

BEST PRACTICES IN CHILD AND ADOLESCENT TUBERCULOSIS CARE

Abstract

The global tuberculosis (TB) and child health community has increasingly prioritized the childhood TB epidemic. In 2013, the childhood TB subgroup developed and published the first *Roadmap for childhood tuberculosis: towards zero deaths*, which has now been updated. The updated Roadmap for child and adolescent tuberculosis: towards ending TB provides an opportune moment to reflect on progress made at global, regional and country levels in scaling up response to childhood TB in the five years since the launch of the 2013 Roadmap. This document compiles examples of best practices at the global, regional and country levels since the launch of the 2013 Roadmap.

Key words

Tuberculosis – prevention and control
Paediatric tuberculosis
Child health
Best practices

Best practices in child and adolescent tuberculosis care

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Special thanks to all contributors who provided global, regional and country examples of childhood TB best practices:

Child and Adolescent TB Working Group Core Team: Farhana Amanullah (Chair); Ben Marais (Vice Chair); Stephen Graham; Shakil Ahmed; Eleanor Click; Anne Detjen; Anthony Enimil; Connie Erkens; Betina Mendez Alcântara Gabardo; Salvaceon Gatchalian; Anneke C Hesselning; Lindsay McKenna; YaDiul Mukadi; Rahab Mwaniki; Elizabeth Maleche Obimbo; Anna Scardigli; Valérie Schwoebel; James Seddon; Alena Skrahina.

Other contributors: Kidist Abayneh (WHO, Ethiopia); Jay Achar (MSF); Kechi Achebe (Save the Children); S Adeyemi (UNICEF, Nigeria); Yaw Adusi-Poku (NTP, Ghana); Feri Ahmadi (NIHRD Indonesia); AI Ahmed (Save the Children); Tahmeed Ahmed (ICDDR, Bangladesh); Yulia Aleshkina (KNCV, Kyrgyz Republic); Aksenova Valentina Aleksandrovna (MoH, Russian Federation); Ruhul Amin (Dhaka Shishu Hospital, Bangladesh); Baryshnikova Lada Anatolyevna (Samara Regional Clinical TB dispensary, Russian Federation); Vasilieva Lyudmila Anatolyevna (Yaroslavl Regional TB dispensary, Russian Federation); Laura Anderson (WHO); Denise Arakaki-Sanchez (NTP, Brazil); Dawit Assefa (Challenge TB, Ethiopia); Magnolia Arango Loboguerrero (Universidad Nacional de Colombia); Blen Ayele (NTP, Ethiopia); Irina Babchonak (Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus); Adama Bangoura (NTP, Guinea); Ahmed Bedru (Challenge TB, Ethiopia); Marion Biremon (KNCV, Kyrgyz Republic); Geoffrey Bisoborwa (WHO AFRO); João Antonio Bonfadini Lima (NTP, Brazil); Franck Bonsu (NTP, Ghana); Martin van den Boom (WHO EURO); Joanna Breitstein (TB Alliance); Mutsa Bwakura-Dangarembizi (University of Zimbabwe); Marcela Calle Paez (Universidad del Bosque, Colombia); Kevin Cain (CDC, Tanzania); Indrani Chakma (UNICEF, Malawi); Dick Chamla (UNICEF); Sharat Chandra Verma (former NTP, Nepal); Rebekah Chang (CHAI); Sarah Cook-Scalise (TB Alliance); Clemax Couto Sant' Anna (Federal University Rio de Janeiro, Brazil); Sheila Cunha Lucena (NTP, Brazil); Masoud Dara (WHO EURO); Abiola Davies (UNICEF Nigeria); Zewdu Gashu Dememew (Challenge TB, Ethiopia); Baronova Olga Dmitrievna (Stavropol regional TB dispensary, Russian Federation); Fernanda Dockhorn Costa (NTP, Brazil); John Paul Dongo (The Union, Uganda); Gunta Dravniece (KNCV); Aimgul Duishekeyeva (KNCV, Kyrgyz Republic); Augustin Dushime (NTP, Rwanda); Ismael Hassen Endris (WHO Ethiopia); Mohammed Farid (NTP Pakistan); Razia Fatima (NTP Pakistan); Erin Ferenchick (The Global Fund); Kathy Fiekert (KNCV); Mike Frick (TAG); Nicholas Furtado (The Global Fund); Tony Garcia Prats (Stellenbosch University, South Africa); Zewdu Gashu (Challenge TB, Ethiopia); Robert Gie (Stellenbosch University, South Africa); Philippe Glaziou (WHO); Daniele Gomes Dell' Orti (NTP, Brazil); Maria das Graças Rodrigues de Oliveira (NTP, Brazil); Tilaye Gudina (NTP Ethiopia); Andrews Gunda (CHAI, Malawi); Kassa Hailu (Addis Ababa City Administration, Ethiopia);

Meherunissa Hamid (Global Health Directorate, Pakistan); Ismael Hassen (WHO, Ethiopia); Rob van Hest (GGD Groningen, Netherlands); Binh Hoa (NTP Viet Nam); Abid Hossain Mollah (Ibrahim Medical College, Bangladesh); Henadz Hurevich (Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus); Hamidah Hussain (Global Health Directorate, Pakistan); Klevno Nadezda Ivanovna (MoH, Russian Federation); Luthful Kabir (Ad-deen Women's Medical College, Bangladesh); Abdulat Kadyrov (NTP, Kyrgyz Republic); Fred Kagwire (UNICEF, Uganda); Aakshi Kalra (FIND India); M Kambanje (Save the Children, Malawi); Maureen Kamene (NTP, Kenya); B Kaneka (Chancellor College, Malawi); Anteneh Kassa (NTP, Ethiopia); Lemma Ketema (Challenge TB, Ethiopia); Daniel Kibuga (WHO AFRO); Dzmitry Klimuk (Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus); Eveline Klinkenberg (Challenge TB, Ethiopia); R Kolola (MoH, Malawi); Kobto Ghislain Koura (The Union); Suvesh Kumar Shrestha (Save the Children, Nepal); Zita Lauska (Children's Clinical University Hospital, Latvia); Hailemariam Legesse (UNICEF, Ethiopia); Taye Letta (NTP, Ethiopia); Keri Lijinsky (USAID); Diana Lolong (NIHRD Indonesia); Thomas Lynch (TB Alliance; Steve Macheso (UNICEF, Malawi); Shelly Malhotra (TB Alliance); Enos Okumu Masini (WHO, Kenya); D Mbori Ngacha (UNICEF); Kimberly McCarthy (CDC Kenya); Corinne Merle (TDR); Patrick Migambi (NTP, Rwanda); Paul Milligan (LSHTM, UK); F Mpanga (UNICEF, Uganda); James Mpunga (NTP, Malawi); Frank Mugabe (NTLP, Uganda); Jules Mugabo (WHO, Rwanda); I Muhammad (Save the Children); Grace Mutembayire (NTP, Rwanda); Bakyt Myrzaliev (KNCV); Anna Nakanwagi (former The Union, Uganda); Jean-Louis Ndiaye (UCAD, Senegal); Anh Tuan Nguyen (NTP Viet Nam); Jürg Niederbacher Velasquez (Universidad Industrial de Santander, Colombia); Christo van Niekerk (TB Alliance); Moiseeva Natalia Nikolaevna (Stavropol regional TB dispensary, Russian Federation); Weston Njamwaha (KNCV, Malawi); Humphreys Nsona (MoH, Malawi); Jesca Nsungwa Sabiiti (MCH, Uganda); Nnamdi Nwaneri (The Global Fund); Andrea Maciel de Oliveira Rossoni (Clinical Hospital Complex of the Federal University of Paraná, Brazil); Iveta Ozere (Riga Eastern Clinical University hospital Centre for Tuberculosis and Lung Diseases, Latvia); Debadutta Parija (FIND, India); Colleen Pero (TB Alliance); Karina Pierantozzi Vergani (Hospital Clemente Ferreira, Brazil); Fátima Pombo (NTP, Brazil); Neeraj Raizada (Independent Consultant, India); Vija Riekstina (Riga Eastern Clinical University Hospital, Latvia); Elana Robertson (TB Alliance); Kefas Samson (WHO); Sanjay Sarin (FIND); Marie Sarr (NTP, Senegal; Cherise Scott (Unitaid); Moorine Penninah Sekadde (NTLP, Uganda); Kunju Shaji (independent consultant); Asim Shrestha (paediatrician, Nepal); Magassouba A Sidiki (NTP, Guinea); Charalampos Sismanidis (WHO); Aliaksandr Skrahin (Belarusian State Medical University); Rinn Song (University of Oxford/Harvard Medical School); Ainur Soorombaeva (KNCV, Kyrgyz Republic); Eric Swedberg (Save the Children); Lissanu Tadesse (FMoH Child Health, Ethiopia); Yared Tadesse (FMoH Child Health, Ethiopia); Ben Tegegn (WHO, Ethiopia); Aisalkun Teshebaeva (National Center of Phtizatry, Kyrgyz Republic); Nafissatou O. Toure (TB research task force, Senegal); Landry Tsague Dongmo (UNICEF); Sentayehu Tsegaye (Challenge TB, Ethiopia); Irina Usherenko (TB Alliance); Kazakov Alexey Vladimirovich (MoH, Russian Federation); Marieke van der Werf (ECDC); Eric Wobudeya (Mulago Hospital, Uganda); Getachew Wondimagegn (Challenge TB, Ethiopia); Zerihun Yaregal (Challenge TB, Ethiopia); Stella Zawedde (former The Union, Uganda); Elena Zdanova (National DR-TB expert committee, Kyrgyz Republic); Texas Zamasiya (UNICEF, Malawi).

Abbreviations and acronyms

aDSM	active TB drug-safety monitoring and management	The Global Fund/ GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
AFD	Agence Française de Développement	HERD	Healthy Ecosystems for Rangeland Development
AFRO	WHO Regional Office for Africa	HEW	health extension worker
BCG	Bacillus Calmette-Guérin	HIV	human Immunodeficiency virus
BDQ	bedaquiline	HMIS	Health Management Information System
BPA	Bangladesh Paediatric Association	HP	Isoniazid-rifapentin
CaP-TB	Control and Prevention of Tuberculosis	HRH	human resources for health
CDC	Centers for Disease Control and Prevention	iCCM	Integrated Community Case Management
CFZ	clofazimine	IGRA	interferon gamma release assay
CHAI	Clinton Health Access Initiative	IMCI	Integrated Management of Childhood Illness
CI	confidence interval	IMNCI	Integrated Management of Neonatal And Childhood Illness
DETECT Child TB	Decentralize Tuberculosis services and Engage Communities to Transform lives of Children with Tuberculosis	INH	isoniazid
DLM	delamanid	IPT	isoniazid preventive therapy
DGIS	Netherlands Ministry of Foreign Affairs	IOM	International Organization for Migration
DOTS	directly observed treatment (short-course)	ITR	individualized treatment regimen
DTG	dolutegravir	IUATLD (The Union)	International Union Against Tuberculosis and Lung Disease
ECDC	European Centre for Disease Prevention and Control	KNCV	KNCV Tuberculosis Foundation
EMA	European Medicines Agency	LTBI	latent TB infection
ERP	Expert Review Panel	LZD	linezolid
FAST	Find cases Actively, Separate temporarily and Treat effectively	MCCH	Maternal, Child and Community Health
FDC	fixed dose combination	MDR-TB	multidrug-resistant TB
FIND	Foundation of Innovative New Diagnostics	MoH	Ministry of Health
GDF	Global Drug Facility	MOQ	minimum order quantities
		MSF	Médecins Sans Frontières
		MUAC	mid upper arm circumference
		NATA	Nepal Anti-Tuberculosis Association

NEPAS	Nepal Paediatrician Society	SIAPS	Management Sciences for Health/ Systems for Improved Access to Pharmaceuticals and Services Program
NGO	nongovernmental organization	SLI	second-line injectables
NPA	nasopharyngeal aspirate	SMC	seasonal malaria chemoprevention
NSP	national strategic plan	STAG-TB	WHO Strategic and Technical Advisory Group for Tuberculosis
NTLP	National TB and Leprosy Programme	STEP-TB	Speeding Treatments to End Paediatric Tuberculosis
NTP	national TB programme	STR	standardized treatment regimen
NTC	national TB centre	TAG	Treatment Action Group
PAHO	Pan-American Health Organization	TB	tuberculosis
PBC	pulmonary bacteriologically confirmed	TB ARC	TB Accelerated Response and Care activity
PEPFAR	President's Emergency Plan For AIDS Relief	TB-SPEED	Strengthen Paediatric TB services for Enhanced Early Detection
PLHIV	people living with HIV	TPMAT	TB Procurement and Market Shaping Action Team
PMI	Peace Management Initiative	TST	tuberculin skin test
PMTCT	prevention of maternal to child transmission of HIV	TWG	technical working group
PQP	WHO's Prequalification Programme	UNDP	United Nations Development Programme
RH	rifampicin-isoniazid	UNICEF	United Nations Children's Fund
RMNCAH	reproductive, maternal, newborn, child and adolescent health	USAID	United States Agency for International Development
RNTCP	Revised National TB Control Programme of India	WHO	World Health Organization
RSSH	resilient sustainable systems for health	WPRO	WHO Regional Office for Western Pacific
SDGs	Sustainable Development Goals	XDR-TB	extensively drug-resistant TB
SEARO	WHO Regional Office for South- east Asia		

Preface

Tuberculosis (TB) in children and adolescents affects a vulnerable population, which can no longer be ignored. The *Roadmap for childhood tuberculosis: towards zero deaths*, published in 2013, provided a strategic framework to address the TB epidemic in children. Significant progress has been made since the first Roadmap was published. It is critical to reflect on the lessons learned in the implementation of interventions at local, national, regional and global levels, to allow replication and scale-up of best practices, and to identify any remaining challenges.

In the past five years, funding opportunities have been provided for responding to childhood TB through Unitaid, The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), United States Agency for International Development (USAID), the Russian Federation, among others. These investments have made it possible to gain better insight into the burden of TB, TB mortality and drug-resistant TB in children. This critical information has been used to bring childhood TB into the spotlight. A wide range of interventions is being implemented, using a lifecycle approach across the cascade of care for children exposed to persons with infectious TB, children with presumed TB disease and children who are diagnosed with and treated for TB. Interventions that integrate childhood TB prevention and care into general child health programmes, including maternal and child health, nutrition, human immunodeficiency virus (HIV) and other programmes, promote family- and people-centred care at all levels of the health system. Many successful examples have been described in this document.

Ending TB in children and adolescents is an integral part of the End TB Strategy, which is aligned with the Sustainable Development Goals (SDGs) and has defined milestones and targets to end the global TB epidemic. Achieving these targets requires provision of TB care and prevention within the broader context of universal health coverage.

Outstanding child and adolescent TB priorities include the need to: find the missing children with active TB and link them to TB care; prevent TB in children who are in contact with infectious TB cases (through implementation of active contact investigation and provision of preventive treatment); and advance integration within general child health services, including maternal and child health/ reproductive, maternal, newborn, child and adolescent health, HIV, nutrition and other programmes.

Programmatic and sustainable scale-up of successful projects and interventions needs to be a priority for health programmes, donors and partners.

We hope that the examples and best practices compiled in this document will stimulate and encourage political leaders, programme managers, health care workers, partners and funders to maintain the momentum in improving the response to child and adolescent TB in all steps of the care cascade – from being susceptible to TB infection to being cured.



Dr Tereza Kazaeva
Director, Global TB Programme
World Health Organization

Executive summary

Increasing advocacy and efforts to address childhood tuberculosis (TB) at global and country levels have brought the child and adolescent TB epidemic into the spotlight. Building on global strategies, the first *Roadmap for childhood tuberculosis: towards zero deaths* was developed by WHO and partners, under the guidance of the then Childhood TB Subgroup, and published in October 2013. The 2013 Roadmap laid out the strategic framework for the fight against childhood TB, aiming for zero TB deaths among children, highlighting ten key actions and the enhanced investment needed to address childhood TB.

In the light of this momentum, the current Child and Adolescent TB Working Group has updated the 2013 Roadmap to *Roadmap for child and adolescent tuberculosis: towards ending TB*. The updated Roadmap provides an opportune moment to reflect on progress made at global and country levels in scaling up the response to childhood TB in the five years since the launch of the first Roadmap.

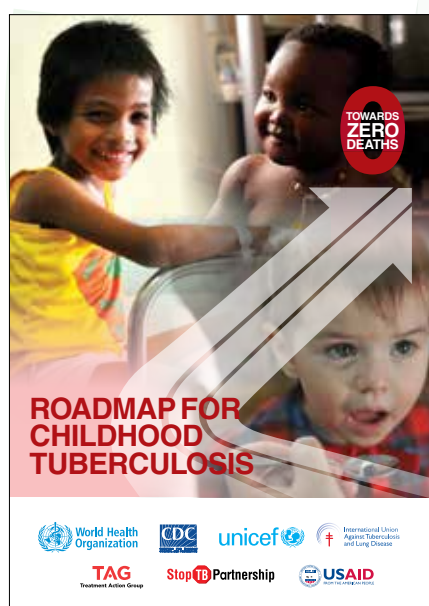
This document compiles examples of best practices at global, regional and country levels since the launch of the first edition of the Roadmap. It describes 36 examples from 24 countries (including 10 TB, two multidrug-resistant TB (MDR-TB) and four TB/ human immunodeficiency virus (HIV) high burden countries) from all the six WHO regions, two regional initiatives and 12 global initiatives. The examples are categorized according to the ten key actions from the 2013 Roadmap.

Introduction

Background

The childhood tuberculosis (TB) epidemic entered the global spotlight, with increasing advocacy, attention and efforts to address childhood TB at global and country levels, led by the Childhood TB Subgroup (established in 2003 as part of the directly observed treatment, short-course (DOTS) Expansion Working Group of the Stop TB Partnership). Historically, the global TB community and the health community have neglected childhood TB, in general. The neglect can be explained by the difficulties in confirmation of a TB diagnosis in children, poor recording and reporting practices as well as misperceptions of childhood TB as a low public health priority and of addressing the childhood TB epidemic by simply containing TB in adults. A misplaced reliance on the protective efficacy of the Bacillus Calmette-Guerin (BCG) vaccine, a lack of research and investment, and a lack of advocacy are additional challenges.

Recent estimates indicate that over one million children under 15 years of age fall ill with active TB disease each year, and 253 000 children (including 52 000 children living with human immunodeficiency virus (HIV) die of this curable and preventable disease. Only 46% of the estimated number of cases are reported by national TB programmes (NTPs) around the world, leaving a gap of over 580 000 children who are not diagnosed, treated and/or reported each year (1).



Building on global strategies (the Stop TB Strategy in 2006 and the recent End TB Strategy as well as the global child survival movement), the first *Roadmap for childhood tuberculosis: towards zero deaths* was developed by WHO and partners, under the guidance of the then Childhood TB Subgroup, and published in October 2013. The 2013 Roadmap laid out the strategic framework for the fight against childhood TB, aiming for zero TB deaths in children, highlighting 10 key actions and the enhanced investment needed to tackle childhood TB (2).

As part of the Sustainable Development Goals (SDGs), the world has committed to ending preventable deaths in children by 2030. Addressing childhood TB is critical in order to achieve this goal. In September 2018, world leaders will renew their commitment to ending TB during the first ever United Nations General Assembly on Tuberculosis (3).

In the light of this momentum, the Child and Adolescent TB Working Group has developed an updated version of the 2013 Roadmap – the *Roadmap for child and adolescent tuberculosis: towards ending TB*.

The updated Roadmap provides an opportune moment to reflect on progress made at global, regional and country levels in scaling up the response to childhood TB in the five years since the launch of the first Roadmap.

Best practices

This document describes progress, best practices and lessons learnt against the original 10 key actions outlined in the 2013 Roadmap.

All WHO regional offices were approached to request contributions and a list was compiled of possible examples of best practices, sourced from reports, published papers and presentations. Potential contributors at global, regional, national and local levels were then invited to submit examples of best practices using a standardized template.

Selection criteria for the contributions included:

- Coverage of all key actions from the 2013 Roadmap
- Coverage of all WHO regions
- Availability of detailed information
- Relevance to one or more of the key actions
- Sustainability and/or possibility for scale-up
- Partnership
- Community involvement
- Impact and/or outcomes.

None of the submitted contributions were rejected.

FIGURE 1: THE 10 KEY ACTIONS FROM THE 2013 ROADMAP FOR CHILDHOOD TUBERCULOSIS



1. Include the needs of children and adolescents in research, policy development and clinical practice



2. Collect and report better data, including on preventive measures



3. Develop training and reference materials on childhood TB for health care workers



4. Foster local expertise and leadership among child health workers at all levels of the health care system



5. Do not miss critical opportunities for intervention



6. Engage key stakeholders



7. Develop integrated family- and community-centred strategies to provide omprehensive and effective services at the community level



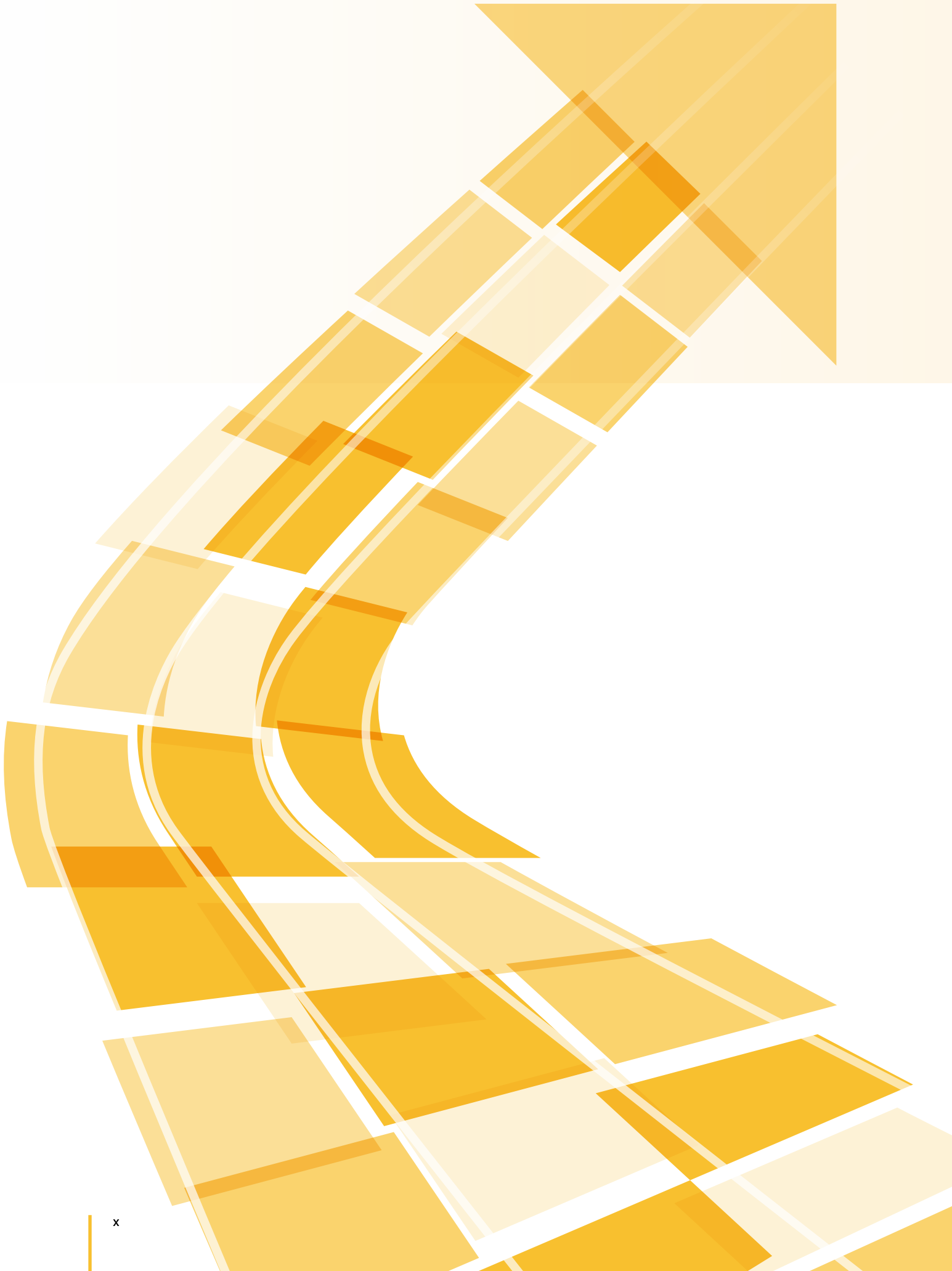
8. Address research gaps



9. Meet funding needs for childhood TB



10. Form coalitions and partnerships to study and evaluate the best strategies for preventing and managing childhood TB, and for improving tools used for diagnosis and treatment





1 Include the needs of children and adolescents in research, policy development and clinical practice

2013 Roadmap for childhood tuberculosis:

- ▶ Ensure inclusion of the needs of children and adolescents in the three pillars of public health: scientific research, policy development and the implementation of appropriate clinical practices.
- ▶ The End TB Strategy is a critical opportunity for addressing childhood TB, but the lack of robust national baseline data for children makes it impossible to set targets for childhood TB.
- ▶ Broaden the strategy from a traditional, vertically delivered public health approach to a more horizontal one, providing an important platform from which to engage the broader child health community.
- ▶ NTPs to develop a framework to support activities addressing childhood TB, including “knowing your epidemic”; evidence-based and relevant policies; identification of priorities and gaps; continued surveillance; training of health care workers; implementation of care strategies for children with TB; operational research; assessment of funding needs; assignment of responsibilities and ensuring accountability; provision of leadership and partnership with all stakeholders; communication across the entire health sector.

