation of treatment response in children with suspected TB. This work is supported by the NIH (R01).

b) Evaluation of TB Lipoprotein as a potential diagnostic biomarker of TB in children.
We are collaborating with Dr Nicole Sampson, Stony Brook University, US, to test a novel serum biomarker, TB lipoprotein (TLP) on a small set of serum samples, as a proof of concept to demonstrate whether the biomarker has potential for the rapid diagnosis of tuberculosis in children.
Dr Sampson is a chemist with a doctoral degree from the University of California, Berkley. Research in the Sampson laboratory focuses on understanding the relationship between protein structure and protein function and synthesizing chemical tools to probe and control biological function. Work is ongoing in the area of tuberculosis steroid metabolism. TB Lipoprotein (TLP) is a specific mycobacterial modification of low density lipoprotein (LDL), a host biomolecule.

For paediatric operational research (lead: Karen du Preez): please refer to the overarching DTTC operational research section below

Students Graduating

Louvina Van der Laan & Jana Winckler Graduating CUM LAUDE in MPhil at UCT

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.

Project updates:

Operational Research Assistance Project

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 a experiential learning course to develop 3 independent study protocols for research to be undertaken in 2017/8. Five mentors from DTTC are supporting the trainees through protocol development, study implementation and publication of their findings.

Key Outputs:

All 3 projects have completed the mentored protocol development stage and were approved for implementation by the Stellenbosch University Health Research Ethics Committee. During data collection, one project was able to complete interim analysis and present findings from the study at the Union World Conference on Lung Health, 2017 in Guadalajara, Mexico. (*Comparing early treatment outcomes in patients on bedaquiline-based regimens vs conventional MDR-TB regimens at PHC facilities in the Cape metro*, Naidoo L, Da Costa D, Garcia-Pratts T, Osman M). A second study has submitted an abstract to the upcoming Union World Conference on Lung Health, 2018 (*Burden, characteristics and treatment outcomes of patients treated for Isoniazid mono-resistant TB in Cape Town, South Africa,* Solomon- da Costa F, Joseph K, Osman M, du Preez K).

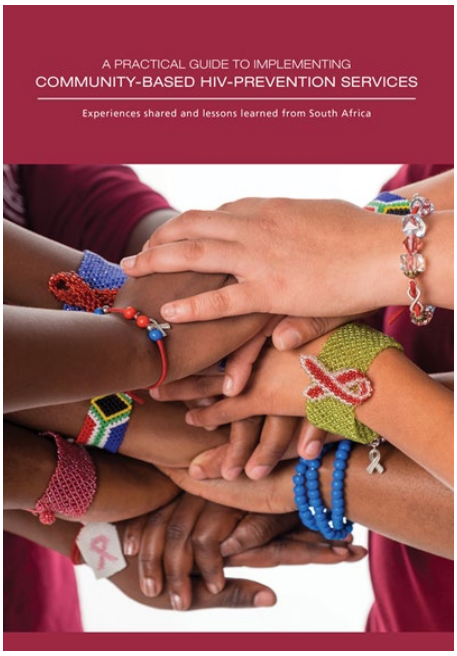
Community HIV/AIDS Prevention Project (COMAPP - Lead: Sue-Ann Meehan)

This project implemented HIV prevention activities between October 2011 and September 2016 in order to address the challenge of reducing HIV transmission in high disease burden communities around Cape Town. In 2017, at the request of the Centers for Disease Control and Prevention in South Africa (CDC-SA), COMAPP launched, "**A practical guide to implementing community-based HIV prevention activities**. **Experiences shared and lessons learned from South Africa."**

The CDC-SA request was made because of the extensive knowledge, understanding and skills generated at the Desmond Tutu TB Centre (DTTC), as a result of more than 10 years of experience in implementing community-based HIV and TB programs, to improve access to HIV testing and linkage to care, as well as strengthen the integration of HIV and TB services, in many communities around Cape Town and in the Winelands.

Key output:

A practical guidance document on how to implement community-based HIV prevention activities. The overall aim of this Guide is to provide practical information on various aspects of implementing community-based HIV services and was produced using knowledge gained from three independent community-based HIV prevention projects implemented by the DTTC between 2008 and 2017.



This Guide was written in close collaboration with numerous stakeholders; individuals and organizations, including local non- governmental organizations (NGOs) as well as Government health partners. It is targeted at program

implementers. Each chapter focuses on a different aspect of implementation, from engaging with stakeholders and communities to how to set up teams and conduct HIV testing services that integrate important other services including screening for TB, sexually transmitted infections and non-communicable diseases.

This guide also includes case studies, best practices, practical tips, photographs and training materials. It was launched on 23 June 2017 at a very well attended function, hosted at the 'One and Only' at the waterfront.

Currently available in English, Afrikaans and French the Guide will soon also be available in isiXhosa, isiZulu, and Portuguese (Available online at: http://www.sun.ac.za/english/faculty/healthsciences/paediatrics-and-child-health/Pages/Home.aspx)

Paediatric operational research (Lead – Dr Karen du Preez)

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

Current projects focusses on optimizing surveillance strategies, prevention and routine data for children with TB, including HIV co-infected children.

Complementary surveillance strategies are needed to better characterise the epidemiology, care pathways and treatment outcomes of tuberculosis in children

The aim of this study was to accurately characterise the burden, spectrum of disease and outcomes of children with TB managed at referral hospital level using combined clinical and laboratory hospital-based surveillance strategies.

A prospective cohort study was conducted, including all children (<13 years) managed for TB at a large referral hospital in Cape Town, South Africa, 2012. Children were identified through clinical surveillance in addition to ongoing laboratory surveillance. Data were collected from clinical records, the National Health Laboratory Service database and provincial electronic TB registers. The study reported overall TB disease burden, spectrum, care pathways and treatment outcomes. Univariate analysis compared characteristics of children by surveillance strategy, to characterise children missed by existing laboratory-based surveillance.

The study identified 395 children (180 [45.6%] <2 years) who were managed for TB at TBH during 2012. Clinical surveillance identified 237 (60%) children in addition to laboratory

surveillance. Ninety (24.3%) children were HIV co-infected; 113 (29.5%) had weight-for-age z-scores <-3. Extrapulmonary TB (EPTB) was diagnosed in 188 (47.6%); 77 (19.5%) with disseminated TB. Favourable TB treatment outcomes were reported in 300/344 (87.2%) children with drug-susceptible and 50/51 (98.0%) with drug-resistant TB. Older children (OR 1.7; 95% CI 1.0-2.8), those with EPTB (OR 2.3; 95% CI 1.5-3.6) and in-hospital deaths (OR 5.4; 95% CI 1.1-26.9) were more frequently detected using laboratory surveillance. TB/HIV co-infected children were less likely to be identified through laboratory surveillance (OR 0.3; 95% CI 0.2-0.5).

Main messages from this study included the substantial burden of paediatric TB disease managed at referral hospital level in this high-burden TB setting, and the importance of adopting complementary hospital-based surveillance strategies for childhood TB. Although clinical surveillance was key to identify all children and provided opportunities for real-time clinical care, laboratory surveillance remains important to understand drug-resistant trends and confirmed disease in children across the TB disease spectrum. *(Manuscript published; BMC Public Health)*

Timing of HIV diagnosis in children with tuberculosis managed at a referral hospital in Cape Town, South Africa

The aim of this study was to investigate the prevalence of and factors associated with simultaneous tuberculosis (TB) and human immunodeficiency virus (HIV) diagnoses in children.

A retrospective cohort study including all TB-HIV co-infected children aged <13 years managed at Tygerberg Hospital during 2012. Data were collected from medical records, laboratory results and electronic anti-tuberculosis treatment registers. A simultaneous TB-HIV diagnosis was defined as an HIV diagnosis made within 7 days before or after a diagnosis of TB.

Hospital records were available for review for 88 (98%) of 90 children with TB-HIV co-infection managed at TBH during 2012; 37 (42%) had a simultaneous TB-HIV diagnosis and 51 (58%) children had been known to have HIV before their TB diagnosis. Interruption of antiretroviral therapy (ART) was reported in 9/32 (28%) children with known HIV infection at TB diagnosis, while missed opportunities for ART initiation were identified in 8/19 (42%) ART-naive children. Simultaneous TB-HIV diagnosis was more likely if maternal HIV infection was unknown at the time of the child's birth (OR 2.7, 95%CI 1.0–7.2) and was associated with unfavourable anti-tuberculosis treatment outcomes (OR 5.9, 95%CI 1.4–25.2).

The study found that TB diagnosis provides an important opportunity to test children for HIV. It further highlighted missed opportunities for HIV prevention, earlier diagnosis and ART

initiation. *(Manuscript in press; International Journal of Tuberculosis and Lung Disease* - 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; 22(5):488-95. doi: 10.5588/ijtld.17.0613. PubMed PMID: 29663952.*)*

Excellent Treatment Outcomes in Children Treated for Tuberculosis Under Routine Operational Conditions in Cape Town, South Africa

Tuberculosis (TB) remains a leading cause of death in children globally. It is recognized that human immunodeficiency virus (HIV) infection increases the risk of developing TB, but our understanding of the impact of HIV on risk of mortality for children treated for TB is limited. This study aimed to identify predictors of mortality in children treated for drug-susceptible TB.

A retrospective analysis of all children (<15 years of age) routinely treated between 2005 and 2012 for drug-susceptible TB in Cape Town was conducted using the programmatic electronic TB treatment database. Survival analysis using Cox regression was used to estimate hazard ratios for death. Logistic regression was used to estimate the odds of unfavourable outcomes.

The study found that of 29 519 children treated for and notified with TB over the study period, <1% died during TB treatment and 89.5% were cured or completed treatment. The proportion of children with known HIV status increased from 13% in 2005 to 95% in 2012. Children aged <2 years had an increased hazard of death (adjusted hazard ratio [aHR], 3.13; 95% confidence interval [CI], 1.78–5.52) and greater odds of unfavourable outcome (adjusted odds ratio [aOR], 1.44; 95% CI, 1.24–1.66) compared with children aged 10–14 years. HIV-infected children had increased mortality compared to HIV-negative children (aHR, 6.85; 95% CI, 4.60–10.19) and increased odds of unfavourable outcome (aOR, 2.01; 95% CI, 1.81–2.23). Later year of TB treatment was a protective predictor for both mortality and unfavourable outcome.

This study showed a dramatic improvement in HIV testing in children with TB over time and excellent overall treatment outcomes. HIV infection and young age were associated with increased risk of death and unfavourable outcome. *(Manuscript published; Clinical Infectious Diseases).*

RESEARCH FOCUS AREA THREE: PRAGMATIC COMMUNITY RESEARCH

HPTN071 (PopART) (Lead: Nulda Beyers, Peter Bock)

The HPTN 071 or PopART study is a cluster-randomized trial which aims to determine the impact of two community-level combination prevention packages, both of which include universal HIV testing and intensified provision of HIV/ART care, on population-level HIV

incidence. The study is being 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 is 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).

Field work for PopART began in January 2014. The study concluded the final annual round of the CHiPs intervention in December 2017. PC follow up will be completed in June 2018. The primary findings of the study will be reported early 2019. Between January 2018 and end June 2019 there will be extensive consultation with stakeholders and dissemination of study results as part of a planned exit from study communities and clinics.

Primary outcomes are 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). The HPTN071 Population Cohort (PC) is currently in its 3rd round (PC 36) of study participant follow up. Progress of the population cohort, South Africa to date is as follows:

CHiPs intervention progress:

- By the end of 2017 for the third annual round for both South Africa and Zambia 152,454 households had been visited by CHiPs
- 168,556 individuals accepted HIV testing among those eligible for HIV testing

PC progress

- PC 0: 18 633 participants were enrolled
- PC12: 12 821 PC assessment visits were completed
- Of the PC assessment visits completed for PC12, 3256 rapid tests were completed
- PC 24: 15 344 PC assessment visits were completed
- Of the PC assessment visits completed for PC24, 3 029 rapid tests were completed

- As of 31st January 2018, 53.9% (n=8269) of population cohort assessment visits had been completed.

Data collection in the population cohort is scheduled to end on the 30th June 2018. Data cleaning and analysis will continue thereafter until the PopART results are disseminated early 2019. Dissemination will involve the announcement of primary results to all HPTN 071 (PopART) stakeholders, as well as a number of community level disseminations in HPTN 071 (PopART) communities in South Africa.

Within PopART there is also an extensive social science component to describe and explain the trial outcomes; inclusive of formative research conducted before intervention implementation and ongoing research throughout the study period. Refer to DTTC social science component for summaries on qualitative work conducted for this trial.

