

RePORT India

**10TH ANNUAL JOINT LEADERSHIP MEETING
TB IN 2021: WHAT'S NEW IN RESEARCH?**

**CONVENED VIRTUALLY
9-11 FEBRUARY 2021**

Participating Institutions

- Bhagwan Mahavir Medical Research Center (BMMRC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)-Johns Hopkins University (JHU) Clinical Research Site (BJGMC-JHU CRS)
- Boston University/Boston Medical Center (BU/BMC)
- Christian Medical College, Vellore (CMC)
- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER)
- Johns Hopkins University (JHU)
- M. Viswanathan Diabetes Research Center (MVDRC)
- National Institute for Research In Tuberculosis (NIRT)
- National Institute for Research In Tuberculosis (NIRT) – International Centers for Excellence in Research (ICER)
- North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS)
- P.D. Hinduja National Hospital and Medical Research Centre (Hinduja)
- Postgraduate Institute of Medical Education and Research (PGI), Chandigarh
- Rutgers University
- University of California—San Francisco (UCSF)
- University of Massachusetts (UMass)
- University of Texas Health Science Center at Tyler (UTT)

Specialized Labs & Collaborators

- All Indian Institute Of Medical Sciences (AIIMS), New Delhi, India
- Cornell University, New York, USA
- Emory University, Georgia, USA
- Fundação Oswaldo Cruz (FIOCRUZ), Bahia, Brazil
- Indian Institute of Science (IISc), Bengaluru, India
- Indian Institute of Technology Bombay (IIT-B) – Proteomics Core, Mumbai, India
- Medgenome, Bengaluru, India
- National Center for Functional Glycomics, Massachusetts, USA
- Office of Cyber Infrastructure and Computational Biology (NIAID), Maryland, USA
- South African TB Vaccine Initiative (SATVI), Cape Town, South Africa
- theraCUES Innovation Pvt Ltd, Bengaluru, India
- Translational Health Science and Technology Institute (THSTI), Faridabad, India

Supporting Organizations

CRDF GLOBAL
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Sponsors



Department of
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National Institute of
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Funding for this conference was made possible [in part] by funding agreement OISE-9531011 from NIH and administered through CRDF Global. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services, nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Contents prepared February 2021



Contents

Overview: **1**

Young Investigator Abstracts: **9**

Data: **23**

Related Grants: **35**

Publications: **45**

Lectures & Presentations: **59**



2020 RePORT India Annual Meeting in Mumbai

RePORT India Overview



CMC-Vellore



BMMRC

Background

RePORT India (Regional Prospective Observational Research for Tuberculosis) is a bilateral, multi-organizational, collaborative research effort established in 2013 under the Indo-US Vaccine Action Program (VAP). RePORT India is now the largest of six regional consortia—China, Brazil, Indonesia, Philippines, and South Africa are also undertaking multi-organizational tuberculosis (TB) research efforts. Each RePORT consortium is designed to support local, in-country, TB-specific data and specimen biorepositories and associated research. Taken together, the anticipated results include greater global clinical research capacity in high-burden settings and increased local access to quality data and specimens for members of each consortia and their domestic and international collaborators. Leveraging the data, specimens, infrastructure, and scientific partnerships established by RePORT India in Phase I, the consortium has now launched Phase II.

Mission

RePORT India is charged with:

1. Advancing regional TB science in India, towards fulfilling the TB strategic goals of the country;
2. Strengthening TB research capacity and infrastructure; and
3. Fostering research collaboration within India and with other countries focused on research that can lead to clinically important biomarkers, vaccines, drugs, and diagnostics.

Phase I

Phase I (2013–18) commenced with six Clinical Research Sites (CRSs) in Western and Southern India that were partnered with five U.S. academic institutions. P.D. Hinduja National Hospital and Medical Research Centre was subsequently added as the seventh Indian site. Initially, each site had its own “Parent Protocol” with distinct research topics. In 2017, RePORT India launched the “Common Protocol” with standardized data elements and harmonized procedures for enrollment. Under the Parent and Common Protocols, CRSs established prospective observational cohorts of participants from whom specimens were collected:

- **Cohort A:** Participants who have active TB disease. Studies involving this cohort of patients focus on TB diagnosis and treatment outcomes.
- **Cohort B:** Participants who are household contacts (HHCs) of an active case of TB. Studies involving this cohort of participants focus on risk of infection and progression to TB disease after exposure.

Parent Protocols (CRS-Specific Objectives)

Each CRS is connected to one or more laboratories where they house their Parent Protocol data and samples at their respective India-based institutions. Samples collected under RePORT India Site-Specific Parent Protocols are kept separate from the Phase I and Phase II Common Protocol samples. On the following pages the CRSs and their Parent Protocols are outlined.

BMMRC & UTT

- **Topic of Study:** Immunologic Markers of Persons at Highest Risk of Progression of Latent TB Infection to TB
- **India PI:** Dr. Vijaya Valluri, Bhagawan Mahavir Medical Research Centre (BMMRC), Hyderabad, India
- **U.S. PI:** Dr. Krishna Vankayalapati, University of Texas Health Science Center, Tyler (UTT), TX, USA
- **Participating Patient Cohort:** Cohort B

BJGMC, NIRT, & JHU

- **Topic of Study:** Host and Microbial Factors Associated with Poor Treatment Response and Progression to Active TB (C-TRIUMPH)
- **India PIs:** Drs. Sanjay Gaikwad, Aarti Kinikar and Shashikala Sangle, Byramjee Jeejeebhoy Government Medical College (BJGMC), Pune, India; Dr. Vidya Mave, BJGMC-JHU CRS, Pune, India; Drs. Padma Chandrasekaran and Bhavani PK, National Institute for Research in TB (NIRT), Chennai, India
- **U.S. PI:** Dr. Amita Gupta, Johns Hopkins University, Baltimore, MD, USA
- **Participating Patient Cohorts:** Cohort A (Adult Pulmonary TB, Pediatric TB, and Extrapulmonary TB) and Cohort B

CMC Vellore & U of Wash/U of Cambridge

- **Topic of Study:** Host Determinants in the Eicosanoid Pathway that Modulate the Inflammatory Response, Disease Outcome, and Treatment Responsiveness in TB
- **India PI:** Drs. DJ Christopher and Balamugesh Thangakunam, Christian Medical College (CMC), Vellore, India
- **U.S. PI:** Dr. Lalitha Ramakrishnan, University of Washington/University of Cambridge, UK
- **Participating Patient Cohort:** Cohort A (Adult Pulmonary TB and TB Meningitis)

Hinduja & JHU

- **Topic of Study:** MDR-TB Treatment Outcomes, Adverse Effects, Mtb Genotyping, and Pharmacokinetic Testing
- **India PIs:** Drs. Zarir F. Udawadia, Tester F. Ashavaid, and Camilla Rodrigues; P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, India
- **U.S. PIs:** Drs. Amita Gupta and Jeffrey Tornheim, Johns Hopkins University (JHU), Baltimore, MD, USA
- **Participating Patient Cohorts:** Cohort A (Adult/Adolescent MDR-TB) and Cohort B

JIPMER, BU/BMC, & Rutgers

- **Topic of Study:** Biomarkers for Risk of TB and for TB Treatment Failure and Relapse
- **India PIs:** Drs. Gautam Roy and Sonali Sarkar, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India
- **U.S. PIs:** Drs. Jerrold Ellner and Padmini Salgame, Rutgers University, Newark, NJ, USA; Dr. Robert Horsburgh, Boston University (BU), Boston, MA, USA; Dr. Natasha Hochberg, Boston Medical College (BMC), Boston, MA, USA
- **Participating Patient Cohorts:** Cohort A (Adult Pulmonary TB and Pediatric TB) and Cohort B

MVDRC, NIRT-ICER, & UMass

- **Topic of Study:** Effects of Diabetes and Prediabetes on TB Severity
- **India PIs:** Dr. Vijay Viswanathan, MV Diabetes Research Centre (MVDRC), Chennai, India; Dr. Subash Babu, National Institute for Research In Tuberculosis (NIRT) – International Centers for Excellence in Research (ICER), Chennai, India
- **U.S. PI:** Dr. Hardy Kornfeld, University of Massachusetts (UMass) Medical School, Boston, USA
- **Participating Patient Cohort:** Cohort A (Adult Pulmonary TB)



JIPMER

MVDRC



Common Protocol (RePORT India-Wide Objective)

The primary objective of the Phase I Common Protocol was to provide data and specimens to Indian biomarker researchers and collaborators to better understand:

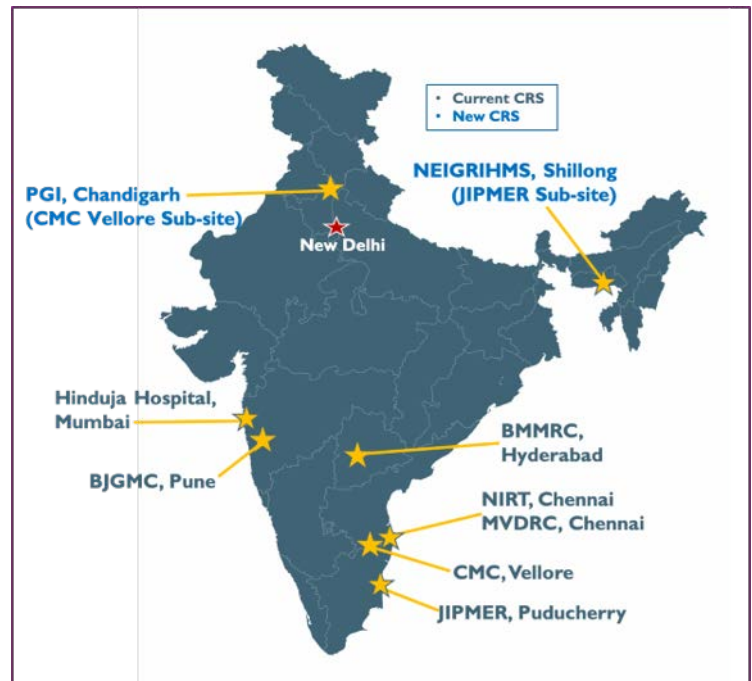
- Prognosis of TB disease; and
- Pathogenesis of progression from TB exposure to disease.

A RePORT India Central Biorepository was established at the National Institute of Research in Tuberculosis (NIRT) in Chennai led by Dr. Luke Elizabeth Hanna.

In addition, a statistical/data management center was established at the Society for Applied Studies (SAS)-Centre for Health Research and Development (CHRD) in New Delhi, and Pharmaceutical Product Development, LLC (PPD) was contracted to provide Common Protocol technical support.

RePORT India Phase II

Under a Phase II Common Protocol, we are pursuing five specific scientific aims including the following cohorts: Diagnostic (New TB suspects), Cohort A (Active TB disease), and Cohort B (HHCs). Samples collected under this protocol will be curated, stored, and managed at the RePORT India Central Biorepository at NIRT where Phase I Common Protocol samples are currently stored. A data management center is being established at JIPMER in Puducherry and PPD will continue to provide technical support. The Phase II Common Protocol Co-Chairs are: Drs. Kamakshi Prudhula Devalraju (BMMRC) and Robert Bollinger (JHU). The consortium has now been expanded to include two new CRSs in Northern India:



North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS)

- **Location:** Shillong, India
- **PI:** Dr. W. Valarie Lyngdoh
- **Linked to:** JIPMER

Postgraduate Institute of Medical Education and Research (PGI), Chandigarh

- **Location:** Chandigarh, India
- **PI:** Dr. Ashutosh Aggarwal
- **Linked to:** CMC Vellore

Phase II Scientific Aims

AIM 1. DIAGNOSTICS

Evaluate Novel Diagnostics & Biomarkers of Diverse States of Mtb Infection

Participating Patient Cohort: Diagnostic (New TB suspects)

Leads: Dr. Sonali Sarkar (JIPMER) and Dr. Jerry Ellner (Rutgers)

Participating Patient Cohort: Cohort B (XDR HHCs)

Leads: Dr. Tester Ashavaid (Hinduja) and Dr. Jeff Tornheim (JHU)

AIM 2. MARKERS OF TREATMENT RESPONSE

Participating Patient Cohort: Cohort A (Active TB disease)

2.A: Identify TB Treatment Response Biomarkers

Leads: Dr. Vijay Viswanathan (MVDRC) and Dr. Hardy Kornfeld (UMass)

2.B: Investigate Host-Related Mechanisms of Treatment Failure

Leads: Dr. Vidya Mave (BJGMC-JHU CRS) and Dr. Natasha Hochberg (BMC)

2.C: Investigate Pathogen-related Mechanisms & Predictors of Recurrence

Lead: Dr. David Alland (Rutgers)

AIM 3. LUNG INJURY & IMPAIRMENT

Identify Markers of Lung Injury Associated with Unfavorable TB Treatment Outcomes.

Participating Patient Cohort: Cohort A (Active TB disease)

Leads: Dr. DJ Christopher (CMC Vellore), Dr. Ashutosh Aggarwal (PGI Chandigarh), and Dr. Akshay Gupte (JHU)

AIM 4. RESISTANCE TO INFECTION

Mechanisms of Protection against TB in Exposed Persons

Participating Patient Cohort: Cohort B (Phase I HHCs)

4.A: Examine Host Antimicrobial Pathways in Inducing their infection resistant (IR) Phenotype in HHC

4.B: Test if IR & Plasma Differ in Modulating Macrophage-Mediated Restriction of Mtb Growth & Evaluate AB Repertoires of Plasma from the IR and infection susceptible (IS) Cohorts

Leads: Dr. Padmini Salgame (Rutgers), Dr. Subash Babu (NIRT-ICER), and Dr. Kamakshi Prudhula Devalraju (BMMRC)

AIM 5. PROGRESSION TO DISEASE

Identify Immunologic Markers of Persons at Highest Risk of Progress of Latent TB Infection to TB.

5.A: Stored Samples: Validation of PREDICT29 in Progressors & Nonprogressors from RePORT Sites

Participating Patient Cohort: Cohort B (Phase I HHCs)

Leads: Dr. Padmini Salgame (Rutgers) and Dr. Luke Elizabeth Hanna (NIRT)

5.B: Immune & Hormone Studies in Freshly Collected Samples

Participating Patient Cohort: Cohort B (Phase II HHCs)

Leads: Dr. Vijaya Valluri (BMMRC) and Dr. Ramakrishna Vankayalapati (UTT)

In addition to these five aims, we will assess cross-cutting epidemiologic and COVID-19 related aims.

Administration

RePORT India has established a collaborative governance structure composed of: 1) an Executive Committee led by two Chairs and two Co-chairs from India and the U.S.; 2) an Indo-U.S. Coordinating Hub; 3) three Scientific Working Groups (Basic Science, Clinical Epidemiology, Behavioral Science); 4) five Operational Working Groups (Common Protocol Leadership, Study Coordination, Publications Committee, Laboratory Management, and Data Management), 5) a Data Coordinating Hub (JIPMER). The EC's mission is to set research priorities, guide scientific activities, and offer administration and logistics in support of research priorities.

The consortium is currently led by:

- Chairs: Dr. Sonali Sarkar (JIPMER, Clinical Epi) and Dr. Amita Gupta (JHU, Clinical Epi)
- Co-Chairs: Dr. Vijaya Valluri (BMMRC, Basic Science) and Dr. Padmini Salgame (Rutgers, Basic Science)

Funding

The RePORT Indian Consortium is supported with bilateral funding from the Government of India's (GOI) Department of Biotechnology (DBT) and the U.S. National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), and Office of AIDS Research (OAR). CRDF Global administers and oversees the funding from the U.S. government.



2021 Young Investigator Abstracts



BJGMC



NIRT



Hinduja



Young Investigator Abstracts

PRESENTED	
TITLE	INVESTIGATORS
Baseline IL-6 is a biomarker for unfavorable tuberculosis treatment outcomes: a multi-site discovery and validation study	Akshay Gupte Pavan Kumar, Mariana Araújo-Pereira, Vandana Kulkarni, Mandar Paradkar, Neeta Pradhan, Padmapriya Darasini, Luke Hanna, Neesha Rockwood, Elsa Du Bruyn, Rajesh Karyakarte, Sanjay Gaikwad, Robert Bollinger, Nikhil Gupte, Vijay Viswanathan, Robert J. Wilkinson, Vidya Mave, Subash Babu, Hardy Kornfeld, Bruno B. Andrade, Amita Gupta
Identification of a six-cytokine biosignature discriminating active tuberculosis from latent infection	Vaishnavi Kaipilyawar , Jason Zhao, Noyal M. Joseph, Sonali Sarkar, C. Robert Horsburgh, Natasha S. Hochberg, Padmini Salgame, W. Evan Johnson, Jerrold J Ellner
Serum markers and integrative multi-omics of TB diagnosis in advanced HIV	Sonya Krishnan , Artur T. L. Queiroz, Amita Gupta, Nikhil Gupte, Gregory P. Bisson, Johnstone Kumwenda, Kogieleum Naidoo, Lerato Mohapi, Vidya Mave, Rosie Mngqibisa, Javier Lama, Mina C. Hosseinipour, Bruno Andrade, Petros C. Karakousis for the ACTG A5274 REMEMBER and NWCS 414 Study Team
Intranasal BCG vaccination induces expansion of lung resident innate immune cells in mice challenged with <i>Mycobacterium tuberculosis</i>	Madeline McAllister , Rajesh Kumar Radhakrishnan, Deepak Tripathi, Padmaja Paidipally Saptarshi Roy and Ramakrishna Vankayalapati
Nutritional supplementation cost-effectively decreases tuberculosis incidence and mortality in India: The Ration Optimization to Impede Tuberculosis (ROTI-TB) Model	Pranay Sinha , Subitha L. Lakshminaryan, Chelsie Cintron, Prakash Babu Narasimhan, Lindsey M. Locks, Nalin Kulatilaka, Padmapriyadarsini Chandrasekaran, Kimberley Maloomian, Senbagavalli Prakash Babu, Madeline E. Carwile, C. Robert Horsburgh, Jr., Carlos Acuna-Villaorduna, Benjamin P. Linas, Natasha S. Hochberg
Comparison of existing tuberculosis gene signatures using original models and gene set scoring methods	Xutao Wang , Padmini Salgame, Natasha S. Hochberg, Jerrold J. Ellner, Prasad Patil, W. Evan Johnson

Young Investigator Abstracts

SUBMITTED	
TITLE	INVESTIGATORS
Knowledge, behaviors, and stigma related to TB in India: a qualitative study among TB patients, their household members, and key stakeholders in Puducherry, India	Madeline Carwile , Lora Sabin, Mahalakshmy T, Senbagavalli Prakash Babu, Selby Knudsen, Lijia Dong, Jessie Stephens, Priyanka Fernandes, C. Robert Horsburgh, Jr, Padmini Salgame, Jerrold J Ellner, Sonali Sarkar, Natasha S. Hochberg
T-cell activation persists among those with advanced HIV and tuberculosis despite treatment	Vandana Kulkarni , Shashikala Sangle, Amol Chavan, Sonali Salvi, Dhananjay Shere, Neelu Nawani, Nikhil Gupte, Amita Gupta, Padmini Salgame, Vidya Mave
A two-gene signature for tuberculosis diagnosis in persons with advanced HIV	Vandana Kulkarni , Artur T. L. Queiroz, Shashi Sangle, Anju Kaga, Sonali Salvi, Amita Gupta, Jerrold Ellner, Dileep Kadam, Valeria C Rolla, Bruno B. Andrade, Padmini Salgame, Vidya Mave
Risk factors for multidrug resistant tuberculosis in a referral hospital cohort	Richu Bob Kurien , D. J. Christopher
Adverse treatment outcomes in pulmonary tuberculosis are characterized by heightened systemic inflammation and microbial translocation	Arun Nancy P , Nathella Pavan Kumar, Kadar Moideen, Vijay Viswanathan, Kannan Thiruvengadam, Shanmugam Sivakumar, Syed Hissar, Hardy Kornfeld, and Subash Babu
TNFRI mediated necroptotic cell death of T2DM mice alveolar macrophages infected with <i>Mycobacterium tuberculosis</i>	Rajesh Kumar Radhakrishnan , Deepak Tripathi, Saptarshi Roy, Padmaja Paidipally, Madeline McAllister and Ramakrishna Vankayalapati
Haematological abnormalities as potential markers for TB diagnosis and outcome prediction	Sathyamurthi P , Brindha B, Kannan T, Kannan M, Anbalagan S, Mangaiyarkarasi S, Murugesan S, Karthika C, Padmapriyadarsini C
Malnutrition leads to distinct patterns in immune pathways and tuberculosis risk signatures in latent tuberculosis infection	Arthur VanValkenburg , Vaishnavi Kaipilyawar, Sonali Sarkar, Subitha Lakshminarayanan, Chelsie Cintron, Senbagavalli Prakash Babu, Selby Knudsen, Noyal Mariya Joseph, C. Robert Horsburgh, Jerrold J Ellner, Prakash Babu, W. Evan Johnson, Padmini Salgame, Natasha S. Hochberg

Young Investigator Abstracts

PRESENTED

Baseline IL-6 is a biomarker for unfavorable tuberculosis treatment outcomes: a multi-site discovery and validation study

Submitting Author: Akshay Gupte

Co-authors: Pavan Kumar, Mariana Araújo-Pereira, Vandana Kulkarni, Mandar Paradkar, Neeta Pradhan, Padmapriya Darasini, Luke Hanna, Neesha Rockwood, Elsa Du Bruyn, Rajesh Karyakarte, Sanjay Gaikwad, Robert Bollinger, Nikhil Gupte, Vijay Viswanathan, Robert J. Wilkinson, Vidya Mave, Subash Babu, Hardy Kornfeld, Bruno B. Andrade, Amita Gupta

Background: Biomarkers of unfavorable tuberculosis treatment outcomes are needed to accelerate new drug and regimen development. Whether plasma cytokine levels can predict unfavorable treatment outcomes is unclear.

Methods: We identified and internally validated the association between 20 a-priori selected plasma inflammatory markers and unfavorable treatment outcomes among adults with drug-sensitive pulmonary tuberculosis in India. We externally validated these findings in two independent cohorts of predominantly diabetic and HIV coinfecting tuberculosis patients in India and South Africa, respectively. We used random effects linear and logistic regression, adjusting for confounders including disease severity, to measure the association between inflammatory markers and subsequent treatment failure, recurrence and all-cause mortality.

Results: Pre-treatment IFN- γ , IL-13 and IL-6 were associated with subsequent treatment failure in the discovery analysis. Internal validation confirmed higher pre-treatment IL-6 concentrations among failure cases compared to controls; we did not find similar associations with IFN- γ or IL-13. External validation among predominantly diabetic tuberculosis patients found an association between pre-treatment IL-6 concentrations and subsequent recurrence and death. Similarly, external validation among predominantly HIV coinfecting tuberculosis patients found an association between pre-treatment IL-6 concentrations and subsequent treatment failure and death. In a pooled analysis of 363 tuberculosis cases from the Indian and South African validation cohorts, high pre-treatment IL-6 concentrations were associated with higher risk of failure (aOR=2.40, 95%CI 1.11-5.22, p=0.02), recurrence (aOR=5.92, 95%CI 2.52-13.90, p<0.001) and death (aOR=4.96, 95%CI 1.84-13.37, p=0.002).

Conclusion: Pre-treatment IL-6 is a biomarker for unfavorable tuberculosis treatment outcomes. Future studies should identify optimal IL-6 concentrations for point-of-care risk prediction.