1.1. WHO Child and Adolescent TB Working Group

Global

Contributors: Farhana Amanullah, Chair of the Working Group

Core team members: Ben Marais, Vice Chair; Stephen Graham, past Chair; Shakil Ahmed; Eleanor Click; Anne Detjen; Anthony Enimil; Connie Erkens; Betina Mendez Alcântara Gabardo; Salvaceon Gatchalian; Anneke C. Hesseling; Hannah Kirking; Lindsay McKenna; YaDiul Mukadi; Rahab Mwaniki; Elizabeth Maleche Obimbo; Anna Scardigli; Valérie Schwoebel; James Seddon; Alena Skrahina

Background

The Childhood TB Subgroup was first established as a subgroup of the Stop TB Partnership's DOTS Expansion Working Group in 2003, in response to the almost total neglect of TB among children within global and national TB control programme activities and priorities.

Among the first achievements of the subgroup was the publication of the first WHO *Guidance for national tuberculosis programmes on the management of tuberculosis in children* in 2006. The Childhood TB Subgroup also successfully lobbied to have children reported to WHO by NTPs in two age categories (0–4 years and 5–14 years) for *all* forms of TB (i.e. not limited to sputum smear-positive TB).

With the expansion of the global TB strategy from the DOTS strategy to the broader Stop TB Strategy in 2006, children were explicitly included for the first time as a “vulnerable population” in need of increased case finding. The number of members and representation from TB endemic countries began to grow steadily from that time until the first international child TB meeting which was held by Stop TB Partnership and European Centre for Disease Prevention and Control (ECDC) in Stockholm in 2011, after which there was acceleration in the growth of the Childhood TB Subgroup with expansion in geographical representation.

In January 2017, the subgroup received full Working Group status and became known as the Child and Adolescent TB Working Group. The Working Group is funded by US Agency for International Development (USAID) through the Stop TB Partnership.

Description

The objectives of the Working Group are to promote research, policy development, formulation and implementation of guidelines, mobilization of human and financial resources, and collaboration with partners working in relevant fields (including maternal and child health, the extended programme on immunization, and HIV) to achieve the goal of decreased childhood TB mortality and morbidity.

Activities

- Provision of global leadership on child and adolescent TB.
- Advocacy for the inclusion of the needs of children and adolescents in research, policy development and clinical practices in line with the WHO post-2015 strategy and targets, including the development of integrated family- and community-centred health services.
- Contribution to the development of evidence-based guidance, training and reference materials for health care workers (specific to infants, children and adolescents), which can be adapted to various country situations and assist national TB programmes with training.
- Provision of input on the management of children and adolescents with TB during national TB programme reviews.
- Provision of technical assistance to country programmes.
- Promotion of key stakeholder engagement in addressing child and adolescent TB.



- Encouraging countries to include the funding requirements for child-specific TB interventions in their national TB strategic plans.
- Holding annual meetings at The International Union Against Tuberculosis and Lung Disease (The Union) Global Lung Health conference.
- Dissemination and sharing of important contributions, progress and successes.
- Support and participation in regional and national child TB task forces or working groups.



Annual Child and Adolescent TB Working Group meeting, Kigali, Rwanda, October 2017 | Photo credit: S Verkuijl

Outcomes/successes

- Membership (external members) increased from 54 in 2007 to 142 in 2013 (just after the launch of the 2013 Roadmap) to 313 in May 2018.
- Development and publication of WHO child TB guidelines, 2006 and 2014.
- WHO rapid advice 2010 with increased recommended dosages of first-line TB treatment in children.
- International Child TB Meeting, Stockholm, 2011.
- First global estimates of TB in children published in the *Global tuberculosis report 2012*.
- Child TB included in WHO and stakeholder monitoring missions.
- Recommended composition of dispersible fixed-dose combination (FDC) therapy for children (Stellenbosch, South Africa 2012).
- Collaborated closely with the TB Alliance in the Unitaied-funded Speeding Treatments to End Paediatric Tuberculosis (STEP-TB) project to develop child-friendly FDCs launched in Cape Town, 2015.
- Represented child TB as WHO Strategic and Technical Advisory Group for Tuberculosis (STAG-TB) member through the development of the End TB Strategy: 2012–2016.
- Acquired and implemented the first TB REACH grant specific for children.
- Contributed to multiple WHO guidelines, including recent development of WHO latent TB infection (LTBI) management guidelines 2018.
- Development of training tools and modules in collaboration with The Union.



Lessons learned

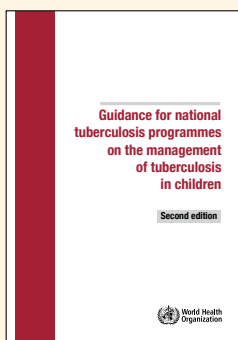
- High TB burden countries rely on global guidance updates, tools and technical assistance and are eager to have child and adolescent TB specifically addressed in their national strategic plans.
- National TB Champions are instrumental in bridging the wide policy to practice gap at the country level.
- Ongoing mentoring by global, regional and national child TB advisers is critical to maintain momentum.

Challenges/outstanding issues to be addressed

- Integration of child TB with other primary care child and adolescent health platforms has not yet been effectively achieved, with child TB still largely centralized to major cities and tertiary care setups in most high burden countries.
- Lack of training/sustained mentoring at all levels of the health-care cascade and efficient use of human resources remain a challenge in high burden settings.
- Effective TB prevention and scale-up continue to be low priority in strategic plans.
- Use of national and local data to inform funding proposals and policy remains suboptimal.

1.2. Updated guidance on child and adolescent TB

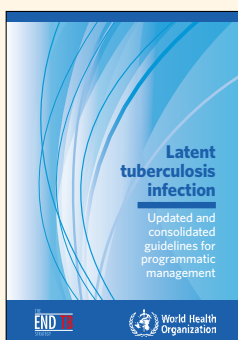
The first edition of the *Guidance for national tuberculosis programmes on the management of tuberculosis in children* was published in 2006. These guidelines assisted countries to revise or develop national guidelines for childhood TB management. New evidence and recommendations necessitated an update of the original 2006 guidance and the second edition of the Guidance was published in 2014 (4). This document included new recommendations on various aspects of childhood TB management, including the use of Xpert MTB/RIF as the initial diagnostic test, updated dosages of anti-TB medicines for the treatment of TB in children, treatment of severe forms of TB in children, BCG vaccination, contact screening and management, isoniazid preventive therapy (IPT), HIV testing, management of TB in children living with HIV, management of drug-resistant TB in children and recording and reporting of children treated for TB in one of two age bands.



World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. 2018.

WHO/CDS/TB/2018.4

<http://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf;jsessionid=6322C92636AB0E37FC4629311EEDB804?sequence=1>



Guidance for national tuberculosis programmes on the management of tuberculosis in children. Second edition. Geneva: World Health Organization; 2014.

WHO/HTM/TB/2014.03

<http://apps.who.int/medicinedocs/documents/s21535en/s21535en.pdf>



In 2018, WHO published the updated and consolidated guidelines for programmatic management on latent TB infection (LTBI), recommending scaling up access to testing and treatment for TB infection, especially among groups who are particularly at risk, such as small children and people living with HIV (5). These consolidated LTBI guidelines increase the number of groups being prioritized for LTBI testing and treatment, testing options and treatment options. It includes new recommendations on preventive treatment for adolescents living with HIV, IPT for infants aged less than 12 months living with HIV with a TB contact, IPT for children aged 12 months or more living with HIV without TB contact, and children living with HIV who successfully completed TB treatment. The document also covers TB preventive treatment in HIV-negative household contacts, with a new recommendation on preventive treatment in children aged five years or more and adolescents who are TB contacts. Recommendations were updated on algorithms to rule out active TB disease in infants, children and adolescents living with HIV, as well as HIV-negative household contacts aged five years or more. New recommendations on treatment options for latent TB infection were incorporated, including alternatives to isoniazid monotherapy for six months: rifampicin plus isoniazid daily for three months; and rifapentine and isoniazid weekly for three months in countries with a high TB incidence. Lastly, a new recommendation was included on preventive treatment of high-risk household contacts (including children below five years of age and people living with HIV) of patients with multidrug-resistant TB (MDR-TB).







2 Collect and report better data, including on preventive measures

2013 Roadmap for childhood tuberculosis:

- ▶ Inclusion of children in all TB surveillance activities.
.....
- ▶ Reporting of TB cases by age, sex, disease type, HIV status and treatment outcome.
.....
- ▶ Collaboration with child health services (including private sector) to improve reporting of childhood TB cases.
.....
- ▶ Reviews and assessments of the burden of TB in children and adolescents; over- and under-diagnosis of TB in children; promotion of electronic recording and reporting systems; evaluation and research on active contact management; evaluation of integration of TB activities into maternal, newborn and child health services.
.....

2.1. Childhood surveillance data

Global

Contributors: Charalampos Sismanidis;¹ Steve Graham;² Cherise Scott;³ Malgorzata Grzemska;¹ Annemieke Brands¹

¹ Global TB Programme, World Health Organization; ² The Union Against Tuberculosis and Lung Disease;

³ Unitaid (former TB Alliance)

The Call to Action for Childhood TB in March 2011 kick-started the work on childhood TB disease burden estimates. A first set of global estimates for TB incidence and TB mortality was published in the WHO *Global tuberculosis report 2012*, with an accompanying description on why such estimates were challenging, as well as a clearly laid out course of action for improving them. The first step in this action plan was to convene a consultation of all relevant stakeholders. In early 2013 the Unitaid funded STEP-TB project, co-led by the TB Alliance and WHO was launched to increase access to quality-assured, affordable TB drugs in suitable doses for children in countries with a high burden of TB (see sections 8.1.1 and 10.1). The project invested heavily in establishing a market for childhood TB and at the same time improved epidemiological estimates of TB disease burden specifically for children.

The STEP-TB funded a global consultation (held in New York, USA in September 2013) that was attended by academia, national TB programmes and leading experts in the field. The main aim of the consultation was to further develop analytical methods and define and prioritize actions needed to obtain new, robust, nationwide, age-specific data. Throughout 2014 different estimation methods for childhood TB disease burden, which were presented and discussed during the global consultation, were published in peer-reviewed journals providing heterogeneous results.

In September 2014 in Bali, Indonesia, a protocol development workshop was held for national TB inventory studies to generate much needed data on under-reporting of childhood TB. In 2015, an attempt was made to consolidate the different estimation methods statistically and publish a single set of estimates supported by the whole TB community. A combined approach was used, in which estimates from case notifications, adjusted for under-detection and under-reporting, were combined with estimates from dynamic modelling. In 2016, detailed burden estimates were produced and published by WHO at the regional level.

In 2017, TB burden estimates were produced at the country level with full age (0–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65+) and sex disaggregation, as well as disaggregation by HIV-status (1). Lastly, in 2018, results available from three large nationwide TB inventory studies in Indonesia, Pakistan and Viet Nam will feed into the estimation process, and further disaggregation into 0–4/5–14 will be published. The figures 2.1 and 2.2 below summarize the chronological milestones in the process of improving childhood TB estimates and global progress in reporting of age-disaggregated TB case notification (including children).

FIGURE 2.1: CHRONOLOGY OF MILESTONES TOWARDS IMPROVING CHILDHOOD TB BURDEN ESTIMATES

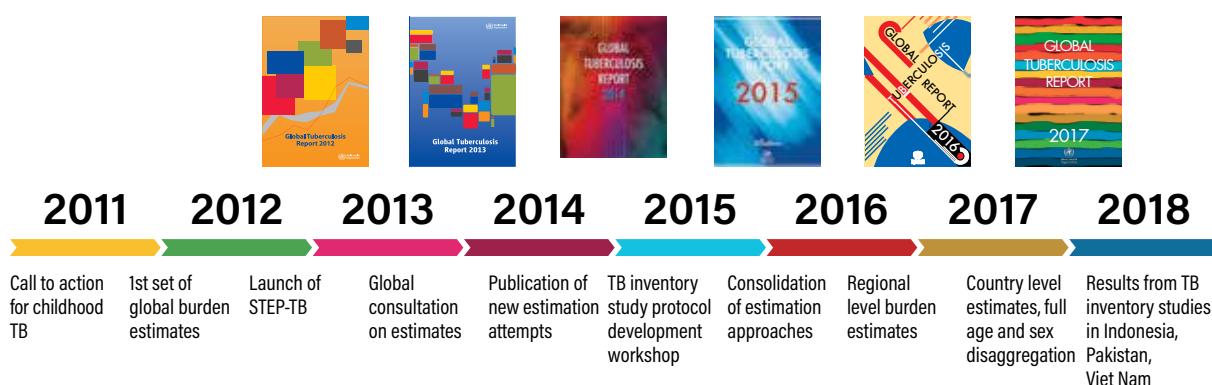
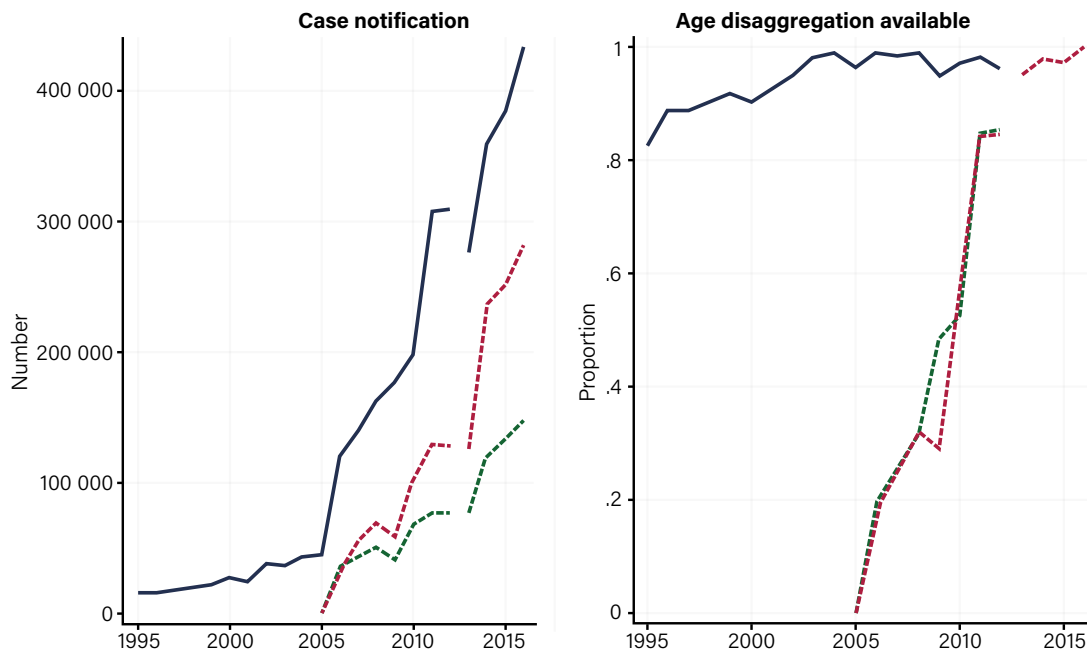


FIGURE 2.2: GLOBAL PROGRESS IN REPORTING OF TB CASES AMONG CHILDREN, 1995–2015



Left panel: Number of notifications of cases among children reported to WHO (blue: 0–14, red: 5–14, green: 0–4). Right panel: Percentage of case notifications reported to WHO that are age-disaggregated (blue: new smear positive, green-dashed: new smear-negative and smear not done, red dash: new extra-pulmonary, red: new and relapse all forms).

Note: Before 2013, childhood case notifications include smear-positive, smear-negative, smear not done and extra-pulmonary TB for all new patients. After 2013 (shown as a gap in the graph) childhood case notifications include all new and relapse cases irrespective of case type.

Source: Methods used by WHO to estimate the global burden of TB disease. Geneva: World Health Organization; 2017 (http://www.who.int/tb/publications/global_report/gtbr2017_online_technical_appendix_disease_burden_estimation.pdf, accessed 18 August 2018).

2.2. The global epidemiological burden of childhood TB: current status

Global

Contributors: Charalampos Sismanidis and Sabine Verkuijl

Global TB Programme, World Health Organization

For the first time, the estimates of the global burden of childhood TB that were included in the *Global tuberculosis report 2012* were based on the number of reported TB cases among children in some countries, extrapolated to non-reporting countries, and the case detection rate for all TB cases globally. The estimates for the year 2011 were that 490 000 children under the age of 15 years developed TB every year (or 6% of the 8.7 million estimated incident cases). To address existing data gaps and improve understanding of burden estimates, complementary methodological approaches were used to evaluate the burden of childhood TB disease, childhood TB mortality and drug-resistant TB in children.

Updated estimates for the burden of childhood TB, drug-resistant TB and mortality played a critical role in the recognition of the importance of this key population in global TB control.

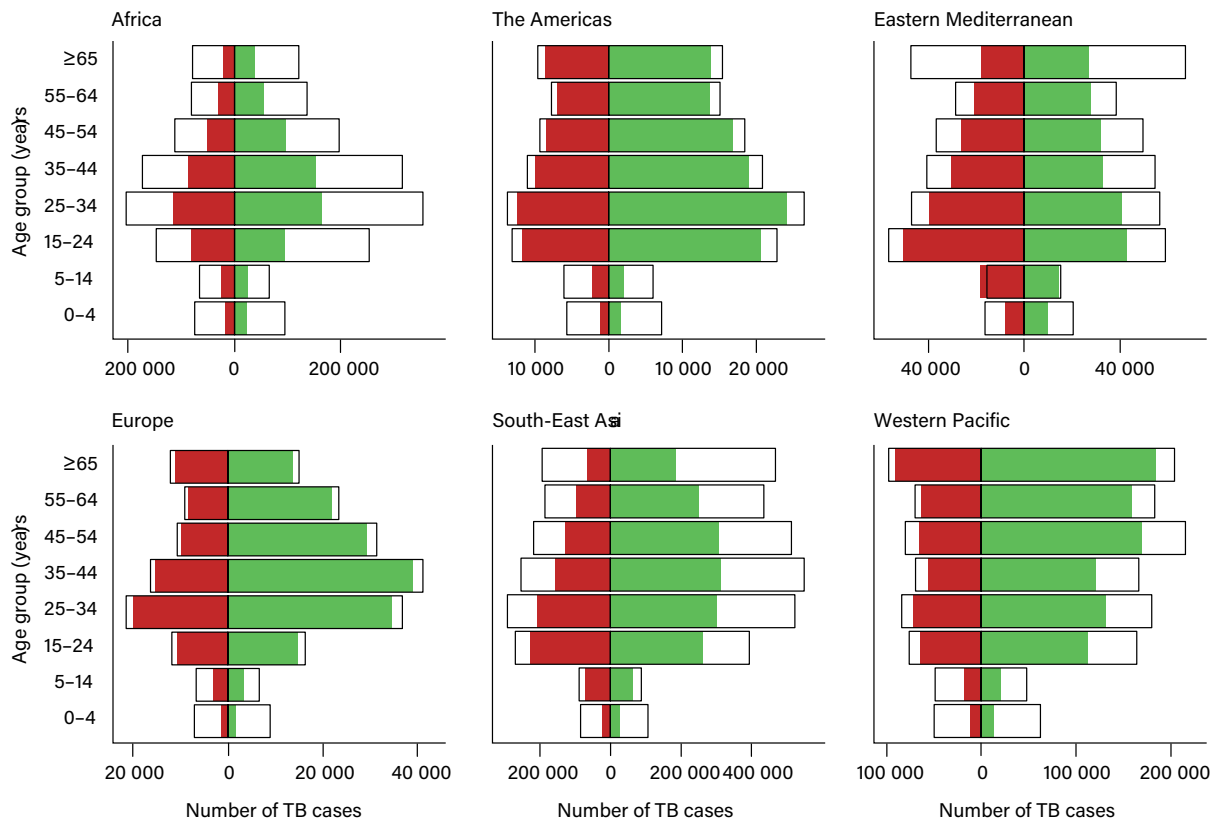


Child TB incidence

The first attempt (6) to estimate the burden of childhood TB with a mechanistic model, used prevalence of TB in adults to estimate rates of infection and disease in children in 22 high-burden countries, accounting for 80% of the global caseload. In 2010, the estimated median number of children who developed *M. tuberculosis* infection was over 7.5 million, with over 650 000 developing active TB disease in these 22 countries. The cumulative number of children with TB infection was estimated at over 53 million. The model suggested that only 35% of childhood TB cases were detected (in 15 of the 22 countries that reported childhood TB notifications). Particularly in young children, the incidence of TB was shown to be much higher than the number of notifications. The estimates of household exposure and cumulative infection highlighted the need for scaling up preventive treatment.

Estimates of TB incidence in children under 15 years reported in the *Global tuberculosis report 2017* were based on case notifications, adjusted for under-diagnosis and under-reporting, combined with estimates derived from dynamic modelling. Results for the 0–14 age group (broken down into the age groups 0–4 and 5–14 years) in each country were then further disaggregated using outputs from an established deterministic model, followed by disaggregation by sex based on results from a meta-analysis of the male-to-female notification ratio.

FIGURE 2.3: REGIONAL ESTIMATES OF TB INCIDENCE AND CASE NOTIFICATIONS DISAGGREGATED BY AGE AND SEX, 2016



Estimates of TB incidence (black line) and case notifications disaggregated by age and sex (female in red; male in green) for the six WHO regions for 2016. Source: WHO *Global tuberculosis report*, page 57.

Child drug-resistant TB incidence

A second modelling study (7) estimated that 850 000 children developed TB disease globally in 2014, including 58 000 with isoniazid mono-resistant TB, 25 000 with MDR-TB, and 1200 with extensively



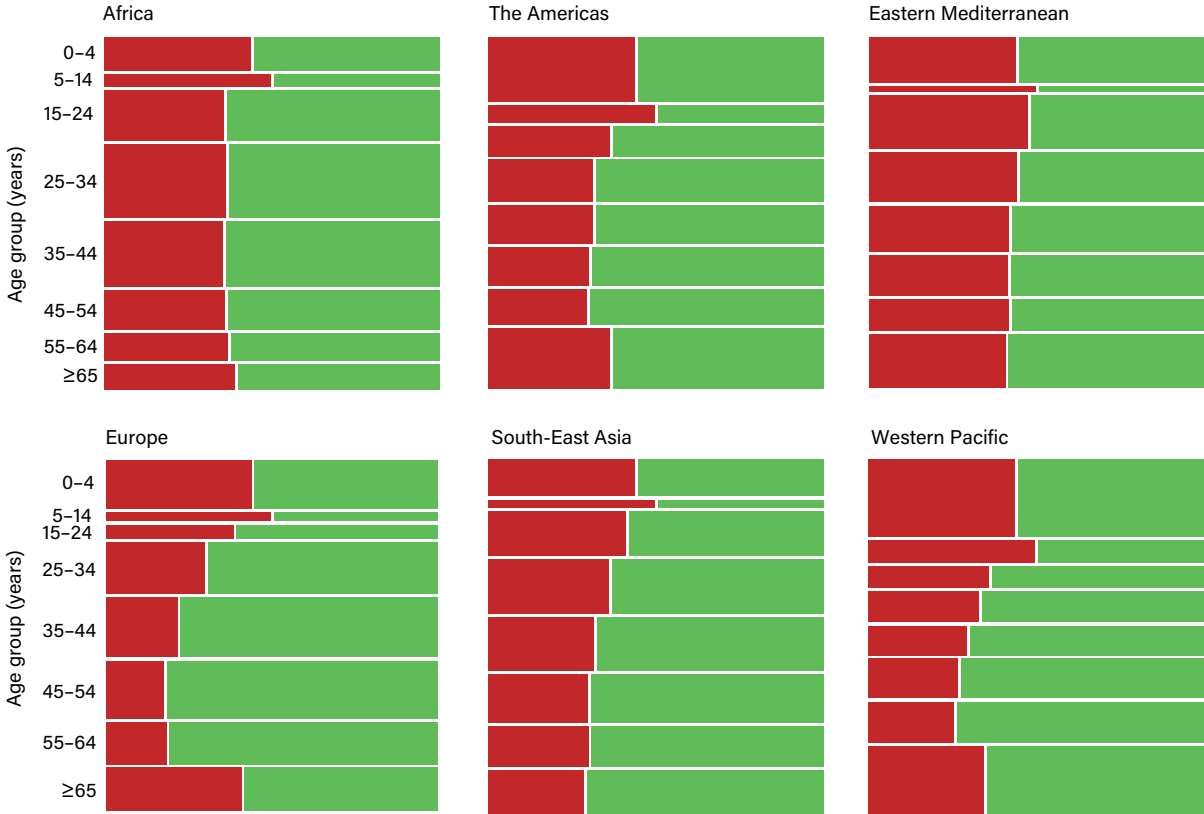
drug-resistant TB (XDR-TB). The study estimated 67 million children to be infected with *M. tuberculosis*, including 5 million with isoniazid mono-resistance, 2 million with MDR-TB, and 100 000 with XDR-TB.

Child TB mortality

A third mathematical modelling study (8) provided estimates for paediatric TB mortality. It estimated that 239 000 children under the age of 15 years died from TB worldwide in 2015, including 80% children under the age of five years. More than 70% of deaths occurred in the WHO South-east Asia and Africa regions. It was also estimated that 17% of paediatric TB deaths (39 000) globally were in HIV-positive children, of which 36% (31 000) occurred in the WHO Africa region. Over 96% (230 000) of all TB deaths occurred in children who were not receiving TB treatment.

In the *Global tuberculosis report 2017*, TB mortality was disaggregated by all age groups and two age groups in children (0–4, 5–14) using the dynamic modelling approach, and then disaggregated by sex, assuming that the male-to-female ratio was the same as that for incidence.

FIGURE 2.4: REGIONAL DISTRIBUTION OF TB MORTALITY IN HIV-NEGATIVE PEOPLE BY AGE GROUP AND SEX, 2016



Regional distribution of TB mortality in HIV-negative people by age group and sex (female in red; male in green), 2016. The total area represents TB mortality and all rectangles are proportional to their share of total TB mortality by region.

