Proposal: TB HCM for children under 5 in India
External

Program background and context

Tuberculosis (TB) stands as one of the leading causes of death globally from a single infectious agent, second to COVID-19. Annually, an estimated 10.6 million incident cases occur, with children accounting for 10%.[1] Around 40% of estimated TB cases remain unnotified in high TB burden, low-and-middle-income countries (LMICs), leading to underdiagnosis and undertreatment, continuing TB transmission within communities.[2]

Children under-5 face the highest risk of contracting TB when residing in households with active TB patients, and they are more prone to rapid disease progression and increased severity of the disease upon infection.[3] The majority of pediatric TB incidence (over 50%) and 80% of mortality occur in this under-5 age group. To combat this challenge, the World Health Organization (WHO) recommends household contact management (HCM) and the use of TB preventive therapy (TPT), particularly emphasizing its importance for children under 5 and those living with HIV.[4] Despite WHO guidelines advocating for TPT initiation after a symptom-based screening, TPT coverage amongst under-5 remains inadequate in high-TB burden countries.[5]

India has the largest burden of TB, accounting for 27% of the world's TB cases[6]. India's national guideline for Programmatic Management of TB Preventive Treatment (PMTPT) was launched in August 2021[7] and recommend TPT for all household contacts of index pulmonary TB patients. Despite the rollout of national guidelines, significant barriers remain, resulting in poor TPT coverage, including:

- *Long regimen with side-effects:* the current TPT regimen is 6-months and a lack of child friendly formulations results in lower TPT initiation and lack of adherence.
- *Loss throughout the cascade of care due to TPT only initiated at the facility:* once identified as a household contact, children still need to be brought in to a health facility for TPT initiation. This leads to several "missed" children at this step or delays in linkage to TPT treatment.
- *Lack of awareness on TPT:* Lower prescriptions for TPT by clinicians due to limited awareness about TB prevention and the availability of newer regimens such as 3HP. Poor community awareness, leading to reluctance amongst caregivers to initiate TPT for healthy children, and lack of adherence to treatment.
- *Limited coverage of private sector patients:* Patient Provider Support Agencies (PPSAs), contracted by the National TB program (NTP) to support patients in the private sector, do not undertake contact tracing or TPT initiation as these activities are not included in their contract.
- *Limited Bandwidth to prioritize TPT:* Expanding National TB program staff mandate to deliver TPT services to all HHCs, has led to significant increase in workload and thus reduced ability to prioritizate of TPT.

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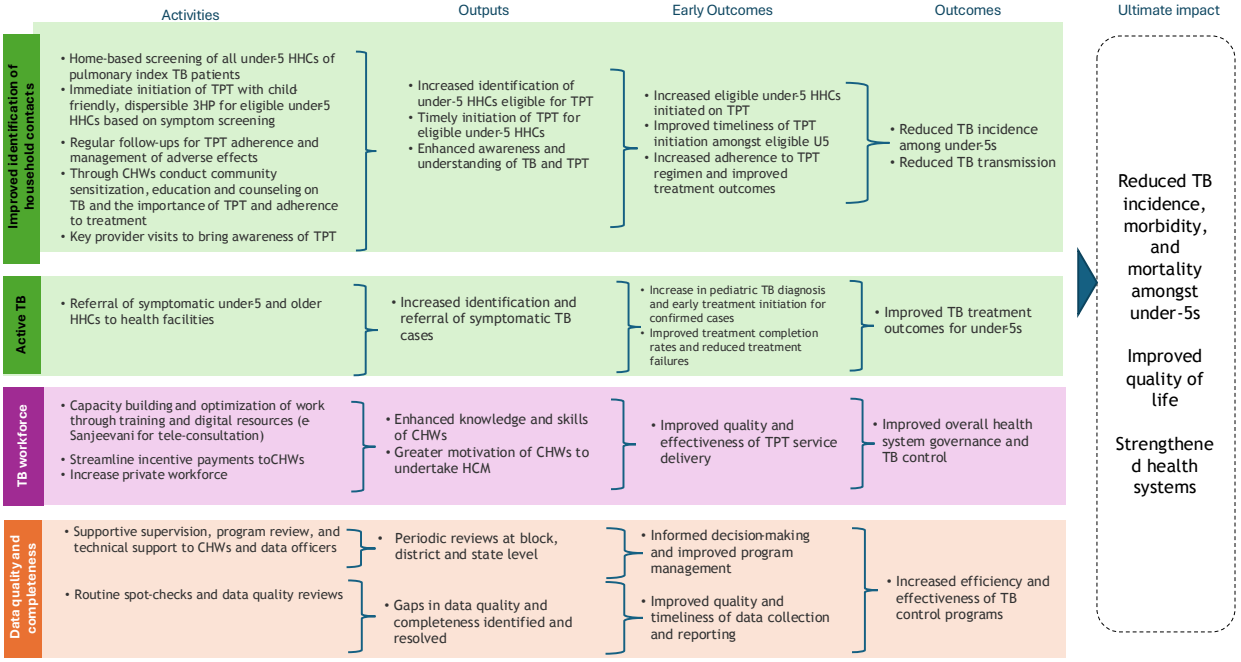
[1] https://www.who.int/publications/i/item/9789240061729
[2] ibid
[3] https://pubmed.ncbi.nlm.nih.gov/32199484/
[4] https://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf
[5] https://www.who.int/publications/i/item/9789240061729
[6] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/tb-disease-burden/1-1-tb-incidence
[7] https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=5621&lid=3664