DTTC GRANT APPLICATIONS AND AWARDS 2017

Description	Grant Application	Date Submitted	Submitted by	Outcome
11th International Child TB Training Course (hosting and international faculty)	NRF Knowledge Interchange & Collaboration (KIC) grant	2017	Gwynneth Hendricks	Awarded
International AIDS Society	CIPHER grant	2017	Adrie Bekker	Awarded
UMOYA Platform (serum diagnostics, respiratory pathogens and lung function in children with TB)				
1.Career fellowship	EDCTP	2017	Marieke van der Zalm	Awarded
2. Personal career award	HB-MJ Thom award	2017	Marieke van der Zalm	Awarded
3.Intra-thoracic tuberculosis in children: Moving towards better diagnosis and improved lung health	SA MRC SIR	2017	Marieke van der Zalm / Liz Walters	Awarded
4. Long-term ipmact of TB onlung health in children	NIH K43	2017	Marieke van der Zalm	Pending
5. Novel serum diagnostic biomarkers for TB in children	NIH RO1	2017	Liz Walters (in collaboration with Tony Hu from Arizona State University)	Awarded
Complementary surveillance strategies for	Early Research Career grant	2017	Karen du Preez	Awarded

paediatric TB				
Promoting uptake of ART at CD4 counts greater than 500 – lessons from three facilities in Metro and Rural Sub-districts, Western Cape Province, South Africa	Decision-Maker Led Implementation Research Grant awards (Centre for Evidence-based Health Care, SU)	2016	Graeme Hoddinott	Awarded
The effect of adherence clubs on quality of clinic care for HIV+ patients on antiretroviral treatment in the Cape Winelands District	Decision-Maker Led Implementation Research Grant awards (Centre for Evidence-based Health Care, SU)	2017	Peter Bock/Sue-Ann Meehan	Awarded
Linked In	Bill and Melinda Gates Foundation	2017	Anneke Hesseling and Muhammad Osman	Awarded
	TB REACH	2017	Anneke Hesseling and Muhammad Osman	Pending
TB-CHAMP (top-up funding)	EDCTP	Q1 2018	Anneke Hesseling	Pending
	GHIT	Q1 2018	Anneke Hesseling	Pending
Post-treatment follow-up to detect recurrent tuberculosis in a high-incidence setting	Wellcome Trust Seed Award	2017	Florian Marx	Pending
TBiMpact: In-depth evaluation of the potential impact of sentinel surveillance of pediatric TB meningitis	NIH K43 EDCTP	2017 2017	Karen du Preez	Pending
Adapting delamanid and levofloxacin for paediatric multidrug-resistant tuberculosis (ADAPT-TB)	EDCTP	2017	Anthony Garcia-Prats	Not awarded
TB-associated mortality in South Africa: longitudinal trends and the impact of health system interventions	South African MRC National Health Scholars Program (SA NHSP)	Period 2017-2020 (PhD)	Muhammad Osman	Awarded
	SACEMA Emerging Researcher	Period 2017-2018	Muhammad Osman	Awarded
Personal career development,	BMRC Fellowship	Period 2018-2022	James Seddon	Awarded

international collaboration (nested work in TB-CHAMP)	Fulbright Scholarship	May – November 2017		Awarded
Postoctoral fellowship	Spanish Paediatric Infectious Diseases Sociecy	2017-2018	Elisa Lopez	Awarded
Stool biome and antimicrobial resistance sub study, TB CHAMP , PhD work	NHLS	Period 2017 - 2019	Kristien Nel van Zyl	Awarded
Familial management of paediatric co-morbid HIV, TB, and diabetes	Wellcome Trust – PhD scholarship	Q1 2018	Dillon Wademan	Pending
Power between client and state in the implementation of expanded home-/community-based HIV services	Wellcome Trust – PhD scholarship	Q1 2018	Hanlie Myburgh	Pending
Social science network for preparedness and response to infectious threats (coordination and support)	EU Horizons 2020	Q1 2018	Graeme Hoddinott	Pending

AWARDS AND OTHER RECOGNITION

1. Dr. Muhamad Osman was awarded Honorary Lecturer in Health Policy and Systems, School of Public Health and Family Medicine, University of Cape Town

2. Professor Anneke Hesseling was voted to serve on the Core Science Group (CSG) for the CDC Tuberculosis Trials Consortium

3. SSA NRF rating: B1 Rating: Major national and international recognition, South African National Research Foundation: 2017-2022

4. Dr. James Seddon , Imperial College London, was appointed as extraordinary Senior Lecturer at DTTC, Stellenbosch University (2017-2020)

5. Professor Kelly Dooley, Johns Hopkins University, was appointed as extraordinary Associate Professor at at DTTC, Stellenbosch University (2017-2020)

6. Professor Amita Gupta, Johns Hopkins University, was appointed as extraordinary Professor at at DTTC, Stellenbosch University (2017-2020)

7. Dr. Dolapo Awoniyi, was awarded the American Thoracic Society International Trainee Award for his research on the "Evaluation of host markers for tracking early treatment response in newly diagnosed pulmonary TB patients."

DTTC SOCIAL SCIENCE COMPONENT (SUPPORTING ALL 3 RESEARCH FOCUS AREAS)

The social science team have successfully implemented a broad range of data collection and analysis activities as components of the wider DTTC research portfolio. These activities ranged in scope from an 18-month cohort of 89 families with hundreds of in-depth interview hours, to an exploratory analysis of four children and their caregivers' experiences of MDR-TB treatment palatability. Across activities, all data collection, management, processing and preparation for analysis is standardised and managed by a dedicated data quality team managed by Hanlie Myburgh. Overall, all activities were implemented successfully per protocol aims and objectives despite the multiple field challenges of conducting this form of social science research. Further, the team was highly innovative in designing and refining novel methods to answer research questions with greater sophistication. A priority for 2018/9 is improving the replicability of these efforts across more platforms and building on the budding culture of publication –

especially guiding relatively junior postgraduate researchers to their first first-author manuscripts.

QUALITATIVE COHORT FOR HPTN 071 (PopART)

The social science team completed data collection as part of the qualitative cohort. The team has collected data for all 5 modules from 74 families over the past 18 months. A data audit has been completed and transcription processes have been streamlined. In January 2018, the team started the final round of Story of the Trial research within the PopART study. The final round will take 9 months. They are particularly interested in any changes that have occurred in PopART communities, post-CHiPs intervention.

HEALTH WORKER ATTITUDES AND PRACTICES SURVEY, ROUND 3 – OPEN COHORT FOR HPTN 071a (stigma ancillary to HPTN 071 (PopART))

The purpose of this cohort is to understand the lived experiences of people living in the context of the implementation of Universal Testing and Treatment implementation – specifically in relation to health behaviour, social drivers or risk, and uptake of health service innovations. Data collection continued from 2016 and was completed in November 2017. During this period, a team of 14 graduate research interns/officers and 12 research assistants (with support from a researcher) collected four 'modules' of data in 9 study communities. Each module included a number of facilitated discussions and participatory research activities over the course of multiple interactions with each participant family. A total of 89 participant families were retained throughout modules two to five, with contributions from over 350 individual members of these families. The dataset now includes over a thousand recorded hours of in-depth interviews/discussions as well as hundreds of days of field observation notes. Data processing (transcription and translation) and analysis is ongoing with 10 manuscripts in development for submission in 2018.

CROSS-SECTIONAL SURVEY OF YOUNG PEOPLE (15-19-YEARS-OLD) EXPERIENCES OF SEXUAL HEALTH AND HIV SERVICES – FOR P-ART-Y

The survey served two broad purposes: (a) as a comparator for the primary outcome (knowledge of HIV status) for the P-ART-Y study in control communities, and (b) to describe the sexual risk profile and HIV-related service needs of young people (15-19-years-old). Data collection commenced on the 26th September 2017 and was completed on the 4th of November 2017. During this period, a team of 14 research assistants (with support from three graduate research officers) collected data in three study communities. Of the 4,118 households (HH) approached, 80.9% had someone present during data collection. Of the total of 3,246 HH that

granted permission to explain the survey, 19.3% included an eligible 15-19-year-old. A total of 835 15-19-year-olds in these households were enumerated, and 667 (80%) consented to participate in the study. The questionnaire was conducted on a smart-phone device. Data cleaning was completed in 2017 and analysis is ongoing with three manuscripts in development for submission in 2018.

MIXED-DATA FORMATIVE RESEARCH FOR HPTN 084 (LIFE)

The purpose of these data was to describe the research community context for the implementation of the HPTN 084 (Life) study and inform the operational planning for the DTTC's new site office space in Kuils River. Data collection was completed between August and September 2017. During this period, a team of 2 research assistants (with support from a research intern) conducted systematic observations and key-informant discussions in 10 neighbourhoods in the site office's catchment area. Further, they (with support from a researcher) prepared an operational report for the HPTN 084 study team. Further data collection is pending the start of the HPTN 084 study.

MIXED-DATA OBSERVATION OF HOW THE POPART INTERVENTION WAS OPTIMIZED AND IMPLEMENTED FOR YOUNG PEOPLE (10-24-YEARS-OLD) AS CLIENTS – FOR P-ART-Y

In the P-ART-Y study, the PopART intervention package was optimized to be more attractive to young people. The purpose of these data was to describe how these optimizations were implemented in real-life contexts. Between November 2016 and June 2017, a graduate research officer, with support from P-ART-Y study staff, documented the implementation of these observations with semi-structured observational tools. Data cleaning is complete. One manuscript reporting on these optimization processes is in preparation.

A PRE- AND POST- EFFECTIVENESS EVALUATION OF THE IMPACT OF A STRUCTURED TRAINING PROGRAMME TO SENSITIZE HEALTH WORKERS TO DELIVER HIV-RELATED SERVICES TO YOUNGER (10-24-YEAR-OLD) CLIENTS

Training of the health workers implementing the PopART intervention was identified as a key optimization mechanism to improve younger clients' experiences. A survey was implemented pre-, immediately post-, and 6-months post- among all health workers receiving this training (n=204) to evaluate its impact on their attitudes toward younger clients. One manuscript is in preparation.

MIXED-DATA IN-DEPTH INTERVIEWS WITH STAFF/STAKEHOLDERS AND OPERATIONAL REVIEW OF CLINIC-BASED COMPONENTS OF THE 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 May and August, 51 in-depth interviews with key informants were collected. Four manuscripts are in preparation for submission in 2018.

MIXED-DATA OBSERVATIONAL AND DISCUSSIONS WITH FIELD STAFF OF THE COMMUNITY-BASED COMPONENTS OF THE POPART INTERVENTION PACKAGE – ANNUAL ROUND 4

A set of structured observations and discussions with implementers conducted annually in 9 study communities between January and March. These data were collected without issue in 2017, with the fifth and final round planned for 2018.

IN-DEPTH PALATIBILITY INTERVIEWS WITH CAREGIVERS AND HEALTH WORKERS FOR CHILDREN ON DRUG-RESISTANT TB TREATMENT

Linked to an honours research project, this included observational and in-depth interviews with caregivers to explore possible topics for understanding palatability of current MDR-TB treatment for young children. The honours research project was successfully completed and this work informs the subsequent acceptability evaluation nested in the MDR-PK2 study to be implemented in 2018.

IN-DEPTH ACCEPTABILITY INTERVIEWS AND OBSERVATIONS WITH CAREGIVERS AND CHILDREN ABOUT A NOVEL FORMULATION OF LEVOFLOXACIN TO BE USED IN THE TB-CHAMP TRIAL

The TB-CHAMP trial users 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 two manuscripts are in preparation for submission in 2018.

IN-DEPTH INTERVIEWS AND OBSERVATIONS WITH CAREGIVERS ABOUT IMPLEMENTATION OF A TRIAL OF MDR-TB NOVEL PROPHYLAXIS IN KWA-ZULU NATAL (ANALYSIS ONLY)

As part of formative research in advance of the TB-CHAMP trial, this research was conducted by a student in KwaZulu-Natal. The data were analysed in 2017 and successfully submitted as part

of an MPhil in Transdisciplinary Health and Development studies dissertation. The student is preparing a manuscript to report on these data for submission in 2018.

IN-DEPTH INTERVIEWS KEY HEALTH SERVICES STAKEHOLDERS ABOUT THE IMPLEMENTATION OF A TB MODULE FOR THE TIER.NET HEALTH INFORMATION SYSTEM (ANALYSIS ONLY)

In July-September 2016, members of the social science team were contracted to conduct a *post-hoc* evaluation of the implementation process of a TB module for the TIER.Net Health information system in three pilot health facilities in the Cape Winelands district. In 2017, this was expanded to include finer analysis of the data and a manuscript reporting on the findings is now in preparation for submission in 2018.