Identification of a six-cytokine biosignature discriminating active tuberculosis from latent infection

Submitting Author: Vaishnavi Kaipilyawar

Co-authors: Jason Zhao, Noyal M. Joseph, Sonali Sarkar, C. Robert Horsburgh, Natasha S. Hochberg, Padmini Salgame, W. Evan Johnson, Jerrold J Ellner

Background & Rationale: The high cost and logistical difficulty of current sputum-based diagnostic tests impedes Tuberculosis (TB) diagnosis in high-burden, resource-poor settings. The development of a cost-effective and rapid triage test would significantly improve the efficiency of TB detection and treatment, further facilitating the reduction in the global TB burden. Our goal was to develop a blood-based biosignature that segregated tuberculosis from latent infection (LTBI) to be subsequently deployed as a triage test.

Methods: Multiplexed, quantitative detection of 23 cytokines/chemokines was performed on plasma samples from a South Indian dataset of 155 TB cases and 208 individuals with LTBI, using Meso Scale Discovery's custom V-plex assays. A random stratified sampling was first applied to split the dataset into a training set (80%) and a validation set (20%). From the training set, an ensemble feature selection pipeline (lasso logistic regression, random forest, and xgboost models and leave-one-out cross-validation) was used to generate a parsimonious cytokine biomarker with robust and unbiased power in differentiating TB from LTBI. An ensemble learning classifier from the training set was then used to evaluate the biomarker's quantitative performance in the validation set.

Young Investigator Abstracts

PRESENTED (Continued)

Results: A biomarker comprising six cytokines (Eotaxin, IFN γ , IL-15, IL-1 β , IL-6, and IP-10) 'CYTO6' was derived from the training set. When tested in the validation set, CYTO6 achieved 0.99 AUC, 100% sensitivity, 92.68% specificity, 60.29% PPV and 100% NPV.

Conclusions: CYTO6 demonstrates strong performance in distinguishing TB from LTBI and thus shows promise as a rapid triage test. Future studies will evaluate the performance of CYTO6 as a community-based triage test.

Serum markers and integrative multi-omics of TB diagnosis in advanced HIV

Submitting Author: Sonya Krishnan

Co-authors: Artur T. L. Queiroz, Amita Gupta, Nikhil Gupte, Gregory P. Bisson, Johnstone Kumwenda, Kogieleum Naidoo, Lerato Mohapi, Vidya Mave, Rosie Mngqibisa, Javier Lama, Mina C. Hosseinipour, Bruno Andrade, Petros C. Karakousis for the ACTG A5274 REMEMBER and NWCS 414 Study Team

Background: Tuberculosis (TB) accounts for a large burden of morbidity and mortality among persons living with HIV (PLWH). Conventional methods of TB diagnosis, including smear microscopy and Xpert MTB/RIF have lower sensitivity in PLWH. Novel high-throughput approaches, such as miRNAomics and metabolomics, may advance our insights into subclinical and difficult to diagnose TB, especially in very advanced HIV.

Methods: We conducted a case-control study leveraging REMEMBER, a multi-country, open-label randomized controlled trial comparing 4-drug empiric TB treatment with isoniazid preventive therapy in PLWH initiating ART with CD4 cell counts <50 cells/ μ L. Active TB was ruled out at baseline. A total of 23 Cases (incident TB within 48 weeks post-ART initiation) were site-matched with up to 2 Controls. We performed miRNA next generation sequencing (QIAGEN), liquid chromatography-mass spectrometry quantitative metabolomic analysis (Metabolon, Inc.), and multiplex immunoassays (Luminex) on serum samples obtained at time of TB diagnosis. Multi-omics data were integrated, and the decision tree algorithm was used to identify the best model for TB diagnosis. The accuracy was measured by receiver operating characteristic (ROC) curve and area under the curve (AUC).

Results: The majority of participants were from South Africa and India. The median time to TB diagnosis was 4.6 weeks (IQR 2-16.1), with 12 pulmonary and 11 extrapulmonary cases. Differentially expressed miRNA analysis revealed 11 altered miRNAs, with fold change higher than ± 1.4 in Cases relative to Controls ($P < 0.05$). Differentially altered metabolite analysis showed no significant alterations in metabolites between Cases and Controls. We found higher TNF α and IP-10/CXCL10 in Cases ($p = 0.011$, $p = 0.0005$), and higher MDC/CCL22 in Controls ($p = 0.0072$). A decision tree algorithm identified gamma-glutamylthreonine and hsa-miR-215-5p as the optimal variables to classify incident TB Cases (AUC 0.965). hsa-miR-215-5p, which targets genes in the TGF- β signaling pathway, was downregulated in Cases. Gamma-glutamylthreonine, a breakdown product of protein catabolism, was less abundant in Cases. Integration of cytokine markers did not improve the AUC.

Conclusions: Use of a machine learning approach in the multi-omics data from advanced HIV participants revealed two variables with the ability to accurately discriminate TB Cases from Controls.

Young Investigator Abstracts

PRESENTED (Continued)

Intranasal BCG vaccination induces expansion of lung resident innate immune cells in mice challenged with *Mycobacterium tuberculosis*

Submitting Author: Madeline McAllister

Co-authors: Rajesh Kumar Radhakrishnan, Deepak Tripathi, Padmaja Paidipally Saptarshi Roy and Ramakrishna Vankayalapati

Background: *Mycobacterium tuberculosis* (*Mtb*) remains to be a leading cause of morbidity and mortality, causing an estimated 1.4 million deaths annually. Previously, it has been shown that activating adaptive immune cells via intranasal or mucosal BCG vaccination in mice has proven to provide superior protection against pulmonary TB, as compared to parenterally administered BCG due to the activation of specific CD69+CD103+ tissue-resident memory T cells. Tissue-resident immune cells are a subset of immune cells which possess a unique CD69+, CD103+, or CD49a+ phenotype and are noncirculating. These site-specific cells play important roles in local tissue homeostasis but have also been shown to play important roles in infection control within various infection models. Although the importance of tissue-resident adaptive cells in protection against infection, including TB infection is known, there is limited information available regarding the immune profile and functional role of tissue-resident (tr) innate cells, such as NK cells and alveolar macrophages, within the lung upon intranasal BCG vaccination or TB infection, despite innate immunity playing a very important role in protection against TB.

Methods: To phenotypically and functionally characterize the tissue-resident innate cells (NK cell and macrophage subsets) within the lungs, C57BL/6 mice were vaccinated intranasally with live-attenuated BCG. After different time points (24h, 48h, 72h, and 7d) lung lymphocytes were isolated and the innate immune cell profile was determined by flow cytometry. In some experiments, three months after vaccination, lung cells from control and BCG vaccinated mice were cultured with γ -irradiated *Mtb* to determine the expansion capacity of lung resident innate lymphocytes. In other experiments, three months after vaccination, control and BCG vaccinated mice were challenged with *Mtb* H37Rv. One month after infection, lung resident innate lymphocytes were determined.

Results: We found that lung resident CD3-NK1.1+CD69+, CD3-NK1.1+CD103+, and CD3-NK1.1+CD69+CD103+ NK subsets expand after BCG vaccination. Three months after BCG vaccination and *in vitro* restimulation of lung resident cells leads to expansion of CD69+ and CD69+CD103+ subsets compared to PBS treated mice lung cells. Similar expansion was noted in the lungs of BCG vaccinated and *Mtb* H37Rv challenged mice. Further, CD3-NK1.1+CD69+, CD3-NK1.1+CD69+CD103+, and CD3-NK1.1+CD103+ subsets from the lungs of BCG vaccinated mice were sorted and administered intravenously to mice infected with *Mtb* to determine their protective role.

Conclusions: Our findings demonstrate that trained immune cells expand within the lungs of BCG vaccinated and *Mtb* challenged mice. Adoptive transfer and functional studies are underway to further determine the functional role of these tissue resident immune cell subsets and their importance in host protection against *Mtb* infection.

Nutritional supplementation cost-effectively decreases tuberculosis incidence and mortality in India: The Ration Optimization to Impede Tuberculosis (ROTI-TB) Model

Submitting Author: Pranay Sinha

Co-authors: Subitha L. Lakshminaryan, Chelsie Cintron, Prakash Babu Narasimhan, Lindsey M. Locks, Nalin Kulatilaka, Padmapriyadarsini Chandrasekaran, Kimberley Maloomian, Senbagavalli Prakash Babu, Madeline E. Carwile, C. Robert Horsburgh, Jr., Carlos Acuna-Villaorduna, Benjamin P. Linas, Natasha S. Hochberg

Background: Undernutrition is the leading cause of tuberculosis (TB) in India and is associated with increased TB mortality. Independent of TB, undernutrition decreases quality of life and economic productivity. We aimed to assess the cost-effectiveness of providing augmented food rations to undernourished Indians through the government's Targeted Public Distribution System (TPDS) to reduce TB cases, TB deaths, and increase quality-adjusted life years (QALYs).

Young Investigator Abstracts PRESENTED (Continued)

Material & Methods: We simulated rate of weight gain among 10,000 undernourished Indian adults with body mass index (BMI) 16-18.4 kg/m² randomly selected from the National Family Health Survey-4 dataset if provided a 2600 KCal/day diet. Using Markov state transition models, we simulated disease progression and mortality among undernourished individuals in three groups: general population, household contacts (HHCs) of people living with TB, and persons with HIV. Transition probabilities were estimated based on RePORT India data and WHO estimates. The models calculate costs associated with provision of augmented rations for undernourished adults until they attain a BMI of 20kg/m² compared to a “do nothing” scenario wherein TPDS rations are unchanged. We employed deterministic and probabilistic sensitivity analyses to test result robustness.

Results: Over 5 years, augmented rations could avert 78% of TB cases and 88% of TB deaths among undernourished Indians. Correspondingly, this intervention could forestall 78% and 43% of TB cases among undernourished HHCs and HIV positive persons and prevent 88% and 68% of deaths, respectively. Augmented rations resulted in a ten-fold higher resolution of undernutrition. Augmented rations were highly cost-effective (incremental cost effectiveness ratio (ICER): \$460.4/QALY). ICER trended towards being lower for HHCs (\$437.3/QALY) and the HIV population (\$406.9/QALY). QALYs gained from improving nutritional status eclipsed those from preventing TB.

Conclusions : A robust nutritional intervention would be highly cost-effective in reducing TB incidence and mortality while reducing chronic undernutrition.

Comparison of existing tuberculosis gene signatures using original models and gene set scoring methods

Submitting Author: Xutao Wang

Co-authors: Padmini Salgame, Natasha S. Hochberg, Jerrold J. Ellner, Prasad Patil, W. Evan Johnson

Background: Blood-based transcriptional biomarkers are useful for studying and understanding tuberculosis (TB) outcomes. Many systematic comparisons of TB gene signatures across independent studies rely on the reconstruction of the original diagnostic model. However, the lack of access to original discovery datasets or missing details about the trained model can make direct comparisons using original models challenging. Alternatively, gene set scoring can be used to evaluate diagnostic ability of the gene set on its own. In this study, we compared the performance of 19 TB gene signatures across 24 transcriptomic datasets using both reimplemented original models and gene set enrichment scoring methods to evaluate if gene set scoring is a reasonable proxy to the performance of the original trained model.

Methods: Existing gene set scoring methods including ssGSEA, GSVA, PLAGE, Singscore, and Zscore were used to evaluate each gene signature’s performance. Area under the curve (AUC) values were calculated for each signature within each study. The sample-size-weighted (weighted) mean AUC value was computed for each signature to measure its overall performance. We also proposed a signature splitting strategy, which evaluates upregulated and downregulated genes within a signature’s gene set separately to improve diagnostic accuracy using ssGSEA and GSVA. Results

Results: PLAGE outperformed the rest of the gene scoring methods, and in some cases the original models, in terms of the signature’s weighted mean AUC values, and the AUC results within individual studies. Wilcoxon-paired tests suggested that the weighted mean AUC value computed by PLAGE, ssGSEA, and GSVA for each signature were equivalent to the results given by the original diagnostic model. Software for applying gene set scoring methods and original models is available in the TBSignatureProfiler platform (<http://www.bioconductor.org/packages/release/bioc/html/TBSignatureProfiler.html>).

Conclusion: Gene set enrichment scoring of existing blood-based biomarker gene sets distinguishes patients with active TB disease with equivalent accuracy as original models. Such toolkits could be used as alternative approaches to profile gene signature performance in a uniform and robust way.

Young Investigator Abstracts

SUBMITTED

Knowledge, behaviors, and stigma related to TB in India: a qualitative study among TB patients, their household members, and key stakeholders in Puducherry, India

Authors: Madeline Carwile, Lora Sabin, Mahalakshmy T, Senbagavalli Prakash Babu, Selby Knudsen, Lijia Dong, Jessie Stephens, Priyanka Fernandes, C. Robert Horsburgh, Jr, Padmini Salgame, Jerrold J Ellner, Sonali Sarkar, Natasha S. Hochberg

Background and Rationale: To capitalize on advances in TB diagnostics and therapeutics, it is critical that people living with active TB (PLWATB) engage in care. One major challenge is stigma, which occurs when PLWATB experience discrimination or rejection due to their disease status, and which can lead to delays in diagnosis and treatment of TB. We aimed to understand TB stigma (anticipated, enacted, and internalized) and evaluate potential interventions to reduce stigma as articulated by PLWATB, their family members, and other key stakeholders in Puducherry and Tamil Nadu, India.

Methods: We conducted 47 in-depth interviews (IDI) with PLWATB and their household members (HHM), together with eight focus group discussions: two each with PLWATB, HHM, healthcare workers, and key informants.

Results: Overall, 38 (80.9%) of IDI participants reported incorrect modes of transmission, though most (70.2%) were aware that TB is curable. Participants reported high levels of perceived stigma; 59.6% of PLWATB chose to hide their disease to avoid stigma in their community. They also reported experiencing enacted stigma from community members, employers, and even healthcare workers, who were often described as scolding patients. Participants supported a range of interventions, including celebrity advocacy in the form of disease awareness through social media, and school-based programming, such as education in textbooks, to increase community knowledge and reduce enacted stigma. They also supported interventions to reduce internalized stigma among PLWATB, including support groups and counseling.

Conclusions: We found high levels of anticipated stigma, which could decrease a PLWATB's willingness to seek treatment. Interventions are needed to increase TB knowledge and decrease stigma; suggestions from this study include advocacy by celebrities, school programs, and support groups. These findings have the potential to inform future interventions to reduce TB-related stigma in India, which could increase engagement in care and result in higher TB treatment success.

T-cell activation persists among those with advanced HIV and tuberculosis despite treatment

Authors: Vandana Kulkarni, Shashikala Sangle, Amol Chavan, Sonali Salvi, Dhananjay Shere, Neelu Nawani, Nikhil Gupte, Amita Gupta, Padmini Salgame, Vidya Mave

Background: Surface markers of T-cell activation (CD38, HLA-DR) are independent predictors of disease progression and mortality in people living with HIV (PLHIV). Although it is known that T-cell activation among HIV-TB may be higher compared to HIV-only, the effect of TB disease among advanced HIV on T-cell activation is not well characterized. We sought to compare T-cell activation markers longitudinally among advanced PLHIV with or without TB.

Methods: HIV-infected adults with and without pulmonary tuberculosis (n=30) with CD4 cell count <100 cells/mm³, tuberculosis treatment naïve with highly active anti-retroviral therapy (HAART)-naïve or experienced at baseline were enrolled and followed up at 8 and 24 weeks. Viral load, CD4 cell count and frequency of T-cells expressing the activation markers CD38 and HLA-DR were evaluated by flow cytometry. Data between HIV-TB and HIV-only were compared using Wilcoxon rank sum test.

Results: We enrolled 16 HIV-TB co-infected and 14 HIV-only groups. Of the 30 enrolled, 23 (77%) were male, median age was 44 (IQR, 35–52), and 26 (87%) were started on HAART during the study. Overall, median CD4 count increased over 24 weeks (51 cells/mm³ at baseline vs. 124 cells/mm³ at 24 weeks, p=0.02); viral load decreased from 5.25 log₁₀ copies/ml at baseline to 2.35 log₁₀ copies/ml at 24 weeks (p=0.002). Compared to HIV-only individuals, percentage of CD4+ T-cells co-expressing CD38 and HLA-DR was higher in HIV-TB group at baseline (p=0.23) and remained elevated at 8 weeks (p=0.02) and 24 weeks (p=0.17) (Figure 1).

Young Investigator Abstracts

SUBMITTED (Continued)

Conclusions: CD4 T-cell activation remained elevated over time among those with advanced HIV and TB despite being on ART and TB treatment. These findings indicate that concurrent ART and TB treatment may not resolve the sustained T-cell activation among people living with advanced HIV. Analysis of other T-cell subsets are in progress.

A two-gene signature for tuberculosis diagnosis in persons with advanced HIV

Authors: Vandana Kulkarni, Artur T. L. Queiroz, Shashi Sangle, Anju Kaga, Sonali Salvi, Amita Gupta, Jerrold Ellner, Dileep Kadam, Valeria C Rolla, Bruno B. Andrade, Padmini Salgame, Vidya Mave

Background: Tuberculosis (TB) is a major cause of death in persons living with HIV (PLWH). Diagnosis of TB in PLWH with advanced immunosuppression and low CD4 T-cell counts remains challenging due to an increased frequency of paucibacillary cases. Although several transcriptional signatures have recently been identified as promising for TB diagnosis, data remain limited in persons with advanced HIV. We performed gene expression profiling to diagnose TB in PLWH with CD4 count < 100 cells/mm³. Transcriptomic signatures for tuberculosis (TB) have been proposed and represent a promising diagnostic tool.

Methods:

We enrolled 30 patients with advanced HIV (CD4<100 cells/mm³) in India; 16 with active TB and 14 without. Whole-blood RNA sequencing was performed; these data were merged with a publicly available dataset from Uganda (n=33; 18 with TB and 15 without). Transcriptomic profiling and machine learning algorithms identified an optimal gene signature for TB classification. Receiver operating characteristic analysis was used to assess performance.

Results: Among 565 differentially expressed genes identified for TB, 40 were shared across India and Uganda cohorts. Common upregulated pathways reflect Toll-like receptor cascades and neutrophil degranulation. The machine-learning decision-tree algorithm selected gene expression values from *RAB20* and *INSL3* as most informative for TB classification.

The signature accurately classified TB in discovery cohorts (India AUC 0.95 and Uganda AUC 1.0; p<0.001); accuracy was fair in external validation cohorts.

Conclusions: Expression values of *RAB20* and *INSL3* genes in peripheral blood compose a biosignature that accurately classified TB status among patients with advanced HIV in two geographically distinct cohorts. The functional analysis suggests pathways previously reported in TB pathogenesis.

Risk factors for multidrug resistant tuberculosis in a referral hospital cohort

Authors: Richu Bob Kurien, D. J. Christopher

Background and Rationale: In 2019, 9.96 million people developed tuberculosis (TB) globally and among them 465,000(6.1%) people suffered from multidrug-resistant TB (MDR-TB) of these 124,000 were from India. History of TB treatment, poor compliance, the presence of DM and other co-morbidities have been described as contributory factors to development of drug resistance. While there are several studies addressing risk factors for drug sensitive TB (DS-TB), studies looking at risk factors for MDR-TB and comparison with DS-TB risk factors are very few. This study was designed to address this.

Methodology: We did a prospective case-control study from March 2019 till July 2020 in a tertiary care centre, in South India. All diagnosed cases of MDR-TB (pulmonary and extra-pulmonary) were recruited along with DS-TB cases matched for age and organ involvement. Asthmatic patients attending the Pulmonary Medicine OPD were recruited as controls. Demographic data, detailed clinical information and laboratory test results including XPERT TB-PCR, AFB smear, culture and DST results were collected. MDR-TB was compared with drug sensitive TB and controls.

Young Investigator Abstracts

SUBMITTED (Continued)

Results: 31 cases of MDR-TB, 56 controls each of DSTB and Asthmatic controls were recruited. Multivariate logistic regression analysis identified the following risk factors for development of MDR-TB.

When compared to DSTB, the following risk factors: Previous TB treatment (OR=16.23; CI=2.76–95.27), household TB case contact (OR=11.84; CI=1.78–78.87), hypertension (OR=7.29; CI=1.01–52.86) and residence in Urban area (OR=4.13; CI=1.10–15.61), showed significant association.

When compared to Asthma controls, the following risk factors: Diabetes mellitus (OR=90.26; CI=4.05–2010.94) and low BMI (OR=12.27; CI=1.44–104.10), showed significant association.

Conclusion: Our study identified important risk factors specific to MDR-TB such as previous TB treatment, household TB case contact, hypertension and residence in an urban area.

Adverse treatment outcomes in pulmonary tuberculosis are characterized by heightened systemic inflammation and microbial translocation

Authors: Arun Nancy P, Nathella Pavan Kumar, Kadar Moideen, Vijay Viswanathan, Kannan Thiruvengadam, Shanmugam Sivakumar, Syed Hissar, Hardy Kornfeld, and Subash Babu

Background and Rationale: Systemic inflammation and microbial translocation are known characteristics of pulmonary tuberculosis (PTB). Whether systemic inflammation and microbial translocation are also associated with adverse treatment outcomes in PTB is not known.

Methods: We examined the presence of systemic inflammation and microbial translocation in a cohort of newly diagnosed, sputum smear and culture positive individuals with drug-sensitive PTB. Participants were followed up for a year following the end of anti-tuberculosis treatment. They were classified as cases (in the event of treatment failure, recurrence or death; n=68) and controls (in the event of successful, recurrence free cure; n=133).

Results: Baseline levels of C-reactive protein (CRP), alpha-2 macroglobulin (a2M), haptoglobin (Hp) and serum amyloid P (SAP) were significantly higher in cases compared to controls and CRP and SAP were associated with increased risk, while Hp was associated with decreased risk of adverse treatment outcomes in both univariate and multivariate (following adjustment for covariates) analysis. Similarly, baseline levels of lipopolysaccharide (LPS), circulating soluble CD14 (sCD14), LPS-binding protein (LBP) were significantly higher in cases than controls and were associated with increased risk for adverse treatment outcomes while endotoxin core IgG antibody (EndoCAB) was significantly lower in cases and associated with decreased risk of adverse treatment outcomes. Longitudinal analysis revealed that levels of CRP and SAP were decreased and sCD14 increased in cases but not controls, while levels of a2M, LPS, LBP and EndoCAB increased in both cases and controls at two months of treatment.

Conclusion: Adverse treatment outcomes in PTB is therefore characterized by heightened systemic inflammation and microbial translocation.

TNFR1 mediated necroptotic cell death of T2DM mice alveolar macrophages infected with *Mycobacterium tuberculosis*

Authors: Rajesh Kumar Radhakrishnan, Deepak Tripathi, Saptarshi Roy, Padmaja Paidipally, Madeline McAllister and Ramakrishna Vankayalapati

Background & Rationale: Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (*Mtb*), is a leading cause of death worldwide. In 2019, globally 10 million people developed active TB disease and 1.4 million died (WHO, 2020). TB causes increased life-threatening events in people with immunocompromised conditions such as malnutrition, aging, diabetes, smoking and alcohol abuse. Further, co-infections with HIV, helminths, or diabetes mellitus alters innate and adaptive immune responses and increases the risk of developing active TB and reduces responsiveness to antimycobacterial treatments. However, the underlying biological mechanisms remain largely unknown. In the current study, we determined the defective mechanisms that make T2DM mice alveolar macrophages more susceptible to *Mtb* infection.