Child TB contacts

In the first dynamic modelling study (6), it was estimated that in 2010, the median number of children (under five years of age) who developed *M. tuberculosis* infection was over 2.6 million in the 22 high TB



burden countries. The cumulative number of children (under five years of age) with TB infection in these countries was estimated at over 6.5 million.

The *Global tuberculosis report 2017* stated that an estimated 1.3 million children under five years of age globally were household contacts of bacteriologically confirmed pulmonary TB cases and were eligible for TB preventive treatment according to current policy recommendations in 2016. Of these, only 13% were reported to have been started on TB preventive treatment (1).

The number of child household contacts eligible for LTBI treatment is defined as the number of children under five years of age who are household contacts of bacteriologically confirmed pulmonary TB cases with confirmed LTBI (in low burden countries) or without LTBI testing (in high burden countries). The following parameters were used for these estimates (9): number of notified bacteriologically confirmed pulmonary TB cases; national proportion of children under five years of age; and national average household size. Prevalence of LTBI among child household contacts under five years of age and average size of the TB cluster per household were estimated by conducting a systematic review of literature and meta-analyses. The proportion of children with active TB among those who had a household contact with TB cases was calculated using number of children sharing the household with an individual with TB and number of children developing active TB disease estimated in the first modelling study (6).

Methods for setting child-focused TB care targets

In order to allocate resources for contact investigations, national TB programmes need to know how many children require care. In 2016, two methods to estimate the number of child contacts aged 0–14 years who need to be evaluated and treated were published (10).

The first method combines local data using simple formulas, based on the number of children in a certain age group, the number of households and the number of adults with pulmonary TB reported in the previous year. From here, the number of children requiring evaluation for active TB disease and those requiring preventive treatment can be estimated.

The second method uses publicly available data (such as data from demographic and health surveys and the World Bank) to estimate the number of children per household. It then combines these results with case notifications and risk estimates of disease and infection.

Based on 2014 adult case notifications, it was estimated that over 2.4 million children aged below five years, and over 5 million children aged 5–14 years need to be evaluated for active TB every year globally, because they live in households with an adult with pulmonary TB. Of these, almost 240 000 child contacts aged below five years and over 400 000 child contacts aged 5–14 years are expected to have active TB disease at the time of contact investigation. Almost 850 000 child contacts aged below five years and over 2.6 million child contacts aged 5–14 years are expected to have TB infection without disease.

This work shows that it is feasible to use available data to set programmatic evaluation, treatment and prevention targets to improve care for child contacts of TB patients.

Lessons learned

The lack of child-appropriate tools to confirm diagnosis of TB disease, standard case-definitions, and the incomplete recording and reporting of children that are diagnosed with TB and put on treatment continue to pose significant shortcomings to the robust estimation of burden due to TB in children. Despite that, remarkable progress has been made since the first official set of WHO estimates for childhood TB was published in 2012. In the five years since then, appropriate global focus has been given to childhood TB, and global interest to improve these burden estimates has been ignited with countries around the world improving their recording and reporting practices for age-disaggregated data. Multiple collaborating research groups are working with WHO to improve understanding of TB disease burden in children. For the first time ever, a number of high priority countries in Asia have implemented national scale studies to measure the level of TB under-reporting in children.



The key contributions to the improvement of the estimation of TB incidence among children include:

- Promotion of case-based electronic recording and reporting systems that facilitate the compilation and analysis of age-disaggregated data at national and subnational levels.
- Implementation of nationwide inventory surveys in high priority countries to measure under-reporting of childhood TB.
- Intensified household contact-tracing activities of index adult TB cases, as well as the integration of TB activities in maternal, newborn and child health services, to identify childhood cases that otherwise go undiagnosed.

2.3. Inventory studies on under-reporting of childhood TB

Countries: Indonesia, Pakistan, Viet Nam

Contributors: Charalampos Sismanidis;¹ Razia Fatima;² Feri Ahmadi;³ Diana Lolong;³ Mohammed Farid;² Anh Tuan Nguyen;⁴ Binh Hoa;⁴ Rob van Hest;⁵ Kunju Shaji;⁶ Laura Anderson;¹ Philippe Glaziou¹

¹ World Health Organization; ² NTP Pakistan; ³ NIHRD Indonesia; ⁴ NTP Viet Nam; ⁵ Regional Public Health Service Groningen, the Netherlands; ⁶ Independent consultant

Background

TB in the three countries

Indonesia	Pakistan	Viet Nam
<p>Indonesia is among the top-five countries with the highest TB burden in the world; and an estimated TB incidence of 1 020 000 cases per year (1). However, only 360 565 were notified in 2016 (treatment coverage 35%) (national database, 2016), with a low contribution of private providers in TB case notification (Indonesia NSP 2016–2020).</p> <p>The 2013–2014 national TB prevalence survey found that 56% of people on TB treatment were not reported to the web- and case-based electronic recording and reporting system called Surveillance Integrated Tuberculosis Information system.</p> <p>Since 2016 it is mandatory for all health facilities to notify TB cases.</p>	<p>Pakistan has an estimated TB incidence of 518 000 cases, at a rate of 268 per 100 000 (1). Treatment coverage was 69% in 2016.</p> <p>An adult inventory study, conducted in 2011, provided evidence for under-reporting of 27%. The unregulated private sector contained a big pool of missing cases. The notified proportion for child TB among all notifications was 12.6% in 2016. Childhood TB is relatively neglected in the country because of its atypical presentation and challenging diagnosis. Therefore, it was expected that the under-reporting of childhood TB would be high.</p>	<p>Viet Nam has an estimated TB incidence of 126 000 cases, at a rate of 133 per 100 000 (1). Treatment coverage was 81% in 2016.</p> <p>NTP providers routinely collect patient data in paper-based registers, which are then entered in the electronic, web-based, case-based Viet Nam TB Information Management Electronic System (VITIMES). Non-NTP providers are required by law to refer or report TB cases to the NTP, but the extent to which this happens is unknown.</p>

TB inventory studies

TB inventory studies provide a customized and more cost-effective alternative to population-based cohort studies and community-based prevalence surveys to quantify detection and report gaps. Inventory studies have two broad objectives: (i) to directly measure levels of under-reporting of detected TB cases; and (ii) to estimate TB incidence through capture-recapture analysis (under certain conditions).



National TB inventory studies can have a retrospective or prospective design. The retrospective design is most feasible in resource-rich settings and uses the national surveillance register alongside other existing national case-based TB-related databases. The prospective design is likely to be useful in most resource-limited settings and requires the creation of additional study registers from a representative national sample of health-care providers who diagnose and/or treat TB. Both designs then link individual records in the national TB surveillance register with those in other databases and/or study registers.

Results from inventory studies have provided a platform and evidence for making programmatic changes to improve the performance of TB surveillance.

Description

Indonesia	Pakistan	Viet Nam
<p>The main objective of the inventory study was to estimate the level of under-reporting of TB cases in the national surveillance system. Specific objectives included: understanding of the relative contribution of health care facility type to TB treatment and under-reporting, as well as assessment of under-reporting by age, sex, geographical area and facility type. Twenty-three districts were selected for the inventory study. Data on TB cases diagnosed by all health care providers within the selected districts was collected prospectively for three months (January to March 2017). Records were linked with the NTP case-based databases to estimate under-reporting.</p>	<p>The primary objective of the inventory study was to quantify the level of under-reporting of diagnosed childhood TB cases to the national surveillance system. Secondary objectives included: facilitating the establishment of linkages between different types of health care facilities and the NTP, as well as describing case management practices of childhood TB to public and private providers.</p> <p>The survey was conducted in all health care facilities (treating at least one childhood TB case in the last quarter) in 12 randomly selected districts, with data collection from April to June 2016.</p>	<p>The main objective of the inventory study was to estimate the level of under-reporting of paediatric and adult TB in the national surveillance system, including from paper registers and non-NTP partners.</p> <p>Prospective, longitudinal surveillance was conducted for diagnosed incident TB cases in 12 randomly selected provinces and five randomly selected districts in Ho Chi Minh City from October to December 2016. NTP data were collected retrospectively from the VITIMES system.</p>

Outcomes/successes

Indonesia:

There were 21 320 TB cases (68% in the public sector, 28% in the private sector and 4% in laboratories, of which 17.8% were aged below 15 years, with 2.5% confirmed bacteriologically and 97.5% diagnosed clinically. When matching the findings with NTP data, it was found that 41% of cases were under-reported by the NTP. For the below 15 years age group, under-reporting was 54%. Clinically diagnosed patients, patients with extra-pulmonary TB and children were more likely to be under-reported. Of the “missing cases”, two thirds were detected but not reported and one third was not detected. Adherence to national treatment guidelines was 84% nationally.

Viet Nam:

A total of 8528 TB cases were identified (66% NTP, 24% public non-NTP and 9% private). Of these, 207 (2.4%) were aged below 15 years, with 8.2% confirmed bacteriologically and 91.8% diagnosed clinically. When matching the findings with NTP data, it was found that 19.8% of cases overall were under-reported by the NTP. For the below 15 years age group, under-reporting was 35.2%.

Pakistan:

A total of 5249 cases of childhood TB were diagnosed (88% clinically) among 7125 children with presumptive TB. The level of under-reporting was 78%; the vast majority among non-NTP providers.



Implications

In Pakistan and Viet Nam, the private health sector has grown rapidly, and TB drugs are available in private pharmacies. The inventory studies clearly identified the need to strengthen TB surveillance and scale up public–public and public–private mix interventions to address high levels of under-reporting from these sectors. The results also informed the development of national strategic plans (NSPs) and funding proposals submitted to The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). In Pakistan, improvements have been noted in child TB notifications from Punjab since the results of the inventory study were shared.

Lessons learned

- TB inventory studies measure the performance of TB surveillance by capturing information on all detected TB cases from different types of health care providers, providing insight on corrective actions required to improve reporting coverage.
- TB inventory studies produce national data on the level of under-reporting (and trends thereof if repeated).
- Under certain conditions, through capture-recapture modelling, inventory studies also provide an important alternative to the indirect estimation of TB incidence. In many endemic countries, this is currently the only option to provide direct measurements needed to improve the understanding of and response to the TB burden in children,
- TB inventory studies provide valuable insights into the health care seeking behaviour of TB patients, reporting practices of health care providers that diagnose and/or treat TB, and existing diagnostic and case management practices in the non-NTP sector.
- TB inventory studies also provide evidence to assess the need for special efforts to improve linkages with other sources that record TB case information (such as HIV information system, hospital information system, national health insurance information system, sample registration system) and reporting by non-NTP providers or sectors (such as private hospitals, private practitioners or laboratories and paediatric specialists).
- TB inventory studies can be used as part of annual quality checks of the TB surveillance system.
- A benefit of prospective inventory studies is a detailed mapping of health care providers in the sampled areas and a clear understanding of the different types of facilities that diagnose and treat TB in the country.
- Results of inventory studies can be used as a follow-up action for public–private mix activities to improve TB notifications.

Sustainability/scale-up

- Unitaid and the Global Fund support the implementation of national TB inventory studies in Asia, including some with a particular focus on children.
- National TB programmes of Indonesia, Pakistan and Viet Nam are to scale-up lessons learnt with successful engagement models in sampled study districts to other districts in the country.

Challenges/outstanding issues to be addressed

- Linkage of records between TB case databases needs to be improved.
- There is a need to move from probabilistic to deterministic record linkage through the use of unique identifiers.
- All health facilities and private practitioners including nurse/midwife private practices need to be included in TB inventory studies (as in many developing countries nurses and midwives contribute informally to TB treatment).







3 Develop training and reference materials on childhood TB for health care workers

2013 Roadmap for childhood tuberculosis:

- ▶ Evidence-based and relevant national guidance on TB in infants, children and adolescents.

- ▶ Training of health care workers on TB in children, including contact screening, diagnosis, treatment and prevention. Integration of training on childhood TB into routine training and supervision activities of all relevant programmes.

- ▶ Development of manuals and algorithms to guide NTPs.

3.1. The Union's Desk-guide for diagnosis and management of TB in children

Global

Contributors: Steve Graham and Valérie Schwoebel

The Union Against Tuberculosis and Lung Disease

Background

Job aids are required to strengthen clinical management and prevention of TB in children in TB endemic, resource-limited settings as many health workers (child health and NTP) lack training and therefore confidence in childhood TB diagnosis, treatment and prevention. These materials should aim to address the need to strengthen clinical diagnosis and management of child TB at the secondary and primary level of health care facilities, which is where most children with TB will first present, and where opportunities for prevention are commonly missed.

There is a growing recognition that while it is difficult to achieve bacteriological confirmation of TB in young children, it is often not difficult to make a clinical diagnosis, which reduces the need to refer every child with presumptive TB to a tertiary level facility for diagnosis and care.

Description

The first edition of the Desk-guide was developed following a consensus workshop at The Union office in Paris, in 2010, led by Steve Graham of The Union and University of Melbourne along with TB clinicians from the WHO Africa region and members of the WHO Child TB subgroup. This edition included algorithmic approaches for the assessment of children with presumptive TB, and for child contacts that did not include diagnostic tools (such as tuberculin skin test (TST)) rarely available in limited-resource settings. It also included guidelines for admission or referral and tables for first-line treatment regimens and dosages.

Stakeholders involved included The Union, WHO Child TB subgroup, WHO Child and Adolescent Health, USAID. The first edition (2010) was funded by USAID through its "Control and Prevention of Tuberculosis" (CAP-TB) project. Hard copies were distributed and available at Union conferences, and the electronic version was made available on the Union website.

The second edition was developed in 2013 and was translated into French with funding from Agence Française de Développement (AFD). This edition included an illustrated section on the diagnosis of lymph node TB.

The development of the third edition (2016) was funded by USAID's Challenge TB project, and translation funded by France's 5% Initiative. This edition included a section on management of MDR-TB in children and dosages for the new child-friendly FDCs, including 3RH (rifampicin and isoniazid for three months) as preventive treatment. The electronic version is freely available on the Union's Child TB Learning Portal (<https://childhoodtb.theunion.org/>; see section 3.2) and The Union website. A total of 3000 hard copies of the third edition (2000 English, 1000 French) have been printed and distributed.



Outcomes/successes

- The Desk-guide is widely used (although use is not monitored)
- It has been used in several countries to support the updating of the NTP guidelines for child TB



- The French language edition is regularly used in The Union international course for TB control (in Cotonou, Benin) which has trained most managers and members of management teams of NTPs in countries of francophone Africa
- It has been used in training for implementation research such as in Uganda's Decentralize Tuberculosis services and Engage Communities to Transform lives of Children with Tuberculosis (DETECT Child TB) project (see section 5.2)
- It has been used as a basis for evaluating diagnosis and management practices for childhood TB at the primary health care level in Uganda.

Lessons learned

- Even though no formal evaluation of the Desk-guide has been conducted, users report that it is extremely useful for training, and as a reference for programme planning and implementation.
- Simplicity and clarity are the best assets of the tool, making it easy to use and be completely accessible to non-doctors (nurses).

Sustainability/scale-up

- The Desk-guide is generic and needs to be adapted by each country. It is therefore important that key personnel at high levels (Ministry of Health (MoH), NTPs and paediatricians) take responsibility on how to use and adapt it.
- Technical assistance may be needed for this adaptation.

Challenges/outstanding issues to be addressed

- A real challenge is that the responsibility of diagnosis, management and prevention of childhood TB often remains restricted to doctors and paediatricians. The Desk-guide is designed as a tool for health staff who are not necessarily doctors; and it can benefit the management of childhood TB only if this restriction is overcome. This may prove difficult in many countries where childhood TB services are highly centralized.
- Similarly, the management of childhood TB, particularly case detection, should be integrated into and implemented by all layers of the health system, and not stay confined only to the NTP. If the use of the Desk-guide is restricted to the NTP and no efforts are made to implement it in primary/secondary health facilities in an integrated way, its success will remain limited.

3.2. The Union's Childhood TB Portal

Global

Contributors: Steve Graham and Valérie Schwoebel

The Union Against Tuberculosis and Lung Disease

Background

Building capacity and reinforcement thereof for health providers on all aspects of management and prevention of childhood TB is an important aspect of programme management. However, access to resources on this topic is limited, particularly in many low-income settings. Furthermore, very few international courses are provided on the childhood TB worldwide and access is limited by financial and other barriers.



Description

A web-based portal with free access to all resources <https://childhoodtb.theunion.org/> was developed in 2013. The portal includes documents and resources (WHO and Union guidelines, practical tools) in several languages, as well as two courses (childhood TB for health care workers and childhood MDR-TB for health care workers) that are accessible both online and off-line (the materials can be downloaded and then executed on your own computer).

The first course “Childhood TB for health care workers” was developed in 2013 under the guidance of WHO and the Union.

It is designed for health care workers at the secondary and primary levels of the health care system and is based on the updated WHO guidelines and the Union Desk-guide. The course has been translated and is available in French, Spanish and Mongolian. A facilitator’s guide has been developed for training in group learning or workshop scenarios.

The development of the course was financially supported by USAID (TB-Care I), and by the AFD.

The second course “Childhood MDR TB for health care workers” has been developed with financial support from USAID (Challenge TB) in 2015. It is available in English language only.

Both courses are composed of several modules that trainees can complete at their own pace. The courses are highly interactive, consisting of clinical case studies designed to allow the health care worker to make decisions in resources-limited settings.



Outcomes/successes

- At the time of writing, about 6000 persons have signed-up to the portal, and 3000 have completed the courses online. An additional 5500 people have downloaded the courses for off-line use.
- The offline version of the “Childhood TB for health care workers” course has been used in 76 health care facilities in the initial training of the DETECT Child TB project in Uganda (see section 5.2). A total of 276 health care workers benefited from the course. The off-line course was further used in the health facilities for refresher training. The increase in TB detection among children during the project, and the sustainable improvement of clinical diagnosis of TB after the project ended are likely attributable to the success of this training.
- Parts of the off-line version of the “Childhood TB for health care workers” course have been used in a training of trainers’ workshop gathering in eight countries in West and Central Africa in 2017, as well as countries in the Asia-Pacific region, including Myanmar in 2016.

Following this workshop, the course has been used in the national training on childhood TB in Madagascar in 2017. The training covered all regional focal points and 53 health facilities throughout the country.



Lessons learned

- The interactivity of the course is unique, and makes completing it easy and fun.
- Situations are adapted to settings with limited resources (such as what to do if the nearest chest radiography machine is more than two hours' drive away?).
- Free access is a key asset of the online course, but access is limited by challenges with internet connectivity in remote areas in low-income countries.
- The off-line version is an excellent alternative and can be used for organizing training. However, facilitators are required to help participants. The facilitator's guide for the first course is available to facilitate off-line training in group learning or workshop scenarios.

Sustainability/scale-up

- Resources in the portal will need to be regularly maintained and updated.
- Individual use of online training will develop if sustained by promotion and advertisements.
- Scale-up is possible and would follow the scale-up of international/national courses on childhood TB.

Challenges/outstanding issues to be addressed

- Translation of courses into additional languages would need additional funding.
- The use of the off-line courses in national/regional training would require support by facilitators who are already familiar with the course.
- Courses will need to be updated in the future following technical advances and changes in international recommendations.

3.3. Capacity development of doctors and health care workers in childhood TB with generic training modules

Country: Bangladesh

Contributors: Shakil Ahmed;¹ ARM Luthful Kabir;² Md Ruhul Amin;³ Abid Hossain Mollah;⁴ Tahmeed Ahmed;⁵ Robert Gie⁶

¹ Shaheed Suhrawardy Medical College, Dhaka, Bangladesh; ² Ad-deen Women's Medical College, Dhaka, Bangladesh; ³ Dhaka Shishu Hospital, Bangladesh; ⁴ Ibrahim Medical College, Dhaka, Bangladesh; ⁵ ICDDR, Dhaka, Bangladesh; ⁶ Stellenbosh University, South Africa

Background

Bangladesh has the eighth highest TB burden in the world (1). Detection of child TB in Bangladesh was static (around 2.5% to 3% of the total TB burden) between 2006 and 2013. The absolute number of childhood TB cases notified was 4044 in 2007 and 5044 in 2013, with only an additional 1000 cases notified in the span of eight years. Case detection was poor in both urban and rural settings including tertiary hospitals, indicating poor capacity of health-care providers to detect and "think TB" among children seeking care.



Description

Members of the Bangladesh Paediatric Association (BPA) developed reference and training materials on childhood TB between 2012 and 2014 (see Table 3.1) to increase the capacity of doctors and health care workers with guidance from the NTP.

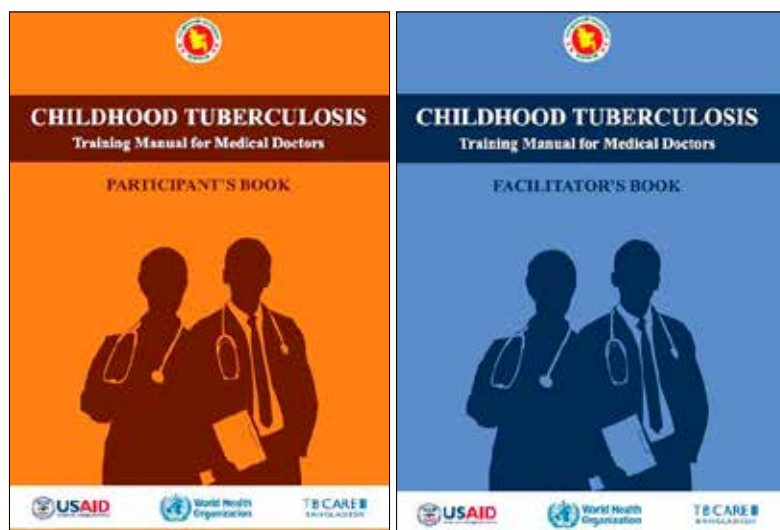
Table 3.1: Guidelines and training material development in Bangladesh

Developments	Year
National guidelines (1st and 2nd edition)	2012 and 2016
Training modules for physicians	2012–2013
Facilitator's guide for physicians training	2012–2013
Training flip chart for health care workers	2013
Interactive training CD for general practitioners	2014
Three teaching videos: ▪ Mantoux test ▪ Gastric aspirate ▪ Examination of a child with TB	2014

Training modules were generic and included the use of local data, cases and resources. The modules applied adult learning methodology and were interactive and participatory through self-learning. For the four-day training for doctors, only one slide presentation was used in the facility-based component. Financial support was provided through USAID (TB CARE II and Challenge TB).

Doctors and health care workers from 21 districts and 144 subdistricts were invited to the trainings by the NTP that were conducted at tertiary hospitals (four-day training of doctors), district hospitals (half-day orientations for general practitioners) and subdistrict hospitals for other health care workers.

Besides developing knowledge and skills, the capacity building programme has stimulated participants to be more engaged with childhood TB. Satisfaction with the trainings was high, with participants describing the training as "very interesting, "one of the best training ever received", "stimulating", "never bored in the last four days". Health care workers at the subdistrict expressed the desire to act more for childhood TB: "we did not know so many children are suffering and dying from child TB", "we need to act more from today".



Outcomes/success

Table 3.2 shows the number of doctors, health care workers and programme personnel who participated in the trainings from 2013.



Table 3.2: Numbers of staff trained

Training Component	Numbers trained
Facilitators training	82
Four-day training of doctors	762
Half-day orientation of general practitioners	544
Health care worker training	10 584
District health managers, programme staff and others	47

The proportion of childhood TB cases, among all TB cases, increased by 53% (from 2.8% in 2013 to 4.3% in 2016) in a period of three years. Absolute numbers of child cases almost doubled from 5044 in 2013 to 9192 in 2016. Over three years 4148 additional cases were notified to the NTP, compared to only 1000 additional cases over the past eight years.

Awareness on childhood TB has increased at all levels of the NTP, resulting in more activities around childhood TB. One doctor has been assigned to the NTP as a childhood TB coordinator and a national child TB advisory group was formulated with NTP, BPA, nongovernmental organization (NGO) members and donors.

In addition, a BPA representative is involved in Technical Working Group meetings.



Self-learning by participants in the four-day training, with two facilitators standing on the left-hand side

General awareness on childhood TB has increased as well; there is more media reporting on childhood TB activities, and the National Anti-Tuberculosis Association of Bangladesh (NATAB; the oldest and largest civil society activist group on TB), has dedicated a time slot for childhood TB in their annual conference over the last four years. IPT for TB infection has been incorporated in the national policy by the NTP.

The Bangladeshi training modules and methodology were successfully replicated in Nepal in 2017, where facilitator training and five regular training sessions were conducted.

Lessons learned

- The interactive facility-based training has been well accepted by doctors and other health care workers.
- Incorporation of the programme component in the training has boosted activities at all levels of the healthcare system (including increased utilization of resources for childhood TB case detection, e.g. Gene-Xpert and child friendly medicine formulations) and led to increased childhood TB notifications.
- Active engagement of professional bodies (such as BPA and academia) with NTP activities enhances policy making, and eases the process of development of training materials on childhood TB.
- The training package can be successfully replicated in other high burden countries.

Sustainability/scale-up

- Scaling up of the programme in the remaining five divisions, 43 districts and 343 subdistricts will have a positive impact on case detection/notification of childhood TB cases in Bangladesh.

Challenges/outstanding issues

- Domestic or donor funding is required to scale up the programme.



3.4. Examples of other resources for national programmes and health care workers

The Sentinel Project on Paediatric Drug-Resistant Tuberculosis

This Project is a global partnership of researchers, caregivers and advocates who share a vision of a world where no child dies from this curable and preventable disease. It is a collaboration to raise the visibility of paediatric drug resistant-TB, and to share evidence and resources that can increase children's access to prompt and effective treatment.