Students Graduating

Angelique Thomas – MA in Political Studies at UWC

Rosemary Brown – MA in Psychology at UKZN

Suzanne Staples – MPhil in Health and Development Studies at SUN

Nina van Tonder – Honours in Psychology at SUN

Stephanie Jacobs – Honours in Anthropology at SUN

Tarshlyn Herandien – Honours in Social Sciences at UWC

OVERALL TRAINING ACTIVITIES AND CAPACITY BUILDING AT DTTC

The TB Clinical Forum 2017, hosted by DTTC at the Stellenbosch University FMHS and organized by the City of Cape Town officials was held monthly between February and November 2017 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. Six speakers from DTTC presented during 2017.

TB Clinical Forum 2017

Date	Topic	Presenter(s)

10th February 2017	The shortened MDR-TB Regimen implementation	Yulene Kock, Julien Te Riele and Jennifer Hughes
10th March 2017	Management of TB/DR-TB in Pregnancy	Jennifer Hughes
7th April 2017	Operational Research for TB Value and application of routine data |Linkage to care	Pren Naidoo and Karen du Preez
12th May 2017	TB Meningitis -adults and children	Ronald Toorn & Graeme Meintjies
14th July 2017	TASK Update on MDR-TB trials	Andreas Diacon
11th August 2017	Paediatric TB-update on Diagnosis is and Management	Simon Schaaf and Liz Walters
8th September 2017	Ethical issues in DR-TB Management	Lesley Londen
6th October 2017	Quarterly Research Update on Paediatric TB treatment Trials - MDR TB & Bedaquiline Study	Anneke Hesseling & Tony Garcia Prats
10th November 2017	Advanced TB Diagnostics /HAIN SL	Grant Theron and Natalie Beylis

The DTTC Academic Meetings 2017, 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.

Academic Meetings 2017

Date	Topic	Presenter(s)
2nd February 2017	Lopinavir/ritonavir 1:1 super-boosting overcomes rifampicin interactions in children	Helena Rabie
16th February 2017	Phenotype and non-humoral functions of B cells during M. tb infection and disease	Andre Loxton
23rd February 2017	Pharmacokinetic model for high dose Rifampicin in adult TB patients	Robin Svenson
9th March 2017	Treatment optimization for TB meningitis: collaborative research from Indonesia and The Netherlands.	Rob Aarnoutse
	Linking rifampicin exposure to treatment response over 6 months in patients with pulmonary tuberculosis.	Elin Svensson
	Crossing Barriers- the role of	Lindsey Te Brake

	efflux pumps and their purpose as a target in TB drug development	
30th March 2017	MDR treatment shortening trial-CTU	Tony Garcia-Prats
6th April 2017	Pyrazinamide resistance -*in M tuberculosis*	Michael Whitfield
11th May 2017	Viral carriage in children with suspected TB	Marieke Van der Zalm
18th May 2017	PK of high dose INH-MDR	Jana Winckler
8th June 2017	Inadequate diagnosis drives development and spread of beyond XDR TB	Marisa Klopper
15th June 2017	TB in healthcare workers	Angela Dramowski
22nd June 2017	Towards innovative and cost-effective TB case case-finding interventions - piloting facility- and household-based active case finding among former TB patients	Florian Marx
13th July 2017	CD8 + T cell Recognition of the MTB infected Cell Implications for TB Diagnostics	Deborah Lewinsohn
27th July 2017	Population Pharmacokinetics of the first line anti-TB drugs in children	Paolo Denti
17th August 2017	Characterization of dormant forms of *Mycobacterium tuberculosis*	Sven Friedrich
31st August 2017	Children with advanced HIV-new WHO guidelines	Lisa Frigati
21st September 2017	A tale of droplets, dusts, handkerchiefs and guinea pigs: Chausse's work on TB transmission	Anne-Marie Demers
5th October 2017	Radiology of Childhood TB: a story of spots, stripes and shadows	Megan Palmer
26th October 2017	Paediatric TB Outcomes in Cape Town: An evaluation of the electronic TB Register	Muhammad Osman

ADVOCACY AND COMMUNITY ENGAGEMENT

World TB Day, March 24, 2017: DTTC hosted an event in the Tyger HUB. The program title was: *State of the art of Paediatric tuberculosis diagnostic biomarker research, therapeutic and operational research for Paediatric TB*. In addition, the PopART Intervention team provided support to the Western Cape Government Department of Health and the City of Cape Town Health Directorate by supporting seven World TB Day Events from the 22 - 24 March 2017. Forty two CHiPs provided HIV testing services to 252 clients in which 23 were diagnosed as HIV positive and referred for HIV care at the local clinic. Fifty six clients were considered presumptive TB cases in which CHiPs collected sputum for laboratory testing. The events were well supported by the community, the government health services, and the local NPO's. PopART provided HIV testing, TB screening, apples, water bottles, and PopART lanyards to attendees as requested by government health services.

P-ART-Y CAB Training, April 22, 2017: Margaret van Niekerk & Getrude van Rensburg delivered the training. The content included sexual development of young people, HIV epidemiology, Reproduction health, Family planning options, and Peer pressure and child sexual abuse.

DTTC CAB General meeting, May 13, 2017: Practical Training- Phoenix & TB CHAMP studies - Basic concepts of TB transmission to effectively inform communities

Madiba Day, July 18, 2017: Scarves distributed to the out-patients of Tygerberg Hospital. HPTN071 Intervention team members tidied up Winelands Clinics in Wellington & Dalvale.

CAB: Budget and Strategy Workshop, August 11-13, 2017: Workshop held at Spier and attended by the CAB Steering committee of 2018. Discussions were held on strategies for 2017 going into 2018 focussing on growth with development, budgets and activities.

World AIDS day, November 29 – December 2, 2017: The PopART intervention team held various functions in the Tygerberg Sub Structure, Khayelitsha and the Cape Winelands (Dalvale & Wellington) Tent testing was offered as well as messaging on treatment and prevention.

DTTC CAB year-end retreat, December 2-3, 2017: FAMCRU, TASK & DTTC members attended. Feedback on counselling, HIV & TB participation and Experiences on strategies followed and outcomes was shared.

Annual DTTC Dissemination meeting, December 8, 2017: The meeting was held at in the TSC Sports hall on Tygerberg Campus. DTTC staff, senior personnel from Stellenbosch University FMHS, personnel of City/Province, members of the DTTC affiliated Community Advisory Board structures and members of the media were in attendance.

THE DTTC COMMUNITY ADVISORY BOARD (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. The CAB members joined other IMPAACT/ACTG CABs in their first development and capacity building event at the **IMPAACT/ACTG CAB Retreat at Goudini Spa, Rawsonville, Western Cape, November 18 -20, 2015**.

Kathy Hinson and Rhonda White of FHI 360 hosted a workshop January 30 to February 01, 2016 in Franschoek on **General CAB development, structure, functions and sustainability – for IMPAACT/ACTG CABs and CLOs**

The formulation of a **DTTC-CAB Constitution and an SOP** was achieved during the development workshops in February and March 2016, followed by the adoption of these documents in April 2016. This was followed by training facilitated by Reverend David Galetta entitled, **"The roles and responsibilities of CAB members"** on May 21, 2016 and "**Leadership and team dynamics**", June 18, 2016. **Research protocol training was conducted by PIs and/or paediatric TB study coordinators** on 21 May 2016 for TB CHAMP, 18 June 2016 for SHINE and 23 July 2016 for P1101.

Monthly General Meetings were conducted throughout the year in 2016 and 2017 and monthly Steering Committee meetings started in addition to these, after the election and appointment of a 7-member steering committee in September 2016.

Other DTTC CAB activities included:

- **IMPAACT Annual Meeting in Washington June 10 -17, 2016 and May, 29th - June 02nd , 2017** – attended by the CLO.
- CAB members and the CLO attended: **6th and 7th International Peace Lecture in 2016/2017 respectively**; Desmond & Leah Tutu Legacy Foundation at the Artscape Theatre.
- **CAB 2017 Strategic Planning Workshop November 25 – 26, 2016**, at FHMS, Tygerberg. Dr Musonda Simwinga from Zambia facilitated the workshop; finalization of the **Strategic**

Document and Budget took place at the **Spier Wine Estate August 11 – 13, 2017**; the final document was presented to the **DTTC EXCO in October 2017**.

- **IMPAACT/ACTG CAB Retreat was held at Goudini Spa, December 2 - 4, 2016** (10 DTTC CAB members attended); and at the **Stellenbosch University Campus, December 1 – 2, 2017** (13 DTTC CAB members attended).
- CAB members attended the **Annual DTTC Dissemination Meeting 2016 at Kirstenbosch, December 9, 2016;** and at the **Tygerberg Campus, December 8, 2017.**
- Represented by 3 members at the **HPTN 084 Stakeholder Meeting, August 9 – 10, 2017**.
- CAB members participated in **a team-building activity on the red open-top bus city sight-seeing tour December 10, 2016** from the Waterfront to Hout Bay; followed by a **team-building cook-out at the CLO's house on December 10, 2017**.

The HPTN 071 (PopART) CAB

Each clinic has 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 HPTN071 (PopART for Young People) COMMUNITY ADVISORY BOARD

The P-ART-Y CAB had two main functions:

1. To advise researchers about how best to implement the P-ART-Y evaluation survey

2. To support the community-level delivery of optimisations of the PopART intervention package for young.

In 2017 the P-ART- Y CAB members were involved in the general and focused meetings in which study processes and CAB issues were discussed. Some of the important meetings other than general routine meetings are noted below:

Cross Sectional Survey- 21 January 2017: This meeting centred on the P-ART-Y cross sectional survey were the survey tool was presented and CAB members reviewed it in detail and discussed the content and appropriateness of the questions. They voted on the sections that they felt were the most topical and relevant to adolescents in their communities and discussed other logistical and ethical issues around survey implementation such as waiver of parental consent and types of devices to be used for the survey. The CAB were engaged throughout the process and offered valuable insights which informed the further development of the survey questionnaire.

World TB Day- 24 March 2017: Two P-ART-Y CAB members, Khanyisa Mcimeli and Luthando Ngwatyu attended the World TB Day which took place at Faculty of Medicine and Health Sciences, Stellenbosch University. The purpose was to commemorate world TB Day. The topic of discussion was "State of the art of paediatric tuberculosis: diagnostics, biomarker research, therapeutics and operational research for paediatric TB".

AIDS Clinical Trials Group (ACTG) Meeting- 27 March 2017: Kathleho Mosimanengape, Luthando Ngwatyu and Jafta Nonklondlo attended the meeting with Allegra from ACTG at Faculty of Medicine and Health Sciences, Stellenbosch University. Allegra presented the ACTG CAB structure and operations. The CAB also gave inputs on CAB structure and functions.

CAB Joint Meeting- 31 March 2017: Five of the P-ART-Y CAB members attended the joint meeting along with CAB members from various studies within Stellenbosch University and University of Cape Town. This meeting was held at University of Cape Town Lung Institute to discuss various studies and issues that CAB members grapple with.

Family Matters Programme (FMP) Workshop-22 April 2017: Gertrude van Rensburg (and Margaret van Niekerk delivered components of the FMP to the P_ART-Y CAB members at the Kolping Conference Centre in Durbanville, Cape Town. 16 members attended the workshop. The content included HIV epidemiology among young people, sexual reproductive health, and peer pressure and child sexual abuse. Training also included role playing. Overall the workshop training was well received by young people and, they were engaged throughout.

P-ART-Y Cross Sectional Survey Training- 14 June 2017: Four ACAB members, Khanyisa Mcimeli, Katleho Mosimanengape, Jafta Nonklondlo and Luthando Ngwatyu were invited to the P-ART-Y training which was held on the 12-15 June 2017 to advise researchers on how to approach young people during implementation of the cross-sectional survey.

DTTC Annual Dissemination Meeting- 8 December 2017: Five CAB members namely Luthando Ngwatyu, Nandipha Anta, Jafta Nonkondlo, Katleho Mosimanengape and Mihlali Ngqawule, attended the annual meeting held at Stellenbosch University. This meeting brought together various stakeholders from the Western Cape Department of Health, City of Cape Town, 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 City of Cape Town representative Dr Virginia de Azevedo shared experiences of working with young people at health facilities and communities.

PARTY CAB members also attended community-level optimisations of the PopART intervention – 'Futures spaces'-an intervention targeted at young people aged 13-24 year old. P-ART-Y CAB members were engaged in these events. The P-ART-Y dissemination plan was also discussed in the last quarter of the year. Given that the P-ART-Y end date was looming, CAB members wanted clarity regarding, the end date and recommendations were made that CAB members apply to be part of the DTTC CAB.

CONFERENCES

Local Conferences

8th SA AIDS Conference in Durban, June 13-15, 2017: DTTC Staff attended and presented posters: Graeme, Hanlie, Lario, Rosemary, Jabu, Nosi & Dionne.