Young Investigator Abstracts

SUBMITTED (Continued)

Methods: In this study, we induced type 2 diabetes mellitus (T2DM) in C57BL/6 mice using streptozotocin (180 mg/kg body weight) and nicotinamide (60 mg/kg body weight). We isolated alveolar macrophages (AM's) from control and T2DM mice and infected with *Mtb* H37Rv. After 3 days of incubation, the cells were collected for mRNA, protein expression and for confocal microscopy. The cell culture supernatants were stored at -80°C and cellular toxicity and cytokine production was measured. For metabolite studies, we collected AM's cell lysates from *Mtb* infected control and T2DM mice in methanol and analyzed through LC/MS.

Results: *Mtb* infected AM's from T2DM mice expressed higher levels of TNFR1 and necroptotic markers (RIPK1, RIPK3 and Mlkl), produced more inflammatory cytokines (TNF- α and IL-6) and less apoptotic as compared to *Mtb* infected AM's of non-diabetic control mice. Anti-TNFR1 antibody treatment of *Mtb* infected AM's from T2DM mice significantly reduced the necroptosis and inflammatory cytokines (TNF- α and IL-6) production. Metabolic comparison of *Mtb* infected AM's from T2DM mice and *Mtb* infected AM's of non-diabetic control mice indicated two metabolites were significantly high abundant, and two metabolites were significantly low abundant in T2DM mice AM's infected with *Mtb* when compared with uninfected control and T2DM and infected control AM's.

Conclusions: Our findings demonstrate that T2DM induces TNFR1 mediated necroptosis of alveolar macrophages (CD11c+F4/80+cells) upon *Mtb* infection. We found that *Mtb* infected T2DM mice AM's and *Mtb* infected non-diabetic mice AM's differ in their metabolic profile. Studies are underway to determine the effects of these metabolites on TNFR1 expression, necroptosis and inflammatory cytokine production by *Mtb* infected AM's from T2DM mice. We are also determining the *in vivo* relevance of our finding by treating *Mtb* infected T2DM and *Mtb* infected control with the above metabolites.

Haematological abnormalities as potential markers for TB diagnosis and outcome prediction

Authors: Sathyamurthi P, Brindha B, Kannan T, Kannan M, Anbalagan S, Mangaiyarkarasi S, Murugesan S, Karthika C, Padmapriyadarsini C

Background: The hematopoietic system is seriously affected during tuberculosis (TB). Analysis of hematological abnormalities associated with TB may help identify valuable markers for TB diagnosis and predictors for treatment outcome.

Objective: To identify haematological changes associated with TB in a cohort of newly diagnosed, HIV-negative, pulmonary tuberculosis (PTB) patients and to identify their usefulness in assisting diagnosis and prognosis of TB.

Methodology: A total of 252 PTB patients (172 males, 80 females) and 442 controls (192 males, 250 females) aged >12 years were included in the analysis. The mean age of the PTB and control groups were 40.9 (13-75) and 33.58 (13-70) respectively. Complete hemogram was performed using an automated five-part hematology analyzer. All the healthy controls were screened for latent TB (LTB) status using TST or IGRA. Mann-Whitney test was used to determine the significance between the groups.

Results: Fifty four percent of the control population were positive for LTB; however, none of the hematological parameters were significantly different between the LTB-positive and negative groups. A number of parameters including RBC, hemoglobin, WBC, neutrophils, lymphocytes, monocytes and platelets were significantly different between the TB and control groups (Table 1). Further, monocyte/lymphocyte ratio (MLR), neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) were also significantly higher in the PTB group. Anaemia was seen in 71% of PTB patients as compared to 40% in the control group, with more males having anaemia in the PTB group (63.1%) and females in the control group (75.4%). Very interestingly, neutrophil and lymphocyte counts, and neutrophil/lymphocyte and monocyte/lymphocyte ratios were significantly higher even at baseline in PTB patients who failed treatment (sputum culture positive at 5 months or later) as compared to those who had a favourable outcome (cure).

Conclusion: Our findings clearly suggest a valuable role for neutrophil and lymphocyte count, and neutrophil/lymphocyte and monocyte/lymphocyte ratio in aiding diagnosis and predicting prognosis in pulmonary TB patients.

Young Investigator Abstracts

SUBMITTED (Continued)

Malnutrition leads to distinct patterns in immune pathways and tuberculosis risk signatures in latent tuberculosis infection

Authors: Arthur VanValkenburg, Vaishnavi Kaipilyawar, Sonali Sarkar, Subitha Lakshminarayanan, Chelsie Cintron, Senbagavalli Prakash Babu, Selby Knudsen, Noyal Mariya Joseph, C. Robert Horsburgh, Jerrold J Ellner, Prakash Babu, W. Evan Johnson, Padmini Salgame, Natasha S. Hochberg

Background: Most individuals exposed to *Mycobacterium tuberculosis* (Mtb) develop latent tuberculosis infection (LTBI) and remain at risk for progressing to active tuberculosis (TB). Malnutrition is an important risk factor driving progression from LTBI to TB. However, the performance of blood-based TB risk signatures in malnourished individuals with LTBI remains unexplored.

Methods: We utilized data from 50 tuberculin skin test positive household contacts of persons with TB - 15 severely malnourished (body mass index [BMI] < 16) and 35 controls (BMI ≥ 16). Whole blood RNA-sequencing was conducted to identify differentially expressed genes (DEGs). Ingenuity Pathway Analysis was applied to the DEGs to identify top canonical pathways and gene regulators. Gene enrichment methods were then employed to score the performance of published gene biomarkers associated with progression from LTBI to TB.

Results: In severely malnourished individuals, pathways involved in neutrophil activation, T-cell activation, pro-inflammatory IL-1 and IL-6 cytokine signaling, and senescence were upregulated while gene regulators involved in T helper (Th) -1 immune responses were downregulated. We found significantly increased expression of the RISK4 (area under curve [AUC] = 0.803) and PREDICT29 (AUC = 0.798) progression signatures, indicating increased risk of progression to TB in severely malnourished individuals.

Conclusion: Severely malnourished individuals display a peripheral immune response profile that is reflective of increased inflammation and suppression of immunomodulation. Malnourished individuals with LTBI exhibited increased expression of TB risk. With validation in prospective clinical cohorts, TB risk biomarkers have the potential to segregate malnourished LTBI for targeted therapy.





CMC
Vellore



ICER Lab



JIPMER

BMMRC

NIRT's Biorepository



Data



BJGMC's Data Management Centre



Hinduja's Hematology Lab



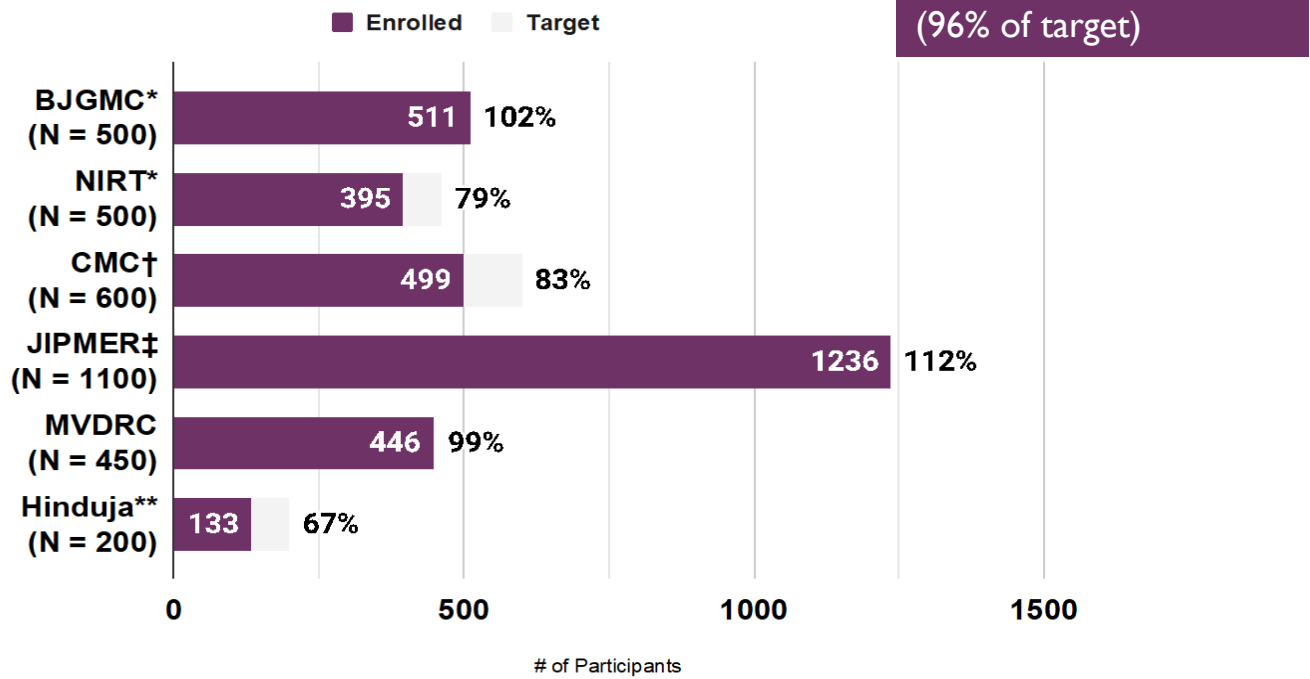
PCR at MVDRC

Centrifuge at BMMRC



Parent Protocol Enrollment

Cohort A: Sample Size & Enrollment



* BJGMC and NIRT jointly implemented a parent protocol. Together, BJGMC and NIRT enrolled 513 PTB (86% of target), 201 Ped (101% of target), and 192 EPTB (96% of target).

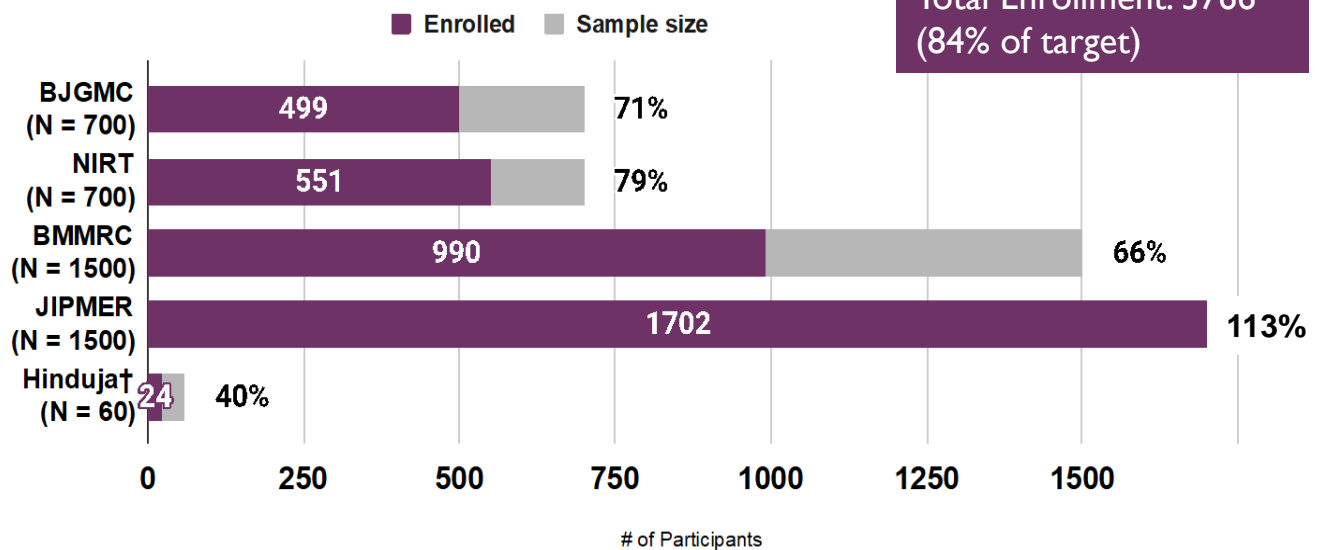
† Of 499 participants at CMC, 186 were PTB and 313 were TBM.

‡ Of 1236 PTB participants at JIPMER, 6 (0.5%) were <15 years old.

** Hinduja launched parent protocol in Oct 2017 and continues to enroll PTB and EPTB patients with MDR-TB >15 years old. Of 133 MDR-TB enrolled, 80 were PTB and 53 were EPTB.

(PTB=Pulmonary TB; TBM=TB Meningitis; EPTB=Extrapulmonary TB; Ped=Pediatric TB (<15 years); MDR=Multidrug-resistant TB)

Cohort B: Sample Size and Enrollment*



* Of 3766 total Cohort B participants enrolled, 675 (18%) were <15 years old.

† Enrollment of Cohort B participants at Hinduja is ongoing.

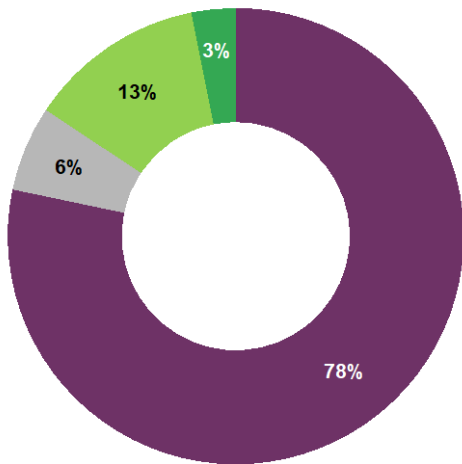
Source: Parent Protocol data was provided by individual sites and aggregated by the RePORT India Coordinating Hub. Data cutoff date: Dec 31, 2020

Parent Protocol Cohort A: Accrual Status

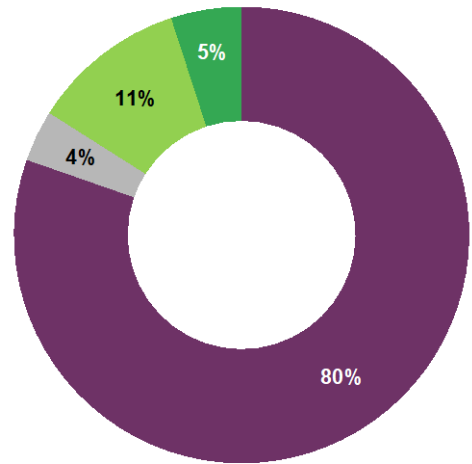


PTB=Pulmonary TB; TBM=TB Meningitis; EPTB=Extrapulmonary TB; Ped=Pediatric TB (<15 years); MDR=Multidrug-resistant TB

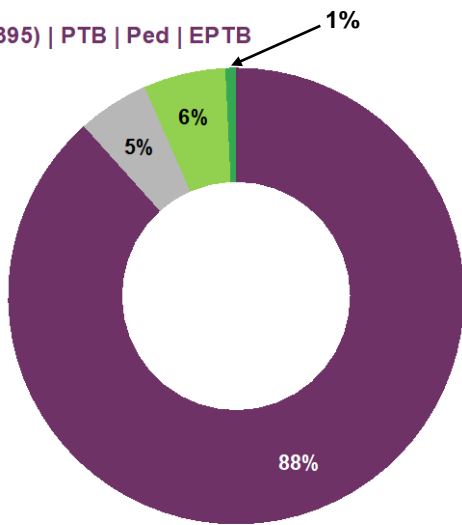
BJGMC (n=511) | PTB | Ped | EPTB



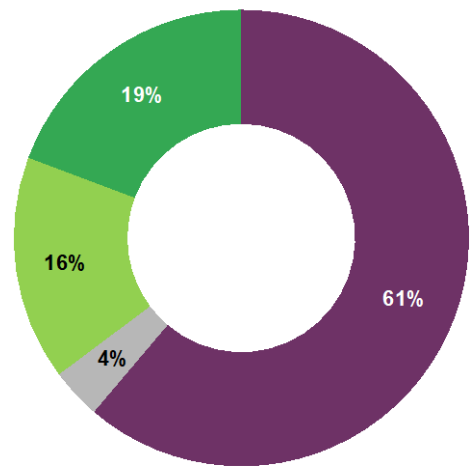
JIPMER (n=1236) | PTB



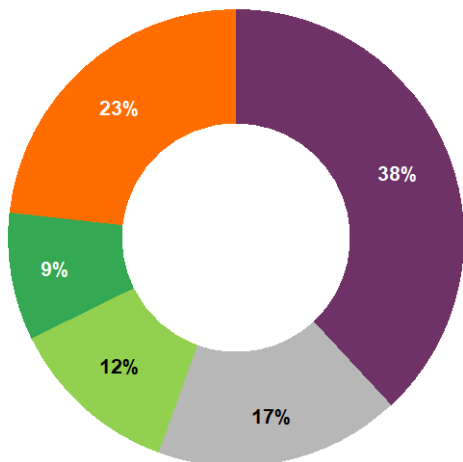
NIRT (n=395) | PTB | Ped | EPTB



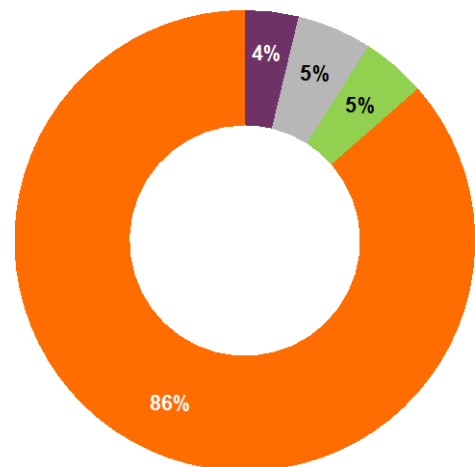
MVDRC (n=446) | PTB



CMC (n=499) | PTB | TBM



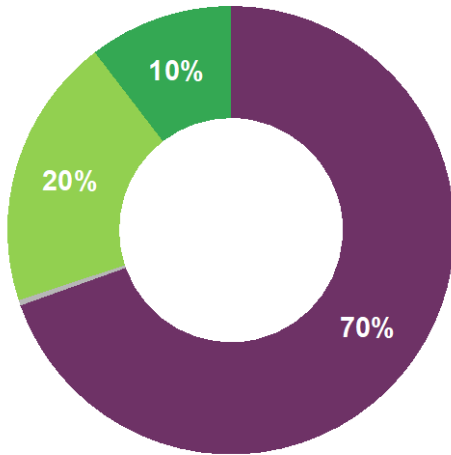
Hinduja (n=133) | MDR-TB



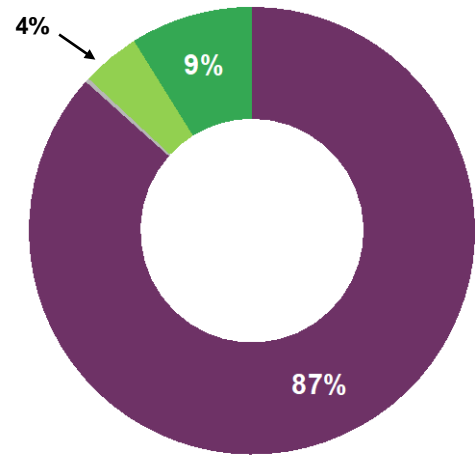
Parent Protocol Cohort B: Accrual Status



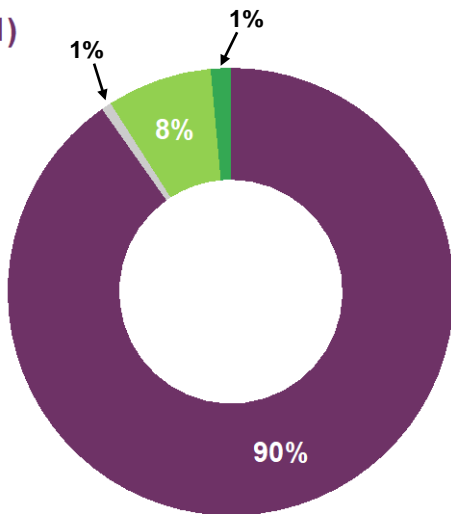
BJGMC* (n=499)



JIPMER (n=1702)**



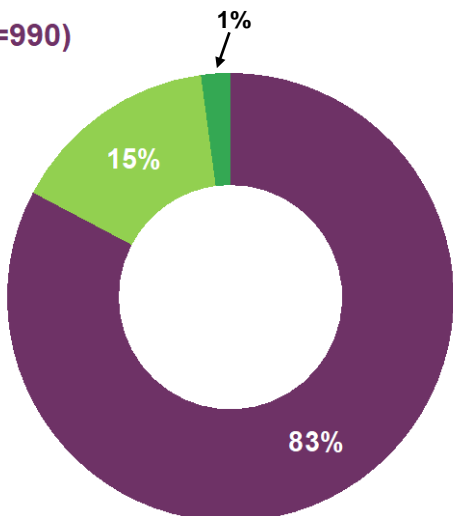
NIRT (n=551)



Hinduja (n=24)



BMMRC (n=990)

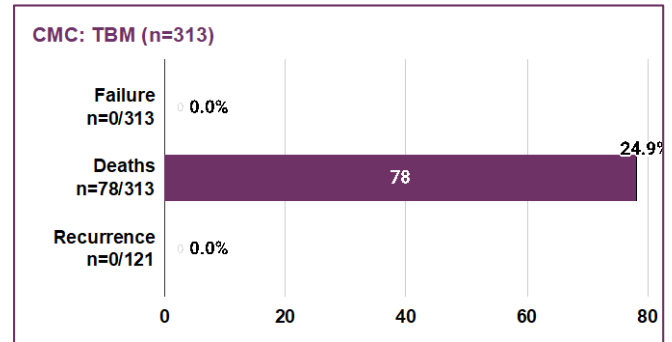
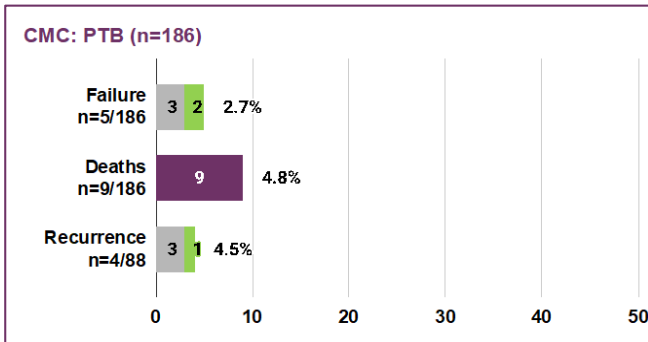
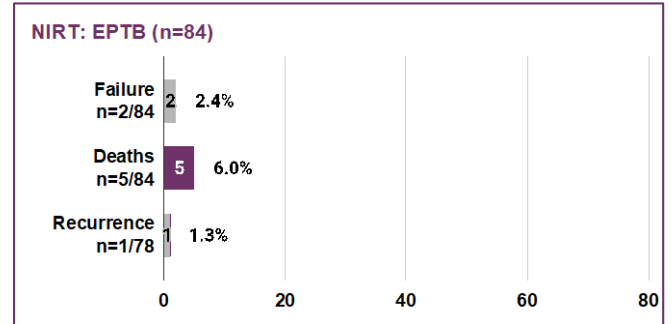
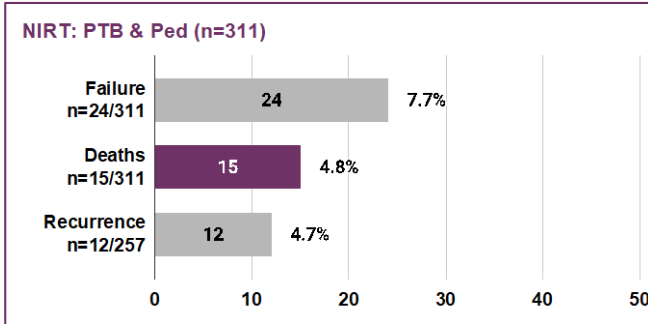
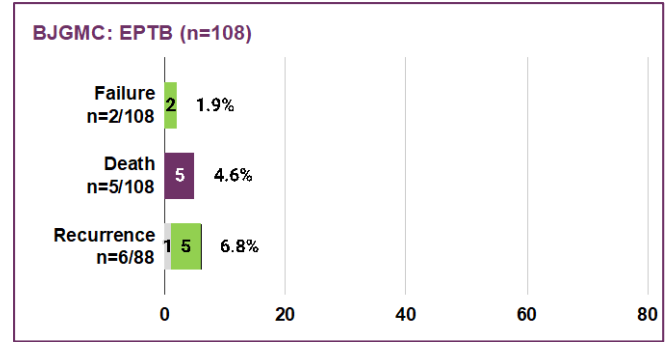
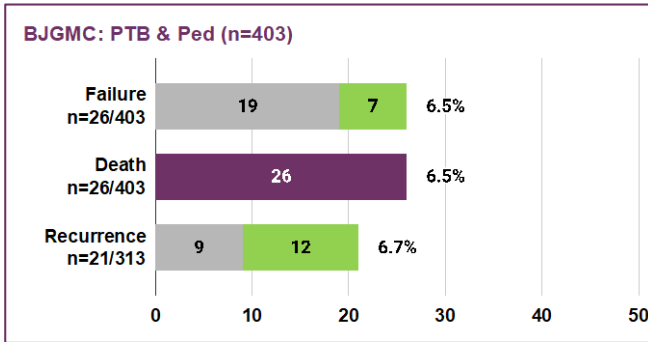


*There were 16 BJGMC participants who were off study because index case diagnosed with MDR-TB.