*"Every child who dies with drug-resistant tuberculosis is a **sentinel** for both ongoing transmission and inadequate treatment delivery systems"* – <http://sentinel-project.org/about/>

Resources available include:

- Rapid clinical advice: The use of delamanid and bedaquiline for children with drug-resistant tuberculosis. Boston: The Sentinel Project; 2016.
- Management of multidrug-resistant tuberculosis in children: A field guide (Third edition). Boston: The Sentinel Project; 2016.
- How to care for people exposed to drug-resistant tuberculosis: a practical guide (First edition). Boston: The Sentinel Project; 2018.
- Brief update on bedaquiline. New WHO "meeting report" discusses evidence on the use of bedaquiline in adolescents treated for MDR-TB. Boston: The Sentinel Project; 2017.
- Webinars (e.g. on paediatric DR-TB treatment regimens, use of new drugs, contact tracing, infection control, adverse effects, adherence, advocacy)
- Internet link: <http://sentinel-project.org/resources/>

Selected job-aids on sputum collection procedures in children

Developed by Children's Foundation and Clinton Health Access Initiative, Swaziland and Baylor College of Medicine, Houston

The image displays three job-aids for paediatric sputum collection procedures:

- Gastric Aspirate:** A poster titled "HOW TO PERFORM A PAEDIATRIC GASTRIC ASPIRATE". It lists materials (N95 masks, gloves, sheet, French catheter, syringes, sterile water, etc.) and provides 11 numbered steps for the procedure, from immobilizing the child to securing the specimen container.
- Nasopharyngeal Aspirate Procedure:** A poster titled "How to Perform a Paediatric Nasopharyngeal Aspirate Procedure". It includes materials, a 6-step procedure for inserting the catheter and aspirating, and instructions for handling the specimen.
- Sputum Induction:** A poster titled "HOW TO PERFORM A PAEDIATRIC SPUTUM INDUCTION". It lists materials and provides 8 numbered steps for inducing sputum collection, including nebulizer use and specimen handling.

The above resources as well as additional ones are available on the Union's childhood TB portal resources page: https://childhoodtb.theunion.org/info/additional_resources?locale=en, accessed 18 August 2018







4 Foster local expertise and leadership among child health workers at all levels of the health care system

2013 Roadmap for childhood tuberculosis:

- ▶ Involvement of health care workers at all levels of the health care system, including the private sector.



- ▶ Childhood TB as an integral part of TB programme reviews.



- ▶ National champions of childhood TB; national childhood TB working group.



- ▶ Role of paediatric associations.



4.1. Formation of AFRO childhood TB task force

AFRO Region

Contributors: Anthony Enimil (Chair);¹ Landry Tsague Dongmo (Vice-chair);² Anne Detjen;² Keri Lijinsky;³ Mutsa Bwakura-Dangarembizi;⁴ Tony Garcia Prats;⁵ Kefas Samson;⁶ Daniel Kibuga;⁷ Annemieke Brands;⁶ Geoffrey Bisoborwa;⁷ Christo van Niekerk⁸

¹ NTP, Ghana; ² UNICEF; ³ USAID; ⁴ University of Zimbabwe, Harare, Zimbabwe; ⁵ Stellenbosch University, South Africa; ⁶ WHO HQ; ⁷ WHO AFRO; ⁸ TB Alliance

Background

Africa contributes 316 000 of the 1 million estimated annual child TB cases worldwide, with an overall child TB mortality of 102 000 (40% of global child TB deaths). The proportion of childhood cases among notified TB cases in Africa ranged from 1% to 14% (1).

In the context of the End-TB Strategy, the need for a task force to address childhood TB in the African region was identified.

Description

At the initiative of the WHO Regional Office for Africa (AFRO) and WHO headquarters, a workshop was held in Kampala, Uganda in March 2017 to establish the AFRO WHO task force for childhood TB and define its terms of reference.

Key stakeholders who participated in the workshop were WHO, USAID, UNICEF, TB Alliance and academia. The task force was established as an advisory body to inform WHO on child TB related issues. Action points included a review of the childhood TB situation in Africa and the development of a regional action plan.



There was extensive deliberation during the two-day workshop leading to the election of executives and the development of a work plan. WHO headquarters and AFRO support implementation, monitoring and evaluation of the activities and timelines determined by the task force.

Outcomes/successes

- An advocacy letter was written by WHO AFRO supporting appropriate inclusion of women, adolescents and children affected by TB in the 2017 funding proposals to the Global Fund.
- An action plan has been developed for 2017/2018.
- The task force facilitated the success of the postgraduate training programme for childhood TB during the 20th Africa Union Meeting Held in Accra, Ghana in July 2017.
- An email list of interest groups and individuals (advocates, policy makers, clinicians, researchers) was set up to share information.



Lessons learned

The task force is relevant in driving towards the End-TB Strategy for childhood TB in the Africa region.

Sustainability/scale-up

Improve communication among the executive members of the task force and AFRO WHO to monitor progress made on set targets. Gather regular updates from member countries on activities related to childhood TB and intervene appropriately.

Challenges/outstanding issues to be addressed

- Meetings between executive members of the task force have not been consistent.
- The task force has yet to review timelines and achievements for the developed action plan.

4.2. WHO Regional Office for Europe child- and adolescent-TB task force

Region: WHO European Region

Contributors: Martin van den Boom;¹ Jay Achar;² Masoud Dara;¹ Connie Erkens;³ Iveta Ozere;⁴ James Seddon;⁵ Alena Skrahina;⁶ Marieke van der Werf⁷

¹ WHO EURO; ² MSF, London, UK; ³ KNCV Tuberculosis Foundation; ⁴ Riga Eastern Clinical University hospital Centre for Tuberculosis and Lung Diseases, Latvia; ⁵ Imperial College, UK; ⁶ Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus; ⁷ European Centre for Disease Control

Background

Childhood TB is a major public health problem worldwide and is responsible for a significant burden of overall TB disease. In the WHO European Region, children under 15 years of age account for 4.1% of all reported TB cases (1). Of around 31 000 estimated TB cases under 15 years of age in the Region, only about 10 000 (one third) are detected and notified. Only 1113 of these (10% of the total) had drug susceptibility test (DST) results available in 2016 (4.9% of these were found to have rifampicin resistant TB). Possible reasons for this include under-diagnosis of childhood TB (to avoid stigma, lack of awareness), paucibacillary disease (with a lower probability of obtaining a sample on which DST can be performed), limited sample collection methods (avoided for lack of infrastructural and technical capacity, as well as being considered invasive), a higher frequency of (more challenging to diagnose) extra-pulmonary TB, TB/HIV co-infection as well as the fact that the diagnosis is often made clinically. In comparison, of all new pulmonary TB cases (of all ages) in the Region, around one third had DST done in 2016.

Of the estimated 14 000 (range 13 000–15 000) children under the age of five years who were contacts of adults confirmed with pulmonary TB in 2016, only 7400 started IPT (55% coverage) through contact investigation. According to 2015 data, 92% of all childhood TB cases were successfully treated (1,11), suggesting a need to focus on finding the missing paediatric cases.

In common with the overall global TB picture, specific challenges, such as a tendency – albeit improving – of unnecessary, and prolonged, hospitalization and high rates of drug-resistant TB, exist. While the overall capacity for diagnosing TB (including in children) has improved in the Region, clinical diagnosis of drug-resistant TB in combination with source case DST results is not often used. In addition, despite improvement and recent updating of the WHO policy guidance on measures for children who have been in contact with drug-resistant TB patients, countries are still generally unsure on to how to deal with such contacts.



Currently, the regional TB action plan covering the period 2016–2020, which was endorsed at the 65th session of the WHO Regional Committee for Europe in September 2015 is being implemented. The plan is in line with the global End TB Strategy. Regarding access to treatment and care of children and adults, plans are in line with the notion of reaching universal health coverage, as stipulated also by Health 2020 (the European policy for health and well-being) and the third SDG. To this end, Member States need to continue to regularly update and adapt or at least revisit their TB NSPs. Childhood TB should be carefully considered for inclusion or re-development/updating, as it falls under several areas of intervention of the regional TB action plan and links to all three pillars of the global End TB Strategy. This context requires concerted efforts to more effectively combat TB in children, one of the most vulnerable patient groups. Strong and well-defined collaboration at international and national levels are important, in order to reduce the burden and suffering of children and adolescents with TB.

Countries in the Region struggle with the introduction of new drug formulations and dosages, including child-friendly dispersible FDCs, as well as child-friendly forms of first- and second-line single drugs. There is insufficient integration within the health system and between medical specialties, such as between pulmonologists, TB specialists, infectious disease specialists, paediatricians and primary health care workers. In addition, there is – to some extent – a lack of diagnostic capacity, motivation and awareness among health care providers, as childhood TB is challenging to diagnose and less frequent than in adults. Apart from general challenges related to the diagnosis, treatment and prevention of childhood and adolescent TB, the actual burden of TB in children is unknown in the Region. Current estimates are debatable, due to under- or over-diagnosis, and under- or over-reporting. For example, children with TB may initially be diagnosed with pneumonia, and diagnosis and treatment of TB is further complicated by other co-morbidities, such as HIV, diabetes or under-nutrition. Young children (under the age of two) are infrequently reported, despite their high risk of developing active TB following infection. BCG coverage is not sufficient in some parts of the Region. The number of countries who have ordered and received new paediatric first-line FDCs, as well as who conduct adequate contact investigation and provide preventive treatment, is still not adequately high.

Description

The WHO/Europe TB Task Force on childhood TB (established in 2012) members and supporters work pro-bono and include stakeholders from different organizations, such as technical partners, national TB prevention and care programmes, academia and NGOs. The Task Force has periodic (virtual) meetings to discuss Region-specific public health and childhood and adolescent TB issues. It has contributed to updating NSPs of TB prevention and care at country level, addressing the aspects mentioned above, as well as advocating childhood and adolescent TB relevant interventions included in regional TB projects and national grants of the Global Fund. The Task Force contributed to organizing two regional child and adolescent TB workshops, in November 2015 and December 2017, during which challenges and further country action plans on effective child and adolescent TB were determined and discussed with more than 30 Member States of the WHO European Region. In addition, the Task Force also contributes to updating the national child and adolescent TB clinical and programmatic guidance documents. It conducted surveys among Member States of the WHO European Region regarding the current situation of policy and practice on several aspects of child and adolescent TB, in an effort to better understand potential gaps and challenges and help support countries in further improving both policies and practices.^{1,2} Individual country examples from the European Region are included in sections 5.4 (Latvia), 5.7 (Russian Federation), 6.1 (Kyrgyzstan) and 8.4 (Belarus).

Outcomes/successes

- Child and adolescent TB has been included in TB NSPs of several countries, and in successful country Global Fund applications.

¹ Dara M, Acosta CD, Rusovich V, Zellweger JP, Centis R, Migliori GB; WHO EURO Childhood Task Force members. Bacille Calmette-Guérin vaccination: the current situation in Europe. *Eur Respir J* 2014;43(1):24–35 (<https://www.ncbi.nlm.nih.gov/pubmed/24381321>, accessed 26 August 2018).

² Blok N, van den Boom M, Erkens C, Dara M, van den Hof S. Variation in policy and practice of adolescent tuberculosis management in the WHO European Region. *Eur Respir J* 2016;48(3): 943–946 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5007218/>, accessed 26 August 2018).



- National child and adolescent TB clinical and programmatic guidance documents were updated in line with WHO recommendations.

The two workshops referred to above were highly successful in driving child and adolescent specific TB interventions.

Lessons learned

Coordination and coordinative platforms at the regional level are well appreciated, as they help bring complementing and synergizing partners together. Regional survey results helped countries better understand their specific challenges and learn from one another.

Sustainability/scale-up

The next steps include:

- The development of a regional child and adolescent-adapted guidance document (by the end of 2018).
- Adaptation and review of existing child and adolescent TB training tool(s) and support for country-level implementation, aiming to increase country-level awareness for the topic, and further build country-level capacity for prevention, diagnosis and treatment of child and adolescent TB.

Challenges/outstanding issues to be addressed

- Although the new WHO pre-qualified FDCs have been assessed by the WHO and are available through the Global Drug Facility (GDF), accessing these drugs is challenging for many countries in Europe. In the European Union, medications need to be approved by the European Medicines Agency (EMA). The very small market for FDCs is a major barrier for drug manufacturers to have paediatric FDCs registered with the EMA.
- There is a potential negative impact of loss of pre-qualified drugs and FDCs for first- and second-line drugs, which may happen during Global Fund transition plans.
- Since child- and adolescent TB concerns different medical and public health specialties, apart from clinical, programmatic and operational public health work, more advocacy at high level is needed, in order to feature it and keep it high on the political agenda. This would include advocacy on the availability of second-line paediatric formulations, rifapentin and child-friendly and more specific LTBI tests.
- Well-tailored advocacy and support to countries is needed, to facilitate and foster further meaningful and sustainable in-country vertical and horizontal integration.

4.3. Brazilian End TB Plan – clinical management of paediatric TB at primary health care level

Country: Brazil

Contributors: Betina Mendez Alcântara Gabardo;^{1,2} Denise Arakaki-Sanchez;³ Fernanda Dockhorn Costa;³ Daniele Gomes Dell' Orti;³ Andrea Maciel de Oliveira Rossoni;⁴ Clemax Couto Sant' Anna;⁵ Maria das Graças Rodrigues de Oliveira;³ João Antonio Bonfadini Lima;³ Karina Pierantozzi Vergani;⁶ Sheila Cunha Lucena;³ Fátima Pombo³

¹ Clinical Hospital Complex of the Federal University of Paraná; ² Regional childhood TB working group – PAHO; ³ NTP, Brazil; ⁴ Federal University of Paraná, Brazil; ⁵ Federal University, Rio de Janeiro, Brazil; ⁶ Hospital Clemente Ferreira, São Paulo, Brazil



Background

Brazil is located in South America and is the only country in the Americas region appearing in two (TB and TB/HIV) of three lists of high-burden countries prioritized by WHO for TB. Although TB is a disease diagnosed and treated universally and free of charge by the Brazilian Unified Health System, it remains a serious public health problem.

In Brazil, 72 770 new TB cases were reported in 2017, including 1155 children under 10 years of age, representing 1.8% of all cases. In 2016, 4483 deaths occurred as a result of the disease, with 26 cases in children under 10 (0.6%).

As Brazil is characterized as a TB high-burden country, it is expected that the proportion of childhood TB is around 10%. These data suggest under-diagnosis of TB cases in this age group.

In the current epidemiological situation, strategies need to be designed to address TB in the country. For this purpose, the country's NTP gathered a group of paediatric TB specialists to elaborate a training model in "clinical management of TB in children" with the aim of capacitating health care professionals on PHC services in TB control interventions. The training model is aligned with pillar one – integrated prevention and care centred on the person with TB, of the national plan for ending TB as a public health problem, published by the NTP in 2017.

Description

In 2016, a Working Group with nine specialists in paediatric TB was established by the NTP. Between 2016 and 2017, the Working Group developed a course on clinical management for paediatric TB, consisting of six educational modules based on concepts of diagnosis and treatment of TB infection, active TB, BCG vaccination, TB-HIV co-infection, among others.

The modules were elaborated through a discussion of clinical cases based on experiences of routine health services. The course helps to build capacity and confidence of medical professionals, nurses and others engaged with TB control in the PHC services, in the prevention, diagnosis and management of TB in children.

Clinical cases are discussed through active participation in an interactive way (using questions and answers). The method consists of three alternative answers, with each alternative linked to a colour card (red, yellow and green). After presenting the question, the participant raises the card with the colour of the alternative s/he thinks is correct. The training facilitator proceeds to discuss the chosen alternatives after knowing the general response of the participants through the colours.

The eight-hour training course is certified by the NTP in partnership with local TB control programmes. At the end, all participants complete a training assessment form to evaluate the strategy and method used.

In the first year, two pilot trainings were carried out, one in the Federal District with 53 professionals and another in Manaus with 192 primary care professionals, hospital professionals and universities who participated actively, thereby contributing to improvement of the module content.



Participants at a training holding up colour cards



With the objective of expanding training to the entire country, in August 2017, the first training of trainers (train the trainer session) of the “clinical management of TB in children” course was organized with 21 professionals from various federative units of Brazil. The list of qualified professionals to apply for management relies on nine facilitators (the authors of the paediatric management course) and these 21 trainers throughout the country.

For 2018, 10 training courses are planned in the capitals of federative units with a high-burden TB: Campo Grande (MS), Fortaleza (Ceará), Goiânia (Goiás), Maceió (AL), Porto Alegre (Rio Grande do Sul), Recife (Pernambuco), Rio de Janeiro (RJ), Salvador (Bahia), São Luiz (Maranhão) and São Paulo (São Paulo).

The cost of travel and organization of local logistics is supported through collaboration with the Health Surveillance Secretariat of the MoH, the state, and municipal coordination of TB control programmes.

Outcomes/successes

The training using the interactive model showed a productive exchange of experiences between participants from different epidemiological scenarios and health professionals working in care, including access to diagnostic tools, medications and basic knowledge.

A total of 266 health professionals were trained in Brazil (including pilot training and roll out of training). The evaluations showed positive feedback regarding the methodology, applicability and performance of the facilitators.

In Manaus, one of the pilot municipalities, paediatric TB services were decentralized to the PHC level, after which good progress was made in the quality of child TB diagnosis. This was evidenced by a 33% increase in case detection of new childhood TB cases (under 10 years of age) in the first four months after the training, compared to the same period during the previous year.

Lessons learned

Training of health professionals in the “clinical management of TB in children” was a collaborative effort by different key stakeholders to improve the quality of care for children in PHC. It resulted in improvement in the establishment of adequate, individualized, family- and patient-centred diagnosis and management of TB in children. In addition, it had a positive effect on the joint work between surveillance professionals and health managers in the development of strategies for paediatric TB control in Brazil.

Sustainability/scale-up

The national programme aims to train all federative units in paediatric clinical management in the next two years, in addition to response requests from the states. Furthermore, the group of paediatric specialists supporting the MoH will contribute to constant updates regarding childcare, and provide technical support to update current recommendations.

Challenges/outstanding issues to be addressed

Brazil has continental proportions with 27 federative units, which makes it highly challenging to conduct multiplication training in the different places targeted for 2018/2019. As the number of paediatricians with experience in TB to support the training is limited, the small group has a very demanding travel schedule.



4.4. Human resource development on TB in children and teenagers in Colombia

Country: Colombia

Contributors: Marcela Calle Paez;¹ Jürg Niederbacher Velasquez;² Magnolia Arango Loboguerrero³

¹ Universidad del Bosque, Bogotá, Colombia; ² Universidad Industrial de Santander, Bucaramanga, Colombia; ³ Universidad Nacional de Colombia, Bogotá, Colombia

Background

Although not a high-burden country, Colombia notified 13 870 TB cases in 2017 (MoH data, 2018). Treatment coverage in 2016 was 84% (1). In 2017, 507 children aged 0–14 years were notified (250 aged between 0 and 4 years, and 243 aged 5–14). The proportion of children (0–14 years) with TB decreased from 6.8% in 2010 to 3.7% in 2017. TB in children and teenagers has been identified as an important issue. However, knowledge about this situation is limited among the population, health care teams, and physicians. As a result, TB cases among children and teenagers are not promptly detected, treatment is delayed, and contact investigation and preventive treatment are not well implemented, resulting in missed opportunities for childhood TB case finding and prevention.

Description

To address the challenges described above, a group of paediatric pulmonologists, engaged with teaching students in the areas of medicine, nutrition, bacteriology and other health care disciplines, collaborate in implementing activities related to education and awareness of child and adolescent TB. Their work centres on theoretical development and practice included in the medical curricular process. Additionally, the group focuses on interaction with students, professionals, health care teams and communities, taking into account integration with maternal and child health, and general health status of young children and adolescents. This work takes place in universities and hospitals, as well as in academic, professional and scientific meetings at local, national and international levels, and in extension programmes within the local communities.

All activities are framed by the Pan American Health Organization (PAHO)/WHO guidelines, the SDGs, and the WHO's End TB Strategy.

The processes and activities that have been developed and implemented include:

- Motivation and sensitization through trainings on maternal and child, childhood and adolescent TB.
- Rolling out training and education to physicians, nurses, health care teams and communities, emphasizing: screening of patients with respiratory symptoms and their contacts, the importance of a prompt TB diagnosis, advantages of new detection methods, and availability of drugs in child-friendly FDCs.
- Participation in forums, congresses, symposiums and meetings of various health disciplines; sharing information about TB in children and teenagers and also about the NTP.
- Relation and interchange with the Ministry of Health and Social Protection, the National Institute of Health, the International Organization for Migration (IOM), the Colombian Anti-tuberculosis League, academia (universities) and scientific societies (Colombian Association of Paediatric Pulmonology, Colombian Society of Paediatrics, National Academy of Paediatrics, societies of pulmonology and infectious diseases).
- Participation in the TB assessment committee of the Ministry of Health and Social Protection and the special TB cases committee (CERCET in Spanish).
- Discussion of consulted cases.



- Participation in the updating of definition of policies and criteria related to childhood TB and in the development of the NSP of the Ministry of Health and Social Protection.
- Advocacy for the inclusion and fulfilment of public health policies that prioritize integrated approaches to TB in children and teenagers, and the inclusion of drugs that are appropriate for these population groups.

Successes

- Maintaining an adequate level of knowledge on TB in children and adolescents in the country.
- Achieving permanent communication with agencies in charge of health care systems.
- Acting as intermediaries between the MoH, the different priority programmes, health sector agencies and the community, on topics about TB in children and teenagers.
- Joint participation with the Colombian Anti-tuberculosis League, Ministry of Health and Social Protection, IOM and Baylor University, in the international training for TB control in special populations with the objective to organize a centre of excellence for TB in Colombia.
- Participation in the Latin American network for the fight against tuberculosis in women, children and adolescents, led by PAHO.

Lessons learned

- It is necessary to strengthen the link between the teaching process and clinical practice in healthcare institutions.
- The activities of education, motivation and sensitization need to be ongoing, with periodic capacitation on TB in childhood and adolescence, according to the guidelines of the NTP.
- It is important to prioritize and collaborate in operational research of TB in children and adolescents.

Outstanding issues to be addressed

It is of vital importance to comprehensively improve all aspects related to the three pillars of the End TB Strategy:

- Attention to integrated and patient-centred care, including prevention.
- Participation in the formulation of policies and support systems.
- Contribution to research and innovation processes.



4.5. Childhood TB benchmarking to intensify childhood TB interventions

Country: Nepal

Contributors: Kathy Fiekert;¹ Sharat Chandra Verma;² Suvesh Kumar Shrestha;³ Shakil Ahmed;⁴ Asim Shrestha⁵

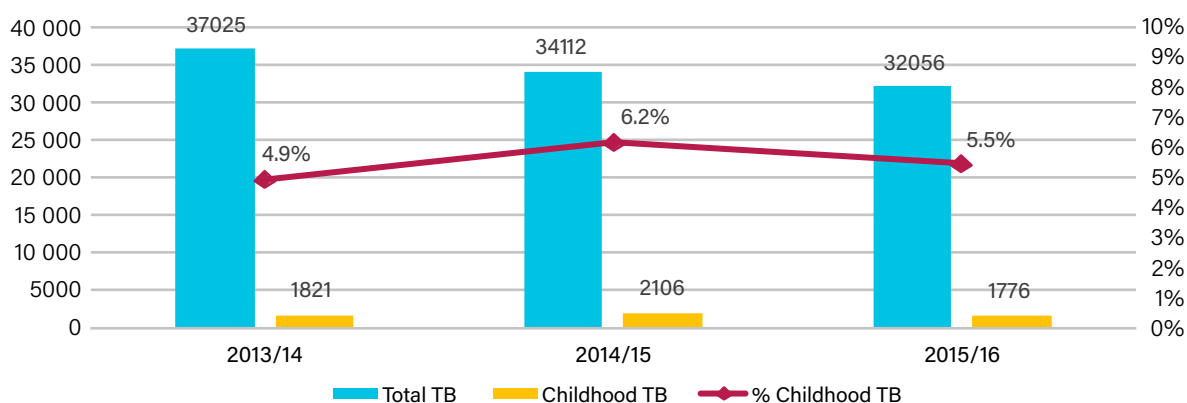
¹ KNCV Tuberculosis Foundation; ² former NTP, Nepal; ³ Save the Children, Nepal; ⁴ Consultant paediatrician, Bangladesh; ⁵ Consultant paediatrician, Nepal

Background

Nepal notified 1226 cases of TB in children (0–14 years of age) in 2016, which accounted for 5.5% of all notified patients in the period (see Figure 4.1) (1).³ While TB treatment coverage (notifications over estimated incidence) for adult patients is estimated at 78%, for children it is only 32% (see Figure 4.2). Childhood TB has been relatively neglected in Nepal, due to challenges posed by the clinical presentation of TB in children, limited availability of effective diagnostic tools, lack of a focal point and a childhood TB roadmap, as well as poor coordination among stakeholders.

At the time of the intervention, contact investigation was not routinely implemented. Most childhood TB patients were detected by paediatricians through chest radiography and clinical examination. Many of the children who were diagnosed with TB were lost during referral. Very few attempts were made to integrate paediatric TB screening into general child health services or to provide active case detection interventions for children. Low case detection among children was identified as a key factor contributing to the overall low case notification (estimated 30% of missing patients).