International Conferences

IAS Conference in Paris, July 23-26, 2017: Attended by Margaret van Niekerk, Blia Yang and Eluid Nkuna.

- Blia Yang presented research abstract: *Feasibility, Uptake and Yield of Household-based Tuberculosis Active Case Finding Within the Combination Prevention Package in the HPTN 071 (PopART) Intervention in High TB/HIV Burden Communities in South Africa*
- Margaret van Niekerk presented the abstract: *Using routine data to describe STI symptom screening by HIV status for men who self-initiated HIV-testing at community-based HIV testing services in Cape Town, South Africa. (Authors: Van Niekerk, M, Draper, H and Meehan, S).*

48th Union World Conference on Lung Health in Guadalajara, Mexico, October 11-14 October, 2017:

- Anneke Hesseling, Simon Schaaf and James Seddon coordinated a scientific symposium: The evolving landscape of paediatric MDR-TB trials
- Sue Purchase – oral presentation: Dissemination of pharmacokinetic lead-in study findings: acceptability and palatability of paediatric levofloxacin tablets in children
- Anne-Marie Demers – poster presentation (on behalf of Marieke vann der Zalm): The detection of respiratory viruses in South African children with suspected pulmonary tuberculosis"

South African Thoracic society, Cape Town: Posters presented by Liz Walters, Marieke van der Zalm (The detection of respiratory viruses in South African children with suspected pulmonary tuberculosis)

SCIENTIFIC MEETINGS AND WORKSHOPS ATTENDED BY DTTC STAFF

PopART Annual Meeting, January 29 – February 3, 2017: Meeting held in Zambia attended by Peter Bock, Anelet James, Blia Yang, Nomtha Mandla, Graeme Hoddinott, Lario Viljoen, Rosa Sloot, Constance and Nozi Makola.

Social Science Proposal writing workshop, February 6-10, 2017: The workshop was hosted by the Centre for Evidence Based Health Care. The CEBHC had a call for proposal for implementation research which was awarded to the DTTC social science team. The title of the research is: *Promoting ART at CD4 counts greater than 500*. There were five grant recipients; the workshop focussed on refining the research proposals for ethical submission.

Research Orientation Day, March 2, 2017: Hosted by Prof Nico Gey van Pittius. Theme: *Unlocking the mysteries of disease- Research at the FHMS* with Exhibitions of work done in the FHMS

HPTN Annual Meeting, April 9-13, 2017: Held in Washington DC attended by PopART staff (Peter Bock, Blia Yang, Redwaan Vermaak, Anelet James, Nozi Makola, , Nomtha Mandla, and a community member Themba Lethu). The annual meeting discussed HPTN 071 (PopART)'s study outcomes and the close-out of study. Nozizwe Makola accepted the Community Engagement Award for 2015-2016 on behalf of the DTTC PopART team. The award was jointly awarded to DTTC and the Zambian team, for being the only Community Engagement team that has published a paper after the writing workshop, conducted by HPTN for all its Community groups in 2015 in North Carolina, USA. (For more information on this meeting: http://www0.sun.ac.za/dttc/a-chance-of-a-lifetime-for-a-dedicated-community-member/)

ANOVA 7th Annual Rural Health Research days, May 18 & 19: 2017: Optimising HTS for young people aged (15-24) presented by Graeme Hoddinott. DTTC also presented 6 posters, 3 of which were from HPTN 071 PopART.

Africa Day, May 25, 2017: Participants displayed FMHS collaborations with institutions and individuals in other African countries in the areas of education, research, community service and interaction.

Annual IMPAACT Meeting, May 29 to June 1, 2017: Held in Washington DC, Gwynneth Hendricks presented a poster: Lessons learnt creating an instant CAB to advise on strategic direction at a clinical research site in Cape Town South Africa (DTTC). The 3-day program focused on: HIV-treatment, complications, cure and prevention; Skills, building Stigma & HIV Disclosure; and Leadership Development & Mentorship.

NIH Transmission Workshop, June 1-3, 2017: The workshop focused on halting TB transmission in HIV endemic settings. Muhammad Osman presented on Childhood TB (especially DRTB) transmission, which was the only paediatric topic at the workshop. Pren Naidoo presented on the TB cascade and highlighted losses in terms of burden, investigated, diagnosed and treated for TB. Florian Marx presented on targeted interventions for those previously treated for TB. Other presentations addressed other elements of transmission and new work done on transmission. Overall, the workshop was limited in that it did not address what is required as the next steps.

PopART Quarterly Interaction meeting, June30, 2017: quarterly meetings held in accordance with human capital management for the preparation of CHIPS Intervention staff contracts to end in December 2017. Staff were informed of Severance Packages & UIF. Psychosocial Support was made available to all staff. To equip the 250 staff members with new job applications, mentors were made available to assist staff in formulating CV's and Cover letters.

Transdisciplinary Health and Development Studies Methods Workshop, July 12, 2017: Open session for students enrolled for the MPhil in Transdisciplinary Health and Development studies methods module to present their research proposals to academic colleagues. 13 DTTC staff members participated in this module either toward degree purposes (3) or as short course only students.

Academic Year Day, August 30, 2017: the following submissions from the paeds team were accepted and presented:

- Oral presentation: Excellent treatment outcomes in children treated for tuberculosis under routine operational conditions in Cape Town M. Osman, K. Lee, K. du Preez, R. Dunbar, A.C. Hesseling, J.A. Seddon
- Poster: The detection of respiratory viruses in South African children with suspected PTB
  M.M. van der Zalm, E. Walters, A.M. Demers, M. Palmer, M. Claassen, G. van Zyl, A.C. Hesseling
- Poster: Optimizing paediatric drug-resistant tuberculosis treatment: population pharmacokinetics of moxifloxacin and linezolid in children A. J. Garcia-Prats, J. Winckler, H. R. Draper, S. Belonwu, H. S. Schaaf, L. Wiesner, A. C. Hesseling, R. Savic
- Poster: Early experiences of the acceptability and palatability of a novel child-friendly levofloxacin formulation in young children S.E. Purchase, P. De Koker, A.J. Garcia Prats, H. R. Draper, D. Wademan, G. Hoddinott

- Oral presentation: Pharmacokinetics and drug-drug interactions of lopinavir/ritonavir administered with first and second-line antituberculotic drugs in HIV-infected children treated for multidrug-resistant tuberculosis. L. E. van der Laan, A. J. Garcia-Prats, H. S. Schaaf, L. Wiesner, M. de Kock, J. Winckler, T. Tikiso, J. Norman, H. McIlleron, P. Denti, A. C. Hesseling [Paolo Denti and Anneke C. Hesseling contributed equally, joint senior authors.]

Implementation Workshop for Science Research (SHIRT), August 17-18, 2017: The workshop was hosted by Mareli Claassens in Namibia, and attended by Anneke Hesseling and Muhammad Osman. SHIRT is conducted in Collaboration with Fogerty Grants for the development of Masters Students.

11th International Child TB Training Course, September 10-15, 2017: Held at Goudini ATKV, Rawsonville. Attended by Simon Schaaf; Anneke Hesseling, Grayson Lamore, Gwynneth Hendricks and Delphine Adams.

40th Semi-Annual TBTC Meeting, October 16-18, 2017: Held in Atlanta, USA and attended by Anne-Marie Demers

HIV Prevention Workshop, October 11, 2017: Integration of PopART Sites for testing amongst Refugees and homeless. 40 were tested for HIV of 70 attendees.

Provincial Health Research Day, October 27, 2017:

- Sue-Ann Meehan presented a poster on behalf of Margaret van Niekerk; *Best Practices in working toward sustainable NPO-led community-based HIV testing services in Cape Town, South Africa.*
- Peter Bock was invited to attend as keynote speaker together with Rodney Ehrlich (UCT). They presented valuable lessons learnt, the impact of CHIPS work in TB Screening, reduction in TB rates and how testing will change. They also spoke about the importance of Community Engagement and Qualitative Research in community based trials
- Barbara Vernon (PopART professional nurse) wrote abstract and presented the poster: *Input in CAB meetings*
- Hanlie Myburgh presented a poster and did a short talk about *experiences within the Study communities and access to services*

Paediatric Day of Excellence, November 1, 2017: Sue-Ann Meehan was invited to present, "*Community-based HTS: Using a case study from Cape Town to provide evidence-based lessons learnt for program implementation*"

HPTN 071 (PopART) Intervention Dissemination, November 27, 2017: Feedback of Research to Community Stakeholders held at SPIER

VISITORS DURING 2017

Portfolio Developer for the Society and Ethics Programme of the Wellcome Trust, Paul Woodgate: visited 27 February 2017 to advise staff working on Wellcome Trust grant applications.

Assistant Professor in Biostatistics, Helen Jenkins, from Boston University School of Public Health: Visited March 6-10, 2017.

P-ART-Y study manager, Dr Joseph Chaila, from Zambia (ZAMBART): joined the P-ART-Y training in South Africa 12th to 15th June 2017.

Institutional Information Officer, Jerall Toi, from Stellenbosch University: presented the Protection Of Personal Information (POPI) ACT to DTTC staff on 14th June 2017

Clinical researcher, Elisa Lopez, from the Barcelona Institute of Global Health (IS Global): visited the paediatric team 26th to 29th June 2017.

Yale student, Kenneth Qinnasekera: joined the Paediatric team at Brooklyn Chest Hospital, gained insight into the Zamstar Prevalence Data and accompanied the CHIPS teams to Delft Community households during his 4-day visit to DTTC 10th to 14th July 2017.

Student, Isabelle De Wandel, from KU Leuven, Belgium: met with Anneke end July 2017.

Social Scientist, Virginia Bond, from Zambia (ZAMBART): joined the HPTN 071(PopART) social science team on 4th to 6th July 2017 to refine implementation of data collection and plan analysis of HPTN 071 (PopART) data.

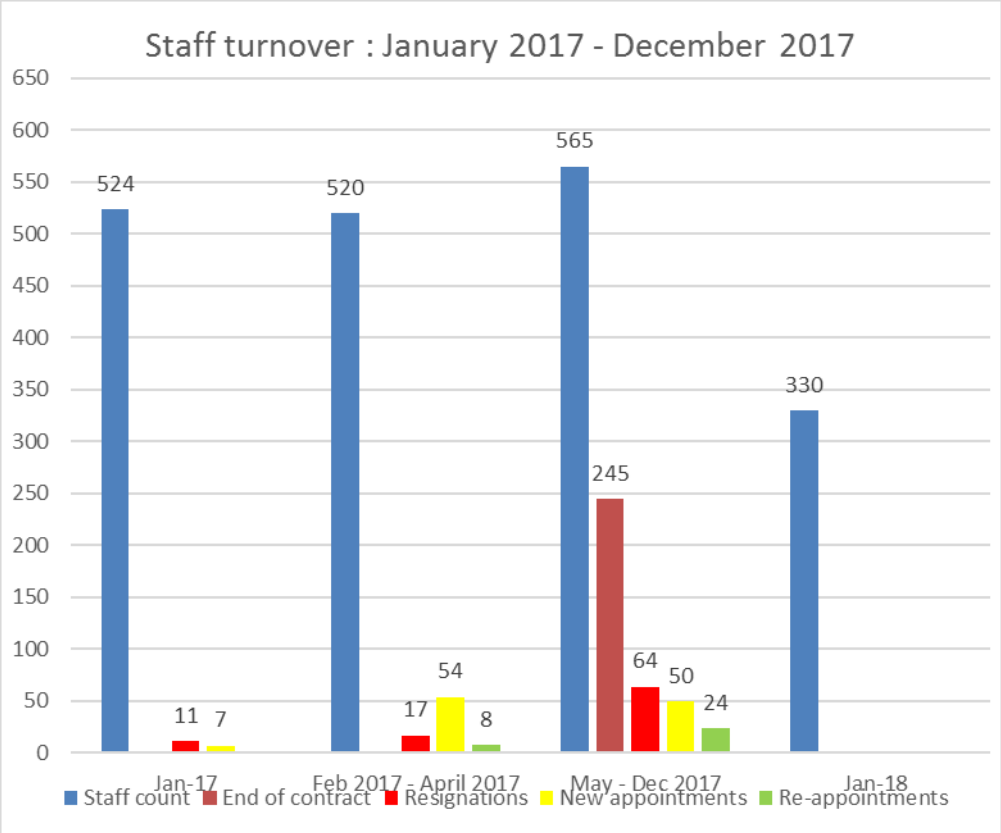
Paediatrician & Clinical Epidemiologist, Jacquie Narotso Oliwa, based at the KEMRI (Wellcome Trust Research Programme in Nairobi): Jacqui is also a Lecturer at The University of Nairobi, School of Medicine, Department of Paediatrics and Child Health and PhD Student at The University of Amsterdam. Following the 11th International Child TB Course, Jacquie spent two weeks (September 15-29) with Liz Walters and the Diagnostics team. To learn from the team at DTTC on the pathways of care here, how diagnostic challenges are addressed to see what could be translated to the Kenyan setting, and any opportunities for collaboration.