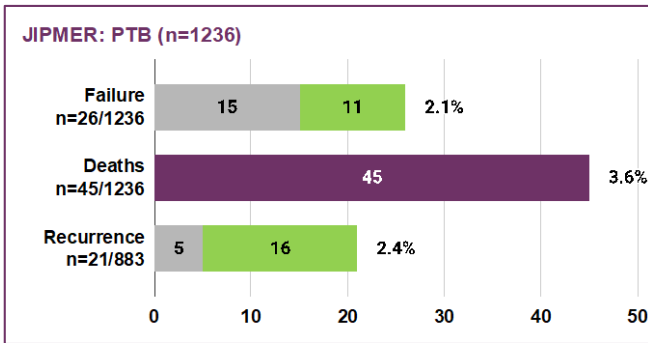
**Follow-up terminated for 83 participants due to study period ending at JIPMER.

Parent Protocol Cohort A: Treatment Outcomes

Treatment Outcomes



■ Bacteriological ■ Clinical ■ Total



For proportion of participants who failed treatment or died, denominator is total number of participants enrolled. For proportion of participants with TB recurrence, denominator is total number of participants who completed treatment.

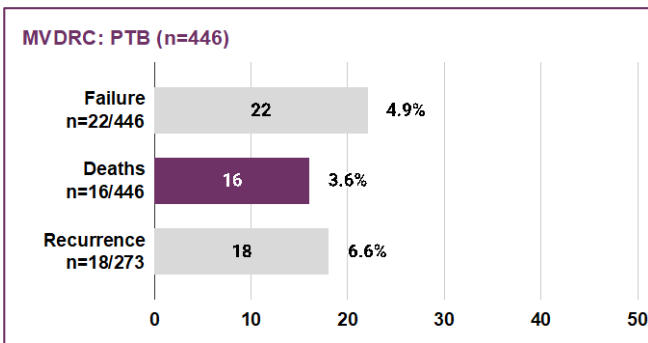
As participants at Hinduja remain in active follow-up, final outcomes are not yet available for this cohort.

Failure=TB patients enrolled in the parent protocol and declared treatment failure between month five and end of treatment.

Deaths=All-cause death

Recurrence=Patients diagnosed with TB after being declared as cured or treatment complete.

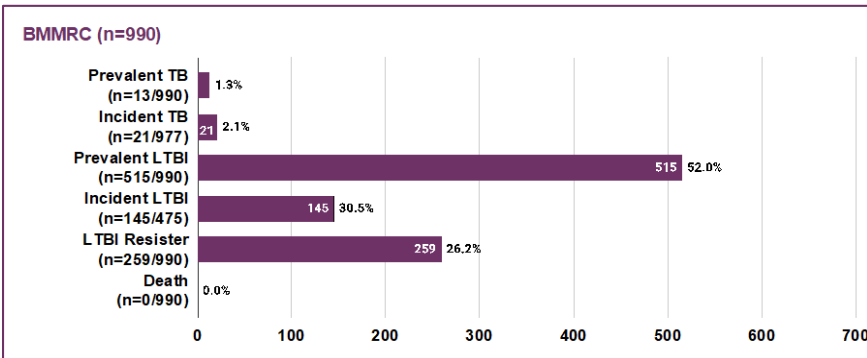
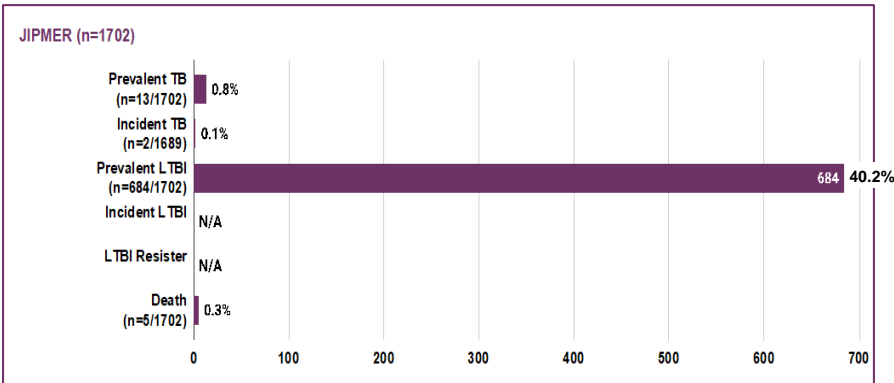
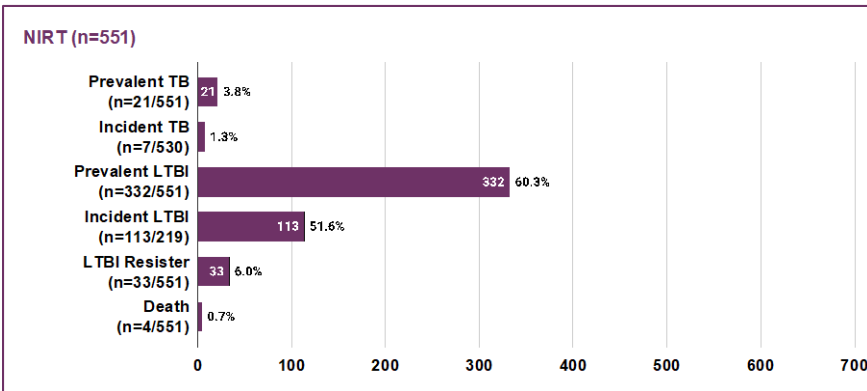
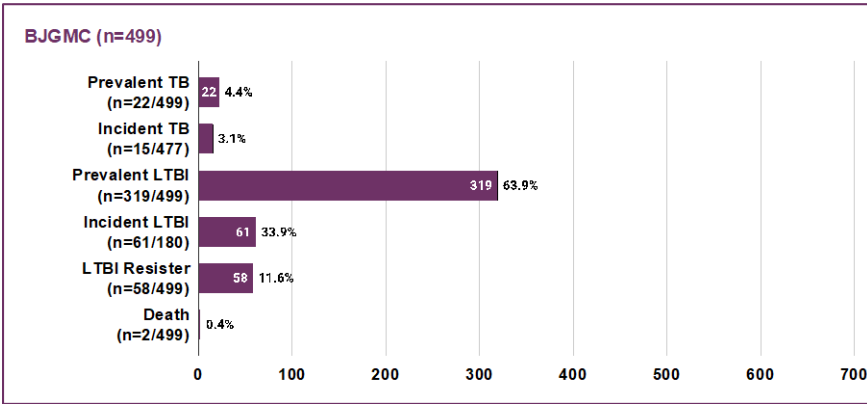
(PTB=Pulmonary TB; Ped=Pediatric; EPTB=Extrapulmonary TB; TBM=TB Meningitis)



of Participants

Parent Protocol Cohort B: Study Outcomes

Outcomes



LTBI=Latent TB Infection

Prevalent TB=TB disease reported at baseline (clinical or bacteriological confirmation).

Incident TB=TB disease diagnosed during follow-up (clinical or bacteriological confirmation). Denominator excludes prevalent TB.

Prevalent LTBI=TST or IGRA positive at baseline.

Incident LTBI=TST or IGRA conversion during follow-ups. Denominator excludes prevalent LTBI.

LTBI Resister=TST and IGRA negative throughout follow-ups.

Death=All-cause death

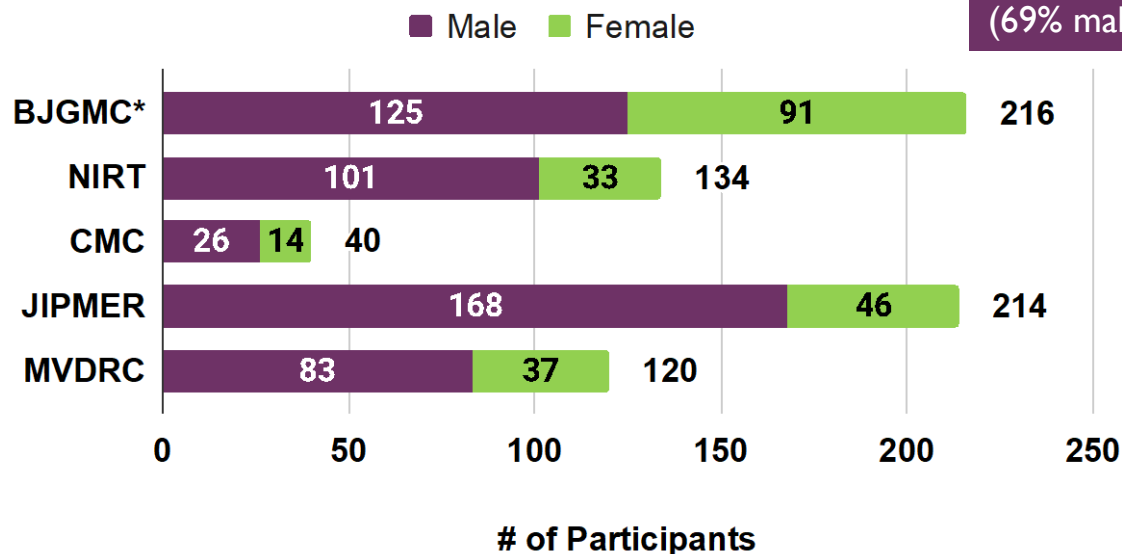
As participants at Hinduja remain in active follow-up, final outcomes are not yet available for this cohort.

of Participants

Common Protocol Enrollment

Cohort A: Enrollment

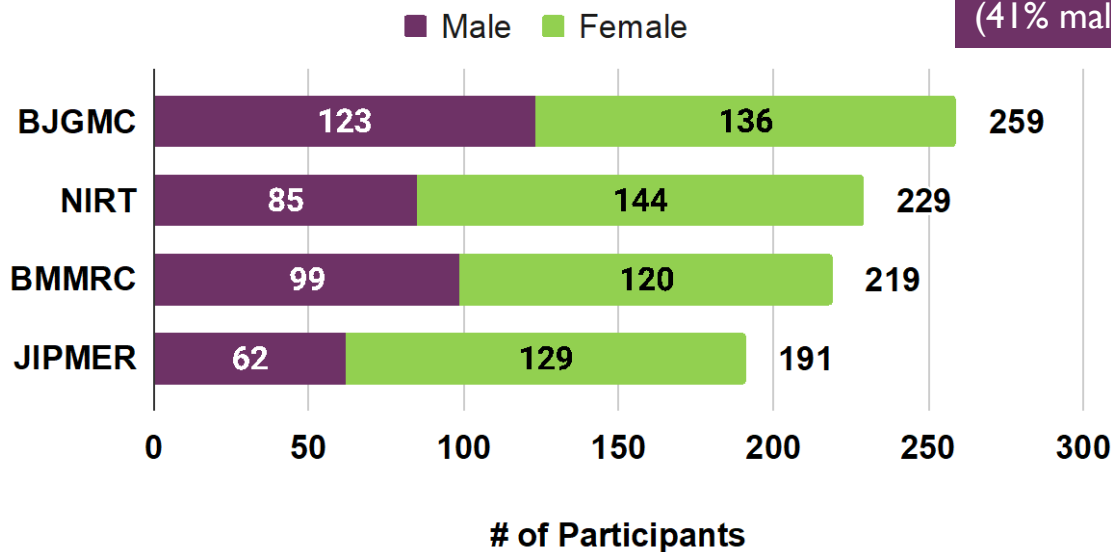
Total Enrollment: 724
(69% male)



*Of 216 participants enrolled at BJGMC, 7 (3%) were <15 years. All other sites enrolled adult pulmonary TB patients only.

Cohort B: Enrollment*

Total Enrollment: 898
(41% male)

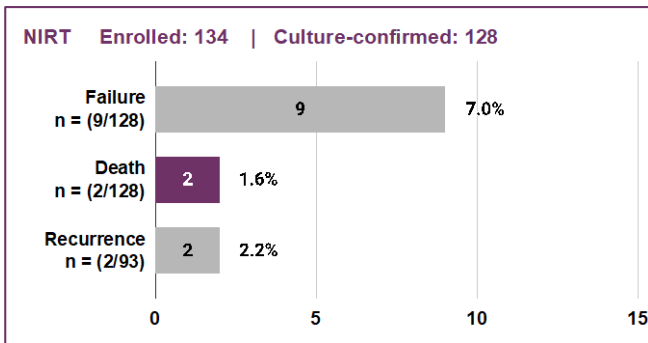
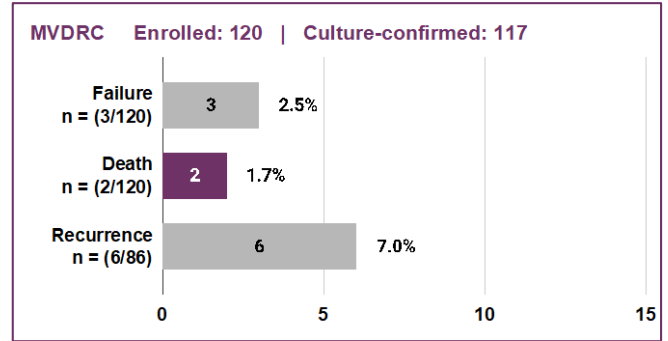
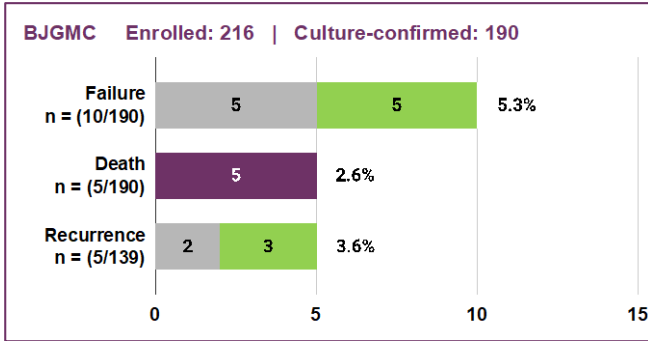


*Of 898 total Cohort B participants enrolled, 134 (15%) were <15 years old.

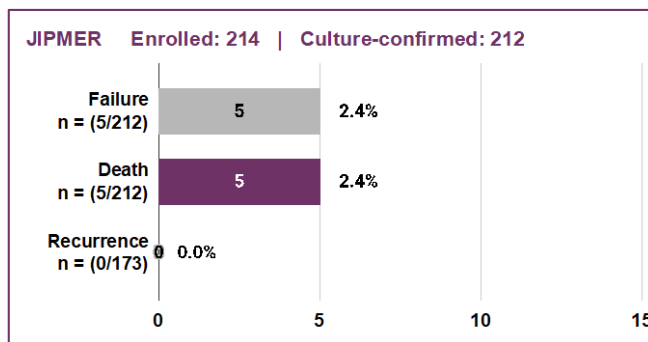
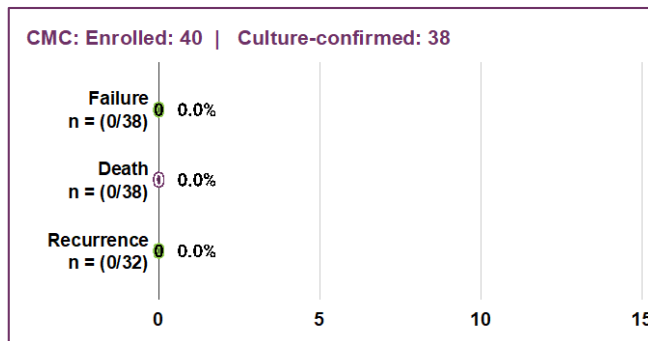
Source: Common Protocol data was provided by individual sites and aggregated by SAS-CHRD. The RePORT India Coordinating Hub prepared graphs. Data cutoff date: Dec 31, 2020.

Common Protocol Cohort A: Treatment Outcomes

Treatment Outcomes



■ Bacteriological ■ Clinical ■ Total



For proportion of participants who failed treatment or died, denominator is total number of participants enrolled and culture-confirmed (i.e. met confirmatory inclusion criteria). For proportion of participants with TB recurrence, denominator is total number of participants who completed treatment.

Failure=TB patients enrolled in the common protocol and declared treatment failure between month five and end of treatment.

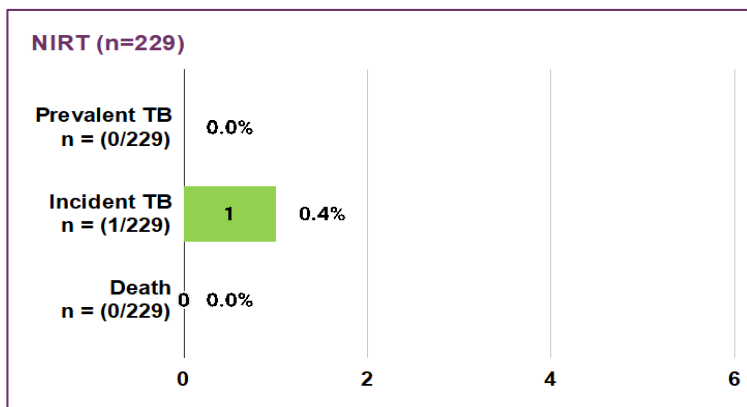
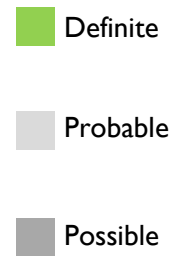
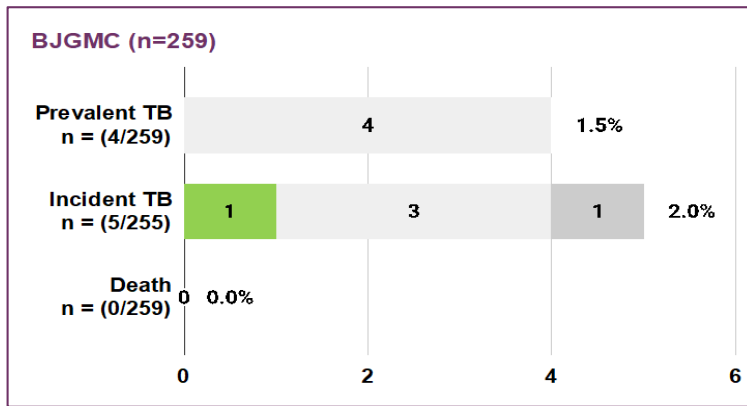
Recurrence=Patients diagnosed with TB after being declared as cured or treatment complete.

Death=All-cause death. Only deaths among participants who met confirmatory inclusion criteria are reported.

of Participants

Common Protocol Cohort B: Study Outcomes

Outcomes

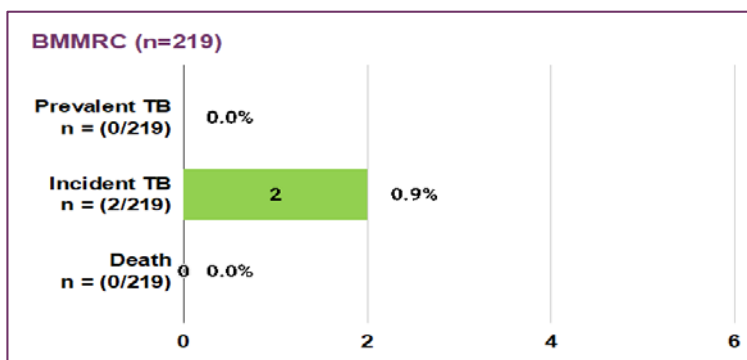
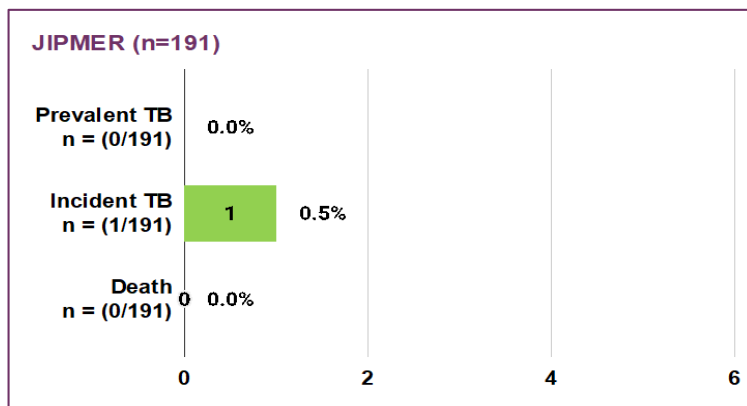


Prevalent TB = TB disease reported at baseline (date of outcome ≤ 30 days from date of HHC enrollment). Total prevalent TB across sites = 4.

Incident TB = TB disease diagnosed during follow-up (date of outcome > 30 days from date of HHC enrollment). Denominator excludes Prevalent TB. Total incident TB across sites = 9.

Death=All-cause death

LTBI outcome data is available upon request.