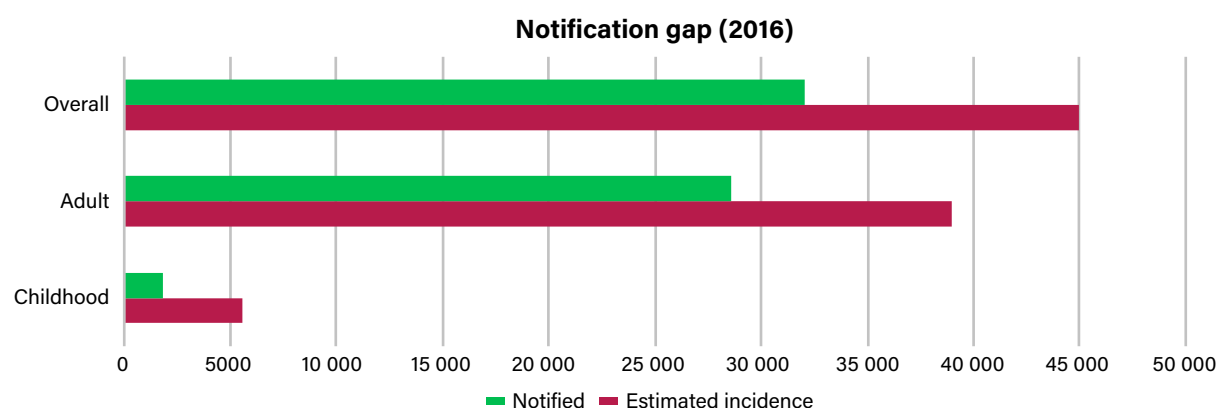
FIGURE 4.1: CHILDHOOD TB NOTIFICATIONS VERSUS ALL TB NOTIFICATIONS



³ National TB programme, Nepal



FIGURE 4.2: NOTIFICATION GAP BY PATIENT GROUP (2016)



The National Strategic Plan for Tuberculosis Prevention, Care and Control (2016–2021) has an objective to increase case notifications among children from 6.2% of total cases (the proportion for 2014/15) to at least 10% (incidence is estimated at 12%) by 2020. The NSP aims to ensure that childhood TB is addressed in the National Tuberculosis Centre’s policies and implementation. Donors (Global Fund and the Netherlands Ministry of Foreign Affairs (DGIS)) and technical partners (KNCV Tuberculosis Foundation (KNCV) and Save the Children) financially and technically supported the ambitions in the NSP.

Description

The intervention aimed to assist the national TB centre (NTC) in assessing the status and challenges of childhood TB interventions by using the childhood TB benchmarking tool and start planning childhood TB improvement interventions. The KNCV benchmarking tool for childhood TB policies, practice and planning⁴ was developed as a self-assessment tool, meant to serve as a basis for discussions, brainstorming and strategic planning, and as a tool for monitoring progress in the realization of childhood TB policies towards alignment with WHO guidelines, in the framework of a TB programme.

In 2017, a team of experts conducted site visits, held key stakeholder interviews in Kathmandu, Pokhara and surrounding areas, and organized a childhood TB benchmarking workshop to: assess the current childhood TB situation in Nepal, and create buy-in of relevant stakeholders to boost childhood TB prevention and care planning and implementation. This activity aimed to complement and strengthen the concurrent development of the Nepal National Guidelines on the Management of Childhood TB, and the Childhood TB training curriculum and manual funded through a Global Fund grant.

The stakeholders involved were:

- Save the Children Nepal (Global Fund – primary recipient).
- KNCV (provides technical assistance to the NTC).
- Two consultant paediatricians who developed the childhood TB guidelines and training package.
- Participants at the two-day childhood TB benchmarking workshop (35): Nepal Paediatrician Society (NEPAS), Nepal Anti-Tuberculosis Association (NATA), Healthy Ecosystems for Rangeland Development (HERD; a research company, promoting evidence informed policies and practices for sustainable development), WHO, UNICEF, Lung Health International Tuberculosis Foundation (Norway), district TB and leprosy coordinators, paediatricians (from referral hospitals and private practice), NTC staff.




The participants used the benchmarking tool to discuss how Nepal is performing on the defined childhood TB benchmarks. They concluded that of the 20 benchmarks, two (10%) were met, nine (45%) were partially met, and nine (45%) were not yet met (see the first part of Table 4.1 below).

⁴ KNCV benchmarking tool for childhood TB policies, practice and planning. KNCV [website].(<https://www.kncvtbc.org/kb/kncv-benchmarking-tool-for-childhood-tb-policies-practice-and-planning/>, accessed 18 August 2018).



Table 4.1: Summary report of benchmarking exercises in 2017 and 2018

Standards and Benchmarks	February	January
	2017	2018
Standard	Benchmark level*	
A: 1.1 There is evidence of political commitment for childhood TB	Partially met	Partially met
B: 2.1 There is an active national working group on childhood TB	Not met	Partially met
D: 3.1 There is national guidance for childhood TB	Not met	Met
E: 3.2 There is effective technical assistance for childhood TB	Partially met	Met
F: 3.3 The childhood TB strategy is fully implemented	Not met	Partially met
G: 4.1 National policies provide guidance for all providers of paediatric care are involved in diagnosis, prevention and treatment of childhood TB	Not met	Partially met
H: 4.2 All providers of paediatric care are involved in diagnosis, prevention and treatment of childhood TB	Not met	Partially met
I: 5.1 All eligible children receive BCG vaccination	Met	Met
J: 6.1 Investigation of childhood contacts of infectious TB patients is part of the national strategy	Not met	Partially met
K: 6.2 Investigation of child contacts of infectious TB patients is fully implemented	Not met	Partially met
L: 7.1 The national strategy provides for preventive treatment of eligible children	Partially met	Partially met
M: 7.2 All eligible children have access to preventive treatment	Partially met	Partially met
N: 8.1 Special approaches for diagnosis of TB in children are included in the national guidance on TB	Not met	Met
O: 8.2 Special diagnostic approaches for TB in children are applied	Not met	Partially met
P: 9.1 The national treatment guidelines for TB and MDR TB have appropriate and specific adjustments for children	Partially met	Met
Q: 9.2 Child friendly formulations are available	Met	Met
R: 9.3 The national treatment strategy of children is universally accessible for children	Partially met	Partially met
S: 10.1 Data on childhood TB are available and used at the NTP	Partially met	Partially met
T: 11.1 There is a plan for human resource capacity building for childhood TB	Partially met	Partially met
U: 12.1 The NTP and partners deploy specific initiatives to promote a patient and family centred approach in childhood TB care	Partially met	Partially met

*  Met  Partially met  Not met

These results were discussed during the workshop and a list of 10 thematic areas for priority action was defined. The first four (bold) topics were deemed to require immediate action:

1. **Identify a childhood TB focal person with a clear mandate and plan.**
2. **Develop childhood TB clinical guidelines.**
3. **Integrate TB into Integrated Management of Neonatal and Childhood Illness (IMNCI), nutrition, and maternal, newborn and child health.**
4. **Develop a comprehensive package to address contact investigation and IPT.**
5. Include childhood TB in the public-private mix guidelines to be developed.



6. Enhance the current childhood TB surveillance system in the health management information system (HMIS).
7. Develop health education materials and an approach to implementation .
8. Develop a transition plan for introduction of the new child-friendly FDCs.
9. Review and develop training materials and training plans.
10. Establish mechanism(s) of co-ordination with broad stakeholder representation.

The Global Fund supported both the childhood TB benchmark workshop and the draft roadmap development, with technical assistance from KNCV, and the concurrent mission to develop paediatric TB guidelines and training curriculum. The activities were conducted as part of the wider Global Fund grant implementation arrangements and were fully integrated into the programme (including relevant monitoring and evaluation activities).

Outcomes/successes

The workshop and consultative process were appreciated as it was recognized as a national self-assessment and planning exercise, which served to facilitate communication and exchange between key stakeholders, leading to a better understanding of the status of childhood TB in Nepal. It further enabled stakeholders to formulate and prioritize recommendations to the NTP towards the development of a national roadmap for childhood TB. Lastly, it enabled the NTP to solicit buy-in, support and commitment from key stakeholders.

The workshop has accelerated planning and implementation of childhood TB interventions:

- Policy:
 - A childhood TB focal person was appointed at the NTC.
 - Childhood TB guidelines were finalized and launched.
- Capacity building:
 - 23 paediatricians were trained as childhood TB trainers in November 2017 and a peer-support WhatsApp group was successfully established among them.
 - Childhood TB orientation of 200 paediatricians was conducted in collaboration with NEPAS.
 - 93 health care providers were trained in childhood TB prevention and care.
- Contact investigation:

This was initiated for all household members of pulmonary bacteriologically confirmed (PBC) index patients in 38 of the high TB burden districts of Nepal which account for 75% of total notified TB patients. During contact tracing, all household members of PBC index patients are screened based on symptoms. This includes all children in those households. Anyone who is positive on symptom screening is subsequently referred for further evaluation. Children under the age of five years who do not have any symptoms are referred for initiation of IPT. Between April and December 2017, 35 282 household contacts (all ages) were screened for TB, of which 198 were subsequently diagnosed with TB. A total of 745 children under five years of age were enrolled on IPT.
- TB screening among malnourished children:

This was initiated from early 2017 onwards in 29 high burden districts. Between March 2017 and January 2018, 20 922 malnourished children were screened for TB, of which 70 were subsequently diagnosed with TB.
- Referral cost:

Since childhood TB cannot be diagnosed in peripheral health facilities where there are no trained human resources or appropriate technology, children with presumptive TB need to be referred to specialized hospitals with adequate facilities and trained health staff. Therefore, the NTP has provided coverage of referral as well as diagnostic costs for all children with presumptive TB.



- Child-friendly TB medicines:

The new child-friendly FDCs for the treatment of TB in children have been procured and introduced.

The childhood TB benchmark assessment was repeated by local stakeholders independently one year after the first assessment and showed remarkable progress: six benchmarks (30%) have now been met and 14 (70%) have been partially met. The results of the childhood benchmarks assessments in 2017 and 2018 are presented below.

Lessons learned

The childhood TB benchmarking tool is a useful for jointly assessing the childhood TB situation and planning with multiple stakeholders. In Nepal, the involvement of multiple stakeholders, including public and non-public actors, led to widespread buy-in, ownership and political commitment at national and regional levels, and the availability of earmarked funding. Simultaneously, capacity building activities created staff awareness on childhood TB and developed their skills to prevent, diagnose and treat childhood TB.

The lessons learned can be summarized as follows:

- Childhood TB needs to be a national priority for all stakeholders to ensure that the country can achieve its national TB programme targets
- All relevant stakeholders (public and non-public) need to be included in the process from the beginning (assessment, planning, implementation and evaluation) to achieve consensus and required commitment.
- Collaboration with the National Paediatric Association and other organizations with high stakes in child health, who might not be associated with TB control traditionally, are of extreme importance, as they can provide valuable resources and much needed expertise. In Nepal, the involvement of NEPAS ensured that paediatricians got involved in developing the childhood TB guideline, became master trainers, trained other health care providers and supported implementation of the childhood TB programme. They can also provide access to relevant points of first contact with health care providers for patients with presumed TB, minimizing diagnostic and treatment delays.
- Systematic contact investigation is key to early diagnosis and treatment of childhood TB and the best approach towards prevention for this vulnerable group.
- Malnourished children are another vulnerable target group, needing priority attention in countries like Nepal with a high burden of malnutrition. Screening malnourished children will help to identify active TB, which is unlikely to be diagnosed if not prioritized.
- The programme needs to focus on capacity building of healthcare providers as diagnosis of childhood TB remains a challenge. After training in childhood management, referral of children with presumptive TB improved and providers were comfortable in conducting diagnostic procedures, such as gastric lavage, as well as treat children with TB.

Sustainability/scale-up

The inclusion of childhood TB in the NSP, the availability of a childhood TB focal person at the NTC and availability of donor funding will safeguard the sustainability and further scale up of the childhood TB interventions. The demonstrated ownership of the activity and the ability of the NTC and stakeholders to conduct periodic assessments of their childhood TB response status utilizing the benchmarking tool leading to adjustments of their strategy and interventions, will ensure that the programme can continue to make the necessary progress towards ending (childhood) TB. Periodic reassessment utilizing the childhood TB benchmarking tool will allow fine-tuning of the programme and facilitate targeted interventions as well as efficient allocation of resources.



Challenges/outstanding issues to be addressed

The NTP and its stakeholders are continuing work to meet the benchmarking standards. Despite all efforts, case notifications have not yet increased as expected. Contact investigation as well as training and awareness needs to be intensified and rolled out throughout all districts. Ultimately, much will depend on simpler, cheaper, better and less invasive diagnostic approaches and technologies for childhood TB.

4.6. Strengthening national level child TB coordination – The role of a child TB technical working group

Country: Uganda

Contributors: Moorine Penninah Sekadde;¹ Frank Mugabe;¹ Eric Wobudeya;² Jesca Nsungwa³

¹ NTP, MoH Uganda; ² Mulago Hospital, Uganda; ³ MCH, MoH Uganda

Background

Uganda is one of the 30 TB/HIV high burden countries. Nearly half of the country's population is less than 15 years of age. A national population-based TB prevalence survey conducted in 2015 showed that the prevalence of TB (253/100 000 population) was higher than previous WHO estimates (154/100 000). Only 50% of the expected annual TB cases (89 000) are notified. In 2012, childhood TB comprised approximately 6% of the notified incident TB cases, which was an underestimate given the high TB burden and the young population. During a consultative meeting held in 2013, the MoH and key stakeholders recognized the need to strengthen national level child TB coordination in order to improve the status of child TB care and treatment. Although there were varied stakeholders providing and/or supporting TB care, there was limited attention and collaboration towards improving child TB specific services. There was also a challenge in championing the translation of policies into practice due to lack of a dedicated forum to support the National TB and Leprosy Programme (NTLP).

Description

A child TB focal point was introduced at the NTLP in 2013, with support from PEPFAR/Centers for Disease Control and Prevention (CDC) through Baylor-Uganda. Subsequently, an NTLP-led child TB technical working group (TWG) was established in the same year. The TWG representation includes the MoH (NTLP, HIV programme, maternal and child health), district health offices, academia, researchers, health care workers, civil society organizations, professional bodies, as well development and implementing partners. The main aim of the TWG is to provide a consultative and consensus forum for NTLP on the implementation of childhood TB activities towards ending TB. TWG meetings are held on a quarterly basis, however, ad hoc meetings are also conducted as the need arises.

Activities that have been implemented by the TWG include: development of the first child TB stand-alone guidelines and training manuals, review of the national TB reporting and recording tools to include child TB specific disaggregated data, definition of child TB indicators and targets, review of information, education, and communication materials to include child TB, and capacity building in child TB (training, mentorship and supportive supervision). A national assessment of childhood TB services was conducted in 2014, which informed interventions, development of annual work plans and a child TB capacity building plan using a cascade approach.



Outcomes/successes

- Updated child TB policy guidelines and training manuals in place.
- Decentralization of frontline health worker capacity to allow management of child TB to lower levels of the health system through training and mentorship.
- Increase in national child TB case notification from 6.9% (3132 child TB cases) among all incident TB cases in 2014/15 to 9% (4007 child TB cases) in 2016/17.

Lessons learned

- Child TB-specific coordination at the national level is critical in driving the child TB agenda.
- A national TB programme-led TWG promotes sustainability of the coordination role.
- An integrated TWG promotes stakeholder buy-in, shared responsibility and optimization of available resources.
- Including child TB specific indicators in the national strategic plan as well as setting annual targets provides a platform to monitor performance and improve advocacy.
- Targeted child TB trainings and regular mentorship are key to building and sustaining health worker confidence for child TB diagnosis and management.

Sustainability/scale-up

- Integrated child TB case finding and management at all the healthcare entry points using continuous quality improvement approach.
- Integrated supervision, mentorship and coaching.

Challenges/outstanding issues to be addressed

- Suboptimal child TB case notification at 9% against an estimated 17% of estimated incident TB cases.
- Limited health worker skills for clinical diagnosis.
- Low uptake of TB preventive treatment among under-five contacts.
- Inadequate health worker capacity for paediatric specimen collection.
- Limited community awareness and advocacy for child TB (including funding).
- Limited attention/advocacy towards TB case finding and treatment among adolescents.







5 Do not miss critical opportunities for intervention

2013 Roadmap for childhood tuberculosis:

- ▶ Use strategies such as intensified case-finding, contact tracing and preventive treatment, and implement policies for early diagnosis.
.....
- ▶ Address the continuum of health states for childhood TB, from susceptibility to cure.
.....
- ▶ Ensure availability of tools for diagnosis and treatment, such as chest radiography; sputum specimen collection; Xpert MTB/RIF as initial diagnostic test; uninterrupted supply of quality-assured anti-TB medicines for children, including for preventive treatment (FDCs as per updated recommendations, paediatric formulations).
.....

5.1. Roll out of the child-friendly TB medicines in Kenya

Country: Kenya

Contributors: Enos Okumu Masini;¹ Maureen Kamene²

¹ WHO, Kenya; ² NTP, Kenya

Roll out of the child-friendly TB medicines in Kenya

Background

Kenya has an estimated burden of childhood TB of 22 000 (13% of the total estimated burden), with an overall treatment coverage rate of 45% (1). In 2016, Kenya reported 6643 cases of TB in infants and children, with those under age five years at greatest risk of having severe forms of TB and dying from the disease. Caregivers had to cut or crush multiple, bitter-tasting pills in an attempt to achieve the right doses for children. This made the six-month treatment journey difficult for children and their families, contributing to treatment failure and death from the disease.

In December 2015, child-friendly FDCs became available through the STEP-TB project – a collaboration between the TB Alliance, WHO and other partners – funded by Unitaid (see sections 8.1.1 and 10.1). The new FDCs are water-dispersible tablets with a pleasant taste, which longer need to be cut or crushed to achieve an appropriate dose. They are improved formulations of currently used medicines recommended for first-line TB treatment.



Dr Jackson Kioko, Director of Medical Services, demonstrates the use of the child-friendly FDCs during the launch

Photo credit: Centre for Health Solutions - Kenya

Description

Kenya was the first country to roll out child-friendly FDCs in 2016. The process began with the approval of the Kenyan Technical Working Group, after which a task force was set up to plan and coordinate the process in the last quarter of 2015. A budget was drawn up and resource mobilization began. Forecasting and quantification was done to estimate the required quantities and stocks ordered, using routine TB notifications for childhood TB. Current stocks were evaluated to guide the roll out date, which was set for 1 October 2016.

Stakeholders' fora were held to agree on the best way forward with the roll out and establish any anticipated challenges.

Training materials and dosing schedules for health care workers were developed. A review of the national paediatric TB guideline was initiated to accommodate the new paediatric treatment regimens.



Commodities arrived into the country by the middle of 2016 and the drugs were distributed to all county medical stores. The initial distribution required significant logistics, but counties would routinely order according to their needs thereafter.

As distribution was ongoing, health care worker sensitizations were done countrywide, initially for county TB coordinators, who thereafter sensitized the subcounty coordinators. Training of 3,500 health care workers was supported by USAID through the TB Accelerated Response and Care activity (TB ARC) of the Centre for Health Solutions–Kenya. On the day of the national launch (27 September 2016), the TB Alliance supported the communication team at Centre for Health Solutions–Kenya to conduct media campaigns and awareness sessions on child TB for both local and international media.⁵

During the launch, a letter presented by a primary school pupil to the Minister of Health on the need to waive chest radiography fees for children triggered discussions on how to achieve this. If implemented it will play an important role in improving access to diagnostics for children.

Outcomes/successes

- As a result of increasing awareness of childhood TB in the communities, the country has experienced a decline in paediatric TB case detection and increasing childhood TB case notifications in most counties.
- From the post roll out assessment done during technical support visits, caregivers and health care workers are happy with the new formulations. They find them easier to use compared to the old medicines.

Lessons learned

- Cascade approach for sensitization on the new FDCs was very useful in rapid dissemination of information and also an opportunity to train the health care workers and increase their index of suspicion for child TB.
- Media campaigns and awareness sessions heightened the support towards child TB as a programme and created awareness on child TB among the general public and health care workers.



A promotional decoration for childhood TB.

Photo credit: Centre for Health Solutions - Kenya

Sustainability/scale-up

Over the past five years, the Government of Kenya has increased its funding towards procurement of first-line TB medicines. In 2017, 70% of all TB medicines, including the paediatric FDCs were purchased through domestic funds.

⁵ Kenya becomes first country to introduce new child-friendly TB medicines; TB Alliance [website] 2016 (<https://www.tballiance.org/news/kenya-becomes-first-country-introduce-new-child-friendly-tb-medicines>, accessed 26 August 2018).



Challenges/outstanding issues to be addressed

- Initial medicine supply missed out on the need to supply measuring cups for estimating the volume of water required in mixing the drugs. Supplying syringes to caregivers in the interim, while cups were being sourced, helped to mitigate this.
- Some counties quickly ran out of commodities after the roll out due to intensified paediatric TB case detection. They were resupplied.
- There was a transition period in which children who started on TB treatment before October 2016 were using the old formulations, while the children who were diagnosed after that date were prescribed the improved formulations. Due to the media awareness that had been created, caregivers in a few cases declined to continue with the older formulations.
- There were limited funds to continue with the health care worker sensitizations especially for those in the maternal, newborn and child health sector. It is hoped that the country will get additional support through the recently submitted Global Fund support request to extend sensitizations to other programmes.
- The fact that dispersible ethambutol is not yet available is still a challenge to caregivers.

5.2. Decentralize Tuberculosis services and Engage Communities to Transform lives of Children with Tuberculosis (DETECT Child TB) project

Country: Uganda

Contributors: Steve Graham;¹ Stella Zawedde;¹ Anna Nakanwagi;¹ John Paul Dongo;¹ Anne Detjen²

¹ The Union; ² UNICEF

Background

Uganda, a high TB-HIV burden country in Africa, reported 3316 paediatric TB cases in 2014 (8% of the total TB burden). The number of children reported to the National TB and Leprosy Program (NTLP) is probably an under-estimate of the true childhood TB burden, as children under 15 years of age represent almost 50% of the total population in Uganda and risk factors for TB such as HIV infection and malnutrition are common. Contact investigation is not routinely implemented in Uganda.

Description

To address the challenges with TB case detection in children, the “Decentralize Tuberculosis services and Engage Communities to Transform lives of Children with Tuberculosis” or “DETECT Child TB” project started as a pilot in two districts (one rural and one peri-urban) in Uganda in 2015. The overall project goal was to strengthen district and community level health care service delivery to improve childhood TB case finding, treatment and prevention (12,13).

The following interventions were implemented:

- Development of training materials and job aids for health care workers (on the diagnosis of TB in children, including clinical diagnosis and implementation of contact screening and management)
- Training of trainers at district level with roll out of training to peripheral level health care workers, including use of an off-line version of The Union’s e-learning child TB course (see section 3.2) for health care workers at lower level health facilities; and training on sputum induction and gastric lavage
- Onsite mentorship and supportive supervision by district level health care workers

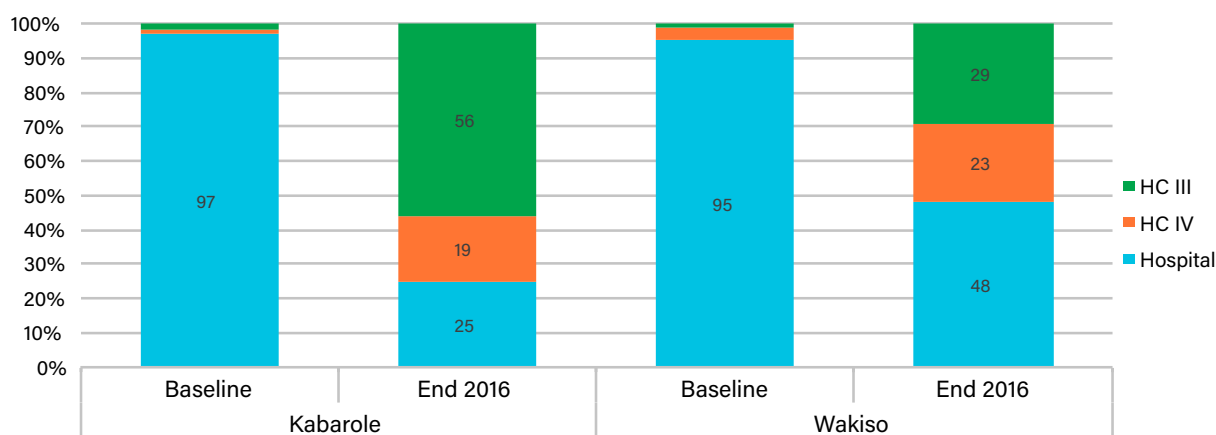


- Development of training materials and job aids for community health workers (on symptom-based screening and management of household TB contacts)
- General health systems strengthening support to improve clinic and laboratory functionality
- Tasks of community health workers: identification, screening and referral of symptomatic contacts for further evaluation for TB disease, and asymptomatic contacts under the age of five years for IPT, as well as monitoring adherence to treatment for index cases, child TB cases and persons on IPT
- Use of a mobile smartphone application to educate and empower frontline health workers to provide TB screening at the community level
- Data collection through routine NTLP tools.

Outcomes/successes

The number of health care facilities offering childhood TB services increased from 65 to 76 in the two districts. Strengthening the diagnosis of child TB at primary and secondary care levels with simple symptom-based screening for child TB household contacts, resulted in an increase in detection and treatment of child TB: from 8.8% of all TB notifications in the year before the project to 15% during the project. The total number of child TB diagnoses in children below 15 years of age more than doubled over this period; there was also a 1.3 fold increase in the number of case notifications in patients over 15 years of age. The project achieved a 95% success rate in treating children diagnosed with TB (up from 65%). A total of 55 children with active TB were identified through contact investigation during home visits to over 2000 child contacts by community health workers, and 74% of 670 eligible children were started on IPT during the project, with an 86% completion rate. Less than 1% of children who were started on IPT developed active TB.