Delegates from Germany, headed by Theresia Bauer (Minister of Research and the Arts) from Baden-Württemberg: the delegates visited DTTC while on business in Cape Town. DTTC facilitated the CHIPS visits to the Sites which included tent testing, HIV trials, TB screening. The visit was organized by Blia Yang and hosted by Nulda Beyers in October 2017. (For more information on this visit: http://www0.sun.ac.za/dttc/high-level-german-delegation-visits-innovative-community-hiv-testing-sites-in-cape-town/)

Representatives of Consul General USA, Steven Smit (Health Attaché) and Virginia Blaser : visited the PopART team to assess progress on the 31st of November 2017.

EMPLOYEES

During 2017 a total of (245) employee contracts ended. The exit of staff included the final annual round of the CHiPs intervention in December 2017. Between May and Dec 2017, a high number of employees (64) resigned, seeking permanent employment elsewhere. The Centre also employed total of (50) new staff members on different studies, linked to different post levels. Total of (24) staff members could be re-employed, which relates our current HR retention strategy.



Month	Staff count	End of contract	Resignations	New appointments	Re-appointments
Jan-17	524	0	11	7	0
Feb-17 to April-17	520	0	17	54	8
May-17 to Dec-17	565	245	64	50	24
Jan-18	330				

DTTC GOVERNANCE

DTTC Executive Committee (ExCo)

The DTTC is governed by its Governing Board, as per its constitution. A new governing board was elected in February 2017, chaired by Professor Andrew Whitelaw, Dept Medical Microbiology and NHLS, Tygerberg; vice-chair: Professor Wolfgang Preiser: Division Head: Medical Virology.

The daily governance of the DTTC is fulfilled by the ExCo. 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 every 2 weeks. In addition, there is a dedicated 2 hour 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.

DTTC Executive Committee Roles and Responsibilities

Name	Role	Responsibility
Prof Anneke Hesseling	DTTC Director and chair of DTTC ExCo	DTTC director; director: paediatric TB studies
Dr Tony Garcia-Pratts	Medical director of the Desmond Tutu TB Centre Brooklyn Chest Hospital Paediatric Pharmacokinetics Unit Principal investigator IMPAACT TB Scientific committee mentored investigator Co-investigator in the newly funded Desmond Tutu TB Centre IMPAACT CRS (site 31790)	Responsible for supervising the clinical care of participants and effective implementation of ongoing trials, as well as supervising the site staff of 15 and overseeing the general functioning of the research unit. Leading two large observational cohort studies evaluating the pharmacokinetics and safety of the second-line TB medications in children. Supporting/Co-supervising two Master's students.
Dr Marieke van der Zalm	Clinical Researcher Paediatric studies Principal investigator Career-development grant of the EDCTP	Lead Clinician of the SHINE study, which is a multi-centre TB treatment shortening study with the DTTC being the only South African site. Co-PI of UMOYA study The Principal investigator assumes overall responsibility and accountability for the efficient planning, implementation and evaluation of the project, ensuring contractual obligations to all stakeholders within the regulations of Stellenbosch University

Dr Frieda Verheye-Dua	Regulatory Coordinator	Coordination of all IMPAACT related activities, with extensive quality assurance and regulatory oversight of all clinical trials conducted under the IMPAACT trial network auspices. Ensures that general and study-specific regulatory-related processes for NIH-funded and other clinical paediatric studies comply with the standard operating procedures (SOPs) as well as the requirements of ethics committees and sponsors, specifically the NIH-trials networks (IMPAACT) and other relevant trials. Interacts extensively with local academic and non-academic stakeholders, and at a very high level with international stakeholders' including the NIH, international regulatory agencies, and international trial networks and investigators.
Prof Simon Schaaf	Lead investigator Paediatric studies	MDR-TB clinical care and research; core member of IMPAACT CRS, clinical and scientific advisor
Sue Ann Meehan	Principal investigator HIV prevention project (funded by PEPFAR/CDC)	The Principal investigator assumes overall responsibility and accountability for the efficient planning, implementation and evaluation of the project, ensuring contractual obligations to all stakeholders within the regulations of Stellenbosch University.
Dr Peter Bock	Co-PI: HPTN 071 / PopART trial IoR designee: HPTN084 trial	The Principal investigator or Investigator of Record assumes overall responsibility and accountability for the efficient planning, implementation and evaluation of the project, ensuring contractual obligations to all stakeholders within the regulations of Stellenbosch University. Staff component of approximately 400 employees (HPTN071). Supporting/Co-supervising PhD and Master's students.
Dr Muhammad	Research Clinician:	Clinician for TB CHAMP (RCT of Levofloxacin vs Placebo for the prevention of MDR TB in

Osman	Paediatric studies Implementation Research PhD student: South African MRC National Health Scholars Program recipient	child household contacts of MDR TB Index cases Operational research assistance program – supervision of multiple projects led by service partners PI on 3 projects contributing to PhD topic of TB mortality in South Africa – responsible for planning, implementation and reporting
Graeme Hoddinott	Senior Researcher Lead Social Scientist, DTTC Co-investigator HPTN 071a (stigma ancillary), PopART for Young people (P-ART-Y), and HPTN 084 (LIFE) Social Science Lead on HPTN 071 (PopART), SHINE, and TB-CHAMP trials	The Principal investigator assumes overall responsibility and accountability for the efficient planning, implementation and evaluation of the project, ensuring contractual obligations to all stakeholders within the regulations of Stellenbosch University. Academic member of the Transdisciplinary Health and Development Studies postgraduate degree programme hosted between the Faculties of Medicine and humanities. Current registered PhD student at UKZN.
Sterna Brand	Human Resources Manager	The HR Manager oversees HR functions at the centre and manages HR processes and procedures within the centre. The HR manager also oversees performance management and compliance and the development and retention of human capital.
Theo Smith	Logistics Manager	The Logistics Manager provides logistical support to the centre's central administrative hub, peripheral research sites and overall

		centre logistics. Duties include management of the following: overseeing vehicle fleet management and reporting, office space and rental agreements, on and off-site storage facilities, fixed asset management, purchase requisition authorisation and assets verification, quotations and tender management and overseeing the non-trial insurance portfolio of the centre.
Anelet James	Operations Manager	The Operations Manager provides operational, financial, administrative and technical support to the centre and its research and support staff. Core responsibilities include financial management, supporting manager centre operations and sample repository management.

FINANCIAL INFORMATION

The information below will be updated once the audited financial statements for financial year ending 31 December 2017 are released by Stellenbosch University.

DTTC carried over a net surplus of operational cash flow from 2016. Total income increased by R13mil from 2016 of which R4mil was from new contracts signed. Total expenditure increased by R30mil (R108, 979, 110 FY2016; R138, 787, 377 FY2017). A total of approximately R2mil was expended on capital purchases. The financial year was closed with a net surplus of R10mil reflecting on the Statement of Income and Expenditure.

Net Surplus as at 01 January 2017 (carried over to FY2017)	R19, 247,932

Total Income in 2017	R129, 819, 730
Total Income from new Contracts in 2017	R4, 242,808
Capital Purchases in 2017	R1, 834, 022
Net Surplus as at 31 December 2017	R10, 408, 303

Income from US Federal funding remains the main source of research funding for DTTC with the major contributor the NIH and CDC for the HPTN071(PopART) study. PopART income for FY2017 totaled to R91mil, approximately 70% of total DTTC income. The CDC funded intervention part of the PopART study was completed in December 2017 with the NIH funded research scheduled to complete in June 2018. This will result in a significant decrease in income for DTTC and many staff contracts ending. The closure of the PopART study has been highlighted in the DTTC risk assessment in preparation of various financial, operational and reputation risks identified and mitigation steps planned against these risks. A summary of income stratified by source is summarized below.

US Federal	R115, 425, 349
US Other	R6, 476, 976
UK	R17, 201, 073
South Africa	R5, 114, 628
Asia	R2, 831, 441
Europe	R1, 124, 657

Operating cash flow per Network as on 31 December 2017 is summarized below.

Network	Carry over 2016	Income 2017	Total
TBTC			**R 7,347,768.51**
TBTC parent grant (CDC)	*R 1,690,903.77*	*R 5,573,060.50*	*R 7,263,964.27*
Study 35	*R 16,324.47*	*R 67,479.77*	*R 83,804.24*
IMPAACT			**R 2,995,876.30**
P1108 and P2003 Protocol Chair (Hesseling)	*R -40,670.90*	*R 694,776.07*	*R 654,105.17*
IMPAACT P1106 co-chair support (Bekker)	*R 92,522.55*	*R 98,131.65*	*R 190,654.20*
IMPAACT P2005 co-chair support (Garcia-Prats)	*R -14,494.67*	*R 53,475.42*	*R 38,980.75*
IMPAACT ITBSL	*R -51,093.56*	*R 1,104.43*	*R -49,989.13*
IMPAACT Laboratory Centre	*R -*	*R 1,713,505.19*	*R 1,713,505.19*
DEMERS IMPAACT CHAIR	*R -*	*R 48,853.69*	*R 48,853.69*
THRASHER URINE	*R -*	*R 399,766.43*	*R 399,766.43*
ACTG			**R 690,204.41**
ACTG AM Demers	*R -16,885.30*	*R 247,731.53*	*R 230,846.23*
DTTC ACTG PIF (A5300)	*R -18,586.86*	*R 357,574.30*	*R 338,987.44*
ACTG Chair AC Hesseling	*R -6,440.84*	*R 126,811.58*	*R 120,370.74*
HPTN			**R 90,992,179.62**
HPTN071 (PopART) Research Trial	*R 4,225,675.70*	R 43,615,850.99	*R 47,841,526.69*
HPTN071 (PopART) Research Trial Intervention	*R 259,685.57*	R 38,457,405.41	*R 38,717,090.98*
HPTN071 (PopART) Research Trial Stigma Study	*R -220,982.97*	R 1,321,747.94	*R 1,100,764.97*
HPTN071 (PopART) Research Trial P-ART-Y	*R 412,404.16*	R 2,920,392.82	*R 3,332,796.98*
DTTC CTU CRS	**R 116,598.19**	**R 3,442,270.27**	**R 3,558,868.46**

Major Cost drivers on the DTTC operational cash flow in 2017 included consultation fees, consumable materials, internal SU interest paid, Levy: ICRR (Indirect Cost), remuneration, travel and workshops. Remuneration was the major cost driver totaling to R83mil, on average 56% of the total operating cash. PopART accounted for 72% of the total remuneration paid in 2017. Another major cost driver was levy paid to SU at R11mil, 7% of the total operating cash.

When taking balance sheet items into account the true net surplus at the end of the FY2017 was R3, 725, 856 (R7mil less than reported above). The decrease is due to R1,6mil of outstanding debt control (funds committed for goods/services not yet received or invoices not yet processed for payment). In addition, just under R500,000 of advance payments had not been processed or reconciled (to be done by faculty finance office) to reflect as expenditures on the DTTC income and expenditure statement. PopART also carried a facility of R5mil at the time of reporting. For financial statements to reflect closer to true cash flow at financial year-end, DTTC procurement office is working on strategies to clear debt control before year-end. A great concern to DTTC is that of advance control, and although it has been taken up to faculty level we still have not been able to find a solution for rapid recon of these expenses. The outstanding expenditures may cause over-expenditure (financial risk) since it does not reflect on the income/expenditure reports from which we generate financial statement reports for monthly financial expenditure management.

Internal interest of R345, 088 was paid to SU during 2017, with PopART the main contributor due to large facilities taken throughout the year. Roughly 1% (R1,8mil) of operating cash flow was lost in FY2017 due to exchange rate loss. The 'WHO FDC in children' cost point lost 14% of the total cash due to exchange rate fluctuations. Both of these losses are addressed in the DTTC risk analysis.

RISK MANAGEMENT
Executive Summary

The Desmond Tutu TB Centre executive committee have identified core risks that may affect study operations, Centre operations (human resources, finance and regulatory) or good Centre governance. Monitoring and evaluation of these risks, as well as steps to mitigate against any risk that realises will be implemented once the plan has been discussed with the DTTC governing board.

Regulatory non-compliance was identified as one of the extreme risks DTTC should mitigate against. The DTTC regulatory office will ensure that no study is commenced without appropriate regulatory approval. Non-compliance will affect all functioning units within DTTC and could result in retraction of funder support leaving DTTC at risk of not being able to honor commitments to debtors or staff.