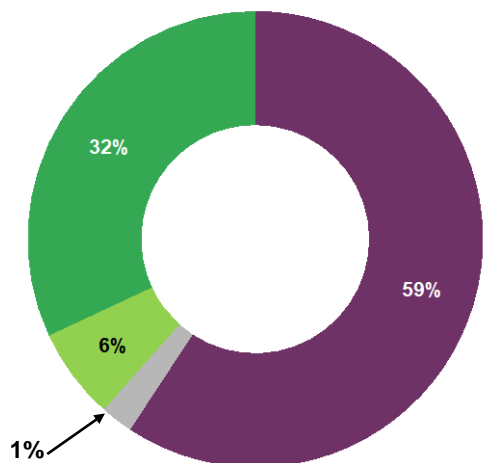


of Participants

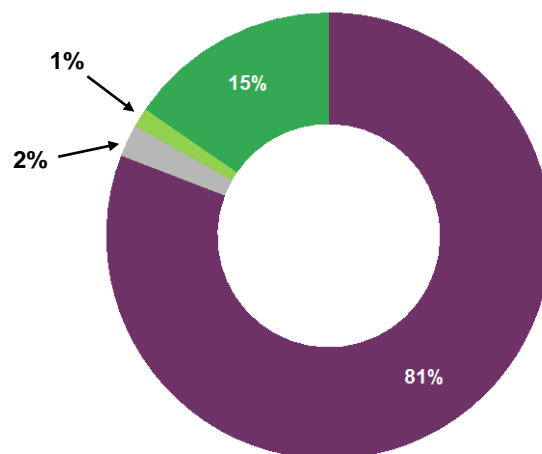
Common Protocol Cohort A: Accrual Status



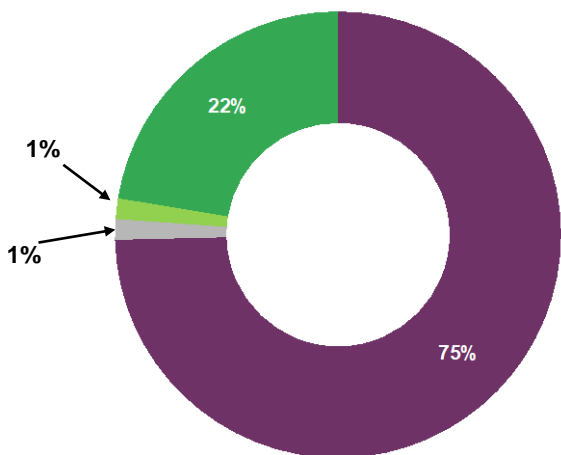
BJGMC (n=216)



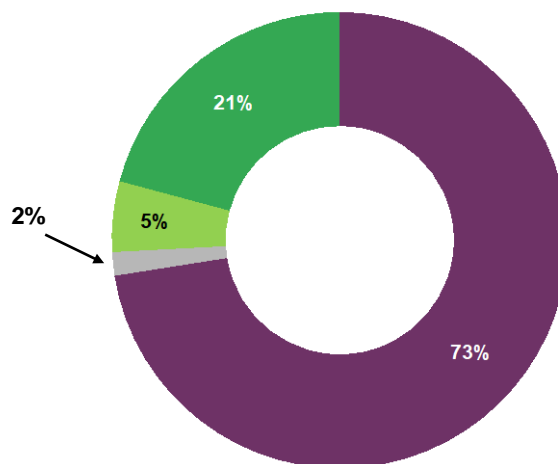
JIPMER (n=214)



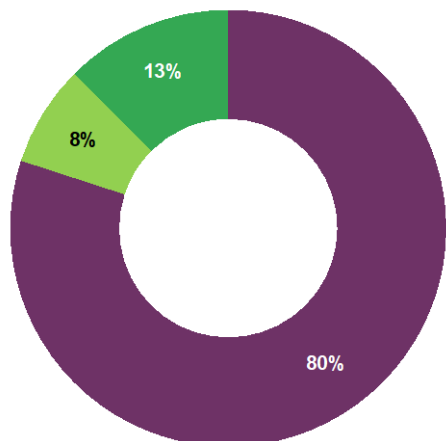
NIRT (n=134)



MVDRC (n=120)



CMC (n=40)



No Cohort A Common Protocol Participants remain in active follow-up.

Completed Follow-up=Participants who met confirmatory inclusion criteria and completed the 6-month post-treatment visit.

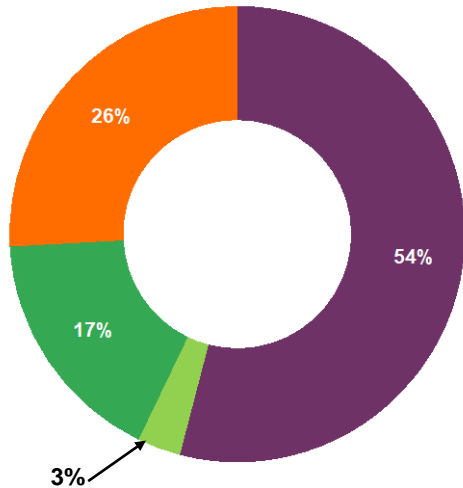
Prematurely Discontinued = Participants who met any protocol-mandated reason for discontinuation, including:

- Provisionally enrolled but culture-negative
- Met an outcome
- Participant withdrawal
- Moved out of area
- Co-enrolled in VPM study

Common Protocol Cohort B: Accrual Status

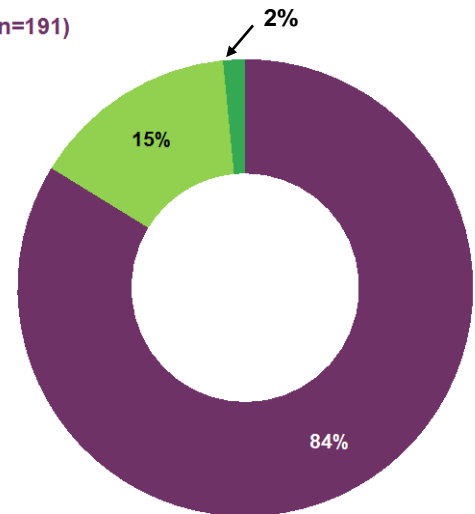


BJGMC (n=259)



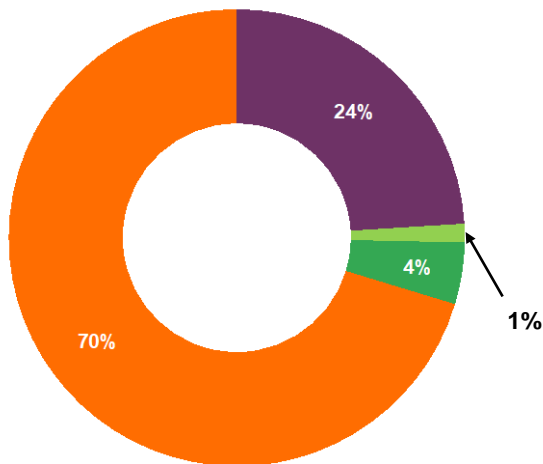
BJGMC: 67 (26%) participants on active follow-up. As part of LOA#2 (started Aug 5 2020), additional follow-up expected for 208 total participants.

JIPMER (n=191)



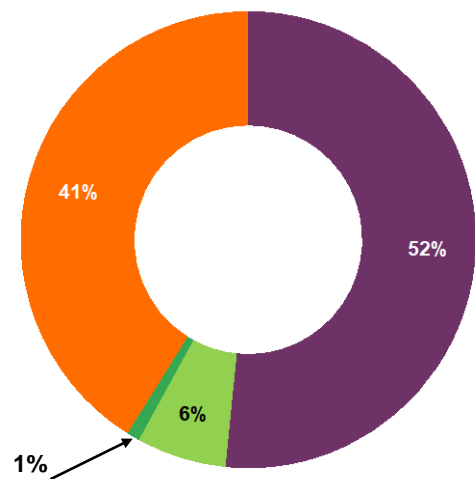
JIPMER: As part of LOA#2 (started Nov 20 2020), additional follow-up expected for 160 total participants.

NIRT (n=229)



NIRT: 161 (70%) participants on active follow-up. As part of LOA#2 (to be started), additional follow-up expected for 211 total participants.

BMMRC (n=219)



BMMRC: 90 (41%) participants on active follow-up. As part of LOA#2 (to be started), additional follow-up expected for 202 total participants.

Completed Follow-up = Participants who completed the 24-month visit.

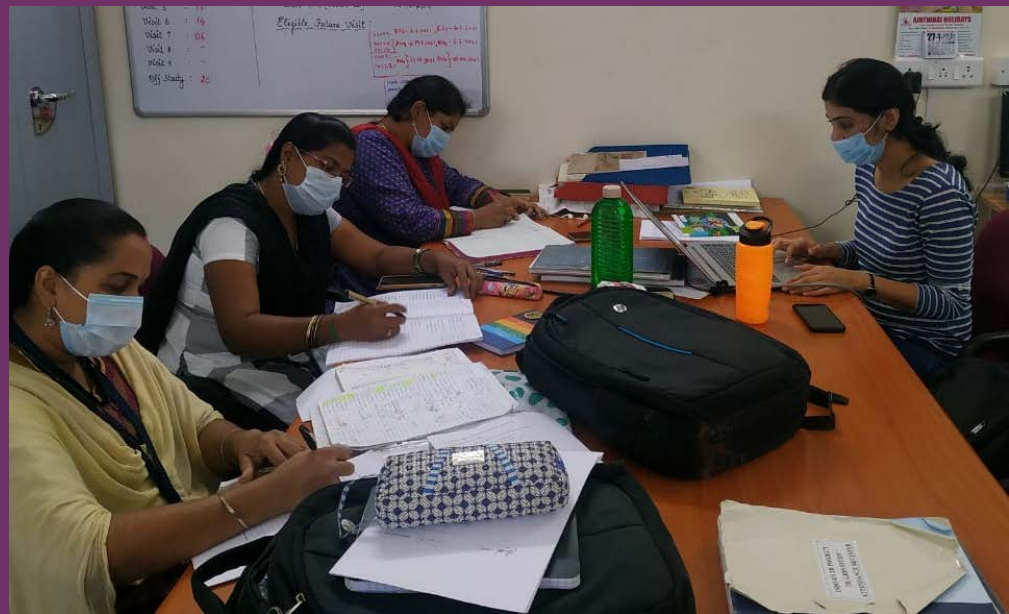
Prematurely Discontinued = Participants who met protocol-mandated reason for discontinuation, including: met an outcome, participant withdrawal, or moved out of area.



RePORT India Related Grants



BJGMC



JIPMER

CMC



RePORT International & CFAR Supplemental Funded Projects AWARDED

	TITLE	PARTNERS	CRDF#	START DATE	INVESTIGATORS
1.	T Cell Biomarkers and T-Regulatory Responses to Pediatric TB	Emory, JHU, BJGMC, NIRT	65373	2020	Rengarajan J, Kagal A, Kinikar A, Mave V, Padmapriyadarsini C, Hanna L, Paradkar M
2.	Pregnancy Associated Immune Responses to TB and HIV in India and South Africa (PARTHISA study)	JHU, BJGMC, Wits Health Consortium, Cornell	65344	2020	Gupta A, Martinson N, Mathad J, Bhosale R, Kagal A, Alexander M, Kulkarni V
3.	Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis	JHU, PD Hinduja, Beijing Chest Hospital, BJGMC, Wits Health	65351	2020	Tornheim JA, Ashavaid T, Rodrigues C, Udadia Z, Duan H, Sangle S, Varaiva E, Dooley K, Ignatius E, Mave V, Gupta A, Shivakumar SVBY, Chawla P, Patil S, Kulkarni V
4.	Inflammasome Genetics and TB Treatment Outcomes	UPenn, JHU, UMass, NIRT, MVDRC, BGJMC	65375	2020	Bisson G, Gupte A, Viswanathan V, Gupta A, Kornfeld H, Hanna L, Babu S, Andrade B, Dhanasekaran M
5.	Host RNA Expression for Diagnosis and Monitoring of Pediatric TB in Africa and India	NIRT, BGJMC, JHU, Univ. Cape Town, Imperial College, London	64080	2019	Kinikar A, Paradkar M, Hissar S, Workman L, Dawre R, Gupte N, Tornheim JA, Kulkarni V
6.	Determination of Efficacy of Xpert PCR Ultra And Transcriptional Signatures In The Diagnosis of Pleural Tuberculosis	CMC, Vellore & University of Cape Town, SA	64074	2018	Christopher DJ, Keertan Dheda
7.	Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients	RePORT Brazil, BMC, BJGMC, JHU	63158	2017	Mave V, Rolla V, Salgame P, Kadam D, Andrade B, Gupta A, Meshram S, Kulkarni V, Ellner J
8.	Molecular Signatures of Tuberculosis-Diabetes Interaction (MSTDl) Study	JHU, UMass, BJGMC, NIRT, MVDRC	63459	2017	Kornfeld H, P Chandrasekaran, Gupte A, Mave V, Bharadwaj R, Golub J, Andrade B, Paradkar M, Luke H, Kulkarni V, Gupte N, Shivakumar SVBY, Gupta A
9.	Biomarkers for TB Diagnosis and Treatment Response	BJGMC, NIRT, Emory, JHU	63069	2016	Rengarajan J, Hanna LE, Mave V, Padmapriyadarsini C, Thiruvengadam K, Toidi A, Gupte N, Kulkarni V, Gupta A and CTRIUMPH team
10.	Impact of HIV and Diabetes Mellitus on TB Drug Resistance and Recurrence	BJGMC, NIRT, JHU, MVDRC, UMass, Rutgers	63221	2016	Mave V, Devi U, Padmapriyadarsini C, Mathema B, Vishwanathan V, Kornfeld H, Kreiswirth B, Golub J, Gupte N, Shivakumar SVBY, Gupta A
11.	MDR-TB and HIV at RePORT Sites India	BJGMC, NIRT, JIPMER, JHU, BMC	63076	2016	Horsburg R, Padmapriyadarsini C, Mave V, Gupta A, Sarkar S
12.	Validation and Fine Tuning of the Computer Aided Diagnosis of Pulmonary Tuberculosis Model for the Indian Subcontinent	CMC	62922	2016	Christopher DJ, Thangakunam B, Lal B, Agrawal A
13.	Extracranial Involvement as Detected by Positron Emission Tomography Scan in Patients with Tubercular Meningitis	CMC	62906	2016	Thangakunam B, Christopher DJ
14.	Inflammatory Biomarkers as a Triage Test for Screening Symptomatic TB	JIPMER, Rutgers, BMC	63466	2016	Ellner J, Salgame P, Sarkar S, Pleskunas J
15.	Characterization of Monocyte Responses in Pulmonary TB Patients with or without Type 2 Diabetes	NIRT-NIH – ICER, MVDRC	62911	2016	Kumar P
16.	Effect of Malnutrition on Latent TB	JIPMER, Rutgers, BMC	62909	2016	Hochberg NS, Negi VS, Mahalakshmy T, Johnson WE, Salgame P, Pleskunas J

RePORT International & CFAR Supplemental Funded Projects AWARDED (Continued)

	TITLE	PARTNERS	CRDF#	START DATE	INVESTIGATORS
17.	Determining Barriers to TB Care	JIPMER, BMC/BU	64020	2016	Sabin L, Sarkar S, Hochberg NS, Fernandes P, Pleskunas J, Amsaveni
18.	TH17 Cell Subsets as Potential Risk Markers of Latency and Active TB Infection in Household Contacts	BMMRC, UT	62916	2016	Devalraju KP, Neela VSK, Valluri VL, Vankayalapati K
19.	Comparison of Available Purified-Protein Derivative (PPD) Tuberculin Skin Test (TST) Antigen Solutions in Detecting Latent Tuberculosis Infection in India	CMC, BJGMC, JIPMER, BMMRC, NIRT, JHU, BMC	61783	2015	Christopher DJ, Shankar D, Roy G, Sarkar S, Prakash Babu S, Gupta A, Deluca A, Cox SR, Hochberg NS, Horsburgh R

RePORT India Related Grants AWARDED

	TITLE	PARTNERS	GRANT SOURCE	START DATE	INVESTIGATORS
1	Rapid Research in Diagnostics Development for TB Network (R2D2 TB Network) Study	CMC, UCSF, NIRT	NIH/NIAID U01AI152087-01	2020	Christopher DJ, Tripathy S, Cattamanchi A, Nahid P, Denkinger C, Balamugesh T
2	Innate immune response of LTBI+HIV+ children	BMMRC, UT	NIH/NIAID RO1 AI42672-01AI	2020	Vankayalapati R and Valluri V
3	Signature of Profiling and Staging the Progression of TB from Infection to Disease	BU, JIPMER	NIH/NIAID: IR21AI154387	2020	Johnson WE, Salgame P
4	Phenotype, Progression and Immune Correlates of Post-Tuberculosis Lung Disease	JHU, BJGMC, DY Patil, NIRT-ICER, UMass	NIH/NIAID: K99AI151094	2020	Gupte A, Gupta A, Gaikwad S, Bollinger R, Babu S, Andrade B, Bisson G, Checkley W, Brown R, Gupte N, Jain S, Kornfeld H, Gupte N, Mave V
5	Dynamics and immune mechanisms of QFT response in close contacts of TB cases	Rutgers, JIPMER, BJGMC, JHU	NIH/NIAID/DMID (via CRDF)	2020	Salgame P, Ellner J, Sarkar S, Gaikwad S, Gupta A, Karyakarte, Bollinger R, Paradkar M, Mave V, Johnson E, Kim S, Prakash Babu S, Joseph N, Hom D,
6	A Nanopore Biosensor for Leveling MTB Antigens in Blood	Tulane University, BJGMC, JHU	NIH/NIAID R01AI144168-01AI	2020	Hu T, Karyakarte R, Bollinger R, Gupta A, Mave V, Paradkar M, Gupte N
7	VITAL-TB (Vitamins And Latency in Tuberculosis)	JIPMER, BU/BMC, Rutgers	U.S. Department of State's Partnership	2020	Hochberg, NS, Salgame P, Sarkar S, Lakshminarayanan S
8	Scaling up Nutritional Interventions to Stop tuberculosis in India	JIPMER, BU/BMC	Boston University Foundation India	2019	Hochberg NS, Lakshminarayanan S, Kulatilaka N, Locks L
9	Impact of TB and HIV Co-infection on Host and Microbial Gene Expression in the Upper Airway	BU/BMC, JIPMER, Rutgers	CFAR Developmental Pilot Award	2019	Johnson WE, Hochberg NS, Salgame S, Lakshminarayanan S, Roy G, Sahu S, Joseph N
10	Evaluation of a urinary biomarker assay for diagnosis and test of cure for tuberculosis	JHU, BJGMC	Johns Hopkins CFAR	2019	Tornheim JA, Mave V, Kagal A, Gupta A, Gilman R, Liotta L, Luchini A, Kulkarni V, Paradkar M, Gupte N, Gaikwad S

RePORT India Related Grants AWARDED (Continued)

	TITLE	PARTNERS	GRANT SOURCE	START DATE	INVESTIGATORS
11	Immune Responses and Effect of Disulfiram on MTB Infected PBMCs as a Potential Host Directed Therapy	BJGMC, NIRT, JHU, THSTI	Funding from Translational Health Sciences and Technology (THSTI)	2019	Singh R, Singhal A, Gupta A, Kagal A, Mave V, Hannah LE, Chandrasekaran
12	Dried Plasma Spots as a Simple Sampling Strategy to Measure Rifampicin Concentration to Facilitate this Service In Resource Limited Settings	CMC	Internal fluid research grant	2019	Christopher DJ, Balamugesh T, Santhosh S
13	Evaluation of diagnostic potential of aptamer-based assays for pulmonary tuberculosis- a pilot study	CMC	THSTI	2019	Christopher DJ, Balamugesh T
14	Markers of Lung Impairment in HIV-TB Co-infected Indian Adults	JHU, BJGMC	leDEA/Treat Asia Supplement	2019	Gupte A, Gaikwad S, Marbaniang I, Paradkar M, Kulkarni V, Gupta A, Mave M, Karyakarte R, Nimkar S, Gupte N, Pradhan N
15	Tuberculosis: Learning the Impact of Nutrition (TB LION)	JIPMER, BMC, Rutgers, Tufts, NIRT	Warren Alpert Foundation	2018-2023	Hochberg NS, Lakshminarayanan S, Ellner JJ, Johnson WE, Wanke C, Salgame P, Cintron C, Sinha S, Chandrasekharan P, Joseph N, Rajkumari N, Mahalakshmy T, Negi VS
16	Removing batch effects in genomic and epigenomic studies	BU, JIPMER	NIH/NIGMS: 5R01GM127430	2018	Johnson WE
17	Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum	Hinduja, JHU	NIH/NIAID 1K23AI135102-01A1	2018	Tornheim JA, Rodrigues C, Udwardia ZF, Ashavaid TF, Gupta A
18	Validating a Th17 Switch as a Novel Correlate of Protective Immunity to TB	NIRT, BJGMC, IISc, Bangalore, JHU	DBT/ IISc	2018	Vyakarnam A, Padmapriyadarsini C, Hanna E, Gaikwad S, Gupta A, Mave V
19	Characterization of Genomics and Metabolomics among Individuals (TB-GWAS)	Emory, BJGMC/JHU, JIPMER/BM / Rutgers, BMMRC/UTT, NIRT, PHRU, McGill	NIH/NIAID 5R01AI139406	2018	Gandhi N, Sun Y, Shah S, Brust J, Gupta A, Gaikwad S, Mave V, Karyakarte R, Paradkar M, Joseph N, Roy G, Sarkar S, Kumar NV, Salgame, P, Hochberg NS, Tripathi D, Padmapriyadarsini C, Hanna LE, Martinson N, Gwinn M, Schurr E, Jones D
20	Validation of Indigenously Developed Technology (TruNat MTB) for Diagnosis of Extra-pulmonary Tuberculosis: Multi-centric Validation	CMC, Hinduja, NIRT, AIIMS	ICMR	2018	Christopher DJ, Singh M, Gomathi, Rodrigues C, Singh U
21	Host and Microbiome Transcriptional Profiling in the Upper Airways for TB Susceptibility	JIPMER, BU/BMC, Rutgers	CTSI Pilot Award	2018	Johnson WE, Hochberg NS, Salgame P, Ellner JJ, Sarkar S, Babu S, Lakshminarayanan S
22	Prevalence of Latent Tuberculosis in Rheumatoid Arthritis and Ankylosing Spondylitis	CMC	Internal fluid research grant	2018	Christopher DJ, Balamugesh T, Varghese DA
23	The Effect of Appropriate Anti Tuberculous Treatment on Recovery of Pulmonary And Pleural Tuberculosis and the Impact of Tuberculosis on Lung Function and Quality of Life in Newly Diagnosed Patients	CMC	Internal fluid research grant	2018	Christopher DJ, Balamugesh T, Roy D
24	Multicenter Phase II/III Double-Blind, Randomized, Placebo Controlled Study to Evaluate the Efficacy and Safety of VPM1002 in the Prevention of TB Recurrence in Pulmonary TB Patients after Successful TB Treatment.	BJGMC/JHU CRS, JIPMER, BMMRC, PGI Chandigarh	Serum Institute	2017-2022	Gaikwad S, Mave V, Sarkar S, Joshi S, Gupta M

RePORT India Related Grants AWARDED (Continued)