FIGURE 5.1: DISTRIBUTION OF CHILDHOOD TB DIAGNOSIS



HC III: Subcounty level primary health care facility, led by a clinical officer, offering out-patient services and maternal health services

HC IV: County-level primary health care facility, run by a medical doctor, offering HC III services and surgical services

Lessons learned

- Decentralized TB services for children allowed the majority of children to be diagnosed at village health centres and other peripheral health facilities, rather than in large hospitals; thus diagnosing the disease earlier and reducing the burden on larger, central health facilities (see Figure 5.1 above).
- Decentralization also resulted in lower rates of patients being "lost to follow up", helping to ensure that patients completed their treatment regimens, as well as decreasing mortality and the risk of new drug resistance.



- Strengthening of community linkages through training and involvement of community health workers resulted in the successful implementation of household contact screening with active case detection and a high uptake and completion of IPT.
- The increased knowledge and confidence of health care workers on TB in general, resulted in more adults with TB being identified.

Sustainability/scale-up

The initiative's success prompted Uganda's MoH to incorporate the DETECT guidelines into the country's national TB action plan and the ministry is currently scaling up the programme to include eight more districts, with funding from the Uganda Global Fund grant, 2018–2020.

Challenges/outstanding issues to be addressed

- More evidence needs to be generated on the role of community health workers in health services delivery at the community level
- Uncertainty on the accuracy of a clinical diagnosis of TB and whether this could lead to over-diagnosis
- Further implementation research on decentralized and integrated childhood TB services within the routine health care system is needed to provide important evidence of impact.

5.3. The Titi study (Transmission Investiguée de la Tuberculose Infantile)

Countries: Benin, Burkina Faso, Cameroon, Central African Republic

Contributors: Valérie Schwoebel and Kobto Ghislain Koura

The Union Against Tuberculosis and Lung Disease

Background

There is substantial evidence on benefits of delivering preventive treatment in children below five years of age who are contacts of bacteriologically confirmed pulmonary TB patients. This has been translated into a strong recommendation on the implementation of this strategy by WHO (5).

Despite evidence-based international and national recommendations, contact investigation among children is poorly implemented with a lack of documentation in many African countries. Pilot studies have demonstrated that contact investigation and provision of preventive treatment is feasible



Nurse and social worker are about to depart for a home visit in Cotonou (Benin). Image: Valérie Schwoebel, The Union



under programmatic conditions (14). The availability of new paediatric formulations with the correct dosage of rifampicin and isoniazid makes it possible to implement a shorter WHO-recommended regimen of preventive treatment (three months of rifampicin and isoniazid (3RH)).

Description

Titi study ("Transmission Investiguée de la Tuberculose Infantile": contact investigation for childhood TB) was an implementation study, conducted in the capital cities of four francophone countries (Benin, Burkina Faso, Cameroon, Central African Republic) since the end of 2015. The study was coordinated by The Union and funded by France's 5% Initiative.

Children below five years of age living in a household with an adult (≥ 18 years) diagnosed with smear-positive pulmonary TB in the participating TB clinics were enrolled after obtaining their parents' informed consent.

These children were evaluated during home and clinic visits using a standardized questionnaire, clinical examination, TST and chest radiography. Children free of active TB were offered preventive treatment using isoniazid for six months in Benin, or rifampicin-isoniazid (RH75/50) for three months in other countries. They were followed-up quarterly for 12 months after completion of the preventive treatment course.

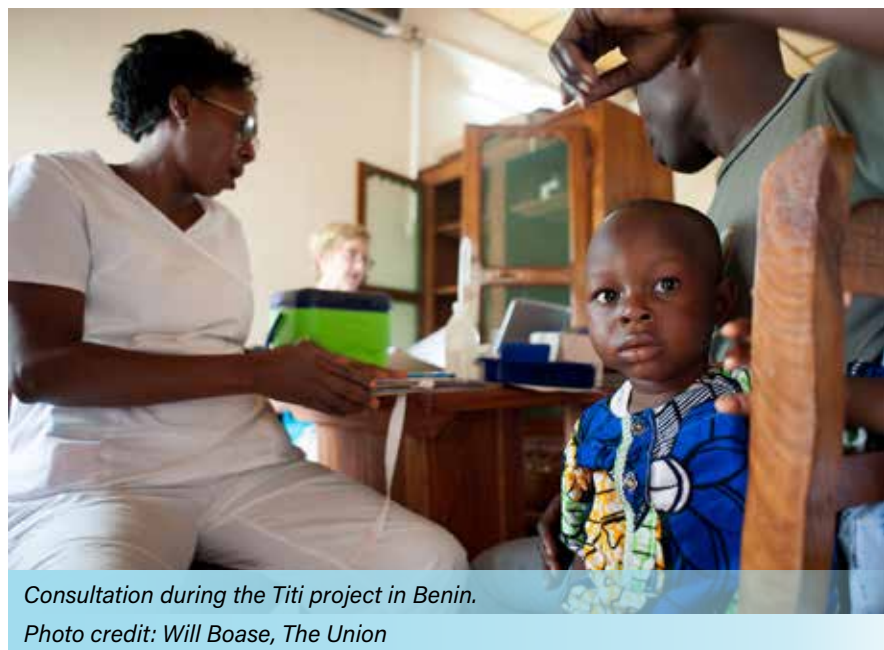
Training of NTP nurses was organized before the study started and standardized tools (weighing scales, preventive treatment register, chest radiography form, drug dosage charts) were distributed.

Outcomes/successes

The inclusion process lasted 18 months up to the end of September 2017, during which 4300 patients notified with smear-positive pulmonary TB in the participating facilities were interviewed for eligibility.

Although this was not routine practice in NTPs, interviewing all patients at the time of TB diagnosis for the presence of children at home appeared feasible.

Participation has been excellent: 92% of eligible parents gave consent and were visited at home. Home visits were very well accepted and clearly provided an added value to the simple interview of index patients at the clinic, in helping to identify contact children and to detect secondary TB cases.



*Consultation during the Titi project in Benin.
Photo credit: Will Boase, The Union*

Preliminary results:

- Close to 2000 child contacts were included in the study
- 5% of them were diagnosed with active TB
- 90% were started on preventive treatment
- Attendance to monthly visits during treatment was good, with over 90% of children completing their course of preventive treatment
- No serious adverse events were reported.
- Follow-up after the end of treatment completion is still ongoing.



Lessons learned

- Training of nurses was essential, since examinations of young children (weighing, clinical examination, gastric aspiration) were not routinely practiced
- Standardized tools were very helpful, such as registers including the outcome of treatment
- Good attendance at the clinic for monthly visits during treatment was facilitated by reimbursement of taxi fares to families
- The wide inter-country differences in chest radiography abnormalities underlines the probable insufficient training of doctors/radiologists on interpretation of chest radiographs in very young children. An external review team is currently performing a blind review of a random sample of chest radiographs to evaluate this aspect.

Sustainability/scale-up

- Elaboration and distribution of standardized tools is needed for scaling-up these activities. This would not require extensive resources.
- Training nurses on TB screening in children needs to be done nationwide
- Results of this study may further support the use of 3RH for preventive treatment in child contacts.

Challenges/outstanding issues to be addressed

- Additional resources and/or involvement of community health workers, depending on countries' programmes, may be needed to implement home visits routinely
- There is a need to clarify and promote the role of nurses in the diagnosis of TB in children, since in some countries only medical doctors have this responsibility
- The use of chest radiography in the paediatric diagnostic algorithm needs to be carefully evaluated. Chest radiography should probably not be used as a TB screening tool for all child contacts, as its performance is not ideal in asymptomatic children
- If used for symptomatic children, chest radiography should be free-of-charge for families, and quality control should be in place to avoid misdiagnosis.

5.4. Transforming the childhood TB programme in Latvia

Country: Latvia

Contributors: Iveta Ozere;¹ Zita Lauska;² Vija Riekstina¹

¹ Riga Eastern Clinical University hospital, Latvia; ² Childrens Clinical University Hospital, Latvia

Background

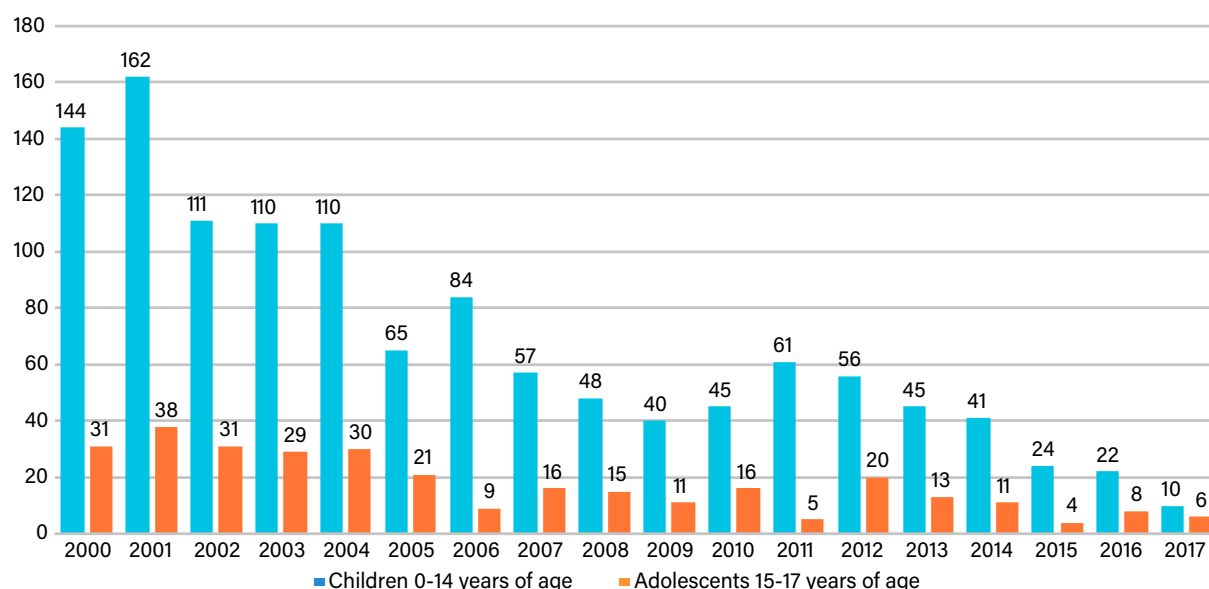
Latvia is a small country located in the Baltic region of Northern Europe with a population of approximately two million and a constrictive population pyramid. Even though TB notification rates have been declining steadily since 2001, Latvia is still among the five high TB incidence countries in the European Union. Latvia is a former Soviet Union country. Until its independence in 1990, TB prevention, identification, diagnosis and treatment was in line with the former Soviet Union regulations. This included BCG vaccination at birth and booster BCG at seven and 14–15 years of age in all TST-negative children; annual TST in children up to 15 years of age with IPT for three months for those with TB infection; isolation and in-patient management in sanatoria and hospitals of TB patients and most patients on LTBI treatment.

Epidemiological surveillance of TB has been strictly conducted in Latvia since the early 1950s. Childhood TB epidemiology trends reflect the ongoing transmission from 1992 and the decrease of transmission rate



since 2001. The proportion of children aged 0–14 years who were diagnosed with TB was never more than 11% of the total number of TB cases and declined with decreasing notification rates of TB in adults. In 2017, children aged 0–14 years made up only 2.1% of all TB cases in the country. The proportion of children (0–14 years) with MDR/XDR-TB was between 2% and 16% from 1998 to 2017. From 1990 to 2010 eleven (0.6%) TB-related deaths occurred among 1950 children (0–14 years) with active TB. The last case of TB meningoencephalitis occurred in 2011.

FIGURE 5.2: TB CASES AMONG CHILDREN AND ADOLESCENTS IN LATVIA, 2000–2017



Description

The country gradually moved towards the WHO recommended approach:

- Regular screening of all children with TST until 15 years of age was changed to targeted TST screening in high-risk groups; interferon-gamma release assay (IGRA) for the diagnosis of LTBI prior to starting preventive treatment was introduced in 2006.
- BCG revaccination was suspended.
- All TB sanatoria were closed, and ambulatory TB treatment started.
- Contact investigation:

Information about household and casual contact children is collected by the pneumonologist by asking the TB patient to list the names of exposed children, and requesting them to come to the hospital for evaluation. If they are not brought in, caregivers are contacted through a letter or phone call. If necessary, family doctors help trace children and manage evaluation. Social workers are involved in some cases to help with logistics (mainly transport). Since 2016, public health workers are participating in the identification of casual contact children (such as in school or kindergarten) who need evaluation. Home visits are not routinely conducted. The coverage of contact investigation is high, with very few cases not being attended to.
- Six months IPT routinely implemented since 2002:

IPT is prescribed by a pneumonologist. Drugs are issued to caregivers for 10–30 days. In the majority of cases IPT is given to the child by the caregiver without direct observation. Regular follow up is provided by the pneumonologist or less commonly by a paediatrician. Frequency of visits varies from weekly to monthly, depending on the child's age, as well as social and medical risk factors. Liver enzymes are checked monthly or more often if indicated.
- The last childhood TB ward was closed in 2017.

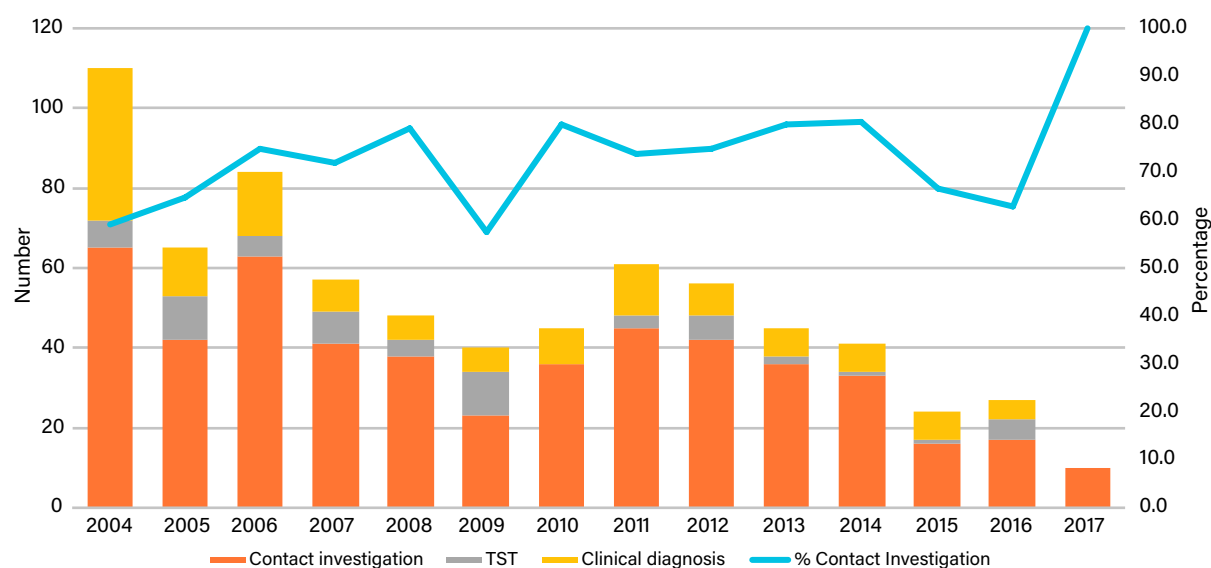


- Use of new drugs for the treatment of drug-resistant TB in children:
Delamanid was used in two 11- and 13-year-old girls in 2015 and one 16-year-old girl in 2017. All of them were diagnosed with pulmonary TB on clinical grounds without bacteriological confirmation and had contact with pre-XDR and XDR-TB patients.

Outcomes/successes

- The implementation of interventions (such as the suspension of booster BCG vaccination and massive TST screening), while TB rates were still increasing due to ongoing transmission of TB in the country was challenging. However, surveillance data showed a continuous decline in the notification rate of TB among children 0–14 years of age and in adolescents 15–17 years of age, along with dropping numbers of adult TB patients since 2002.
- There has been no TB death in children since 2010, and no cases of TB meningitis have been registered since 2011
- Childhood TB data from 2004 through 2017 show that:
 - 708 children aged 0–14 years were diagnosed with TB
 - Of these, 507 (71.6%) were identified through contact investigation, 142 (20.1%) presented with suggestive signs and symptoms and 59 (8.3%) were identified during evaluation after a positive TST
 - The figure below shows the trends over time (from 2004) in methods of case identification in the country.

FIGURE 5.3: TRENDS IN CASE DETECTION BASIS IN CHILDREN (0-14 YEARS) FROM 2004 TO 2017



- Treatment outcomes of drug-resistant TB in children:
Between 2005 and 2016, 59 children (0–14 years) were treated for MDR-/XDR-TB: nine (15%) had bacteriologically confirmed TB, while 50 (85%) were clinically diagnosed. Nine children were cured (15%), treatment was completed in 49 children (83%), and treatment failed in one child (2%). A total of 58 (98%) children reached a successful treatment outcome, including the three who received delamanid.

Lessons learned

- The best strategy for TB case detection in children is contact investigation, allowing early diagnosis, preventing death and providing successful treatment outcomes of TB disease and prevention of progression of LTBI due to preventive treatment.
- Epidemiology of TB in children is mainly influenced by ongoing transmission of TB by infectious adult patients.



- Booster BCG vaccinations and case detection through yearly TST do not have a role to play in preventing childhood TB.
- The best method to reduce the number of TB cases in children is by reducing the number of adult TB patients in the community through active and early case finding, and ensuring successful treatment outcomes in adults.

Sustainability/scale-up

- BCG vaccination should still be continued in all newborn children.
- Directly observed preventive treatment with regimens containing isoniazid plus rifampicin (3HR) and isoniazid plus rifapentin (3HP) should be implemented for children with *M. tuberculosis* infection.

Challenges

- The major challenge for Latvia is the large reservoir of children, adolescents and adults who have latent MDR/XDR-TB infection. Implementation of appropriate treatment of drug-resistant LTBI is very important.
- Identification and registration into the National TB Registry of all household contacts of MDR-/XDR-TB patients to provide early diagnosis of TB and appropriate preventive treatment when it becomes available.

5.5. Introducing routine TB contact investigation with facility-level self-performance monitoring in Malawi

Country: Malawi

Contributors: Rebekah Chang;¹ James Mpunga;² Andrews Gunda;¹ Weston Njamwaha³

¹ Clinton Health Access Initiative; ² NTP, Malawi; ³ KNCV/Challenge TB Malawi

Background

Paediatric case detection is low in Malawi. At the time of this project (2015/2016) it was at a low 39% (1827 notified cases below 15 years of age of 4100 estimated incident cases) (15). Improving routine contact investigation was identified as a key strategy to improve childhood TB case detection and IPT coverage among child contacts below five years of age. Malawi's national TB guidelines recommend contact investigation of households and priority contacts of TB patients; however, implementation has been variable. A TB assessment conducted in 2015 revealed low levels of follow-up screening of household contacts and inconsistent use of TB contact investigation registers. This intervention was designed to build a model that would be scalable by the NTP, if successful. As such, emphasis was placed on undertaking activities using existing NTP staff and resources and strengthening of existing systems for these activities.

Description

In the fourth quarter of 2015, the Clinton Health Access Initiative (CHAI) and NTP developed a package of training materials and tools to facilitate routine contact investigation by facilities, including standard operating procedures, an appointment slip, a revised register, a training curriculum, a job aid for community health workers, screening forms and supervision tools (see Figure 5.4). These materials were initially piloted at three facilities, after which the materials were reviewed and prepared for roll out. During this planning period, CHAI also facilitated a learning trip for NTP staff to Rwanda (see section 7.4) (where contact tracing was already being undertaken routinely), to learn about best practices in contact tracing and paediatric TB.



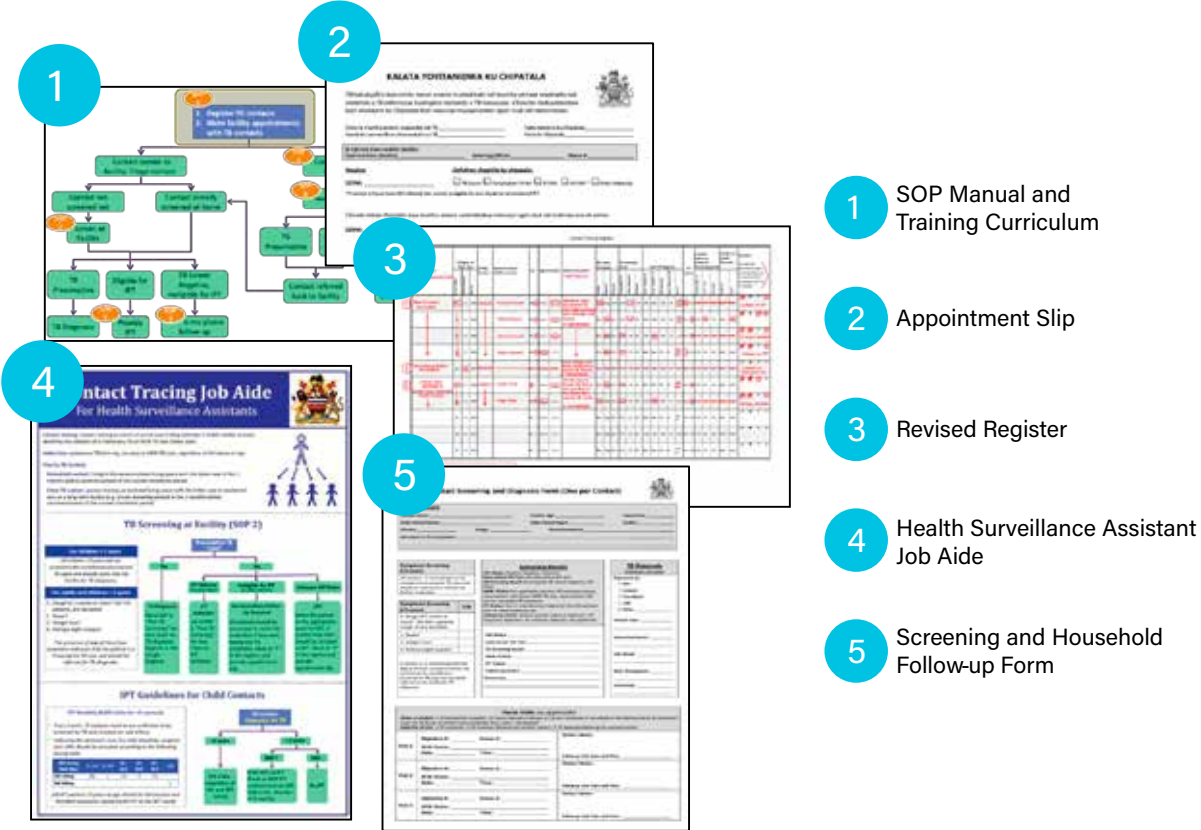
CHAI and NTP staff developed the tools and materials for this intervention and led the initial roll out in five districts. USAID funded Challenge TB project implementer – KNCV – was later engaged to scale up this intervention to other districts.

From August to December 2016, trainings were conducted in 40 high-volume public facilities offering TB services across five districts. The two-day training involved all key facility staff, including community health workers, TB officers, nurses and clinicians. Staff were trained on the standard operating procedures and new tools. Trainings were then followed up with supervision activities. A facility self-assessment tool was introduced through facility visits, which required facility staff to review their contact tracing performance data from their registers on a monthly basis and develop monthly action plans to address areas where the facility was falling short of targets. District and zonal TB officers also integrated review of contact investigation activities in their routine supervision trips.

New tools and training materials were printed, including the standard operating procedures manual, job aides, registers and other new forms. Existing NTP staff-led trainings, and contact investigation activities were implemented by existing facility staff. The only costs that were incurred were one-off costs for printing and implementing trainings.

Pre- and post-intervention analyses were conducted to measure the impact of activities on screening, TB notification and IPT initiation of eligible household contacts. This included primary data collection to collect six months of baseline data. End-line data were collected at the conclusion of the intervention period.

FIGURE 5.4: TOOL AND MATERIALS DEVELOPED



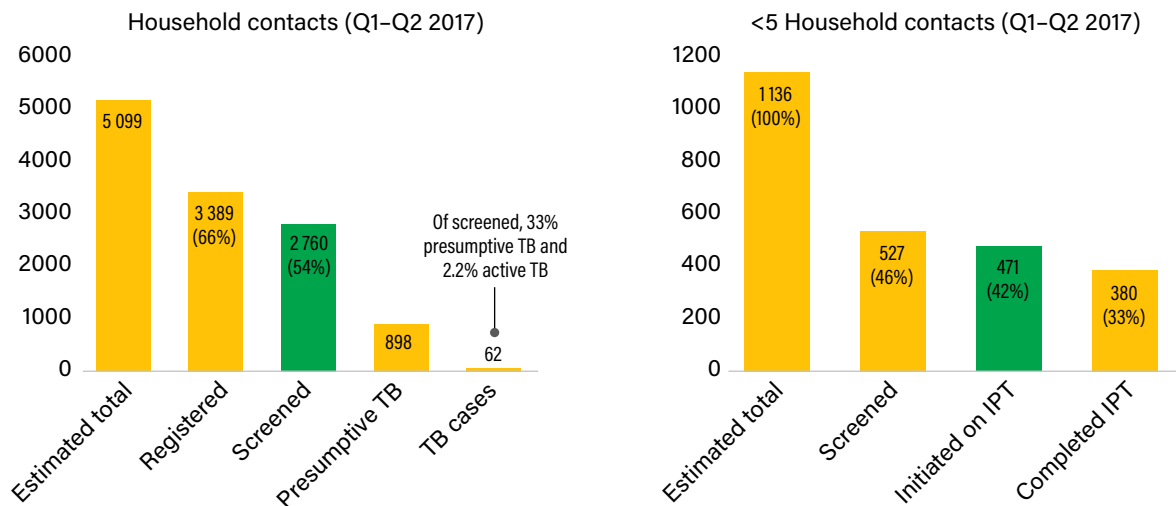
Outcomes/successes

Trainings and subsequent supervisory visits were conducted in 40 facilities, covering 222 health care workers, comprising 69% of public facilities managing TB patients in the five districts. High-volume sites, accounting for 90% of district TB patient burden, were prioritized for training. Across the five districts, this



resulted in an increase in the household contact screening rate from 26% to 54% and the TB preventive treatment coverage rate for child contacts improved from 19% to 42%. In the last two quarters of the project (January to June 2017), IPT initiation was 89% among child household contacts who were screened and not symptomatic. In that period, IPT completion was 81% for this population (see Figure 5.5 below).