Key proposed interventions

CHAI proposes to implement community-based TB household contact management (TB HCM), specifically targeting under-5 household contacts of index pulmonary TB cases. Leveraging the combined strengths of the NTP and general health system, the program will engage Accredited Social Health Activist (ASHA) and TB Health Volunteers (TB-HVs) for patients in the public sector to optimize their bandwith and prioritize TPT. Moreover, to address the gaps in the private sector CHAI will contract PPSAs to expand TPT coverage amongst patients seeking care in the private sector. These three cadres of CHWs will go to households for contact tracing, management, and care, ultimately bridging the gap between healthcare facilities and communities. This approach is expected to improve TPT initiation rates. In addition to this household-based primary intervention, all household TB contacts who are symptomatic will be referred to the base health facility for additional diagnostic screening. To address behavioral barriers at the provider and household level, the project will build the capacity of CHWs to effectively counsel households and raise awareness with them on the benefits of TPT, while providers will be sensitized on need for TPT and latest advancements in TPT through periodic medical education seminars. The intervention will also introduce pediatric formulation of 3HP, a weekly 3-month regimen in dispersible form, that will improve convenience and initiation to TPT.

Theory of change



Proposed scale of implementation

The planned program includes 26 high-TB notification districts Bihar and 44 high-TB notification districts Uttar Pradesh, for a total of 70 districts. Collectively, these states represent 26% of the population and 32% of TB prevalence in India. The intervention will be implemented through State governments, with CHAI providing TA support for capacity building of CHWs, strengthening review

mechanisms for TPT at district and state level, establish robust monitoring and supportive supervision systems, support streamlining of CHW incentive payment mechanisms, and strengthen drug quantification and supply chain systems to improve availability of TPT.

Market shaping opportunities

CHAI sees a potential market shaping opportunity to reduce the price of pediatric rifapentine (RPT) through the development and introduction of a co-packaged RPT DT + Isoniazid (INH) DT product, commonly referred to as the 3HP regimen. A summary of the potential for this is provided below:

Therapeutic	Current Negotiated price ($/pill)	Aspirational negotiated price ($/pill)	% reduction (aspirational to current negotiated price)
Pediatric rifapentine	$0.138*	$0.110	20%
Pediatric isoniazid	$0.030*	$0.024	20%

*The current negotiated price ensures this price is accessible only until December 2024.

The co-packaged products will enable countries to buy both products together, minimizing supply chain disruptions, avoiding instances where one of the therapies in the regimen is not available. The co-packaged product would also effectively increase demand for the pediatric TPT products and provide suppliers with the opportunity to increase sales volumes allowing for manufacturing efficiencies and profitability at lower margins. CHAI anticipates that these price reductions can be achieved by 2025/26. The pediatric 3HP formulation will be offered in intervention districts in the pilot to evidence impact and accelerate programmatic uptake. The volume commitment from the project procurement will be used to achieve the proposed price reductions.

Monitoring and Evaluation Framework

The M&E framework will include multiple components to ensure that the program is successful and information is obtained to help further scale this project if successful. The framework will include components such as routine program monitoring, formative research, and an independently evaluated impact evaluation.