	TITLE	PARTNERS	GRANT SOURCE	START DATE	INVESTIGATORS
24	Transcriptomic and Metabolomic Analysis of Microbiologically Confirmed Pediatric Tuberculosis Patients and Uninfected Household Contacts	BJGMC, JHU	Ujala Foundation Wyncote Foundation	2017	Tornheim JA, Paradkar M, Dutta N, Bader J, Kulkarni V, Bharadwaj R, Raja R, Sreenivasmurthy S, Karakousis P, Mave V, Pandey A, Gupta A
25	Therapeutic Outcomes with Second-Line Drug Exposures in a Cohort of South African and Indian Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment	Hinduja, PHRU, JHU	DBT/South Africa MRC	2017	Ashavaid TF, Variava E, Rodrigues C, Udhwadia ZF, Gupta A, Tornheim JA, Chawla P, Martinson N
26	Association of Lipid Mediators of Inflammation with TB Treatment Outcomes	JHU, NIRT, BJGMC	Gilead Foundation	2017	Shivakoti R, Padmapriyadarsini C, Mave V, Kulkarni V, Gupte A, Gupte N, Shivakumar SVBY, Nimkar S, Dalli J, Natarajan S, Karunaianantham R, Gupta A
27	The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection	U Colorado, JHU, BJGMC	NIH/NIAID /DMID: 1R21AI134129	2017	Weinberg A, Segano Z, Mave V, Gupte N, Paradkar M, Suryavanshi N, Kulkarni V, Bharadwaj R, Gupta A
28	Effect of pregnancy and HIV on the development of tuberculosis	Cornell, JHU, BJGMC	NIH/NIAID: 1K23-AI129854	2017	Mathad J, Gupta A, Bhosale J, Naik S, Alexander M, Kulkarni V, Gupte N
29	IFN- γ Independent Inhibition of MTB Growth in Human Macrophages + Administrative Supplement: Thyroxine (T4) hormone inhibits expansion of immunosuppressive CD4CD25+Foxp3+ (Tregs) cells	BMMRC, UTT	NIH/NIAID: R01AI123310-01A1	2017	Vankayalapati K, Valluri V and others
30	Predictors of Resistance Emergence Evaluation in MDR-TB Patients on Treatment (PREEMPT)	JIPMER, NIRT, BJGMC, RePORT Brazil, Vanderbilt, Rutgers, CDC, JHU, BMC, Hinduja	NIH/NIAID/ DMID 5R01AI134430	2017	Horsburgh R, Sterling TR, Pelloquin C, Alland D, Mave V, Ciegelski P, Collins J, Gaikwad S, Lokhande R, Gupta A, Rolla V, Kritski A, Sarkar S, Hom D, Rodrigues C, Udhwadia Z, Tornheim J, Padmapriyadarsini C, Palnivel C, Premarajan KC, Sahu S, Joseph NM, Muthuraj M, Govindarajan S
31	MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB – MUKT)	Hinduja, JHU	Hinduja	2017	Udhwadia ZF, Rodrigues C, Ashavaid TF, Tornheim JA, Gupta A
32	Measuring TB Drugs in Hair as a Tool to Monitor Adherence, Exposure and Response	BJGMC, NIRT, JHU	NIH/NIAID: 5R21 AI127149-02	2016-2018	Mave V, Dooley K, Ramachandran G, Gupta A, Bacchetti, Sushant M, Gupte N, Gandhi M
33	Role of Iron Deficiency in Resistance of Women of Child-Bearing Age to Tuberculosis	JIPMER, BMC	NIH	2016-2017	Ellner J, Salgame P, Sarkar S, Hochberg NS, White L, Jayalakshmy R, Joseph NM, Senthilkumar GP
34	The Role of Monocyte Subpopulation in HIV+LTB+ Individuals and Development of Active TB	BMMRC, UTT	NIH/NIAID R21AI127178	2016	Vankayalapati K, Valluri V, and others
35	Studying T cell Memory Responses for Understanding Protective Immune Response in Tuberculosis (TB)	CMC, NIRT, Saint Louis U	American Society of Tropical Medicine and Hygiene/ Burroughs Wellcome Fund)	2016	Christopher DJ, Chatterjee S, Balamugesh T

RePORT India Related Grants AWARDED (Continued)

	TITLE	PARTNERS	GRANT SOURCE	START DATE	INVESTIGATORS
36	Maternal inflammation, diet and gut microbiome in HIV: impact on infant outcomes	BJGMC, NIRT-ICER, JHU, UMD, Columbia	NIH/NICHD: K99-HD089753	2016	Shivakoti R, Gupta A, Naik S, Shouche Y, Ravel J, O'Toole PW, Gupte N, Ghanem KG, Caulfield L, Babu S
37	Impact of Immune Changes of HIV and Stages of Pregnancy on TB	BJGMC, NIRT, JHU	NIH/NICHD: 5R01HD081929	2015-2020	Gupta A, Mathad J, Bhosale R, Alexander M, Mave V, Gupte N, Pradhan N, Kulkarni V, Hannah LE, Babu S
38	Impact of Pregnancy on Tuberculosis	JIPMER, BMC	NIH/NIAID: 5R01AI124217	2015-2018	Ellner J, Sarkar S, Hochberg N, Horsburgh CR, Salgame P, Savic R, Dartois V, Joseph NM, Jacob SE, Jayalakshmy R, Plakkal N, Ramachandran G, Sasirekha R, White LF
39	Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study	BJGMC, NIRT, JHU	UJALA/ Gilead Foundation	2015-2017	Gupte A, Gupta A, Meshram S, Kadam D, Mandar, Gupte N, Padmapriyadarsini C, Salvi S, Golub J, Selvaraju S
40	D4GDI-mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, UTT	NIH/NIAID: R21AI120257	2015-2017	Vankayalapati K, Valluri V and others
41	Understanding of Tuberculosis Infection and Preventive Therapy Among Skin-Test Positive Household Contacts of Tuberculosis Cases	BJGMC, NIRT, JHU	NIH CFAR and JHU/BJGMC D43	2015	Deluca A, Suryavanshi N, Mave V, Kadam D, Padmapriyadarsini C, Shivakumar SVBY, Pardeshi G, Thomas B, Kolhi R, Gupta A
42	T-regs Mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, UTT	UT	2015	Vankayalapati K, Valluri V and others
43	Compare Drug Levels in Newly Diagnosed or Relapsed PTB/ EPTB Following Daily ATT vs DOTS Regimen	CMC	Internal fluid research grant	2015	Christopher DJ, Balamugesh T
44	Impact of Personal Exposure to Black Carbon on Pulmonary Tuberculosis Severity	JIPMER BMC	Potts Memorial Foundation	2014-2018	Ellner J, TS Ravikumar, Hochberg NS, Reddy D, Jonathan Levy, Roy G, Sahu S, Vinod Kumar, Joseph NM
45	Yield of TB using GeneXpert (Xpert MTB-Rif) by Induced Sputum Compared to Standard Sputum Samples	CMC	Internal fluid research grant	2014	Christopher DJ, Balamugesh T

RePORT India Related Grants NOT AWARDED

	TITLE	PARTNERS & IRB STATUS	GRANT SOURCE	SUBMISSION DATE	INVESTIGATORS
1	VITAL-TB (Vitamins And Latency in Tuberculosis)	JIPMER, BU/BMC, Rutgers	NIH ROI	2020	Hochberg, NS, Salgame P, Sarkar S, Lakshminarayanan S
2	Immune Mechanisms of Protection against Mycobacterium tuberculosis Center	CMC, UCSF	(IMPACT-TB) NIAID AI	2019	Ernst J, Cattamanchi A, Nahid P, Christopher DJ,
3	Analysis and Consequences of Humoral Responses during Mycobacterium tuberculosis Infection	Rockefeller, JHU, Emory, BJGMC	NIAID P01	2019	Ravetch J, Ahmed R, Gupta A, Gandhi NR, Chandele A, Amara R
4	Protective Immune Responses and Effective Vaccines to End TB (PREVENT-TB) (IMPACT-TB)	Emory, JHU, Tulane, RePORT Brazil, RePORT India	NIH	2018	Rengarajan J, Sterling T, Gupta A, Bollinger RC, Gaikwad S
5	Sex and TB Immunity (SATI) (IMPACT-TB)	Rutgers, JHU, Stanford, Saint Louis, Tulane, Emory	NIH	2018	Gennaro ML, et al.

RePORT India Related Grants NOT AWARDED (Continued)

	TITLE	PARTNERS & IRB STATUS	GRANT SOURCE	SUBMISSION DATE	INVESTIGATORS
6	Effect of Helminths on Tuberculosis Severity	JIPMER, BMC, Rutgers, NIRT, NIH	NIH R21	2018	Hochberg NS, Salgame P, Babu S, Ellner JJ, Johnson WE, Parija S, Sarkar S, Mahalakshmy T, Joseph N, Rajkumari N
7	Analysis of IgG-FcR Interactions in TB	Rockefeller, JHU, Emory, BJGMC	Bill & Melinda Gates Foundation	2018	Ravetch J, Ahmed R, Gandhi NR, Gupta A, Mave V, Gupte N
8	RePORT India Tuberculosis Research Training Program	RePORT India	NIH Fogarty: D43	2018	Gupta A, Kornfeld H, Bollinger RC, Christopher DJ, Rodrigues C, Tripathy S, Mehendale S
9	Memory-like NK Cells and Household Contacts of TB Patients	BMMRC, UT	NIH R21	2018	Vankayalapati K, Valluri V, and others
10	RePORT India TB Transmission Training Program	RePORT India	NIH Fogarty: D43	2017	Gupta A, Christopher DJ, Bollinger R, Deluca A, Golub J
11	Systems Approaches for Predicting TB Clinical Outcomes	BJGMC, Emory, Knowledge Synthesis, NIRT, Texas A&M, UTX-Tyler, WITS Health Consortium	NIH: U19	2017	Karakousis P, Bader J, Bharadwaj R, Padmapriyadarsini C, Dutta N, Gupta A, Gupte N, Joerger T, Kadam D, Hanna LE, Martinson N, Mave V, Pandey A, Rengarajan J, Salamon H, Shivakoti R, Vankayalapati K
12	Developing a Rapid Point-of-Care TB Diagnostic	RePORT International	NIH/NIAID: R01	2017	Walt D (Tufts PI), Rushdy A (Broad Institute co-PI), Rolla V, Santos M, Kristi A, Sterling T, Li Y, Mave V, Cristopher DJ, Gupta A, Pim A, Walzl G, Hamilton C, Duffy D, Gillette M
13	Research and Interventions for HIV, Alcohol, Tobacco and Tuberculosis in India and South Africa (The HATT Consortium)	BJGMC, NIRT, JHU	NIH/NIAAA: R01	2017	Gupta A, Chander G, Heidi H, Thomas B, Kadam D, Suryavanshi N, Padmapriyadarsini C, Mave V, Gupte N
14	Bio-markers for Risks of Development of LTBI and TB Disease in a Cohort of Childhood Contacts of Sputum Positive TB Patients	CMC	RePORT India Supplemental Funding	2017	Christopher DJ, Rose W
15	Innate Immune Responses in Household Contacts	BMMRC/LEPRA, BJGMC, NIRT, JHU, UT	NIH/NIAID: R01	2017	Vankayalapati K, Valluri V, Gupta A, Mave V, Kadam D, Bharadwaj R, Hanna LE, Shivakumar SVBY, Prudhula, Padmapriyadarsini C, Gupte N
16	Impact of Air Pollution on Inflammation and Anti TB Immunity	BJGMC, NIRT, JHU	RePORT India Supplemental Funding	2016-2017	Shivakoti R, Gupta A, Padmapriyadarsini C, Chandrakumar D, Golub J, Mave V, Babu S, Elf J, Hannah LE, Kulkarni V, Gupte N
17	Characterizing the Host Inflammatory Response, and its Association with Treatment Outcomes and Lung Health in Adult Pulmonary TB Patients Undergoing Treatment in India	BJGMC, NIRT, JHU	RePORT India Supplemental Funding	2016-2017	Gupte A, Padmapriyadarsini C, Gupta A, Babu S, Mave V, Gupte N, Kornfeld H
18	Association of Recent Active Tuberculosis Disease with Significant Coronary Artery Disease at JIPMER, Puducherry: A Hospital-based Case Control Study	JIPMER, BMC	RePORT India Supplemental Funding	2016	Kar S, Sarkar S, Ellner JJ, Santhosh Satheesh
19	Novel Serum Based Biomarkers for Diagnosis of TB and Treatment Monitoring in HIV-infected and Uninfected Children	BJGMC, NIRT, DTTC, Cape Town, JHU	India SA RFA	2016	Valvi C, Hesselting AC, Chandanwale A, Kulkarni R, Paradkar M, Mave V, Gupte N, Padmapriyadarsini C, Shivakumar SVBY, Danasekaran K, Thiruvankadam K

RePORT India Related Grants NOT AWARDED (Continued)

	TITLE	PARTNERS & IRB STATUS	GRANT SOURCE	SUBMISSION DATE	INVESTIGATORS
20	Pediatric TB Biomarkers for Diagnosis and Treatment Response	BJGMC, NIRT, JHU	NIH/NIAID: R01	2016	Karakousis P, Paradkar M, Tornheim JA, Gupta A, Padmapriyadarsini C, Bader J, Mave V, Gupte N, Kulkarni V, Bharadwaj R, Valvi C, Shivakumar SVBY, Hannah LE, Pandey A
21	Biomarkers for Treatment Response and Disease Recurrence in Pulmonary and Extrapulmonary Tuberculosis Disease	IGIB, BJGMC, SA, NIRT, JHU	India SA RFA	2016	Gokhale R, Kana B, Swaminathan S, Padmapriyadarsini C, Mave V, Gupta A, Shivakumar SVBY
22	Novel Blood Biomarker to Predict Progression to Active TB Disease Among Recently Exposed Adult and Pediatric Household Contacts of TB Patients in India and South Africa	BJGMC, NIRT, SA, JHU	India SA RFA	2016	Padmapriyadarsini C, Scriba T, Mave V, Paradkar M, Shivakumar SVBY, Gupte N, Gupta A, Danasekaran K, Khan S, Thiruvengadam S, Tripathy S, Prasad K
23	Annual Screening of Healthcare Personnel Using TST & QGFT and Identification of Bio-markers & the Role of Pet Scan	CMC	RePORT India Supplemental Funding	2016	Christopher DJ, Balamugesh T
24	Radiological Treatment Response in Pulmonary Tuberculosis	CMC	RePORT India Supplemental Funding	2016	Balamugesh T, Christopher DJ
25	Does Tubercular Infection Adversely Affect Cardiovascular Risk?	JIPMER, BMC	RePORT India Supplemental Funding	2016	Kar S, Sarkar Si, Negi VS, Prasanna MD, Roy G, Premarajan KC, Hochberg N, Lakshminarayanan S
26	Geographical and Genotypic Distribution of TB Cases Under RePORT India – Tools for Understanding Epidemiology	JIPMER, BMC, BU	RePORT India Supplemental Funding	2016	Sarkar S, Roy G, Mahalakshmy T, Lakshminaraya S, Joseph NM, Jenkins H, Amsaveni, Hochberg NS
27	Progression of Tuberculosis Infection to Disease Among HIV-Infected and HIV Seronegative Individuals: A Prospective Cohort Study in South India and South Africa	CMC, BMMRC/LEPRA, NIRT, PHRU, UWITS, JIPMER	Indo-South Africa	2016	Valluri VL, Martinson N, Christopher DJ, Variava E, Priyadarsini P, Bhavna G, Ziyaad W, Melissa C, Prudhula DK, Sanjeev NV

RePORT India Related Grants PENDING

	TITLE	PARTNERS	GRANT SOURCE	SUBMISSION DATE	INVESTIGATORS
1.	Microbiome-Associated Effects of Diabetes and BMI on Tuberculosis Severity	UMass, MVDRC	NIH/NIAID R01 for PA-20-184	2020	Viswanathan V, Kornfeld H, Bucci Vanni
2.	TB Learning the Impact Of Nutrition Enteropathy and Systemic Susceptibility (TB LIONESS)	Rutgers, BMC	NIH R01	2021	Hochberg NS, Salgame P



MVDRC Freezers



NIRT PBMC
Processing Lab

Publications



BMMRC



Hinduja

PAPERS: 2015–PRESENT



Data for 2021 includes 3 published and 6 accepted papers

RePORT India Consortium

1. Building capacity for advances in tuberculosis research; proceedings of the third RePORT International meeting

Van der Heijden YF, Abdullah F, Andrade BB, Andrews JR, Christopher DJ, Croda J, Ewing H, Haas DW, Hatherill M, Horsburgh CR Jr, Mave V, Nakaya HI, Rolla V, Srinivasan S, Sugiyono RI, Ugarte-Gil C, Hamilton C. *Tuberculosis (Edinb)*. 2018;113: 153-162. PMID: 30514497; PMCID: PMC6349374.

2. RePORT International: Advancing tuberculosis biomarker research through global collaboration

Hamilton CD, Swaminathan S, Christopher DJ, Ellner J, Gupta A, Sterling TR, Rolla V, Srinivasan S, Karyana M, Siddiqui S, Stoszek SK, Kim P. *Clinical Infectious Diseases (CID)*. 2015 October 15; 61(Suppl 3): S155–S159. PMID: 26409277; PMCID: PMC4583572.

Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

1. Defective expansion and function of memory like natural killer cells in HIV+ individuals with latent tuberculosis infection.

Devalraju KP, Neela VSK, Krowvidi SS, Vankayalapati R, Valluri VL (Submitted: *PLOS One*)

2. Young household contacts of tuberculosis (TB) patients with reduced T4 and IL-1 production are at a highest risk for developing active TB disease

Devalraju KP, Tripathi D, Neela VSK, Paidipally P, Bogam AK, Mallidi V, Sykam A, Singh KP, Ansari MS, Vankayalapati R, Valluri VL. (Submitted: *Journal of Clinical Investigation*)

3. IL-22 produced by type 3 innate lymphoid cells (ILC3s) reduces the mortality of type 2 diabetes mellitus (T2DM) mice infected with *Mycobacterium tuberculosis*

Tripathi D, Radhakrishnan RK, Sivangala TR, Paidipally P, Devalraju KP, Neela VSK, McAllister MK, Samten B, Valluri VL, Vankayalapati R. *PLoS Pathog*. 2019 Dec 6;15(12):e1008140. PMID: 31809521.

4. Toll-like receptor 2 polymorphisms and their effect on the immune response to ESAT-6, Pam3CSK4 TLR2 agonist in pulmonary tuberculosis patients and household contacts

Mandala JP, Ahmad S, Pullagurla A, Thada S, Joshi L, Ansari MSS, Valluri VL, Gaddam SL. *Cytokine*. 2020 Feb;126:154897. doi: 10.1016/j.cyto.2019.154897. Epub 2019 Oct 31. PMID: 31678868.

5. Down regulation of RANTES in pleural site is associated with inhibition of antigen specific response in tuberculosis

Pydi SS, Ghousunnissa S, Devalraju KP, Ramasari SS, Gaddam R, Auzumeedi SK, Vankayalapati R, Valluri VL. *Tuberculosis (Edinb)*. 2019 May;116S:S123-S130. PMID: 31103419.

Continued

Bhagwan Mahavir Medical Research Centre
University of Texas Health Science Center at Tyler (CRU 107)

- 6. Alcohol enhances type I interferon- production and mortality of young mice infected with Mycobacterium tuberculosis**
Tripathi D, Welch E, Cheekatla SS, Radhakrishnan R, Venkatasubramanian S, Paidipally P, Van A, Samten B, Devalraju P, Neela V, Valluri V, Mason C, Nelson S and Vankayalapati R. PLoS Pathog. 2018 Aug 2;14(8):e1007174. doi: 10.1371/journal.ppat.1007174. eCollection 2018 Aug. PMID: 30071107; PMCID: PMC6072099.
- 7. IL-17 and IL-22 production in HIV+ individuals with latent and active tuberculosis**
Devalraju KP, Neela VSK, Ramaseri SS, Van A, Chaudhury A, Krovvidi SS, Vankayalapati R, Valluri VL. BMC Infect Dis. 2018 Jul 11;18(1):321. doi: 10.1186/s12879-018-3236-0. PMID: 29996789; PMCID: PMC6042451.
- 8. Defective MyD88 and IRAK4 but not TLR-2 expression in HIV+ individuals with latent tuberculosis infection**
Devalraju KP, Neela VSK, Gaddam R, Chaudhury A, Van A, Krovvidi SS, Vankayalapati R, Valluri VL. Cytokine. 2018 Oct;110:213-221. doi: 10.1016/j.cyto.2018.05.005. Epub 2018 May 17. PMID: 29778672; PMCID: PMC6103807.
- 9. Interleukin-21 regulates Natural Killer cell responses during mycobacterium tuberculosis infection**
Paidipally P, Tripathi D, Van A, Radhakrishnan RK, Dhiman R, Venkatasubramanian S, Devalraju KP, Tvinnereim AR, Valluri VL, Vankayalapati R. J Infect Dis. 2018 Mar 28;217(8):1323-1333. doi: 10.1093/infdis/jiy034. PMID: 29390153; PMCID: PMC6018723.
- 10. Association of TNF- , IL-10 and IL-6 promoter polymorphisms in pulmonary tuberculosis patients and their household contacts of younger age group**
Joshi L, Chelluri LK, Valluri V, Gaddam S. Comp Immunol Microbiol Infect Dis. 2018 Feb;56:20-26. doi: 10.1016/j.cimid.2017.12.001. Epub 2017 Dec 26. PMID: 29406278.
- 11. IL-6 and IL-18 cytokine gene variants of pulmonary tuberculosis patients with co-morbid diabetes mellitus and their household contacts in Hyderabad**
Ponnana M, Sivangala R, Joshi L, Valluri V, Gaddam S. Gene. 2017 Sep 5;627:298-306. doi: 10.1016/j.gene.2017.06.046. Epub 2017 Jun 23. PMID: 28652186.
- 12. IL-21-dependent expansion of memory-like NK cells enhances protective immune responses against Mycobacterium tuberculosis**
Venkatasubramanian S, Cheekatla S, Paidipally P, Tripathi D, Welch E, Tvinnereim AR, Nurieva R, Vankayalapati R. Mucosal Immunol. 2017 Jul;10(4):1031-1042. doi: 10.1038/mi.2016.105. Epub 2016 Dec 7. PMID: 27924822; PMCID: PMC5462891.
- 13. NK-CD11c+ cell crosstalk in diabetes enhances IL-6-mediated inflammation during Mycobacterium tuberculosis infection**
Cheekatla SS, Tripathi D, Venkatasubramanian S, Nathella PK, Paidipally P, Ishibashi M, Welch E, Tvinnereim AR, Ikebe M, Valluri VL, Babu S, Kornfeld H, Vankayalapati R. PLoS Pathog. 2016 Oct 26;12(10):e1005972. doi: 10.1371/journal.ppat.1005972. eCollection 2016. PMID: 27783671; PMCID: PMC5082658.
- 14. Polymorphisms of IFN- (+874A/T) and IL-12 (+1188A/C) in tuberculosis patients and their household contacts in Hyderabad, India**
Thada S, Ponnana M, Sivangala R, Joshi L, Alasandagutti M, Ansari MS, Schumann RR, Valluri V, Gaddam S. Hum Immunol. 2016 Jul;77(7):559-65. doi: 10.1016/j.humimm.2016.04.016. Epub 2016 Apr 22. PMID: 27108964.
- 15. Cytokine production and mRNA expression in pulmonary tuberculosis patients and their household contacts of younger age group**
Joshi L, Ponnana M, Sivangala R, Chelluri LK, Nallari P, Valluri VL, Gaddam S. J Immunol Methods. 2016 May;432:65-71. doi: 10.1016/j.jim.2016.02.012. Epub 2016 Feb 12. PMID: 26876300.

**Byramjee Jeejeebhoy Government Medical College
National Institute for Research in Tuberculosis
Johns Hopkins University (CRUs 106 & 105)**

1. Measuring tuberculosis drugs in hair in adults and children as a tool to monitor exposure and outcomes

Mave V, Kadam D, Gaikwad S, Kinikar A, Aguilar D, Chavan A, Paradkar M, Shivakumar SVBY, Bharadwaj R, Kagal A, Suryavanshi N, Golub J, Kulkarni V, Dooley K, Gupta A, Bachetti P, Gerona R, Gupte N, Gandhi M. *Int J Tuberc Lung Dis*. 2021 Jan 1;25(1):52-60. doi: 10.5588/ijtld.20.0574. PMID: 33384045.