FIGURE 5.5: LEFT: CHILDHOOD TB CASE DETECTION THROUGH CONTACT INVESTIGATION; RIGHT: PROVISION OF IPT THROUGH CONTACT INVESTIGATION⁶



CHAI and NTP designed a model to carry out routine contact investigation in public facilities using existing facility staff. Health care workers were motivated to undertake activities given the ongoing mentorship and supervision on these activities. These activities were fully institutionalized within the NTP and district TB teams by the conclusion of the implementation period.

Lessons learned

- High levels of IPT initiation suggested that low levels of contact tracing were the main barriers to initiating IPT.
- The results of the pilot project showed the potential to strengthen contact investigation systems through training and supervision and empower health care workers to monitor their own performance by using simple self-assessment tools.
- Supporting facility staff to learn to complete the simple facility self-assessment tool on a monthly basis ensured that they were reviewing their register data to see whether contact investigation targets were being met. This monthly exercise was very effective in helping facility staff to see gaps in their contact investigation activities and facilitated the development of facility-specific action plans to address these gaps.

Sustainability/scale-up

Given the success of this intervention, the USAID funded Challenge TB project supported the scale-up of these activities in four other priority districts. Further scale-up planning is in consideration by other implementation partners and the NTP.

The following factors need to be considered for scaling up:

⁶ Nyirenda G, Mlauzi L, Chang R, Stillson C, Berman L, Mbendera K, et al. Introduction of a systematic TB contact investigation model with facility-level self-performance monitoring in Malawi. OA-208-14. 48th World Conference on Lung Health, Guadalajara, Mexico, 11-14 October 2017.



- Availability of facility staff to conduct TB contact investigation activities and community health worker staff linked to health facilities.
- Training and mentorship capacity: classroom training of facility staff, on-site training on the self-assessment tool with facility staff, continued mentorship support visits to facilities.
- Capacity to integrate TB contact investigation activities within the health system.

Challenges/outstanding issues to be addressed

- Access to chest radiography services was a key barrier to TB evaluation in children, which could be addressed in other contexts by providing transport vouchers to health facilities with radiography services.
- While supplementary funding for community health workers was not available for this project, funds for transport to households in remote areas or for airtime to follow up with households would have facilitated higher screening rates.
- Many TB patients are diagnosed at the secondary district hospital level and then transferred back to their local health centre for treatment initiation or continuation. This transfer process can cause confusion between sending and receiving sites in terms of who should initiate the process for contact investigation and requires follow-up in supervision visits.

5.6. Zero TB Cities initiative in Kotri, Jamshoro, Pakistan

Country: Pakistan/EMRO

Contributors: Farhana Amanullah;¹ Hamidah Hussain;² Meherunissa Hamid²

¹ *The Indus Hospital, Karachi, Pakistan;* ² *Indus Health Network, Karachi, Pakistan*

Background

The estimated TB incidence in Pakistan in 2016 was 268 new cases per 100 000 population with approximately 51 000 (10%) cases in children. Of these, only 71% were notified to the national programme (1).

One of the objectives of the Zero TB Cities initiative in Pakistan was to enhance the capacity for child TB detection and management, and provide access to free diagnostics and quality assured paediatric TB drugs for effective TB care in children in a rural setting in Pakistan. The biggest challenge identified in Kotri, Jamshoro was access to free quality diagnostics and physicians willing to manage children with TB.

Description

A TB REACH project conducted in rural Sindh in 2015 showed that supporting public sector facilities with trained human resources and screeners resulted in a seven fold increase in child TB notifications from Kotri, Jamshoro. Building on this experience Kotri was included as an intervention area in the Zero TB/child TB proposed budget for 2017/2018. The Global Fund under its reprogramming mechanism approved this intervention. A large regional chest diseases clinic, where drug-resistant TB programmatic services were already supported, was approached and the proposal for child TB service establishment was made. Local media channels ran the news about free diagnostics and respiratory health illness care provision at the chest diseases hospital. A local health care worker was trained in screening children for TB suggestive symptoms/risk factors and a paediatrician with prior clinical experience was trained in child TB management. Children could now access quality chest radiography and Xpert MTB/RIF testing as a first-line diagnostic test for free. The chest diseases hospital, which was already a reporting site for adult TB patients, was now a child TB reporting site as well. The hospital was also provided with child TB FDC regimens from the Pakistan national TB control programme.



Programmatic monitoring and evaluation was conducted on a weekly basis by the programme manager and clinical oversight was provided on a continuous basis by a local experienced paediatrician and a clinical expert based out of Karachi on WhatsApp and Skype as needed. Refresher trainings were conducted every few months.

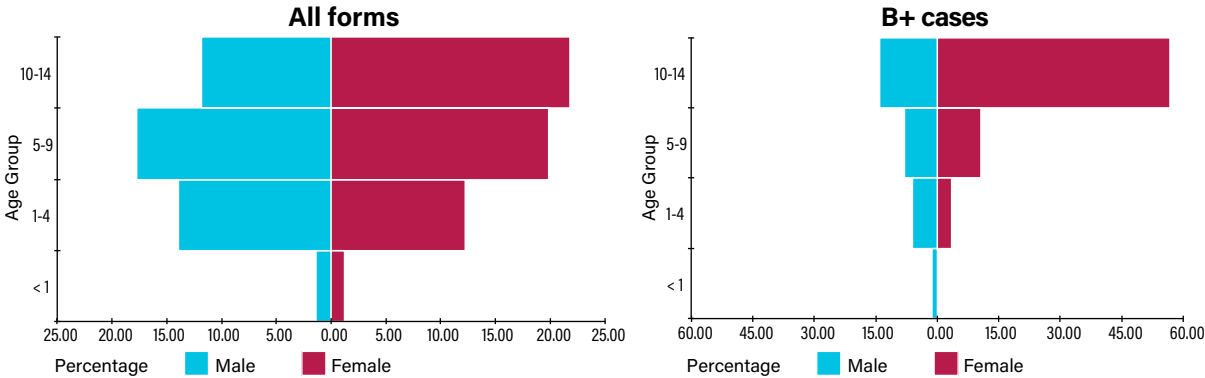
Outcomes/successes

Over a three-month period of programme implementation, of the 9192 children screened for TB symptoms at the chest diseases clinic, 807 children (9%) were diagnosed with TB. In comparison, the average number of child TB cases identified before the project started was around 100 per quarter. Bacteriological confirmation on sputum samples was available in 52/754 (7%) of children diagnosed with pulmonary TB (see Table 5.1).

Table 5.1: Paediatric TB cases in Kotri

Chest clinic	Bacteriologically positive		Clinical diagnosis		Total
	N	%	N	%	N
	52	7%	755	93%	807

FIGURE 5.6: TB CASES BY AGE GROUP AND GENDER



November 2016 to January 2017 (Blue: boys; Red: girls; B+: bacteriological positive)

Lessons learned

- The significant increase in child TB notifications from Jamshoro district from a single centre-based intervention showed that focused, area-specific interventions could be a start to finding missing children with TB.
- The identification of bacteriological positivity in 52 children (when access to Xpert MTB/RIF testing as a first-line diagnostic for children was provided) was an important finding. Further capacity strengthening for specimen collection is needed.
- Local community engagement and media involvement helped raise awareness and direct families to the chest clinic for evaluation.

Sustainability/scale-up

The intervention clearly showed that by supporting and restructuring existing service platforms in a high burden setting and ensuring access to free quality diagnostics and quality assured drugs, a significant increase in case detection can be achieved. The national TB programme, instead of operating in silos,



should implement TB symptom/risk factor screening across all health platforms where families seek care and ensure that clear referral links are available to bring appropriate diagnostics and management services to the families.

Challenges/outstanding issues to be addressed

Capacity for in-patient care was not available at this clinic and gastric aspirates could not be performed. Space and back-up services for induced sputum and nasopharyngeal aspirate collection could not be established and hence full advantage of the Xpert MTB/RIF testing capacity could not be taken. A last limitation of this intervention was that only respiratory samples were tested, thus limiting the bacteriological diagnosis of extra-pulmonary TB.

5.7. Regular screening of children for TB in the Russian Federation

Country: Russian Federation

Contributors: Aksenova Valentina Aleksandrovna;¹ Baryshnikova Lada Anatolyevna;² Klevno Nadezda Ivanovna;¹ Kazakov Alexey Vladimirovich;¹ Vasilieva Lyudmila Anatolyevna;³ Baronova Olga Dmitrievna;⁴ Moiseeva Natalia Nikolaevna⁴

¹ National Medical Research Centre of Tuberculosis, Pulmonology, and Infectious Diseases of the Ministry of Health of the Russian Federation; ² Samara Regional Clinical TB dispensary named after N.V. Postnikov; ³ Yaroslavl Regional TB dispensary; ⁴ Stavropol regional TB dispensary

Background

The main goal of TB control is not only the detection of active TB, but also the prevention of disease. Individuals with latent infection are at high risk for developing active TB. Prophylactic measures are particularly important for this patient group. Tuberculin has been used worldwide for the diagnosis of LTBI for the past century. The main disadvantage of the tuberculin test is the considerable number of false positive results due to the cross-reactivity of the purified protein derivate antigens present in many mycobacteria and in the BCG vaccine strain. Therefore the test has a low specificity in countries where mass BCG vaccination is used (including the Russian Federation). The discovery of antigens specific for *M. tuberculosis* that are absent in *M. bovis*, BCG and in most environmental mycobacteria, has resulted in the development of in-vitro assays, based on measurement of interferon gamma production (IGRA) in response to stimulation with these antigens. These tests have demonstrated high sensitivity and almost absolute specificity. Factors precluding widespread use of IGRA include lack of financial support (as these assays are expensive) and the need for laboratory equipment and highly qualified personnel.

Description

In October 2009, the introduction of a new skin test (the Diaskin test⁷) with a recombinant TB allergen was initiated in the Russian Federation. It contained two antigens present in the virulent strains of *M. tuberculosis* that were absent in the BCG vaccine strain and in the majority of non-TB mycobacteria. Preclinical and multicentre clinical studies of phases I, II and III demonstrated a 95% sensitivity (confidence interval (CI) 98–100) and specificity (CI 90–100) of the Diaskin test in the detection of TB infection, as well as the lack of BCG vaccination effect on the results of this new skin test.

⁷ The performance of the Diaskin test has not yet been evaluated by WHO and as such WHO cannot recommend the use of the test for the diagnosis of LTBI in any setting or patient group. The Diaskin test is used in some countries, mostly in The Russian Federation and other former Soviet Union Republics.



From 2009 to 2014, the Diaskin test was used in the TB service in population groups at risk of TB disease, including for all children with positive TST with subsequent reading of test results 72 hours after the test. Preventive treatment was indicated in patients with positive Diaskin test results (induration of 15 mm and more).

Informed consent was obtained from parents or persons representing the interests of minor children.

Since 2014, the Diaskin test has been used for all children over eight years of age as a screening method instead of TST; in children under eight years of age, it is used in the presence of a positive TST.

Outcomes/successes

In 2014, the Ministry of Healthcare of the Russian Federation analysed test results obtained in 2012 and 2013 for 1 830 432 children and adolescents. This analysis demonstrated that the use of the Diaskin test allowed the identification of individuals with TB infection who should receive targeted preventive therapy. This resulted in a 25% reduction in the number of patients subject to follow-up by TB specialists and a dramatic decrease in the cost of preventive treatment for patients at risk (by more than 50%) compared with previous cost when TST was used. The professional medical community and the Russian Society of TB specialists support the use of the Diaskin test in children.

Since 2012, the occurrence of TB decreased by 41% in children (0–14 years), and by 34% in adolescents (15–17 years). The decreasing trend of TB in children continued in 2017. In the past year, the incidence decreased by more than 14.6% in children and by 9.9% in adolescents. Screening with the Diaskin test resulted in significantly improved early detection of TB and permitted administration of targeted preventive interventions in individuals at high risk for developing TB rather than in all children and adolescents with a positive reaction to TST (as was the case in Russia until 2009); while also increasing the adherence of parents to having their children tested for TB. This measure addresses all aspects of the WHO TB action plan for the European Region 2016–2020. It provides regular screening of individuals in contact with TB patients and of people at high risk. It offers complex, affordable and cost-effective patient-oriented approaches for prevention of further transmission of TB.

Lessons learned

- The incidence of TB in Russian children has decreased in the second decade of the 21st century and the trend continues.
- Widespread use of the intradermal test with the recombinant TB allergen (the Diaskin test) for screening allows timely identification of individuals with TB infection who require preventive treatment.
- The proposed intervention, used along with other anti-TB measures, helps decrease the incidence of TB in children and adolescents through targeted preventive therapy of children and adolescents at risk of developing TB.
- Long-term results of the use of this systematic screening include a significant reduction in the incidence of TB in young people.

Sustainability/scale-up

This is a long-term programme that does not require significant additional financing or workforce. The broader strategy includes wider use of the screening in children, adolescents and adults at high risk.

The results obtained with the Diaskin test in the Russian Federation show the possibility of this tool significantly contributing to reducing the incidence of TB and helping achieve the SDGs by 2030. It can also serve as a valuable experience for other countries, particularly where mass BCG vaccination is used.







6 Engage key stakeholders

2013 Roadmap for childhood tuberculosis:

- ▶ Effective communication and collaboration among the healthcare sector and other sectors that address social determinants of health and access to care: such as global and national policy-makers; maternal, newborn and child health services, HIV services, health education institutions; private health care sector; community based organizations and NGOs; community leaders; researchers and advocacy groups
-

6.1. Implementing a drug-resistant TB patient triage approach in children through stakeholder collaboration

Country: Kyrgyz Republic

Contributors: Bakyt Myrzaliev;¹ Aisalkun Teshebaeva;² Ainur Soorombaeva;¹ Abdulat Kadyrov;³ Yulia Aleshkina;¹ Elena Zdanova;⁴ Aimgul Duishekeyeva;¹ Marion Biremon;¹ Gunta Dravniece⁵

¹ KNCV Tuberculosis Foundation, Kyrgyz Republic; ² National Center of Phtiziatry, Kyrgyz Republic; ³ NTP, Kyrgyz Republic; ⁴ National DR-TB expert committee, Kyrgyz Republic; ⁵ KNCV Tuberculosis Foundation HQ, The Netherlands

Background

In Kyrgyzstan, the number of newly detected cases of TB among children (0–17 years) is increasing at an average rate of 1.6% per year over the past 25 years. In 2016, 639 childhood TB cases were registered, of which only 36 cases had MDR-TB. The low proportion of children with MDR-TB compared to the rates in adults was due to an outdated diagnostic algorithm without access to rapid susceptibility testing for second-line drugs.

In addition, there was no access to the shortest possible and most effective new treatment options for children with drug-resistant TB, including XDR-TB. There was limited contact tracing, a lack of trained staff to perform sputum induction and gastric lavage, and limited health care worker capacity as aspects around childhood TB were not sufficiently covered in trainings. Limited data existed on the estimation of drug needs for children.

Description

Within the framework of the USAID Challenge TB project, KNCV and partners supported the introduction of the TB patient triage approach. Implementation of appropriate diagnostic and treatment algorithms allows for the early allocation of the best drug-resistant TB treatment regimen to rifampicin-resistant TB patients. From the very beginning of the Challenge TB project it was agreed with the NTP and all other stakeholders that children and adolescents will be included.

The approach was supported by national and international partners, including the MoH, NTP, Global Fund, United Nations Development Programme (UNDP), WHO country office, Médecins Sans Frontières (MSF), GDF and the Sentinel project.

Drug-resistant TB diagnostic algorithms and clinical guidelines were revised. Selection of standardized treatment regimen (STR) or individualized treatment regimen (ITR) was based on confirmation of drug resistance by Xpert MTB/RIF, GenoType MTBDRsl, as well as drug resistance patterns of the source of infection or suspected additional resistance to second-line drugs. Patients without resistance to second-line injectables (SLI) and/or fluoroquinolones were allocated to a STR. Patients with extensive resistance to second-line drugs were allocated to standard-length treatment (20–24 months) with addition of new and/or repurposed drugs to the regimen (ITR).

Patient enrolment on STR and ITR was started in January 2017 in two pilot sites (Bishkek city and Chui Oblast). NTP and KNCV teams provided trainings, on-the-job trainings and ongoing supportive supervision on diagnosis and treatment of drug-resistant TB among children by childhood TB experts, including international experts and MDR-TB expert committee members.



Outcomes/successes

A total of 40 children and adolescents with drug-resistant TB were enrolled on second-line treatment between January 2017 and March 2018: 28 on STR and 12 on ITR (5 with bedaquiline, 3 with delamanid, 4 with repurposed TB drugs only). Interim treatment results are promising: 12 children already successfully completed STR and the remaining patients are all still on treatment.

Case study: Aibek getting back on his feet

Four-year-old Aibek is so small he looks half that age. He has spinal and intra-thoracic lymph node TB, a very rare and dangerous form of the disease that mostly occurs in young children. A few weeks ago, he was finally able to stand again, for the first time in two years.

Nine months into his treatment, Aibek no longer has any pain. When he took his first steps in two years, his mom was brought to tears. *“I don’t have the words to explain what we’ve been through, and even less to describe what I felt when I saw my son finally walking again. Now he can even run and play along with the other children, and his doctors assure me that he will grow up normal and healthy.”*

With the assistance of the USAID-funded Challenge TB project, Aibek is receiving an ITR containing the new drug delamanid for XDR-TB. His health is improving each day and he doesn’t have any side-effects from the drugs. After nine long months of hospitalization in Bishkek’s National Tuberculosis Centre, he is now being treated as an outpatient, back home in their mountain village, a few hours away from the capital. He still has over a year of treatment left, but he can now enjoy a near-normal life and start forgetting the ordeal he has been through.

Until recently, Aibek’s life hung in the balance, and his parents had started to lose hope. It took over a year for doctors to properly diagnose him and find a treatment that would help. It all started when Aibek was two. He suddenly stopped walking and could not even sit; he would just lie down day and night. The first doctors his parents consulted in their region said that the boy had rheumatism. Others thought he had a dislocated hip and fitted him with a spica body cast. He endured the cast for eight months, but nothing changed, he still could not take a single step. *“When a painful lump appeared on his buttocks and kept growing, the doctors didn’t change their diagnosis and even accused us of giving him some sort of injections,”* said his mom.

Aibek’s health kept getting worse, he cried all day and stopped smiling; he lost his appetite, and just didn’t act like a child anymore. Doctors wanted to perform surgery to remove the lump, but his parents refused because they thought he was too young. It was only when a sample from the lump was analysed that Aibek was correctly diagnosed with TB and started on treatment. After two months he was found to have drug-resistant TB and his treatment was changed. It turned out that Aibek got XDR-TB from his aunt, who initially refused to be treated, but the Challenge TB team managed to convince her and started her on an ITR with the new drug bedaquiline.

TB is entirely curable, including its drug-resistant strains, but the diagnosis of TB in children remains difficult and often comes late, putting the lives of the smallest patients at risk. In order to raise the profile of the disease among doctors and health care workers, Aibek’s case was presented during a Challenge TB countrywide training on paediatric TB. Training is provided to ensure that health care providers recognize the signs of TB in children, and encourage early diagnosis and follow-up on all close contacts of patients, to find more TB patients who have been missed by the health system.



Since October 2017, based on the success of the first pilot sites, implementation of the new diagnostic algorithm and new treatment approaches was rolled out to all regions in the country.

Lessons learned

The TB patient triage approach for children enabled access to timely diagnosis of drug-resistant TB, followed by prescription of the most effective and shortest possible drug-resistant TB treatment. The experience from the first pilot sites stimulated countrywide expansion of access to STR and ITR in just one year after enrolment was initiated. The use of new regimens is well accepted by clinical teams and appreciated by the children and their parents. Sharing success stories with examples of how new treatments influenced the lives of little patients played a crucial role in advocacy among clinical staff, patients and also politicians.

The Kyrgyz programme is a great example of a very effective, well-coordinated collaboration among key stakeholders and partners:

- Global Fund/UNDP fully supported the introduction of new drugs and regimens and ensured access to drugs, laboratory consumables and safety monitoring tests.
- MSF supported updates on national policies and regulatory framework, and also provided trainings on gastric lavage in Jalalabad and Oblast.
- The GDF and the Sentinel project supported access to child-friendly second-line drug formulations; with support through Challenge TB/KCNV, the NTP has ordered new formulations.

Sustainability/scale-up

Challenge TB/KCNV supported the NTP team in building health care worker capacity in all regions. This was done through trainings and on-the-job trainings with the involvement of international childhood TB experts. The drug-resistant TB training modules and national guidelines include updated information on drug-resistant TB management in children. Specific standard operating procedures on diagnosis and treatment of drug-resistant TB among children are under development and will soon be available for childhood TB experts in all regions in Kyrgyzstan. Management of TB among children and adolescents is included in the agenda of all supportive supervision visits facilitated by Challenge TB/KCNV and NTP teams.

Whenever it is necessary the national childhood TB expert committee is involving international childhood TB experts for distance consultations.

Challenges/outstanding issues to be addressed

- Although it is being scaled up, contact tracing and investigation is still insufficient.
- Limited access to advanced diagnostics such as CT scan.
- Lack of sustainable supervision and clinical mentoring system.
- Insufficient quality of out-patient care.







7 Develop integrated family- and community-centred strategies to provide comprehensive and effective services at the community level

2013 Roadmap for childhood tuberculosis:

- ▶ Use a family/community-centred approach, integrating the diagnosis, treatment and prevention of childhood TB into maternal, newborn and child health, HIV, and nutrition services.
- ▶ Ensure effective coordination and communication among different service providers.
- ▶ Opportunities occur in existing widely used programmes, such as Immune Mechanisms of Protection Against *Mycobacterium tuberculosis* center, integrated management of childhood illness (IMCI), integrated community case management (iCCM) of childhood illness, child HIV care, prevention of mother-to-child transmission, nutritional programmes for children family planning/fertility services.
- ▶ Engage NGOs, community-based organizations and civil society organizations.
- ▶ Critical areas include: increased case finding; treatment support; advocacy for/support of patients and their families; training and supervision for community health workers and volunteers; research.

7.1. Strengthening community and primary health systems for TB. A consultation on childhood TB integration

Global

Contributors: Anne Detjen;¹ Malgorzata Grzemska;² Annemieke Brands;² Cherise Scott;³ Shelly Malhotra;³ Irina Usherenko;³ Joanna Breitstein;³ Sarah Cook-Scalise;³ Elana Robertson;³ Colleen Pero;³ Sabine Verkuijij²

¹ UNICEF; ² WHO Global TB Programme; ³ TB Alliance

Background

To achieve the SDG target for ending preventable maternal and child deaths, the epidemics of TB and HIV need to be addressed. The majority of childhood TB cases remain undiagnosed, because these children do not access care or because TB is not considered as a cause of their illness at the entry point to health care at primary or community level where most children with TB present first. Systematic screening of contacts and high-risk groups for TB and integrated, patient-centred care are important components of the WHO's End TB Strategy.

The strengthening of health systems and the move from vertical, disease-specific programmes to integrated approaches are key to addressing childhood TB. This is especially important at the community and primary care levels, where children and their families affected by TB access care, and where preventive and curative services for women and children are provided.

Description

To engage key stakeholders that have traditionally not been as involved in childhood TB, and to continue the dialogue on how to mainstream childhood TB within the continuum of care for women and children, UNICEF, in collaboration with WHO and TB Alliance, organized a consultation in New York in June 2016 (16).

The objectives of the meeting were to:

- Contribute to the understanding of integrating childhood TB in the scale-up of community and primary care systems for maternal and child health
- Identify opportunities and knowledge gaps
- Learn from country experiences and reflect on key health system functions involved.

Seventy-four experts from different countries and regions, representing country governments, UN organizations, international NGOs, donor organizations, academic institutions and researchers participated in the meeting. Together, they combined expertise in TB, HIV, maternal and child health, nutrition, health systems strengthening, governance, health financing, human resources, health financing, procurement and drug-supply as well as service delivery.

Outcomes

The meeting represented an important step forward in addressing TB as part of broader efforts to end preventable maternal and child deaths and strengthen comprehensive primary care systems.

Participants agreed that there are overall challenges, many of them related to health systems, faced by the TB, HIV, nutrition and maternal, newborn and child health communities that hinder successful implementation of high impact interventions and building of functional and effective primary care programmes. Attempts to better link with maternal and child health initiatives are not unique to TB and





Participants at the global consultation on childhood integration, June 2016

have much in common with those for HIV and nutrition, among others. There are ample opportunities for engagement, calling for increased commitment and leadership of all stakeholders and better collaboration and coordination of efforts.