- Routine program monitoring: CHAI proposes to conduct routine program monitoring activities to be fully developed with key stakeholders to understand program roll-out and enhance sustainability. The types of activities will include tracking process indicators to ensure program roll out such as telecaller data, weekly visit data, and data quality spot checks (not a comprehensive list).

- Formative research: Before the launch of the pilot, CHAI in development with co-investigators and key stakeholders, proposes to conduct formative research to refine the design and roll-out of the pilot, leveraging qualitative and participatory approaches with community health workers and facility managers to understand how to optimize implementation. Example questions include: What is the optimal workflow for CHWs to be dispatched to index households?

- Independent evaluation: To minimize conflict of interest and prove that the program had the impact as intended, IDinsight India has been hired to conduct an impact evaluation and accompanying process evaluation on the program over the first 2 years of the 4-year grant. For the impact evaluation, the primary outcome of interest is the impact of the CHW-based model on TPT initiation rates amongst eligible children-U5. The impact evaluation will thus be a cluster randomized controlled trial comparing the impact of the TB HCM approach on TPT coverage amongst U5, compared to standard TPT delivery which is currently a facility-based model. Secondary outcomes include impact on ASHA and TBHV's time allocation; TPT completion; and other indicators related to the cascade of care. The qualitative process evaluation will document the perspectives of the program; interviews will be conducted from control and intervention areas among household members, implementing staff, and key stakeholders at midline and endline. The cluster RCT is intended to run for 2 years at which point all remaining districts will laucn the CHW-based program. The full development of this evaluation will be conducted along with co-investigators and key stakeholders within India.

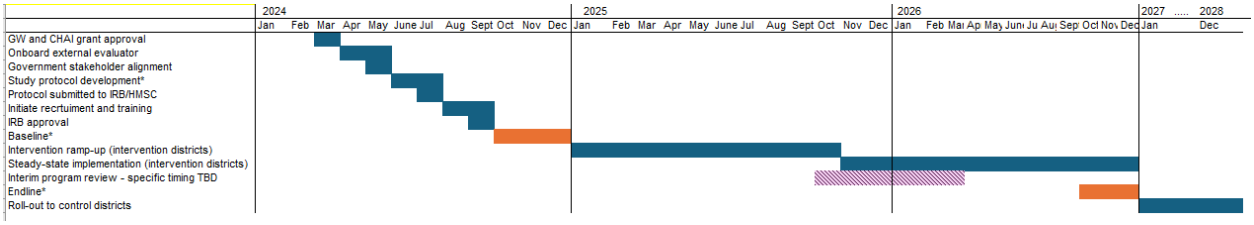
The roles and responsibilities of CHAI, Co-Investigators and IDinsight for different M&E components is provided below:

	CHAI Role	Co-Investigators	IDinsight Role
Routine program monitoring	• Lead routine program monitoring activities: • Develop CHW M&E tools • Develop dashboards for program review • Review/ensure data quality • Build analytical capacity • Analyse routine data to refine operations • Prioritize key questions for process evaluation	• Review periodic reports as produced by CHAI	• Review periodic reports as produced by CHAI
Formative research	• Contract agency to research patient, provider, and CHW beliefs/issues and integrate findings into implementation	• Research key implementation questions • Review findings	
Impact evaluation – cluster RCT to evaluate primary outcome Measurement of secondary outcomes	• Provide inputs on the impact evaluation protocol • Generate list of potential co-PIs and facilitate introductions as necessary • Help IDinsight obtain in-country research approvals • Support IDinsight to obtain state/district level data collection permissions • Collect insights from existing data forms/systems • Review periodic reports and results	• Co-lead protocol development	• Co-lead protocol development • Final decision on co-PI • Obtain ethical and regulatory approvals • Collaborate with co-PIs • Implement baseline and endline data collection • Synthesize findings

Process evaluation – qualitative study with key stakeholders	• Provide inputs into design of interview guides • Support IDinsight to shortlist stakeholders, as necessary • Facilitate introductions to stakeholders, as necessary • Provide programmatic context to interpret findings • Identify opportunities to incorporate findings into program design • Review period reports and results	• Co-lead the impact evaluation protocol and review all findings.	• Co-lead the impact evaluation protocol • Lead the development of the shortlist of stakeholders to be interviewed and sampling strategy of stakeholders • Lead interview guide design • Collaborate with CHAI to shortlist stakeholders to be interviewed • Conduct interviews • Synthesize findings

Timeline

The program's duration will extend over a total of 4 years and 9 months. The initial 9 months will be dedicated to finalizing the evaluation design, developing a protocol, and obtaining necessary in-county approval and set-up. Following this preparatory phase, a pilot M&E will be conducted over a period of 2 years [from Jan 2025 to Dec 2026, tbc]. Subsequently, program implementation will proceed for subsequent 2 years [Jan 2027 to Dec 2028, tbc] from across all pilot sites, with gradually reduced CHAI's involvement.