2. Unhealthy alcohol use independently associated with unfavorable tuberculosis treatment outcomes among Indian men.

Cox SR, Gupte AN, Thomas B, Gaikwad S, Mave V, Padmapriyadarsini C, Sahasrabudhe RT, Kadam D, Gupte N, Hanna LE, Kagal A, Paradkar M, Thiruvengadam K, Jain D, Atre S, Sekar K, Raskar S, Shivakumar SVBY, Santhappan R, Deshmukh S, Pradhan N, Kulkarni V, Kakrani A, Barathwal MS, Sawant T, Deluca A, Suryavanshi N, Chander G, Bollinger R, Golub JE, Gupta A. (Accepted: *IJTLD*)

3. A two-gene signature for tuberculosis diagnosis in persons with advanced HIV

Kulkarni V, Queiroz ATL, Sangle S, Kagal A, Salvi S, Gupta A, Ellner J, Kadam D, Rolla VC, Andrade BB, Salgame P, Mave V. (Accepted: *Frontiers in Immunology*)

4. Substantial early mortality among tuberculosis patients with diabetes mellitus, particularly among patients not receiving metformin, in India

Mave V, Gaikwad S, Barthwal M, Chandanwale A, Lokhande R, Kadam D, Dharmshale S, Bharadwaj R, Kagal A, Pradhan N, Deshmukh S, Atre S, Sahasrabudhe T, Meshram S, Kakrani A, Kulkarni V, Raskar S, Suryavanshi N, Kornfeld H, Dooley KE, Chon S, Gupta A, Gupta A, Gupte N, Golub JE. (Accepted: *OFID*)

5. Host lipidome predicts tuberculosis treatment outcomes

Shivakoti R, Newman J, Hanna LE, Queiroz ATL, Borkowski K, Gupte A, Paradkar M, Satyamurthi P, Kulkarni V, Selva M, Pradhan N, Shivakumar SVBY, Natarajan S, Karunaianatham S, Gupte N, Thiruvengadam K, Fiehn O, Bharadwaj R, Kagal A, Gaikwad S, Sangle S, Golub JE, Andrade BB, Mave V, Gupta A, Padmapriyadarsini C. (Submitted: *European Respiratory Journal*)

6. Baseline IL-6 is a biomarker for unfavorable tuberculosis treatment outcomes: a multi-site discovery and validation study

Gupte AN, Kumar P, Araujo-Pereira M, Kulkarni V, Paradkar M, Pradhan N, Padmapriyadarsini C, Hanna LE, Du Bruyn E, Rockwood N, Karayakate R, Gaikwad S, Bollinger R, Gupte N, Viswanathan V, Wilkinson RJ, Mave V, Babu S, Kornfeld H, Andrade BB, Gupta A. (Submitted: *AJCCRM*)

7. Comparative immune responses to M. tuberculosis in individuals with latent infection or sterile protection against infection

Jalbert E, Liu C, Mave V, Lang N, Kagal A, Valvi C, Paradkar M, Gupte N, Lokhande R, Bharadwaj R, Kulkarni V, Gupta A, Weinberg A. (Submitted: *PLoS Pathogens*)

8. Integration of metabolomics and transcriptomics reveals novel biomarkers in the blood for tuberculosis diagnosis in children

Dutta NK, Tornheim JA, Fukutani KF, Paradkar M, Tiburcio RT, Kinikar A, Valvi C, Kulkarni V, Pradhan N, Shivakumar SVBY, Kagal A, Gupte A, Gupte N, Mave V, Gupta A, Andrade BB, Karakousis PC for the CTRIUMPH RePORT India Study Team. *Scientific Reports*. 2020 Nov 11;10(19527). PMID: 33177551; PMCID: PMC7658223.

9. Assessment of persistent depressive symptoms among tuberculosis patients in India

Suryavanshi N, Sane M, Gaikwad S, Paradkar M, Mave V, Padmapriyadarsini C, Shivakumar SVBY, Gupta A, Gupte N, Thomas B for CTRIUMPH RePORT India study. *IJTLD*. 2020 Nov 1;24(11):1208-1211(4). PMID: 33172530.

10. Higher IL-6 levels and changes in TGF- are associated with lung impairment in pulmonary tuberculosis

Gupte AN, Selvaraju S, Gaikwad S, Mave V, Kumar P, Babu S, Andrade BB, Checkley W, Bollinger R, Gupta A for the CTRIUMPH study team. *ERJ Open Research*. 2020 September. DOI: 10.1183/23120541.00390-2020

Continued

Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

11. Tuberculosis preventive treatment should be considered for all household contacts of pulmonary TB patients in India

Paradkar M, Padmapriyadarsini C, Jain D, Shivakumar SVBY, Thiruvengadam K, Gupte AN, Thomas B, Kinikar A, Sekar K, Bharadwaj B, Dolla CK, Gaikwad S, Elilarasi S, Lokhande R, Reddy D, Murali L, Kulkarni V, Pradhan N, Elizabeth Hanna L, Pattabiraman S, Kohli R, Nayagam R, Suryavanshi N, Shrinivasa BM, Cox SR, Sriram Selvaraju S, Gupte N, Mave V, Gupta A, Bollinger RC, for the CTRIUMPH-RePORT India Study Team. *PLoS One*. 2020 July 29;15(7):e0236743. <https://doi.org/10.1371/journal.pone.0236743>. PMID: 32726367; PMCID: PMC7390377.

12. Transcriptomic profiles of confirmed pediatric tuberculosis patients and exposed household contacts identifies tuberculosis disease, infection, and response to treatment among Indian patients

Tornheim JA, Madugundu A, Paradkar M, Gupte N, Fukutani KF, Gupte AN, Kinikar A, Kulkarni V, Balasubramanian U, Sreenivasamurthy S, Raja R, Pradhan N, Shivakumar SVBY, Valvi C, Hanna LE, Andrade B, Padmapriyadarsini C, Mave V, Pandey A, Gupta A for the CTRIUMPH RePORT India Study Team. *J Infect Dis*. 2019 Dec 4. pii: jiz639. doi: 10.1093/infdis/jiz639. [Epub ahead of print]. PMID: 31796955.

13. Lipid mediators of inflammation and resolution in individuals with tuberculosis and tuberculosis-diabetes

Shivakoti R, Dalli J, Kadam D, Gaikwad S, Barthwal M, Colas RA, Mazzacuva F, Lokhande R, Dharmshale S, Bharadwaj R, Kagal A, Pradhan N, Deshmukh S, Atre S, Sahasrabudhe T, Kakrani A, Kulkarni V, Raskar S, Suryavanshi N, Chon S, Gupte A, Gupta A, Gupte N, Arriaga MB, Fukutani KF, Andrade BB, Golub JE, Mave V. *Prostaglandins Other Lipid Mediat*. 2019 Nov 11;147:106398. doi: 10.1016/j.prostaglandins.2019.106398. [Epub ahead of print] PMID: 31726221.

14. MAL adaptor (TIRAP) S180L polymorphism and severity of disease among tuberculosis patients

Saranathan R, Sathyamurthi P, Thiruvengadam K, Murugesan S, Shivakumar SVBY, NS Gomathi, Kavitha D, Paradkar M, Puvaneshwari R, Kannan M, Madheswaran A, Pradhan N, Kulkarni V, Gupte AN, Gupte N, Mave V, Bollinger RC, Gupta A, Padmapriyadarsini C, Hanna LE. *Infection, Genetics, and Evolution*. 2020 Jan(44). Epub ahead of print 2019 Oct 31. PMID: 31678649.

15. Age-specific prevalence of TB infection among household contacts of pulmonary tuberculosis: Is it time for TB preventive therapy?

Dolla CK, Padmapriyadarsini C, Thiruvengadam K, Lokhande R, Kinikar A, Paradkar M, Gupte A, Gaikwad S, Pradhan N, Kulkarni V, Shivakumar SVBY, Suryavanshi N, Gupte N, Pattabiraman S, Kagal A, Shrinivas BM, Murali L, Bharath TK, Pirthivi M, Kumaran P, Mave V, Gupta A. *Trans R Soc Trop Med Hyg*. 2019 Oct 11;113(10):632-640. doi: 10.1093/trstmh/trz049. PMID: 31225622; PMCID: PMC6792162.

16. Delays and barriers to early treatment initiation for childhood tuberculosis in India

Valvi C, Chandanwale A, Khadse S, Kulkarni R, Kadam D, Kinikar A, Joshi S, Lokhande R, Garg P, Gupte N, Jain D, Suryavanshi N, Golub J, Shankar A, Gupta A, Dhumal G, DeLuca A, Bollinger RC. *Int J Tuberc Lung Dis*. 2019 Oct 1;23(10):1090-1099. doi: 10.5588/ijtld.18.0439. PMID: 31627774.

17. Smoking, alcohol use disorder and TB treatment outcomes: A dual co-morbidity burden that cannot be ignored

Thomas B, Thiruvengadam K, Rani S, Ovung S, Sivakumar S, Shivakumar SVBY, Paradkar M, Gupte N, Suryavanshi N, Gupte AN, Kohli R, Pradhan N, Sivaramakrishnan GN, Gaikwad S, Kagal A, Dhanasekaran K, Deluca A, Golub JE, Mave V, Padmapriyadarsini C, Gupta A, CTRIUMPH-RePORT India Study. *PLoS One*. 2019 Jul 31;14(7):e0220507. doi: 10.1371/journal.pone.0220507. eCollection 2019. PMID: 31365583; PMCID: PMC6668833.

18. Infection free “resisters” among household contacts of adult pulmonary tuberculosis

Mave V, Padmapriyadarsini C, Chavan A, Shivakumar SVBY, Danasekaran K, Paradkar M, Thiruvengadam K, Kinikar A, Murali L, Gaikwad S, Hannah LE, Kulkarni V, Pattabiraman S, Suryavanshi N, Thomas B, Kohli R, Sivaramakrishnan GN, Pradhan N, Banu B, Kagal A, Golub J, Gupte A, Gupte N, Swaminathan S, Gupta A. *PLoS One*. 2019;14(7):e0218034. Published 2019 Jul 18. doi:10.1371/journal.pone.0218034. PMID: 31318864; PMCID: PMC6638997.

Continued

Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

19. Mobile phone access and comfort: Implications for HIV and tuberculosis care in India and South Africa

Cox SN, Elf JL, Lokhande R, Ogale YP, DiAndreth L, Dupuis E, Milovanovic M, Mpongose N, Mave V, Suryavanshi N, Gupta A, Martinson N, Golub JE, Mathad JS. *Int J Tuberc Lung Dis*. 2019 Jul 1;23(7):865-872. doi: 10.5588/ijtld.18.0542. PMID: 31439120.

20. Assessment of lung function in successfully treated tuberculosis reveals high burden of ventilatory defects and COPD

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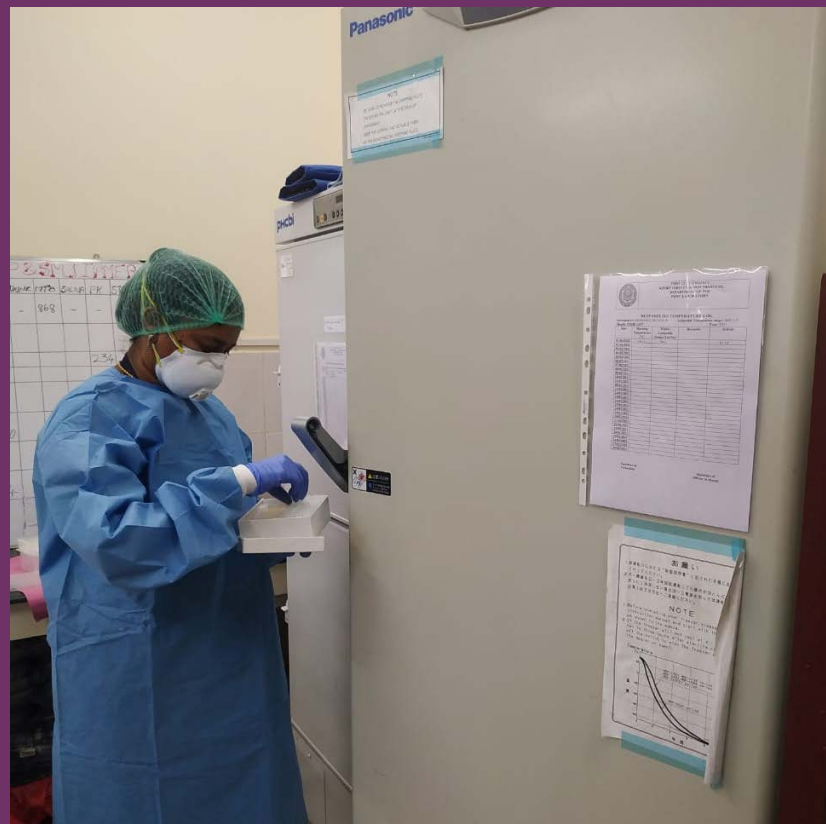


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Lectures & Presentations



CMC



MVDRC



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PGI Chandigarh



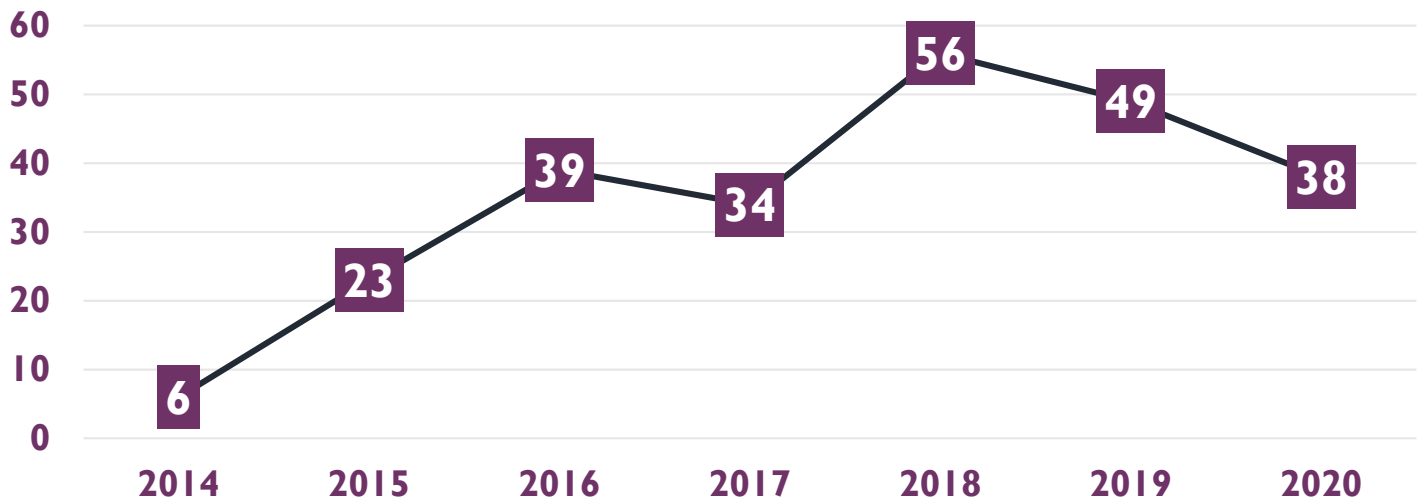
NEIGRIHMS

Hinduja

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LECTURES & PRESENTATIONS 2014–2020



LECTURE: Individual presentation on a topic of field of expertise. Lectures from prior RePORT India annual conferences are not included in this list but are available upon request.

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RePORT India Consortium

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Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

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Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

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2. Christopher DJ. Smoking, alcohol, air pollution & TB. TB RiCC Virtual Meeting. September 28-30, 2020.
3. Christopher DJ, Post TB bronchiectasis. Presented at: Nexptore Bronchiectasis Conclave. Candolim, Goa, India; December 14, 2019.
4. Christopher DJ. Experiences with LTBI screening of healthcare workers in an Indian referral hospital. Presented at: 50th Annual Union World Conference on Lung Health. Hyderabad, India; October 30–November 2, 2019.
5. Christopher DJ. TB-diabetes link. Presented at: Prof. Dr. M. Viswanathan Oration at the Research Society for the study of Diabetes in India, Annual Conference. Dindigul, Tamil Nadu, India; August 10, 2019.
6. Christopher DJ. Is India's endeavor to end TB by 2025 achievable? Presented at: 36th AP Tuberculosis & Chest Diseases Conference. Madanapally, Andhra Pradesh, India; November 10–11, 2018.
7. Christopher DJ. Addressing diagnostic challenges for TB meningitis—From clinical staging to PET Scanning. Presented at: 49th Union World Conference on Lung Health. The Hague, The Netherlands; October 24–27, 2018.
8. Christopher DJ. Is India's endeavor to end TB by 2025 achievable? How can RePORT align with this? Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.
9. Christopher DJ. Determination of efficacy of expert PCR ultra and transcriptional signatures in the diagnosis of pleural tuberculosis. Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.
10. Christopher DJ. Healthcare personnel TB—Fact of life in high burden countries. Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.

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Christian Medical College, Vellore

University of Cambridge–University of Washington (CRU 101)

LECTURES

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12. Christopher DJ. Battling the white plague (TB) in our campuses. Presented at: The Quality Circle, Christian Medical College. Vellore, India; April 14, 2018.
13. Christopher DJ. Targeted LTBI testing. Presented at: LTBI Knowledge Seminar. Hyderabad, India; January 11, 2018.
14. Christopher DJ. LTBI screening in high TB prevalence setting. Presented at: Qiagen Knowledge Seminar. Bangalore, India; November 2, 2017.
15. Christopher DJ. LTBI Screening: A clinician's perspective. Presented at: CME organized by Qiagen. New Delhi; India. April 5, 2017.
16. Christopher DJ. LTBI: To screen or not to screen. Presented at: Three T's of TB Prevention: Test, Treat, and Track Symposium. Asia Pacific Regional Conference; International Union against Tuberculosis. Tokyo, Japan; March 23, 2017.
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18. Christopher DJ. Healthcare worker TB: A Panel Discussion. Presented at: TB Symposium. Convened by Krishna Medical College in collaboration with McGill University (Canada). Manipal, India; December 21, 2016.
19. Christopher DJ. Evolution of drug resistant TB in India. Presented at: Annual Update in Tuberculosis. Convened by CMC Vellore. Vellore, India; November 19, 2016.
20. Christopher DJ. Screening for LTBI in healthcare personnel to assess TB risk—Lessons from India. Presented at: 5th Meeting of Asian Experts Community. Taipei, Taiwan; August 26–28, 2016.
21. Christopher DJ. TB risk in healthcare workers: Myth or reality? Presented at: RePORT International 2016 Meeting. Durban, South Africa; July 14–15, 2016.
22. Christopher DJ. From lab to clinic: Optimizing the importance of new diagnostics. Presented at: Advancing TB Research—An Exploration of Opportunities. Convened by PD Hinduja Hospital and NIH (USA). Mumbai, India; March 23–24, 2016.
23. Christopher DJ. Lessons from healthcare—TB research in India. Presented at: CMC Winter Symposium and the RePORT India 2016 Joint Leadership Group Meeting. Vellore, India; February 12–13, 2016.
24. Christopher DJ. Pleural tuberculosis. Presented at: Association of Physicians of India Meeting. Hyderabad, India; January 29–31, 2016.
25. Christopher DJ. TB in healthcare workers. Presented at: National Update in Respiratory Medicine. Convened by PD Hinduja Hospital. Mumbai, India; November 27–29, 2015.

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Christian Medical College, Vellore

University of Cambridge–University of Washington (CRU 101)

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28. Christopher DJ. Relevance of TST and IGRA in current day practice. Presented at: ASHRAICON Conference 2014. Ahmedabad, India; July 27, 2014.

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2. D. J. Christopher, Coelho Victor, Dr. Ebby Simon, Deepa Shankar, Balamugesh T Incremental Yield of Xpert MTB/RIF Ultra over Xpert MTB/RIF in the diagnosis of extrapulmonary tuberculosis (25062)) Presented at Virtual ERS International Congress 2020, Barcelona, Spain; September 7 to 9 2020.
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Christian Medical College, Vellore

University of Cambridge–University of Washington (CRU 101)

PRESENTATIONS | ABSTRACTS

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11. Christopher DJ. Experiences with LTBI screening of healthcare workers in an Indian referral hospital. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India; October 30–Nov 2, 2019.
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Christian Medical College, Vellore

University of Cambridge–University of Washington (CRU 101)

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 23. Christopher DJ, Balamugesh T, Dhahi P. The prevalence of active and latent tuberculosis infection in patients with type 2 diabetes mellitus in a tertiary care hospital of South India. Presented at: RePORT India 2016 Joint Leadership Meeting. Vellore, India; February 12–14, 2016.
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 25. Christopher DJ, Mitra S, Saroini JS, Balaji V, Gupta M, Therese M, Yadav B, Jeyaseelan L. Burden of diabetes among patients with tuberculosis: Ten-year experience from an Indian tertiary care teaching hospital. Presented at: 45th Union World Conference on Lung Health. Barcelona, Spain; October 28–November 1, 2014.
 26. Christopher DJ, Denkinger C, Thangakunam B, Sarojini JS, Pai M, Schumacher S. Point-of-care implementation of Xpert: Evaluating the impact of product and process innovation in TB diagnosis. Presented at: 45th Union World Conference on Lung Health. Barcelona, Spain; October 28–November 1, 2014.
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Jawaharlal Institute of Postgraduate Medical Education & Research

Boston Medical Center / Boston University

Rutgers (CRU 102)

LECTURES

1. Hochberg, NS. Malnutrition and TB. TB RiCC Virtual Meeting. September 28-30, 2020.
2. Hochberg, NS. Tuberculosis: The fundamentals and the sea changes. Presented at: MPH Course: Global Health Priorities & Approaches. Tufts University School of Medicine. Boston, MA, USA; 2019.
3. Hochberg, NS. Malnutrition and tuberculosis. World TB Day, National Regional Conference, Albany, NY, USA; 2019.
4. Hochberg, NS. Malnutrition and tuberculosis. Providence/Boston CFAR TB/HIV Scientific Working Group TB Interest Group Round Table. Boston, MA, USA; 2019
5. Hochberg, NS. The skinny on tuberculosis: Why malnutrition matters. Infectious Diseases Grand Rounds. Presented at: Boston Medical Center. Boston MA, USA; 2019.
6. Hochberg NS. Indo-U.S. TB cohort: Study design and preliminary results. Presented at: TB Research Unit (TBRU) Investigators Meeting. Boston, MA, USA; September 2017.

Continued

Jawaharlal Institute of Postgraduate Medical Education & Research Boston Medical Center Rutgers (CRU 102)

LECTURES

7. Hochberg NS. Updates in tuberculosis: The era of sea changes. Medicine Grand Rounds. Presented at: Carney Hospital. Dorchester, MA. USA; March 2017.
8. Hochberg NS. Malnutrition and TB in India: Intersection and implications. Presented at: Northeastern World TB Day Symposium. Boston, MA, USA. March 6–7, 2017.