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, duel 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 has developed a 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 was also identified as a potential risk for 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. Line management within field offices has been improved to mitigate against any HR irregularities (attendance, working hours) that may arise at site offices.

Due to the lack of sustainable funding DTTC are at risk of losing core support staff when big studies are closed out. DTTC is investigating new sources of sustainable core funding such as leveraging competencies and resources within DTTC to ensure highly trained and skilled core staff can be retained without reliance on grant funding for salary support.

Other human resource risks include that of staff safety, temporary staff contracts and staff diversity.

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. 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, and continue to provide staff with infection control training.

Temporary staff contracts leads to employee insecurity, demotivation and often to early exit. DTTC hopes to mitigate against losing study staff during an active study by offering employee contracts for the full term of the study cycle. DTTC also requires faculty level discussions to better support female staff members on temporary contracts during maternity leave.

DTTC also requires faculty intervention during the HPCSA registration process for foreign doctors. Delays experienced during this process puts the Centre at risk of non-adherence to funder time-lines.

DTTC is committed to adhere to SU diversity policies during their recruitment processes. In addition, DTTC has identified, trained and promoted many staff members from disadvantaged backgrounds to senior management positions.

DTTC employs a cadre of finance staff who work closely with the faculty research grants management office (RGMO) to ensure no misappropriation of research funds takes place. Regular expenditure allocation, reporting and finance meetings are held to mitigate against any misappropriation. Correct budgeting in collaboration with RGMO will also mitigate against large exchange rate losses experienced by DTTC in 2017. Advanced cash payments to study staff for reimbursement of study participants has become a great risk to DTTC (as well as other faculty departments) as fraud and robbery has increased. Investigations to implement use of an 'electronic wallet' has been taken up with the faculty, however this solution is not ideal for our current setting and nature of our research. Alternative solutions, such as daily dispensing form an internal DTTC cashier, are being investigated.

The DTTC risk plan will be implemented and updated on a regular basis and a risk management report will be included in the 2018 Annual report.

DTTC Listing
Collaborators | Funders | Partners

INTERNATIONAL

-Arizona State University
-Bill & Melinda Gates Foundation
-BMRC
-Boston Children's Hospital
-Columbia University
-CDC
-Department of Health & Human Services
-EDCTP
-HPTN
-IMPAACT
-Imperial College London
-International Initiative for Impact Evaluation
-International Union Against TB & Lung Disease
-Johns Hopkins University
-NIAID
-NIDA
-NIH
-NIMH
-PEPFAR
-Radboud University
-Seattle Children's Hospital
-Stony Brook University
-TB Alliance
-UMC Utrecht | Wilhemina Children's Hospital
-Uppsala University
-UCL
-UK AID
-Welcome Trust
-ZAMBART Project

SOUTH & SOUTHERN AFRICAN

-City of Cape Town
-Department of Science and Technology
-Department for International Development
-Desmond Tutu TB Centre
-EHPSA
-FAMCRU
-HB & MJ THOM
-NHLS
-NRF
-PHRU
-SACEMA
-SARChI Chair in Paediatric TB (Prof AC Hesseling)
-SA MRC
-Stellenbosch University
-TASK
-Wits Reproductive Health & HIV Institute
-Western Cape Government

International Collaborators | Funders | Partners

South African Collaborators | Funders | Partners

SARChI Chair in Paediatric TB (Hesseling)

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

CDC Guidance Document

Meehan, S, Yang, B, Van Niekerk, M, Boffa, J, Dunbar, R, Felix, R, James, A, Makola, N, Mandla, N, Molaolwa, J, Naidoo, V, Ndiki, Z, Nel, K, Scheepers, M, Theart, M and Viljoen, L. **A Practical Guide to Implementing Community-Based HIV-Prevention Services. Experiences shared and lessons learned from South Africa.** Cape Town: Stellenbosch University, 2017. Available online at:
http://www.sun.ac.za/english/faculty/healthsciences/paediatrics-and-child-health/Pages/Home.aspx

Journal Articles (NON-subsidised)

ABRAHAM DR. A portrait of my life with Lupus. *Joint Ability* 2017; **1**:4-5.
DU PLESSIS L, DETJEN AK, HESSELING AC, DU PREEZ K. Operational implementation and impact of the Union's online childhood TB training course in South Africa. *Public Health Action* 2017; **7**(2):175-177.

DTTC Students January 2017 – April 2018				
Currently Registered Trainees: Masters Degree				
Name of trainee	Current position	Degree	Supervisor	Research Topic
Megan Palmer, MD, FCP	Research pediatrician	MPH (UCT))	Robert Gie, Anneke Hesseling	Validity of chest radiographic reading methods in children with suspected tuberculosis
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 postmortem studies and notifiable diseases including TB
Louvina van der Laan, MD	Research medical officer	MPhil Clin Pharm (UCT)	Anneke Hesseling	MDR-TB in HIV-infected children: drug drug interactions and safety
Jana Winckler, MD	Research medical officer	MPhil Clinical Pharm (SU)	Tony Garcia-Prats	Pharmacokinetics and safety of high-dose INH in children with MDR-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
Elizabeth Batist, MPh	Study coordinator, TB-CHAMP	MPhil in HIV management (SU)	Frieda Verheye-Dua	HIV-related stigma among HIV-positive men who have sex with men
Thando Wonxie, PGD.	Research Intern	MPhil in HIV management (SU)	Dr C Clive	Health Care workers' experiences on HIV testing
Chulumanco Mdingi, BA Hons.	Research Intern	MA (NMMU)	Jenna Larsen	Vulnerabilities of small scale citrus farmers in Ngqushwa.
Rosemary, Brown, BA (Hons)	Social science research officer	MSocSc (UKZN)	Nicholas Munro	Participation in an early intervention programme, social support and parental stress in parents of deaf children
Jabulile, Baleni, 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
Thomas, Angilique, BA (Hons)	Social science research officer	Master's Politics (UWC)	Dr Cherrel Africa	The role of faith-based organisations on reducing crime and violence on the Cape Flats
Lubabalo, Mdedetyana, BA(Hons)	Social science research officer	Master's Anthropology (UWC)	Dr Sashimi Mfecane	Medical Circumcision: tradition or transformation

Gabriela Carolus, BA (Hons)	Social science research officer	Master's Sociology (SU)	Thomas Cousins	Politics and performance of a literacy intervention in Cape Town: School libraries and the new subjection of volunteerism.
Christopher Mahwire, MD	Medical officer, DOH	MSc Epid (SU)	Pren Naidoo	Has the use of Xpert[R] 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)
Noleen Mohononi, BScHons	Data Capturer	MPH Nutrition (SU)	TBA	The Impact of Fermented foods/beverages on TB Treatment Outcome
Sue Purchase, MD, DCH	Research Medical Officer	MSc Epid (SU)	Simon Schaaf Anneke Hesseling	Operational implementation of treatment of MDR-TB prevention in a community based clinical trial
Nosivuyile Vanqa	Social science research officer	MPhil Transdisciplinary Public health and development studies (SU)	Lindsey Reynolds	The roles of traditional healers in supporting the implementation of Universal Testing and Treatment
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
Rene Raad	Social science research intern	MA Anthropology (SU)	Thomas Cousins	Termination of pregnancy service providers' experiences
Khanya Mama		MCom (SU)	Ronelle Burger Graeme Hoddinott	TB patients with confirmed diagnoses who decline/delay taking up treatment – exploring why
Bianca Leigh Hamman		MSc (Medical Microbiology) (SU)	M Newton-Foot Andrew Whitelaw Marieke Van der Zalm	The role of respiratory co-infections and the microbiome in the clinical presentation and response to treatment in South African children with suspected PTB
Currently registered PhDs				
Adrie Bekker, MD, FCP	Neonatologist, Research fellow	PhD (SU)	Anneke Hesseling Simon Schaaf	Prevention and treatment of maternal and infant tuberculosis in the HIV era
Dillon Wademan	Social science, research officer	(registration Q3) 2018	Lindsey Reynolds/Graeme Hoddinott	Chronic conditions and care: Intergenerational experiences of living with HIV, TB, and diabetes in South Africa
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), MRCGP (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
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.
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, COMAPP PI	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.
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"
Rory Dunbar, MSc	Senior data manager	PhD (SU)	Nulda Beyers Pren Naidoo	Operational modelling to optimise the impact of Xpert MTB Rif on TB and MDR-TB yield and costs
Pren Naidoo, MD, MBA	Senior researcher, lead operational researcher	PhD (SU)	Nulda Beyers	Evaluating the impact of an Xpert® MTB/RIF- based TB diagnostic algorithm in a routine operational setting in Cape Town
Lario Viljoen, MA	Social science researcher	PhD (SU)	Lindsey Reynolds	Young women's sexual decision-making in the context of earlier ART-access
Sinazo, Nomsenge, MA	Social science research officer	PhD (RU)	Professor Monty Roodt	Relative impact of NGO-delivered/partnered school interventions to improve learning outcomes in the Eastern Cape
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
Anthony Garcia-Prats, MD, Msc	Paediatric PI BCH PK Unit Medical Director	PhD (SU)	Anneke Hesseling Simon Schaaf	Optimizing and operatioanlizing MDR-TB treatment in 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	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
Post docs current				
Marieke van der Zalm		Postdoc (SU)	Anneke Hesseling	Lung function and respiratory pathogens in children with suspected TB
Mareli Claassens		Postdoc (SU)	Nulda Beyers	Impact of HIV on TB outcomes and mortality
Jody Boffa		Postdoc (SU)	Anneke Hesseling	Epidemiological comparison of MDR-TB in Cape Town and rural Kwa-Zulu Natal
Rosa Sloot		Postdoc (SU)	Pren Naidoo	Epidemiology – HPTN071(PopART)

SOUTH2SOUTH PROGRAMME FOR COMPREHENSIVE FAMILY HIV CARE & TREATMENT

Acting Director: Ms C du Toit

South to South Programme
Final Programme Report

November 2012 – September 2017

Implementing Mechanism: HIV Innovations for Improved Patient Outcomes in South Africa (Developing & Institutionalizing an Innovative Capacity Building Model to Support SA Government Priorities & to Improve HIV/TB Health Outcomes for Priority Populations

Cooperative Agreement No: AID-674-A-12-00031

South to South Programme for Comprehensive Family HIV Care & Treatment, Stellenbosch University

Contents

Executive Summary

South to South Programme for Comprehensive Family HIV Care & Treatment (South2South) is currently implementing an innovative capacity building programme and intervention that addresses capacity building at different levels of the health system in South Africa with the overall goal of improving maternal and child HIV/TB health outcomes. The South2South capacity building model is an integrated and multi-level intervention aimed at improving the capacity of individuals, organisation and systems of the National Department of Health (NDOH) to implement, scale up, and institutionalize innovations to improve patient outcomes of key populations.

Key features of the multi-level South2South capacity building programme were: (1) activities at an individual health worker level, (2) programme activities at an organisational level and (3) programme activities at a systems or policy level. Individual level capacity building activities conducted by South2South are aimed at the individual health care worker. Organisational level capacity building activities conducted by South2South are aimed at supporting health facilities, cluster of facilities, district/sub-district multidisciplinary teams, provincial regional training centres, Master Trainer networks. At a systems or policy level, South2South programme activities are targeted at attendance and responding to request from the National Department of Health (NDoH) such as to participate in technical working groups and supporting the Human resources directorate.

Programme Background

The rapid roll-out of antiretroviral therapy and the human resource challenges created by the rapid expansion of Africa's health system response to the HIV/TB epidemic necessitated an urgent response from local institutions. In May 2006, in response to the urgent need to build paediatric HIV care and treatment capacity among African healthcare professionals, the Department of Paediatrics and Child Health in the Faculty of Medicine and Health Sciences at Stellenbosch University (SU) partnered with the International Center for AIDS Care and Treatment Programme (ICAP) at Columbia University to launch the South to South Partnership for Comprehensive Paediatric HIV Care and Treatment Programme (S2S Partnership). The aim of the programme created by this partnership was to support indigenous capacity building whereby multidisciplinary healthcare teams throughout Africa could learn from other African institutions and staff to implement paediatric HIV care and treatment services successfully.

In March 2008, the ICAP-SU partnership was concluded and the programme was re-launched as the South to South Programme for Comprehensive Family HIV Care and Treatment (S2S Programme), broadening its activities to respond to specific clinical and systems-strengthening needs within South Africa only. During 2010, USAID-South Africa indicated that funding of S2S would be administered by Right to Care under an Umbrella Grants Management (UGM) mechanism. Throughout the period 2006-2012 S2S continuously refined and improved capacity building and health systems strengthening programme activities, in response to the needs of South African Government stakeholders.