Budget

The overall grant budget over 4 years and 9 months is approximately $15.4M (TBC).

Previous CHAI experience in India

Immunization

CHAI's affiliate, William J Clinton Foundation (WJCF)'s Immunization programme, funded by BMGF, supports the government's goal of achieving 90% Full Immunization Coverage equitably in Bihar, Madhya Pradesh, and Uttar Pradesh, which comprise 42% of India's annual birth cohort (~12 million) and face significant routine immunization coverage and equity challenges. WJCF employs a two-pronged approach in Bihar and Uttar Pradesh to enhance government capacity for improved and sustainable programme performance at the state, district, and block levels.

Firstly, WJCF strengthens public health systems for improved Management and Governance of the Universal Immunization Programme (UIP) by innovating data-based decision-making, converging different health system datasets, improving data quality, and promoting data-driven problem identification. WJCF also strengthens review platforms and meetings owned and managed by government officials and healthcare

workers. The organization is gradually transitioning districts out of this capacity enhancement support to enable the government to build on the programme's gains.

Secondly, WJCF conducts research to uncover the root causes of Zero Dose children, who are the most vulnerable to Vaccine-Preventable Diseases and other childhood issues. Based on these findings, WJCF prototypes community-led solutions to reduce the Zero Dose problem in identified population segments, aiming to develop highly contextualized packages for improving routine immunization outcomes, which can be implemented and scaled by state governments.

To address the unique challenges in urban segments of Bihar and Madhya Pradesh, WJCF is innovating GIS-enabled mapping solutions to bring rapidly evolving urban populations into the public health fold. The organization is also strengthening supply and governance systems in urban areas to deliver immunization services effectively.

IMPAACT4TB

The IMPAACT4TB program - Increasing Market and Public health outcomes through scaling up Affordable Access models of short Course preventative therapy for TB - funded by UNITAID, was led by the South Africa-based Aurum Institute as the Primary Recipient, with a consortium of partners including CHAI, Johns Hopkins University, and the Royal Netherlands Central Association to Fight Tuberculosis as Secondary Recipients. CHAI coordinated the program in 4 countries, including India, WJCF, collaborated with 5 Indian-based institutes (National Institute for Research in TB, National AIDS Research Institute, Regional Medical Center - Bhubaneswar, National Institute of TB and Respiratory Disease, Byramjee-Jeejeebhoy Government Medical College) and aimed to provide local evidence for the National Technical Working Group (NTWG) on TPT. As a result of this consortium with the importation of Rifapentine from Global Drug Facility and development of training material for health workers, in May 2020, the NTWG included 3HP for all eligible populations, and a large order (5M courses) for 3HP was placed by the Government of India in March 2024.

Joint Effort for Elimination of Tuberculosis (JEET 1.0)

Joint Effort for Elimination of Tuberculosis (JEET) project, which focused on finding "missing patients" in the private sector. Funded by a the Global Fund grant of $18.28M from 2018-2021, WJCF implemented the JEET Patient-Provider Support Agency (PPSA) model across 47 districts & (150+ districts in a light touch manner) in seven states, engaging with over 25,000 private providers. The project facilitated linkages between private sector patients and India’s National TB Elimination Program (NTEP) services, including free molecular diagnostics, drugs, and nutritional support. JEET's impact at a national level was significant, contributing to 29%, 66%, and 68% of total private sector notifications in 2018, 2019, and 2020, respectively, despite the challenges posed by COVID-19.

The success of JEET, demonstrated the effectiveness of mobilizing and engaging India's unorganized private sector to address public health challenges. JEET's achievements laid the foundation for the Government of India to transition towards direct financing of Private Sector Engagement (PSE) programs through domestic budgets, showcasing WJCF's ability to successfully hand over projects to the government. As a result, the NTEP has approved PPSAs in 385 districts, with 203 districts having functional PPSAs as of June 2022. This domestic scale-up, built on the lessons and successes of JEET, highlights WJCF's expertise in managing large-scale projects and facilitating smooth transitions to government ownership.