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2. VanValkenburg A, Kaipilyawar V, Sarkar S, Lakshminarayanan S, Cintron C, Babu S, Knudsen S, Joseph N, Horsburgh CR, Babu P, Ellner J, Johnson WE, Salgame P, Hochberg NS. Malnutrition is associated with increased inflammation and increased tuberculosis risk signatures in individuals with latent Mycobacterium tuberculosis infection. 2020.
3. Kaipilyawar V, Verma S, Stringari LL, Ellner JJ, Alland D, Dietze R, Ribeiro-Rodrigues R, Salgame P. Innate immune mechanisms of protection against Mycobacterium tuberculosis infection. RePORT India 9th Annual Joint Leadership Meeting: Next Gen RePORT. Mumbai, India: February 10-12, 2020.
4. Abilasha N, Bharath B, Priyanga J, Senbagavalli P, Prakash B, Vinod K, Subitha L, Roy G, Salgame P, Muthuraj M, Roy G, Sarkar S, Hochberg NS, Noyal J. Effect of diabetes prevalence on circulating components of blood, disease severity and drug susceptibility in patients with pulmonary tuberculosis. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 30–November 2, 2019.
5. Chua A, Mowry WB, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas J, Sarkar S, Hochberg NS, Reddy D. Does the form of tobacco product used by smokers influence pulmonary tuberculosis severity? Presented at: ATS 2018. San Diego, CA, USA; May 18–23, 2018.
6. Abilasha N, Bharath B, Priyanga J, Senbagavalli P, Prakash B, Vinod K, Subitha L, Roy G, Salgame P, Muthuraj M, Roy G, Sarkar S, Hochberg NS, Noyal J. Effect of diabetes prevalence on circulating components of blood, disease severity and drug susceptibility in patients with pulmonary tuberculosis. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
7. Schenk NM, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas J, Sarkar S, Hochberg NS, Reddy D. Influence of type of tobacco product on chest X-ray findings in pulmonary tuberculosis patients in India. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
8. Hoyt K, White L, Sarkar S, Pleskunas J, Zhou T, Noyal J, Muthuraj M, Vinod K, Roy G, Ellner JJ, Horsburgh Jr CR, Hochberg NS. Effect of malnutrition on tuberculosis mycobacterial burden and chest radiographic findings. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
9. Reddy D. Wood fuel usage is associated with a higher leukocyte count in pulmonary tuberculosis patients. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
10. Forsyth M. Alcohol use and clinical presentation of tuberculosis at time of diagnosis in Puducherry and Tamil Nadu, India. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.

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Jawaharlal Institute of Postgraduate Medical Education & Research Boston Medical Center Rutgers (CRU 102)

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12. Johnson WE. Parsimonious gene signatures for TB outcomes. Presented at: JIPMER. Pondicherry, India; November 2017.
13. Johnson WE. Addressing unwanted heterogeneity in genomic data: Applications in RNA-sequencing and prediction. Presented at: Department of Statistics, University of Connecticut. Storrs, CT, USA; November 2017.
14. Svadzian A, Sahu A, Pleskunas JA, Sarkar S, Roy G, Ellner JJ, Hochberg NS, Reddy D. Association between wood fuel usage and disease severity among pulmonary tuberculosis cases. Presented at: American Society of Tropical Medicine & Hygiene Meeting. Atlanta, GA, USA; November 2016.
15. Stigma as a barrier to tuberculosis care: A literature review. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
16. Roy G, Sivaprakasam A, Kubiak R, Govindarajan S, Salgame P, Ellner J, Hochberg N, Sarkar S. Description of new pulmonary tuberculosis cases in Southern India. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
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18. Conversion among pulmonary tuberculosis cases in India. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
19. Predictors of 2 month sputum conversion among tuberculosis patients in India. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
20. Prolonged cough among tuberculosis patients in Tamil Nadu and Pondicherry, India. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
21. Reddy D, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas JA, Sarkar S, Hochberg NS. Association between biomass fuel, tobacco use and two-month sputum smear conversion among pulmonary tuberculosis cases in India. Presented at: American Thoracic Society Conference. San Francisco, CA, USA; May 2016.
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24. Reddy, D, Sahu S, McIntosh A, Kubiak R, Roy G, Ellner J, Sarkar S, Hochberg N. Association between latent tuberculosis infection and indoor air pollution among household contacts of pulmonary tuberculosis cases. Poster presented at: 46th Union World Conference on Lung Health of the International Union Against TB and Lung Disease. Cape Town, South Africa; December 1–5, 2015.

MV Diabetes Research Centre – NIRT-NIH-ICER University of Massachusetts (CRU 103)

LECTURES

1. Kornfeld H. TB and diabetes from bench to bedside and back. Presented at: 2nd International Symposium on Frontiers in Biomedical Science of Infection Control Convergence Medical Research Center, MMRC. Chungnam National University. Daejeon, Korea; October 15, 2019.
2. Kornfeld H. AMP kinase activation as host-directed therapy for tuberculosis. 49th Union World Conference on Lung Health. The Hague, Netherlands; October 23–26, 2018.
3. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. Effect of standard tuberculosis treatment on circulating levels of pro-inflammatory cytokines in tuberculosis-diabetes comorbidity. Presented at Keystone Symposia -Tuberculosis: Translating Scientific Findings for Clinical and Public Health Impact. Whistler, BC, Canada; April 15–19, 2018.
4. Kornfeld H. TB and diabetes from bench to bedside and back. Presented at: American Thoracic Society International Conference ATS San Diego, CA, USA; March 22, 2018.
5. Kornfeld H. Diabetic immunopathy and TB. Presented at: TB Conference. The Union-North American Region, Chicago, IL, USA; March 3, 2018.
6. Kornfeld H. TB and diabetes from bench to bedside and back. Presented at: Division of Infectious Disease, Boston University School of Medicine. Boston, MA, USA; January 25, 2018.
7. Kornfeld H. TB and diabetes from bench to bedside and back. Presented at: Division of Endocrinology, University of Massachusetts School of Medicine. Worcester, MA, USA; January 9, 2018.
8. Kornfeld H. Clinical and immunological findings from the Effect of Diabetes on TB (EDOTS) study in India. Presented at: 48th Union World Conference on Lung Health. Guadalajara, Mexico; October 11–14, 2017.
9. Kornfeld H. Impact of diabetes and hyperlipidemia on host defense. Presented at: 48th Union World Conference on Lung Health. Guadalajara, Mexico; October 11–14, 2017.
10. Kornfeld H. Sugar, fat, and consumption. Presented at: Infectious Diseases Grand Rounds, Perelman School of Medicine, University of Pennsylvania. Philadelphia, PA, USA; September 28, 2017.
11. Kornfeld H. Intersection between TB & diabetes. Presented at: New England TB Clinicians' Conference, University of Massachusetts Medical School. Worcester, MA, USA; May 11, 2017.
12. Kornfeld H. Diabetic immunopathy and TB. Presented at: Rollins School of Public Health, Emory University. Atlanta, GA, USA; April 20, 2017.
13. Kornfeld H. Diabetic immunopathy & TB. Presented at: Meakins-Christie Laboratories, McGill University. Montreal, Canada; April 10, 2017.
14. Kornfeld H. Diabetic immunopathy and TB. Presented at: National TB Conference. Atlanta, GA, USA; 21 April 2017.
15. Kornfeld H. Tuberculosis and diabetes: From bench to bedside and back. Presented at: Workshop on Integrated Care and Research for Tuberculosis, Diabetes, and HIV/AIDS: Challenges, Strategies, and Clinical Solutions. NIAID, International Union for Tuberculosis and Lung Disease, Bill and Melinda Gates Foundation. Liverpool, UK.; October 24, 2016.

Continued
MV Diabetes Research Centre – NIRT-NIH-ICER
University of Massachusetts (CRU 103)

LECTURES

16. Kornfeld H. Diabetic immunopathy. Presented at: Boston University School of Medicine Inflammation Symposium. Boston, MA, USA; May 23, 2016.
17. Kornfeld H. Developing a comprehensive therapeutic research strategy for the converging epidemics of TB, T2DM, and HIV. Co-Organizer and Speaker. NIAID Workshop. Rockville, MD, USA; May 10–11, 2016.
18. Kornfeld H. Workshop on advancing TB research: TB, diabetes, and host-directed therapies. Presented at: P.D. Hinduja Hospital. Mumbai, India; April 23–24, 2016.
19. Kornfeld H. The impact of Mycobacterium tuberculosis immune evasion on protective immunity: Implications for TB vaccine design. Co-Organizer, NIAID TB Workshop. Rockville, MD, USA; March 7–8, 2016.
20. Kornfeld H. Symposium on Tuberculosis Co-Morbidities & Immunopathogenesis. Organizer and Speaker, Keystone, CO, USA; February 28–March 2, 2016.
21. Kornfeld H. Sugar, fat, and consumption. Presented at: Pulmonary Center, Boston University School of Medicine. Boston, MA, USA; January 16, 2016.
22. Kornfeld H. Environmental epigenetics—Diabetes and tuberculosis. Presented at: Joint Retreat for the Centres for Biodiscovery & Molecular Development of Therapeutics and Biosecurity and Tropical Infectious Diseases (Australian Institute of Tropical Health & Medicine). Port Townsend, Australia; September 22, 2015.
23. Kornfeld H. Determinants of TB severity. Presented at: Shenzhen-Hong Kong Institute of Infectious Diseases. Shenzhen, China; November 20, 2015.
24. Kornfeld H. Tuberculosis: The rise of comorbidities. Presented at: Medical Grand Rounds. University of Massachusetts Medical School. Worcester, MA, USA; June 4, 2015.
25. Kornfeld H. TB and diabetes. Presented at: Singapore Immunology Network. Singapore; February 27, 2015.
26. Kornfeld H. Keystone Symposium on Granulomas in Infectious and Non-Infectious Disease: TB and Diabetes. Invited speaker, Santa Fe, NM, USA; January 22–27, 2015.
27. Kornfeld H. The effects of diabetes on TB susceptibility. Presented at: No.4 People’s Hospital of Nanning. Nanning, China; January 12, 2015.
28. Kornfeld H. Sugar, fat, and consumption. Presented at: University of Texas, Health Science Center at Tyler. Tyler, TX, USA; August 22, 2014.

PRESENTATIONS | ABSTRACTS

1. Nancy, A, Kumar NP, Moideen K, Viswanathan V, Dhanasekaran M, Sivakumar S, Hissar S, Kornfeld H, Babu S. Metformin use is associated with diminished plasma cytokines/ chemokines and acute phase proteins in incident tuberculosis with known diabetes mellitus. RePORT India 9th Annual Joint Leadership Meeting: Next Gen Report. Mumbai, India: February 10-12, 2020.
2. Devarajan A, Kumpatla S, Dhanasekaran M, Sahukar SB, Babu S, Kornfeld H, Viswanathan V. Glycaemic status in screen detected versus known cases of DM TB patients and its effect on treatment outcomes: EDOTS Study from South India. RePORT India 9th Annual Joint Leadership Meeting: Next Gen RePORT. Mumbai, India: February 10-12, 2020.

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MV Diabetes Research Centre – NIRT-NIH-ICER
University of Massachusetts (CRU 103)

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3. Kumar NP, Nancy A, Moideen K, Viswanathan V, Dhanasekaran D, Sivakumar S, Hissar S, Kornfeld H, Babu S. Elevated unstimulated and TB antigen stimulated levels of IL-36 isoforms in tuberculosis-diabetes comorbidity. RePORT India 9th Annual Joint Leadership Meeting: Next Gen RePORT. Mumbai, India; February 10-12, 2020.
 4. Shruthi BS, Sivakumar S, Arutselvi D, Kumar NP, Babu S, Menon PA, Natarajan M, Sathyavani K, Kornfeld H, Viswanathan V. Association of diabetes mellitus with INH mono-resistance. Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, India; February 4–6, 2019.
 5. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. Altered circulating levels of eicosanoids in tuberculosis-diabetes co-morbidity and reversal upon standard tuberculosis treatment. Presented at: Keystone Symposia -Tuberculosis: Mechanisms, Pathogenesis and Treatment. Banff, Alberta, Canada; January 17–21, 2019.
 6. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. Elevated circulating levels of monocyte activation markers among tuberculosis patients with diabetes co-morbidity Presented at: IMMUNOCON 2018 45th Annual Meeting of Indian Immunology Society. TSHTI, Faridabad, India; November 1–3, 2018.
 7. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. Effect of anti-tuberculosis treatment on the systemic levels of matrix metalloproteinases and tissue inhibitors of MMP in tuberculosis–diabetes comorbidity. Presented at: 5th Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
 8. Moideen K, Kumar NP, Bethunaickan R, Sivakumar S, Menon PA, Viswanathan V, Shruthi BS, Kornfeld H, Babu S. Altered systemic levels of neutrophil and mast cell granular proteins in tuberculosis-diabetes comorbidity and changes following treatment. Presented at: 5th Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
 9. Shruthi BS. Impact of metformin use on TB severity in diabetes. Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
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 11. Kumar NP. Effect of standard tuberculosis treatment on circulating levels of monocyte activation markers and RAGE ligands in tuberculosis–diabetes comorbidity. Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
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P.D. Hinduja National Hospital & Medical Research Center
Johns Hopkins University (CRU 108)

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1. Rodrigues C. Targeted NGS in TB diagnosis. TB RiCC Virtual Meeting. September 28-30, 2020.
2. Udwardia ZF. India's COVID response: The Good and The Bad. COVID TB Webinar, RePORT India. July 27 2020.

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P.D. Hinduja National Hospital & Medical Research Center Johns Hopkins University (CRU 108)

PRESENTATIONS | ABSTRACTS

1. Chawla PK, Keny Bhamini, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Soman R, Sunavala A, Mullerpattan J, Rodrigues C, Gupta A, Tornheim JA, Martison N, Ebraham V, Ashavaid TF. Serum linezolid levels in MDRTB patients. Abstract submitted at: RICC 2020, September 2020
2. Chawla PK, Naik PR, Lokhande RV, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Development & validation of plasma Bedaquiline levels. Presented at: 33rd Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; June 30, 2020. (Awarded 1st Prize for Best Laboratory paper)
3. Naik PR, Chawla PK, Lokhande RV, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Plasma moxifloxacin levels in Indian MDR-TB patients. Presented at: 33rd Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; June 30, 2020. (Awarded 2nd Prize for Best Laboratory paper)
4. Tornheim JA, Gajjar I, Shivakumar SVBY, Gupte AN, Gutpe N, Kishore G, Karane M, Rodrigues C, Gupta A, Udwardia ZF. Increased Moxifloxacin Dosing among MDR-TB Patients with Low-Level Resistance to Moxifloxacin did not Improve Treatment Outcomes in a Tertiary Care Center in Mumbai, India. Presented at: Johns Hopkins Department of Medicine Research Retreat. 28 February 2020. Baltimore, MD.
5. Naik PR, Chawla PK, Lokhande RV, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Therapeutic Drug Monitoring of moxifloxacin in Indian MDR-TB patients. Presented at: RePORT India 9th Annual Joint Leadership Meeting: NEXT GEN RePORT, Mumbai, India, February 10-12, 2020.
6. Gajjar I, Kharat N, Tornheim JA, Sawant N, Pandya H, Kishore G, Chalwa PK, Karane M, Sayed S, Rodrigues C, Ashavaid TF, Gupta A, Udwardia ZF. A case report on cycloserine induced late onset of psychosis and linezolid induced peripheral neuropathy in an adolescent with drug resistant tuberculosis from the Private sector in Mumbai. Presented at: RePORT India 9th Annual Joint Leadership Meeting: NEXT GEN RePORT, Mumbai, India, February 10-12, 2020.
7. Kamblil P, Ajbani K, Sadani M, Kazi M, Khillari A, Shetty A, Tornheim JA, Rodrigues C. Targeted next generation sequencing (tNGS) for detection of drug resistant mutations in TB. RePORT India 9th Annual Joint Leadership Meeting: Next Gen RePORT. Mumbai, India: February 10-12, 2020.
8. Gajjar I, Tornheim JA, Kharat N, Kishore G, Shivakumar SVGY, Chalwa PK, Rodrigues C, Ashavaid TF, Gupta A, Udwardia ZF. Impact of cycloserine treatment on depression among patients treated for multidrug-resistant tuberculosis in the private sector in Mumbai. Presented at: RePORT India 9th Annual Joint Leadership Meeting: NEXT GEN RePORT, Mumbai, India, February 10-12, 2020.
9. Kharat N, Gajjar I, Tornheim JA, Sawant N, Pandya H, Shivakumar SVGY, Chalwa PK, Rodrigues C, Ashavaid TF, Gupta A, Udwardia ZF. Monitoring household contacts of drug resistant tuberculosis patients for incident infection from the private sector in Mumbai: An ongoing study. Presented at: RePORT India 9th Annual Joint Leadership Meeting: NEXT GEN RePORT, Mumbai, India, February 10-12, 2020.
10. Chawla PK, Naik P, Lokhande R, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Therapeutic drug monitoring of moxifloxacin in Indian MDR-TB patients. Presented at: Association of Clinical Biochemists of India. 15th Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB) Congress. Jaipur, India; November 17-20, 2019.

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P.D. Hinduja National Hospital & Medical Research Center Johns Hopkins University (CRU 108)

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11. Tornheim JA, Gajjar I, Shivakumar SVBY, Gupte AN, Kishore G, Karane M, Rodrigues C, Gupta A, Udwardia ZF. Increased moxifloxacin dosing among MDR-TB patients with low-level resistance to moxifloxacin did not improve treatment outcomes in a tertiary care centre in Mumbai, India. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 30-November 2, 2019.
12. Chawla PK, Lokhande RV, Naik PR, Dherai AJ, Udwardia ZF, Mahashur AA, Pinto L, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Therapeutic drug monitoring of clofazimine in Indian MDR-TB patients. Presented at: MSACL 2019 EU. Salzburg, Austria; September 22–26, 2019.
13. Chawla PK, Lokhande RV, Naik PR, Dherai AJ, Udwardia ZF, Mahashur AA, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. Determination of plasma clofazimine levels by liquid chromatography-mass spectrometry. Presented at: 32nd Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; March 2, 2019 & RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
14. Chawla PK, Lokhande RV, Naik PR, Dherai AJ, Udwardia ZF, Mahashur AA, Soman R, Rodrigues C, Gupta A, Tornheim JA, Ashavaid TF. Determination of serum linezolid levels by HPLC. Presented at: 32nd Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; March 2, 2019 (Awarded 2nd Prize for Best Laboratory paper) & RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
15. Tornheim JA, Udwardia ZF, Porwal S, Kishore G, Gajjar I, Karane M, Shivakumar SVBY, Rodrigues C, Gupta A. Impact of standard or increased moxifloxacin dose among MDR-TB patients in Mumbai with low-level resistance. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
16. Gajjar IN, Tornheim JA, Udwardia ZF, Kishore G, Karane M, Sayed S, Chawla P, Rodrigues C, Ashavaid T, Shivakumar SVBY, Gupta A. Quality of life among MDR-TB patients from the public sector in Mumbai. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
17. Shivakumar SVBY, Tornheim JA, Gajjar I, Porwal S, Kishore G, Karane M, Chawla P, Rodrigues C, Ashavaid T, Gupta A, Udwardia ZF. Mental health and TB: High prevalence of depression among drug-resistant TB patients not associated with cycloserine. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
18. Kampli P, Tornheim JA, Soundararajan L, Priyadarshini S, Gupta R, Ramprasad VL, Gupta A, Rodrigues C. Whole genome sequencing of Mycobacterium tuberculosis directly from clinical samples accurately identifies drug resistance. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
19. Ajbani K, Kazi M, Naik S, Soman R, Shetty A, Rodrigues C. Simultaneous rapid detection of tubercular meningitis and drug susceptibility testing using pyrosequencing on uncultured cerebrospinal fluid samples. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
20. Nambiar R, Tornheim JA, Diricks M, Katrien DB, Sadani M, Shetty A, Rodrigues C. Linezolid resistance in Mycobacterium tuberculosis isolates at a tertiary care center in Mumbai, India, by whole genome sequencing. Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.

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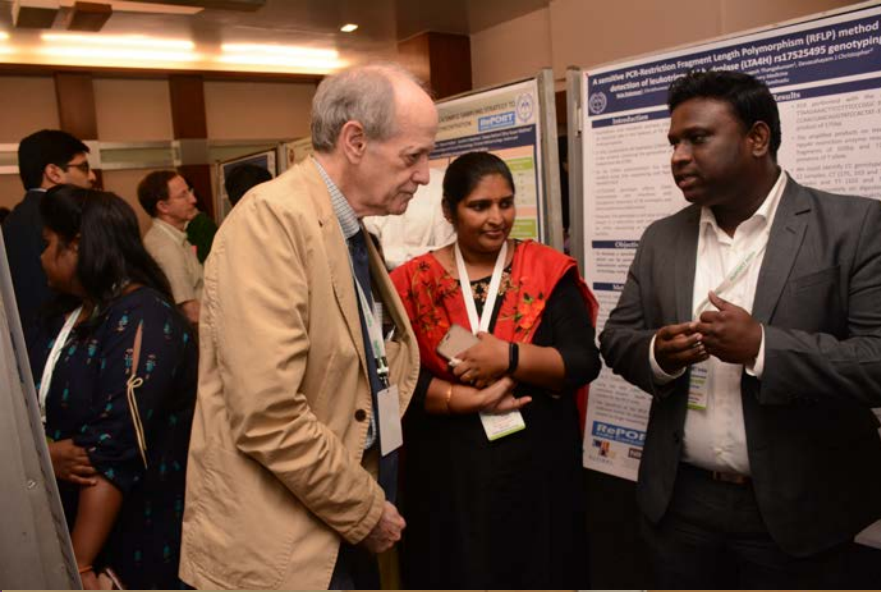
PRESENTATIONS | ABSTRACTS

21. Chawla PK, Lokhande RV, Naik PR, Singh S, Dherai AJ, Udwadia ZF, Pinto L, Soman R, Rodrigues C, Patel J, Ashavaid TF. Implications of acetylase genotype on plasma rifampicin and isoniazid levels in TB patients. Presented at: 45th National Conference of Association of Clinical Biochemists of India (ACBICON 2018). Goa, India; October 25–27, 2018.
22. Chawla PK, Lokhande RV, Naik PR, Dherai AJ, Udwadia ZF, Rodrigues CR, Mahashur AA, Soman R, Patel J, Ashavaid TF. Implication of acetylase genotype of plasma rifampicin and isoniazid. Oral Presentation at: 31st Annual Research Day. (Awarded 1st Prize for Best Laboratory paper) P.D. Hinduja Hospital and MRC. Mumbai, India; March 3, 2018.
23. Tornheim J, Ganatra S, DeLuca A, Banka R, Rodrigues C, Gupta A, Udwadia Z. Linezolid experience among MDRTB patients in Mumbai. Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
24. Chawla PK, Lokhande RV, Naik PR, Dherai AJ, Udwadia ZF, Mahashur AA, Soman R, Patel J, Ashavaid TF. Therapeutic drug monitoring of rifampicin and isoniazid and implications of acetylase genotype on plasma levels. Presented at: 15th International Congress on Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT). Kyoto, Japan; September 27, 2017.
25. Tornheim J, DeLuca A, Ganatra S, Radhika B, Gupta A, Udwadia Z. It simply won't work here: Few eligible for the newly recommended short course MDR-TB regimen in a Mumbai private clinic. Presented at: American Thoracic Society 2017 International Conference. Washington, DC, USA; May 21, 2017.
26. Tornheim JA, Ganatra S, DeLuca A, Banka R, Gupta A, Udwadia ZF. Impact of drug susceptibility testing on drug choice in a tuberculosis cohort with high rates of drug resistance from the private sector in Mumbai. Presented at: RePORT India 2016 Joint Leadership Meeting. Hyderabad, India; February 3, 2017.
27. Udwadia ZF, Tornheim JA, Ganatra S, DeLuca A, Banka R, Gupta A. Impact of drug susceptibility testing on drug choice in a tuberculosis cohort with high rates of drug resistance from the private sector in Mumbai. Presented at: IDWeek 2016. New Orleans, LA, USA; October 27, 2016.



Until We Gather Again ...





Production Team

Content Management: Daphne Martin

Data Visualization: Samyra Cox, Prasad Bogam, Mandar Paradkar

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