S2S piloted a Quality Improvement (QI) model in the Moretele district (North West province) from October 2009 till March 2012. Based on the successes demonstrated in Moretele district, the

capacity building model was refined.

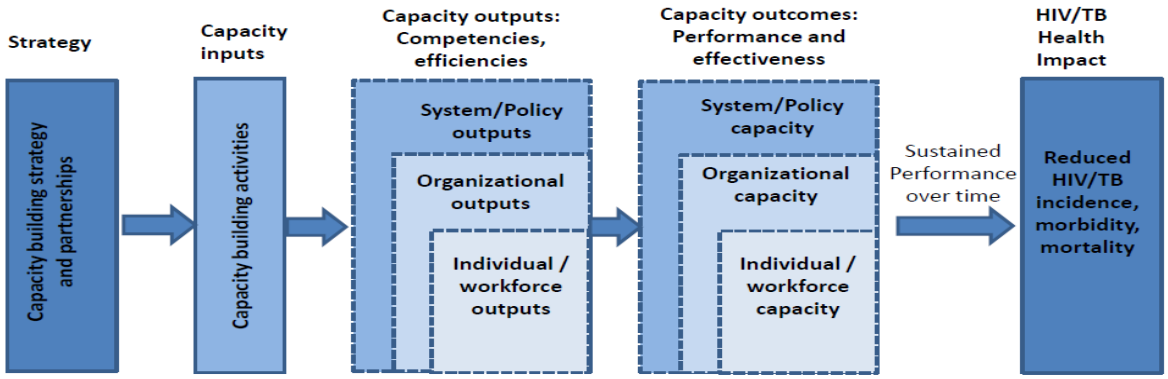
In November 2012, South2South was awarded a 5-year, $15-million cooperative agreement by PEPFAR/USAID to develop an innovative capacity-building programme to support the South African Government in improving the HIV/TB health outcomes of pregnant women, infants, children, and adolescents.

The program funded through this award overlapped with the Right to Care sub-award program. The 1-year overlap of funding created the situation where S2S had to implement a training and mentoring program (the RTC sub-award program) as well as develop a new capacity building program (the USAID Innovations program).

Programme Results Framework

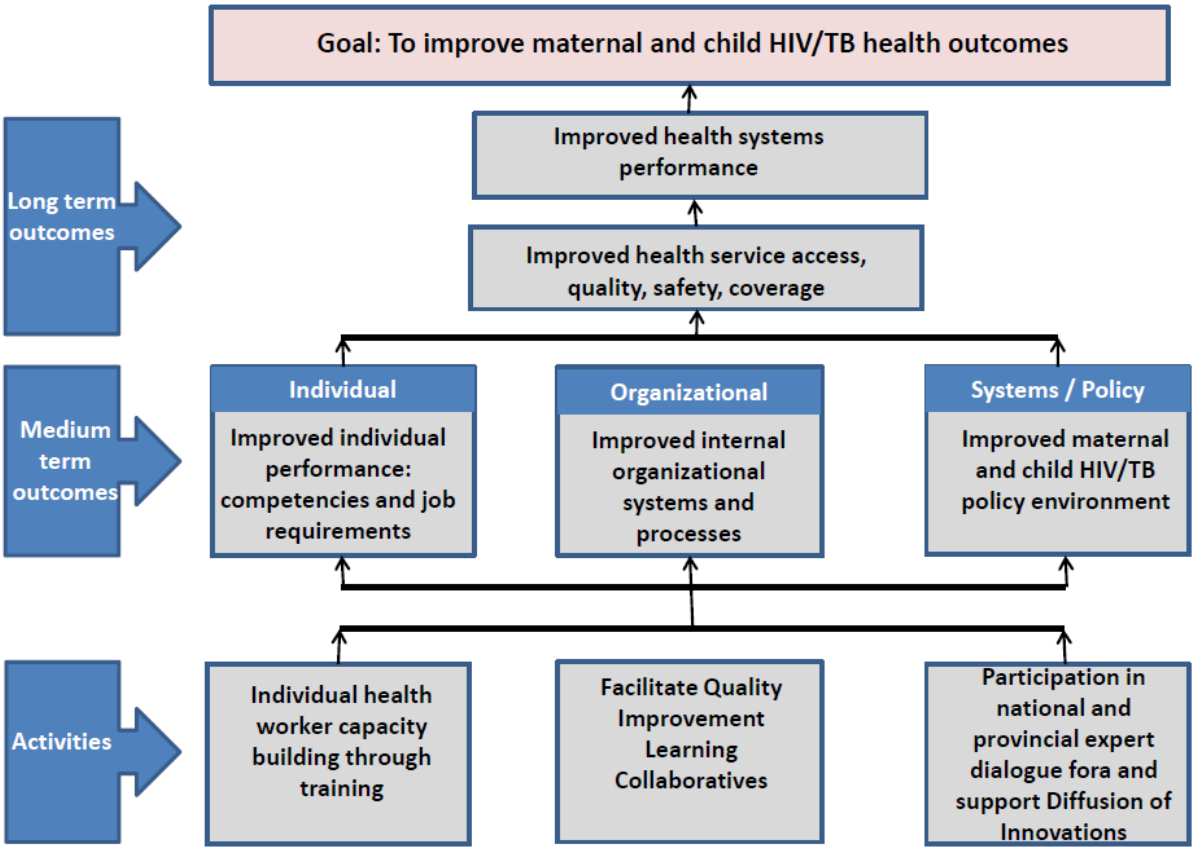
Programme effect theory describes the causal mechanisms through which programme activities were predicted to bring about programme outcomes. The programme effect theory for the capacity building work funded by the USAID Innovations Cooperative Agreement is outlined in Figure 1: Programme results framework.

Figure 1: Capacity building results framework



Capacity building is an integral component in the effort to improve HIV/TB health outcomes in priority populations. Capacity is defined as the ability of individuals and organizations to perform functions effectively, efficiently, and sustainably. Capacity building is an evidence-based process of strengthening the abilities of individuals, organizations, and systems to perform core functions sustainably, and to continue to improve and develop over time (PEPFAR, 2012). During Year 1 of this program, the South2South Program developed a program model that reflected integrated, multi-level strategies for capacity building.

Figure 2: Innovations Program Results Framework



The success of this program can be defined through the achievement of improved health outcomes for the priority populations targeted, as defined by the National Strategic Plan on HIV, STIs, and TB (2012-2016). The capacity building support targets that will enable the achievement of improved health outcomes are outlined in the table 1 below.

Table 1: Program objectives and success measures for the Innovations Program

Objective	Success measures (Outlined in Cooperative Agreement No. AID-674-A-12-00031; HIV-Innovations for Improved Patient Outcomes in South Africa)
Develop innovations and plans for capacity building and support for scale up of effective and efficient models and approaches for HIV-related services in line with SAG priorities	Improving the number of health workers attending in-service learning Improving the number of facilities with clinical mentoring and supportive supervision programmes in place Improving the number of professional health workers trained on HIV/AIDS and TB related programs Improving the number of professional nurses trained on Paediatric NIMART/IMCI-Plus, PMTCT, Breastfeeding, and Quality Improvement Improving the number of doctors trained on paediatric HIV treatment and PMTCT Improving the number of doctors trained on paediatric HIV treatment and PMTCT Improving the number of non-professional trained on HIV/AIDS and TB-related programs Improving the number of nurses currently mentored on ART initiation in all facilities
Support SAG to develop, scale up, and institutionalize	Improving the number of children started on ART and managed by nurses

innovations to inform strategies for improving patient outcomes of key populations	Achievement of improved health outcomes for the priority populations targeted, defined by the SAG in: NSP 2012-2016 eMTCT Action Framework Blue Print for Action for Paediatric and Adolescent HIV/TB
Sustainability (not included in Cooperative Agreement No. AID-674-A-12-00031; HIV-Innovations for Improved Patient Outcomes in South Africa)	Uptake of innovations in national policies, guidelines, and standards Institutionalization of capacity building approaches in DOH organizational systems and structures Uptake of innovations in pre-service and in-service training curricula Endorsement of innovations by SAG institutions Uptake of innovations in at least 20% of the target population

Programme execution

Programme Goal

Developing and institutionalizing an innovative capacity building model to support South African Government Priorities and to improve HIV/TB health outcomes for priority populations.

Objectives

1) Develop innovations and plans for capacity building and support for scale up of effective and efficient models and approaches for HIV-related services in line with SAG priorities
2) Support SAG to develop, scale up and institutionalize innovations to inform strategies for improving patient outcomes for key populations (Children and Pregnant Women in S2S case)

S2S adopted the Institute for Healthcare Improvement's (IHI) ***Quality Improvement Collaborative*** approach (see Figure 4) in order to achieve organisational level changes. The collaborative model uses the Model for Improvement (see Figure 5) to develop, test and disseminate best practices in order to achieve improved health outcomes in maternal and child health. This model has been widely adapted and applied to developed and developing world health contexts.

Figure 4: Quality Improvement Collaborative Approach

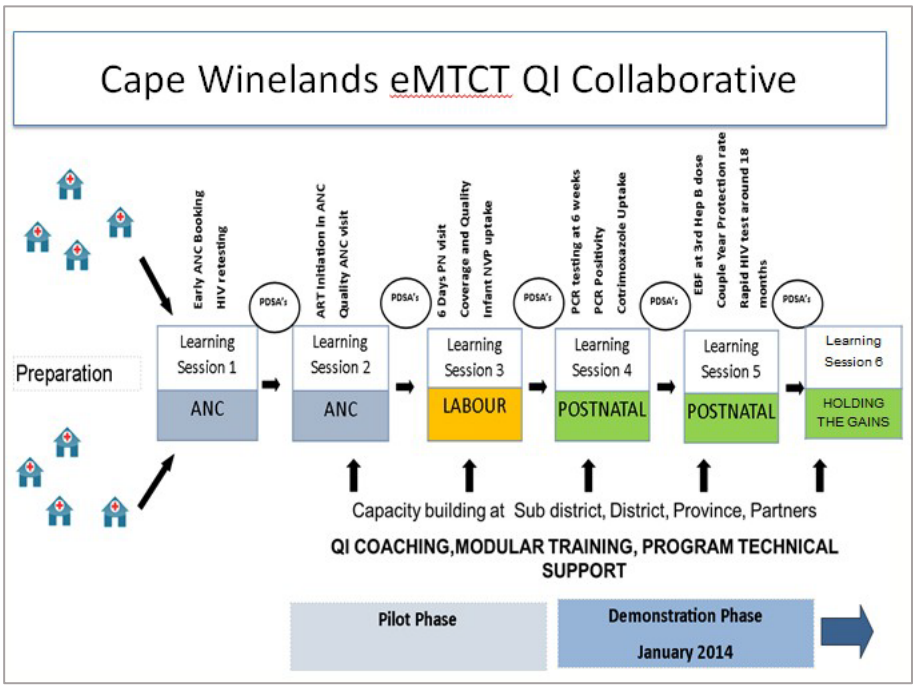
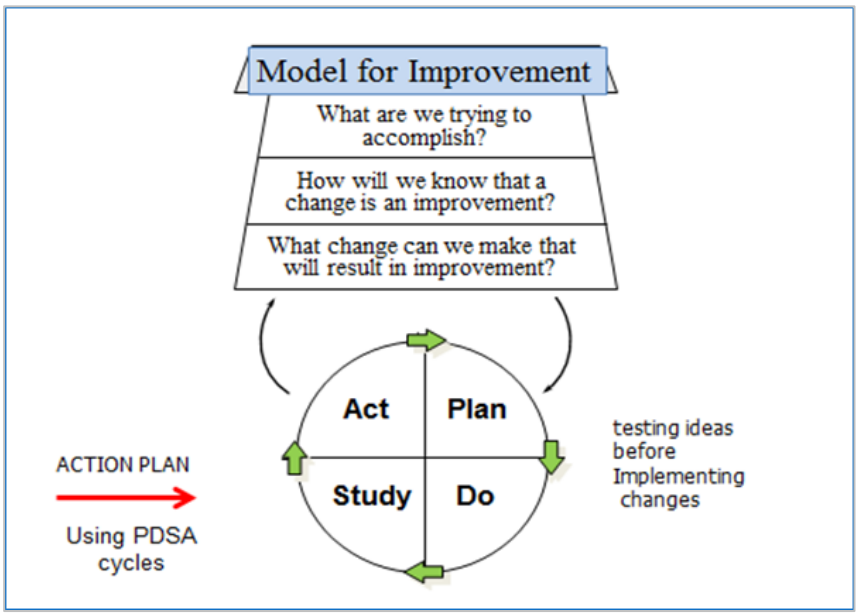


Figure 5: Model for Improvement (adapted from IHI 2003)



From March 2012 to March 2015 S2S piloted these individual-, organisational- and systems/policy-level activities in three districts across three provinces: Amathole (Eastern Cape), Cape Winelands (Western Cape) and Pixley ka Seme (Northern Cape).