Joint Effort for Elimination of Tuberculosis (JEET 2.0):

WJCF was a primary recipient to a Global Fund grant in India that aimed to improve TPT coverage amongst household contacts of drug-sensitive pulmonary TB patients. WJCF worked with CHWs and the health system across 11 states from Sep 2021 to March 2024 to implement contact tracing using a facility-based intervention model.

Under JEET 2.0, WJCF has supported TPT initiations to household contacts of all age groups, including U5 contacts, across 71 districts (in 11 states). Project staff visited index TB patient houses for contact enumeration, and symptom screening. Contacts were then linked to a health facility for testing and TPT initiation. Project staff also supported HHCs through the course of treatment to facilitate better adherence and completion rates. Moreover, NTEP staff, medical officers and private providers were trained on TPT guidelines. The project also supported training and capacity building of CHWs on undertaking HCM and TPT initiations. WJCF has developed communication tools that field staff use for engaging providers, TB patients and their families to overcome low awareness and stigma associated with TPT.

TB Free Chennai Initiative (TFCI)

The TB Free Chennai Initiative (TFCI) was an ambitious program led by the Greater Chennai Corporation (GCC) and funded by USAID, aiming to improve timely detection and appropriate treatment of TB cases in Chennai. CHAI played a crucial role as the technical support group (TSG) for TFCI from 2017 to 2022, supporting GCC in various aspects, including ideation, strategy, procurement, M&E, and operations related to several active case-finding (ACF) interventions. Key components of TFCI included the procurement and operationalization of mobile diagnostic units (MDUs) retrofitted with digital x-ray machines and AI, conducting a pilot vulnerability mapping-led ACF campaign, a large-scale prospective study among ~85,000 households using behavioral science and machine learning, and implementing an omnichannel mHealth campaign targeting a highly vulnerable group.

The outcomes of TFCI were significant, with the procurement of seven MDUs equipped with x-ray machines leading to the screening of over 100,000 individuals in high-risk areas of Chennai between January 2019 and March 2020. This increased case-finding from ~13 per 100,000 from routine campaign-mode ACF to >500 per 100,000 screenings under the revised methodology. Additionally, an index of individual vulnerability with greater specificity towards TB was designed, and an ~8 month mHealth campaign showed directional improvements in knowledge, attitudes, behavior (KAB), and time to care-seeking.

The experiences and learnings from TFCI played a significant role in shaping the ACF approach for other programs in reaching high-risk populations and improving case detection rates. The insights gained from the large-scale prospective study informed the development of targeted interventions and communication strategies, while the successful implementation of the omnichannel mHealth campaign demonstrated the potential of digital technologies in reaching and engaging high-risk groups. Following the success of TFCI, the Tamil Nadu Government planned and allocated funds for scaling up the number of MDUs from 16 to 44.

Radical Technology for Tuberculosis: RADTECH4TB Delhi Study

WJCF partnered with the Delhi State National Tuberculosis Elimination Program from August 2022 to March 2024 in 3 primary health centers and one chest clinic in Delhi to validate a computer-aided application (CAD) for TB detection using the WHO protocol. The study involved 1,411 individuals from three high-burden

primary health centers, with 354 confirmed TB cases. Chest x-ray images were independently interpreted by a local radiologist and analyzed using Qure.ai's qXR software version 3.2.9 (qXRv3). The findings indicated that qXRv3 performs comparably to local radiologists in India, particularly in primary health centers.

Subsequently, as part of the main study, WJCF updated the TB case-finding algorithms at these three PHCs using dCXR and CAD technology. Among 45,094 walk-in patients, 8,860 received chest x-rays, with 1,186 showing a CAD score suggestive of TB and 312 having microbiologically confirmed TB. This led to a 53% increase in drug-sensitive TB notifications and a 60% reduction in the turnaround time from screening to diagnosis.

The study provided evidence for two Global Fund tenders in 2023, conducted by WJCF on behalf of India's National TB Elimination Program (NTEP), resulting in the procurement of 225 dCXR systems. Additionally, operational guidelines were developed for using ultraportable digital chest x-rays at primary healthcare facilities. These guidelines have been adopted by the government for the operationalization and deployment of dCXR-CAD systems nationwide.