QIC	Western Cape - Cape Winelands District:	Northern Cape – Pixley ka Seme District:	Eastern Cape – Amathole District:
Pilot phase	8 health facilities where supported in the Breedevalley sub-district from October 2012 until September 2014	5 health facilities (3 primary healthcare clinics and 2 community health centres) where supported in the Siyancuma sub-district from June 2012 until December 2013	4 health facilities where supported in the Mnquma sub-district in 2013
List of facilities	De Doorns CHC Empilisweni CHC Orchard clinic Rawsonville clinic Sandhills clinic Touws River clinic Worcester CHC Worcester District Hospital	Griekwastad CHC Breipaal PHC Campbell PHC L. Adams PHC Douglas CHC	Nozuko clinic Butterworth hospital Nqamakwe CHC Hebe Hebe clinic
S2S Advisors	Carolin Diergaardt Olatunji Adetokunboh Maxime Molisho Katherine Brittin Samantha Hanslo	Christalien Hüsselmann Justine Geiger Madoda Sitshange	Dorothy Williams Gina Bernhardt
Learning Sessions	Learning session 1: Early ANC Booking, HIV retesting Learning session 2: ART initiation in ANC, Quality ANC visit Learning session 3: 6 Days PN visit, Coverage and Quality, Infant NVP uptake	Learning session 1: Early ANC Booking, HIV retesting Learning session 2: ART initiation in ANC, Quality ANC visit Learning session 3: 6 Days PN visit, Coverage and Quality,	Learning session 1 (27 Jun 2013): Early ANC Booking, HIV retesting Learning session 2 (10 Sep 2013): ART initiation in ANC, Quality ANC visit

		Infant NVP uptake	Learning session 3 (21 Feb 2014): 6 Days PN visit, Coverage and Quality, Infant NVP uptake
Demonstration phase	18 health facilities where supported in the Langeberg and Witzenberg sub-districts from January 2014 to March 2015	14 health facilities where supported in the Siyancuma,Renosterberg, Thembelihle and Emthanjeni sub-districts from January 2014 to March 2015	14 health facilities where supported in the Mnquma sub-district from January 2014 to March 2015
List of facilities	**Langeberg sub-district** Bergsig Nkqubela clinic McGregor clinic Cogmanskloof clinic Zolani clinic Montagu CHC Happy Valley clinic Robertson hospital Montagu hospital **Witzenberg sub-district** Annie Brown clinic Prince Alfred's Hamlet Nduli clinic Wolseley clinic Op die berg clinic Tulbagh clinic Bella vista clinic Breede river clinic Ceres Hospital	**Siyancuma sub-district** Griekwastad CHC Breipaal PHC Campbell PHC L. Adams PHC Douglas CHC **Renosterberg sub- district** Keurtjieskloof PHC Petrusville PHC Masibambane PHC **Thembelihle sub-district** Hopetown PHC Hopetown CHC **Emthanjeni sub-district** De Aar Town clinic De Aar Day hospital Montana PHC K.E. Twani PHC	**Butterworth Centane cluster** Nozuko clinic Ibika clinic Ndabakazi clinic **Butterworth cluster:** Butterworth hospital Butterworth Gateway clinic CL Bikitsha clinic Highview clinic **Nqamakwe cluster:** Nqamakwe CHC Hebe Hebe clinic Kotana clinic Mnyibashe clinic Ntseshe clinic **Centane cluster:** Macibe clinic Tutura clinic
S2S Advisors			
Learning Sessions	Learning session 4: PCR testing at 6 weeks, PCR Positivity, Cotrimoxazole Uptake Learning session 5: Couple Year Protection rate, Rapid HIV test around 18 months, EBF at 3rd Hep B	Learning session 4: PCR testing at 6 weeks, PCR Positivity, Cotrimoxazole Uptake Learning session 5: Couple Year Protection rate, Rapid HIV test around 18 months, EBF at	Learning session 4 (6 Jun 2014): PCR testing at 6 weeks, PCR Positivity Learning session 5 (24 Oct 2014):

	dose Learning session 6: Holding the Gains	3rd Hep B dose Learning session 6: Holding the Gains	Couple Year Protection rate, Rapid HIV test around 18 months Learning session 6 (27 Mar 2015): Holding the Gains

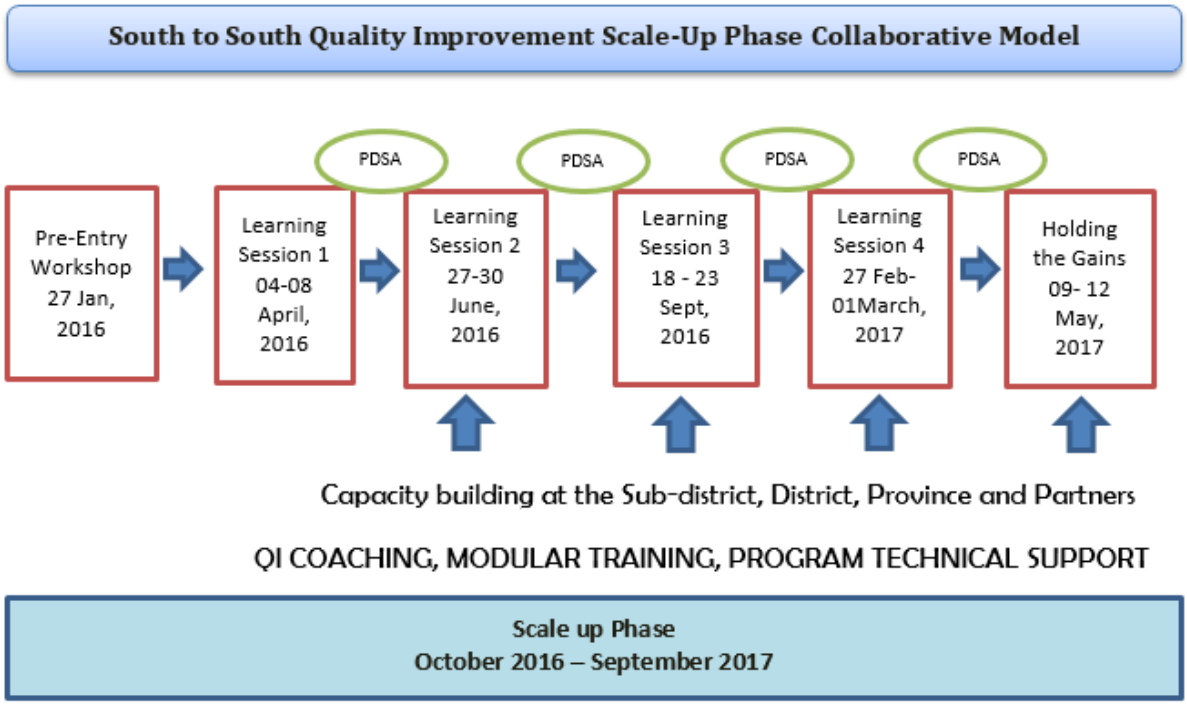
The purpose of the scale-up phase of the project was to achieve eMTCT and successful implementation of Paediatric HIV treatment and care programme, to facilitate translation, and implementation of the eMTCT Action Framework.

Table 3. S2S facility support profile for Amathole sub-districts from October 2015 to May 2017

SCALE -UP PHASE SUPPORTED FACILITIES (OCTOBER 2015 – MAY 2017)			
AMAHLATHI	**MBASHE**	**MNQUMA**	**NKONKOBE**
Komga Clinic	Badi Clinic	Butterworth Gateway Clinic	War Memorial Clinic
Stutterheim Clinic	Bolotwa Clinic	Dr CL Bikitsha Clinic	Middledrift CHC
Peddie Extension Clinic	Bomvana Clinic	Gcaleka Clinic	Victoria Gateway Clinic
Cumakala 2 Clinic	Fort Malan Clinic	Gqunqe Clinic	Lower Regu Clinic
Donnington Clinic	Gwadana Clinic	Grainvalley Clinic	Thozamile Madakana Clinic
SS Gida Gateway Clinic	Hobeni Clinic	Hebe-Hebe Clinic	Hillside Clinic
Ngqwele Clinic	Idutywa Nqabara Clinic	Highview Clinic	Newtown Clinic
Mooiplaas Clinic	Idutywa Village CHC	Ibika Clinic	Bedford Clinic
Nompumelelo Gateway Clinic	Keti Clinic	Kotana Clinic	Adelaide Gateway Clinic
Ndwayana Clinic	Kotyana Clinic	Macibe Clinic	Seymour Clinic
Cata Clinic	Lota Clinic	Mgcwe Clinic	Lulama Kama Clinic
Cathcart Clinic	Madwaleni Hospital	Mnyibashe Clinic	Balfour Clinic
Gxulu Clinic	Mahasana Clinic	Mpukane Clinic	Bezuidenhoutville Clinic
Jaji Clinic	Melitafa Clinic	Mqambeli Clinic	Debe Nek Clinic
Robert Mbelekane Clinic	Mpame Clinic	Ncizele Clinic	Fort Beaufort Gateway Clinic
Daliwe Clinic	Mpozolo Clinic	Ndabakazi Clinic	Nomakhwezi Makhenyane Clinic
Horton Clinic	Mqhele Clinic	Ngqusi Clinic	Mzamomhle Clinic (Bedford)
Lenye Clinic	Msendo Clinic	Nozuko Clinic	Melani Clinic
Tyata Clinic	Nkanya Clinic	Nqancule Clinic	Msobomvu Clinic
Twecu Clinic	Nqabeni Clinic	Ntseshe Clinic	Assina Mandla Clinic
Philani Clinic(KWT)	Nqadu Clinic	Qina Clinic	Gilton Clinic
Norah Clinic	Nyhwara Clinic	Qolora-By-Sea Clinic	Njwaxa Clinic

Mgwali Clinic	Soga Clinic	Springs Clinic	Mxhelo Clinic
Nompumelelo Hospital	Sundwana Clinic	Tafalofefe Gateway Clinic	Healdtown Clinic
Stutterheim Hospital	Taleni Clinic	Tanga Clinic	Adelaide Hospital
SS Gida Hospital	Vukukhanye Gateway Clinic	Tutura Clinic	Bedford Hospital
Cathcart Hospital	Willowvale CHC	Tyali Clinic	Fort Beaufort Hospital
Komga Hospital	Xhora CHC	Zazulwana Clinic	Victoria Hospital

In the Amathole District, South to South supports 112 facilities in all 4 sub-districts in the Amathole District. The quality improvement collaborative is comprised of learning sessions and action periods focusing on key PMTCT/IMCI, and paediatric care and support indicators to support the treatment and care pathway. South to South also conducted 1-2 hour need based facility training in supported facilities. This is complemented by the Train the Trainer course being conducted by S2S for Department of Health (DoH) Trainers and Implementing partners to support Management of Paediatrics and adolescent HIV/AIDS and PMTCT thereby ensuring sustainability of all capacity-building activities.



Financial Summary

	FY1 (ZAR)	FY2 (ZAR)	FY3 (ZAR)	FY4 (ZAR)	FY5 (ZAR)
Personnel compensation	1 333 688.95	13 355 952.28	13 538 277.89	18 049 184.01	
Procurement consumables	0	100 952.63	48 711.93	103 461.24	
Travel	221 559.74	1 689 586.79	1 581 957.28	3 697 834.30	
Operating and direct costs	376 108.88	5 447 660.88	7 983 287.04	11 924 846.84	
Subcontracted services	27 657.35	292 207.81	1 746 152.04	1 790 088.87	
Assets	0	605 426.92	93 993.02	287 000.16	
Total Expenditure	1 959 014.92	21 491 787.31	24 992 379.20	35 852 415.42	
Total Expenditure FY1 – FY5					

Factors affecting project results

Staff turnover is a barrier to QI team functionality, meaning that all staff needs to have a basic understanding of QI, to sustain the projects that are happening in their facility.

Some teams lacked motivation due to perceived slow progress of QI projects and setting too high targets for their clinics- *clinic should set their own targets.*

Perceived time constraints: some staff felt that QI projects were an extra burden and did not see the value that they added.

It is crucial that all staff at the facility have a basic understanding of the QI process.

The availability of managers to accompany S2S Advisors on clinic visits limited the transfer of QI skills.

It was difficult to get buy-in from hospital for the collaborative.

Challenges were experienced in scheduling S2S activities with facilities/sub district management due to short-notice planning of district and sub district activities.

The assessment of QI capacity and competency shows that, health workers who participated in training on QI methods, staff at all levels are not participating in QI efforts.