Key messages

- TB remains invisible on the broader agenda of ending preventable maternal and child deaths.
 - Opportunities for childhood TB in the era of the SDGs and the End TB Strategy to be addressed strategically.
 - High level global and national leadership and champions to drive the agenda.
 - Increasing and broadening the critical mass of people engaged in advocacy, awareness and implementation.
 - Childhood TB to be included in global policy documents and guidance pertaining to child survival/maternal and child health.
- Integration is merely a means that can be used to save children’s lives – it is not an aim by itself.
 - A common understanding of what integration means is needed.
 - Equitable access and comprehensive care for children and their families affected by TB is needed.
- Strengthening the community and primary health centre platforms is essential and could avert up to 77% of maternal, newborn and child deaths.
 - More horizontal programming through better harmonization and coordination of all stakeholders engaging at the primary care level to streamline and facilitate work of health care workers to serve their communities more efficiently.
 - Use of existing platforms, strategies and tools for maternal and child health, HIV and nutrition to address TB at the primary care level.
 - Strengthening of linkages between community providers and facilities as well as referral systems between all levels.
- The current funding environment contributes to fragmentation and verticalization.
 - Funding should allow for integrated approaches and systems strengthening.
 - Inclusion of childhood TB, integration and strengthening of primary care in TB NSPs as well as maternal and child health strategies to promote resource mobilization.
 - An investment case for TB: What is the cost of NOT addressing TB in children?



- Good quality, reliable data are key.
 - Strengthening global and national childhood TB estimates to raise awareness and mobilize resources.
 - Using (sub) national data to inform programme planning.
 - Generation and dissemination of operational data to show the impact of integrated care on childhood TB as well as other child health outcomes.
- Clear policies and guidance are needed but leadership for implementation is crucial.
 - Implementation of policies, scale-up of successful pilots and high impact interventions.
 - Definition of milestones and benchmarks.
 - Clear roles and responsibilities for all stakeholders engaged.

Key actions:

- Raise awareness and increase demand and care seeking.
- Undertake routine screening of TB contacts at the household/community level to identify children with TB and those in need of preventive treatment.
- Ensure routine risk management and referral among sick children to improve early case finding.
- Decentralize diagnostic capacity for childhood TB to all facilities that can initiate treatment.
- Ensure that generic training materials and management tools for integrated community case management in high TB and HIV burden settings are available.
- Document and share lessons learnt, best practices, cost and impact to inform scale up.

7.2. TB/HIV adapted Integrated Community Case Management

Countries: Malawi, Nigeria and Uganda

Contributors: Anne Detjen;¹ Chamla D;¹ Davies A;² Macheso S;^{3,4} Kambanje M;⁴ Kaneka B;⁶ Chakma I;³ Zamasiya T;³ Nsona H;⁷ Mpunga J;⁷ Kolola R;⁷ Adeyemi S;² Muhammad I;⁵ Ahmed AI;⁵ Achebe K;⁵ Mbori Ngacha D;¹ Swedberg E;² Nsugngwa J;⁸ Sekadde M;⁸ Kagwire F;⁹ Mpanga F⁹

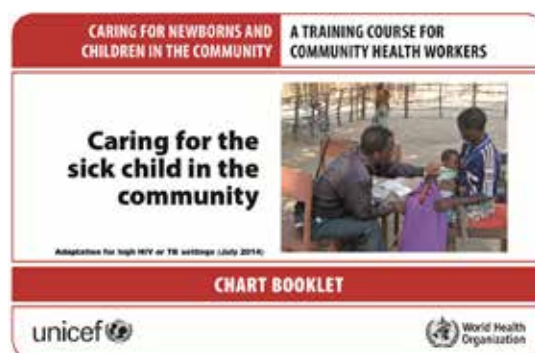
¹ UNICEF, New York; ² UNICEF, Nigeria; ³ UNICEF, Malawi; ⁴ Save the Children, Malawi; ⁵ Save the Children, USA; ⁶ Department of Population Studies, Chancellor College, Blantyre, Malawi; ⁷ Ministry of Health, Malawi; ⁸ Ministry of Health, Malawi; ⁹ UNICEF, Uganda

Background

There are major gaps in paediatric TB and HIV programmes around case finding and access to prevention and treatment that particularly affect young children under the age of five years. Case finding and prevention can be improved by implementing family-centred approaches, targeting affected households through index case testing for HIV and contact screening for TB, and child-centred approaches targeting sick children. Key strategies to provide care for sick children under five years at the community and lower facility level include Integrated Community Case Management (iCCM) and Integrated Management of Childhood Illness (IMCI). There is currently a lot of momentum regarding primary health care for women and children, especially since research has shown that strengthening the implementation of comprehensive packages of services for women and children at the community and primary health care levels could avert 77% of maternal, newborn and child deaths (17).



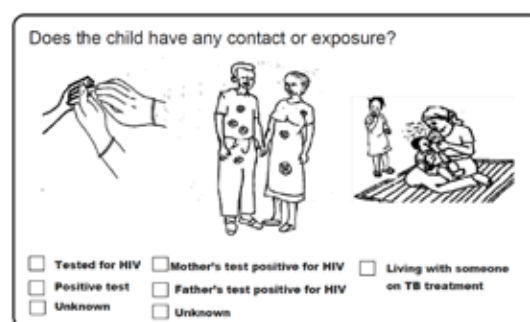
iCCM is an equity-focused strategy that complements and extends the reach of public health services by training community health workers to provide timely and effective treatment of key causes of child morbidity and mortality (especially targeting malaria, pneumonia and diarrhoea) to populations with limited access to facility-based healthcare, and to ensure referral of children showing danger signs (18). In 2014, WHO and UNICEF with partners revised the generic iCCM training and management tools to include risk assessment for TB and HIV.⁸ To assess acceptability, feasibility and operational challenges of adding TB and HIV components to iCCM, UNICEF and Save the Children, together with government partners, piloted the TB/HIV iCCM in Malawi, Nigeria and Uganda – countries with a high burden of TB and TB/HIV as well as a significant paediatric TB case detection and antiretroviral treatment gap.



Nigeria had an estimated incidence of TB in 56 000 children (0–14 years) in 2016, but a case detection rate of 9.4% with only 5244 children (1621 aged 0–4 and 3623 aged 5–14 years) reported to the NTP. Uganda had an estimated 8700 child TB cases, with a case detection rate of 41%. In Malawi, an estimated 2200 children develop TB every year, while 62% of those were reported to the NTP in 2016. Antiretroviral treatment coverage among children living with HIV was 17%, 47% and 49% in Nigeria, Uganda and Malawi, respectively.

Description

National iCCM materials were adapted in all countries to include additional questions on HIV and TB risk. HIV risk was defined as: one or both parents have HIV and the child has not been tested (unknown status); or the parent's HIV status is unknown (unknown exposure). TB risk was defined as: the child lives in a household with someone who is on TB treatment. The community health worker iCCM package, including the chart booklet, sick child recording form, and iCCM register, supervision and mentorship checklists, was updated with this additional information. Identification of a child at risk of either TB or HIV should prompt the community health worker to advise referral to the primary health care facility.



Adapted community health worker chart booklet for iCCM, Uganda

The TB/HIV adapted approach was first piloted in Blantyre District in Malawi, with 10 linked primary health care facilities and 27 trained community health workers (health surveillance assistants), for nine months in 2015/2016. In 2016 and 2017, Nigeria and Uganda started their pilot projects. In 2016, WHO held a regional training of trainers on the generic TB/HIV iCCM package in Uganda with participants from Ethiopia, Malawi, Uganda and Zambia. In Nigeria four local government areas in Adamawa state implemented the pilot with 390 trained community health workers linked to 38 primary health care facilities. In Uganda it was implemented in three districts (Kayunga, Sheema and Wakiso), with 220 trained community health workers (village health teams), linked to 13 primary health care facilities.

Outcomes

In Malawi, of the 10 794 sick children under-five years of age seen by health surveillance assistants, 17 (0.2%) were identified as at risk for TB, nine were known HIV-positive and 419 (4%) were identified as at risk of HIV.

⁸ Caring for the sick child in the community, adaptation for high HIV or TB settings. Geneva: World Health Organization; 2014 (http://www.who.int/maternal_child_adolescent/documents/newborn-child-community-care/en/, accessed 18 August 2018).



To estimate the number of children that would be expected to have TB exposure during the study period, the method described by Yuen et al. (10) (see section 2.2) was applied to Blantyre District: 34 under-five child contacts would require evaluation over the pilot period of nine months, who would require either TB treatment or preventive treatment. Of these three children would be expected to have active TB disease.

The project identified 17 children at risk for TB, or 50% of the estimated number of child contacts. Ideally, these children should have been detected through household contact screening before presenting with illness to a healthcare provider.

In Nigeria, 17 509 sick children were attended to by community health workers, of whom 71 (0.4%) were identified as at risk of TB, none were known HIV-infected, and 6071 (35%) were identified as at risk of HIV. While the data could not be disaggregated, health workers reported that a large number of HIV-risk children were identified due to unknown HIV status of the parents.

In Uganda, of the 8645 children seen by village health teams, 48 (0.6%) were living with someone on TB treatment, 19 (0.2%) were known HIV-positive and 69 children (0.8%) had known HIV exposure with unknown status. However, almost all other children seen by village health teams (8308, 96%) were marked in the iCCM registers as “unknown HIV exposure”. Qualitative assessments showed that stigma, especially around HIV, was a major factor affecting the consistency and quality of risk assessment (not all community health workers correctly applied the new questions), trust and openness to disclose HIV status by caregivers, and issuance and uptake of referrals, highlighting the need for stigma reduction, counselling skills and supportive supervision.

There were challenges in all countries around uptake of referral as well as preparedness of primary health care facilities, especially in paediatric TB diagnosis.

Lessons learned

- Overall, stakeholders positively embraced the integrated approach and recognized its potential impact on TB and HIV case finding among young children, as well as on child-centred service delivery and quality of iCCM.
- The community platform is an important entry point for preventive and promotive paediatric TB and HIV interventions, including stigma reduction, awareness and demand generation, care seeking, identification of children and families at risk as well as treatment support.
- It is feasible to add TB and HIV risk assessment to iCCM and does not seem to negatively impact community health workers’ assessment for the “standard” conditions. However, clear guidance, clinical practice lessons, follow up, mentorship and supervision were perceived as crucial by all actors to reinforce knowledge and assure quality regarding the newly introduced as well as “standard” interventions and tools.
- In Nigeria and Uganda, a large proportion of children with unknown HIV exposure were identified. This highlighted the need to refer caregivers with unknown HIV status and to strengthen access to and uptake of HIV testing and counselling services.
- The risk assessment for TB only identified children with current TB exposure but should be expanded to identify children with exposure during the past one to two years when risk of disease progression remains high. Community health workers should be aware of additional factors that help to identify TB risk in a child.
- **Stigma** was a major factor impacting whether community health workers assessed children for TB and HIV risk especially in Nigeria and Uganda; whether caregivers disclosed HIV status or TB exposure; and whether they adhered to referral.
- Major **health system barriers** that impacted children’s access to diagnosis, prevention and treatment include:
 - Weak community–facility linkages for referral and back referral impacts the flow of information and clients.
 - Cost of transportation and distance affect uptake of referrals by caregivers.



- Primary health facilities do not always provide HIV testing for children under 18 months of age, and there was very little or no capacity specifically around childhood TB diagnosis; some facilities faced stock outs of basic commodities including for TB, HIV and key childhood illnesses (such as dispersible amoxicillin).
- Fragmentation of services at facilities negatively impacts the management of TB in children.
- Data systems across different levels of care and health programmes complicate patient tracking.

Sustainability/scale-up

- Stakeholders in Nigeria defined actions to strengthen the continuum of care from community to facility level, to improve referral mechanisms and facility readiness to manage children with TB and HIV. This should be achieved through better collaboration between state level iCCM, TB and HIV coordinators. Specific indicators were added to be addressed by primary health care supervisors including the verification of uptake of HIV testing, TB screening and TB treatment initiation at referral facilities.
- The Malawi MoH IMCI unit and TB programme discussed ways to scale-up TB/HIV iCCM to all districts in the country.
- The Uganda team plans to further consolidate capacity and ensure adequate support for continuation and further strengthening of ongoing activities in the three implementation districts. Scale-up to other districts, led by the iCCM technical working group, would depend on the capacity of those districts to provide full support and build capacity to ensure quality. National level leadership as well as endorsement of integrated activities by all vertical health programmes is required.

Challenges/outstanding issues to be addressed

- Decentralization of diagnostic, treatment and preventive services for paediatric TB to primary care level, with training of health care workers and ongoing mentoring and supervision.
- Strengthening of the referral system to ensure that children who are identified as 'at risk' at community level, reach the referral facility and receive necessary care in terms of evaluation for active TB, TB treatment and/or preventive treatment.
- Stigma is a major barrier for community health workers, caregiver and communities. Community health workers need to be equipped with basic skills to address stigma and counsel families on TB and HIV.
- Algorithms for risk assessment should be revised to include clear actions for unknown HIV exposure as well as to better define TB exposure.
- For higher impact, a health systems approach is needed, addressing all building blocks of the health system: governance and leadership; financing; health information; health workforce management; supply chain management; and service delivery.

7.3. Integrated approaches for intensifying TB active case finding: lessons learned from pilot projects in West Africa

Countries: Guinea Conakry, Senegal and Ghana

Contributors: Corinne Merle;¹ Franck Bonsu;² Yaw Adusi-Poku;² Marie Sarr;³ Nafissatou O Toure;⁴ Adama Bangoura;⁵ Magassouba A Sidiki;⁵ Paul Milligan;⁶ Jean-Louis Ndiaye;⁷ staff of National Malaria, TB and Nutrition programmes of Ghana, Guinea and Senegal

¹ *Special Programme for Research and Training in Tropical Diseases (TDR)*; ² *NTP, Ghana*; ³ *NTP, Senegal*;

⁴ *TB research task force*; ⁵ *NTP Guinea*; ⁶ *London School of Hygiene and Tropical Medicine, UK*; ⁷ *UCAD, Senegal*





Home visit during SMC activities in Guinea

Background

Despite ongoing efforts TB case detection is estimated to be around 60% in sub-Saharan Africa. Intensified case finding is necessary to better control the epidemic and to achieve milestones for TB case reduction set by the End-TB Strategy. This is particularly the case for children under five of age who are often under-diagnosed in the Region. Intensified case-finding strategies targeting “at-risk” populations have been piloted but are sometimes too expensive to be sustainable in the long-term when implemented by vertical NTPs. Integrating health activities potentially increases cost-effectiveness and favours sustainability, but this implies service integration and collaboration across vertical, independent programmes. The NTPs of Ghana, Guinea and Senegal tested whether piggy-backing a TB screening programme onto a door-to-door outreach campaign providing malaria prophylaxis could increase TB case detection among children under five years of age.

Description

The objectives of these pilot projects were to assess the feasibility, acceptability, efficacy and cost of a strategy among children integrating systematic clinical TB screening within door-to-door seasonal malaria chemoprevention (SMC) activities.

All children who received SMC were checked for: (i) symptoms suggestive of TB (i.e. cough, failure to thrive, loss of appetite, fever and fatigue/reduced playfulness); (ii) nutritional status assessment using the mid-upper arm circumference (MUAC); (iii) a history of TB contact. If a child presented with one or more symptom(s) or a MUAC measurement revealing moderate or severe malnutrition, s/he was referred to the health post for further investigations (sputum collection, smear microscopy, chest radiography, TST, Xpert MTB/RIF, depending on the setting and availability of services). In Ghana and Guinea, health care workers in charge of SMC did the initial screening, whereas in Senegal a TB staff member joined the SMC health care worker teams. In Ghana, clinical TB symptoms were also checked in adults living in the same household as the children screened.

Outcomes/successes

In one week around 300 000 children below the age of 15 years were screened (150 000 in Ghana, 141 264 in Guinea and 11 799 in Senegal). All guardians/parents consented to TB screening of their children. A total of 5608 presumptive TB cases were identified in children under 15 years of age (1.9% of children screened). Of these, 1922 were under the age of five years (1.0% of under-fives screened). A total of 37 cases of TB were diagnosed in children under 15 years (0.7% of those with presumptive TB), with 23 under-fives (1.2% of under-fives with presumptive TB). No TB cases were diagnosed in Senegal, but 30 childhood TB cases were found in Ghana (18 in children under five years) and seven childhood TB cases in Guinea (five in children under five years) (see Table 7.1). Twenty additional adult TB cases (parents or guardians of the children) were identified in Ghana during the same week. A total of 48 severely malnourished children were also detected and referred for nutritional rehabilitation.



Table 7.1: Results of the integrated TB and malnutrition screening during SMC

	Ghana		Senegal		Guinea	
	<15	<5	<15	<5	<15	<5
Children <15 years screened	150 000	117 490	11 799	5 403	141 264	71 318
Presumptive TB	493	249	1 778		3 337	1 673
<i>% presumptive TB among children screened</i>	<i>0.33%</i>	<i>0.21%</i>	<i>15.1%</i>		<i>2.4%</i>	<i>2.3%</i>
TB diagnosis	30	18	-	-	7	5
<i>% TB diagnosis among presumptive TB cases</i>	<i>6.1%</i>	<i>7.2%</i>	-	-	<i>0.21%</i>	<i>0.30%</i>
Started TB treatment	30	18	-	-	7	5
Adult TB diagnosis		20		0		0
Severe acute malnutrition		26		17		5

Lessons learned

At the national level, opportunities for integrating national programme activities exist but efforts to implement them effectively are rarely undertaken. The integration of SMC, TB and malnutrition screening, as piloted in Ghana, Guinea and Senegal, are examples of successfully integrated activities. These three pilot studies demonstrated that an integrated approach with TB and malnutrition screening along with SMC is feasible, acceptable and effective. Because of this one-week intervention, the notification of TB cases in children under the age of five years drastically increased in the district where the pilot was conducted in Ghana and Guinea (see Table 7.2).

In Senegal, the intervention was not fully integrated (i.e. an extra TB staff member joined the SMC teams), whereas in Ghana and Guinea health care workers delivering malaria preventive treatment were also the ones screening for TB and malnutrition. Therefore, with the same budget (around US\$ 20 000), a lower number of children could be screened in one week in Senegal compared to Ghana and Guinea. In addition, although a higher proportion of presumptive TB cases were identified in children, their referral and follow-up were less effective and no children were (known to have been) diagnosed with TB. This advocates for a full integration of activities of the two programme activities in order to increase efficiency.

These pilot projects helped sensitize and increase the capacity of health care workers and health staff to detect TB in children. The trend of TB notifications in children in the districts where the pilots were conducted will be analysed to assess the potential long-term effect on improving TB diagnosis in children in these countries.

Sustainability/scale-up

SMC programmes are led by national malaria control programmes and supported by national governments, UNICEF, Peace Management Initiative (PMI), Unitaid, World Bank, and a number of other NGOs, with commitments from the Global Fund to contribute funds for SMC continuation in a number of countries. Cost-effectiveness analyses of the integrated approach are currently underway to provide more evidence for the scale-up of this integrated strategy in all countries where SMC is done. In 2017, 12 countries in West and Central Africa implemented SMC, treating around 18 million children. Because of its scale and

Table 7.2: Increased case notification during SMC/TB integration pilot projects

	2015/2016	SMC/TB integration pilot
Ghana	1 case notified in one year (2015)	18 cases diagnosed in one week
Guinea	3 cases notified in one year (2016)	5 cases diagnosed in one week



outreach capacity, combined with secured funding by partners, SMC provides a unique opportunity for reducing under-diagnosis of TB in children in West and Central Africa by integrating TB screening in SMC door-to-door activities, which is acceptable to the families.

Challenges/outstanding issues to be addressed

Further operational/implementation research is needed to maximize the cost-efficiency of this integrated model. For instance, cost-effective strategies need to be found for improving the referral system and ensuring sustainability of this strategy at low cost. This is an ongoing exercise. The NTP of Burkina Faso will conduct a similar pilot in 2018 with improvements in the strategy tested thus far. For example, health care workers will be involved in the follow-up of children with presumptive TB to improve the referral system. In addition, preventive treatment will be offered to children under-five years of age who are identified as contacts of TB patients, and not receiving TB preventive treatment.

Political willingness of national programmes to collaborate is needed for defining and scaling-up cost-effective, integrated strategies that would benefit populations and programmes. Implementation research of similar programmes needs to be conducted at increased scale to convince policy makers of the cost-effectiveness of such integrated approaches.

7.4. Contact investigation and integration of TB into IMCI in Rwanda

Country: Rwanda

Contributors: Patrick Migambi;¹ Jules Mugabo;² Mutembayire Grace;³ Augustin Dushime³

¹ NTP, Rwanda; ² WHO, Rwanda; ³ MoH, Rwanda

Background

TB remains a major health public issue among adults and children. Children under the age of five years and exposed to a person with TB disease in the household have been shown to have much higher rates of TB prevalence and mortality than the general population. WHO recommends that all children in close contact with TB cases be screened for TB and referred for diagnosis and treatment if they have symptoms of disease; or given TB preventive treatment after exclusion of TB infection. According to the WHO *Global tuberculosis report 2017*, only 13% of the 1.3 million children estimated to be eligible for preventive TB treatment had started TB preventive treatment in 2016 (1).

Rwanda's history is marked by the 1994 genocide that led to the death of over one million people, displacement of millions more and devastated the health system and economy. In the years that followed, Rwanda put in place a decentralized health system with community-based health insurance and performance-based financing systems as key components.

Over the past decade, Rwanda has demonstrated significant progress in fighting TB. TB incidence dropped from 98 per 100 000 in 2000 to 50 per 100 000 in 2016 and the TB mortality rate decreased from 17 per 100 000 to 2.7 per 100 000 over the same period. The treatment coverage rate was 100% in 2016. Although Millennium Development Goal 6 was achieved, the proportion of TB cases among children below 15 years has seen a decrease from 10.8% to 5.7% of total TB cases between 2007 and 2014.

To improve TB detection and TB case management among children, the NTP in collaboration with the Rwanda Paediatric Association, developed a TB diagnostic algorithm specific to children in 2008. In 2014, the first stand-alone childhood TB guideline was developed.



Rwanda acknowledges the challenges of TB diagnosis among children and of the roll out of the TB childhood guideline. To augment childhood TB diagnosis and management, the MoH decided to integrate TB management into IMCI guidelines and tools.

Description

Contact investigation

- In 2008, the Rwandan NTP initiated TB contact screening among children and adults at all health facilities and subsequently the following activities were implemented:
- Development of a policy for TB screening, diagnosis and treatment for all contacts of bacteriologically confirmed TB cases. The patient treatment card was revised to include contact tracing.
- Regular training of health care providers on the policy.
- Preparation of lists of names of all contacts living with the index case before treatment initiation.
- Home visits for TB symptom screening. If a contact is absent during the home visit, the health care provider involves the community health worker nearest to the index case to explain the importance of screening to family members.
- Provision of IPT to all children under five years of age without active TB. At initiation of IPT a supply of isoniazid (INH) for two weeks is provided to the caregiver after which follow up is done monthly.
- Symptomatic children are referred to the TB clinic for full physical examination and diagnostic testing according to the national algorithm to confirm or exclude TB.

Integration of TB into IMCI

In 2013, Rwanda developed the TB NSP (2013–2018) that addressed childhood TB as one of the major TB control interventions. One of the strategic interventions to improve TB case detection among children was to integrate TB into IMCI guidelines and tools. A concept note of integration of childhood TB into IMCI was developed and approved by the NTP and Maternal, Child and Community Health (MCCH) division.

The following activities have been conducted to implement the strategy in collaboration with MCCH, NTP, WHO, UNICEF, and the Technical Working Group:

- Coordination meetings to develop the terms of reference and roadmap for the integration of childhood TB into IMCI.
- A workshop to review and update the national IMCI guidelines, training materials and tools in 2014.
- Integration of childhood TB into IMCI guidelines, training materials and tools.
- Establishment of the Childhood TB Technical Working Group to coordinate and oversee the implementation of activities and conduct monitoring and evaluation.
- Capacity building of health care providers through a cascade of trainings on childhood TB and IMCI integration at district hospitals and health centre level. Distribution of new tools.

Supervision was conducted from central level to district hospitals and from district hospitals to health centres along with quarterly evaluation meetings to discuss data quality and provide recommendations for improvement.



Mentoring on TB integrated IMCI in a clinic

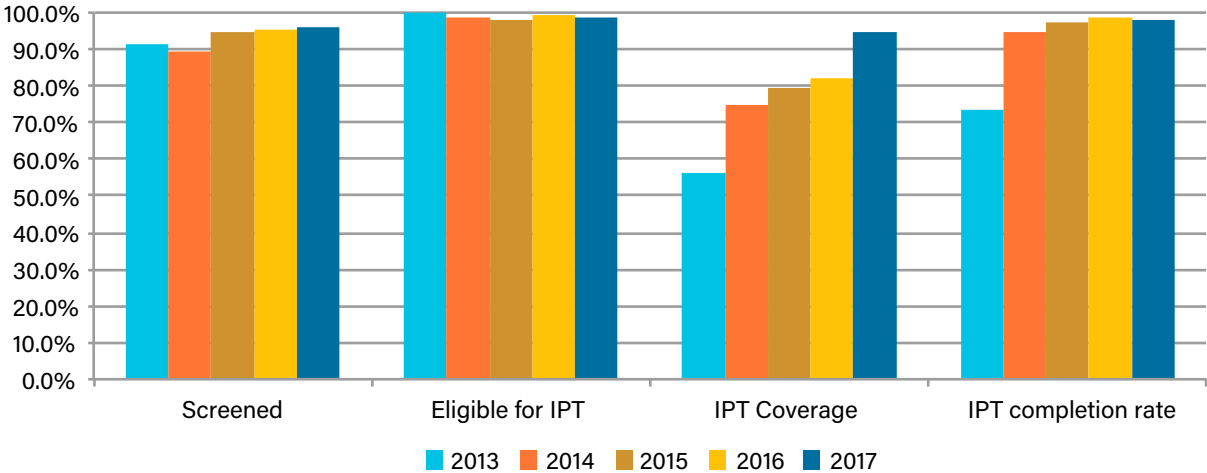


The NTP conducted a rapid service quality assessment at least once a year to evaluate the implementation of the strategy and the quality of health services provided.

Outcomes/successes

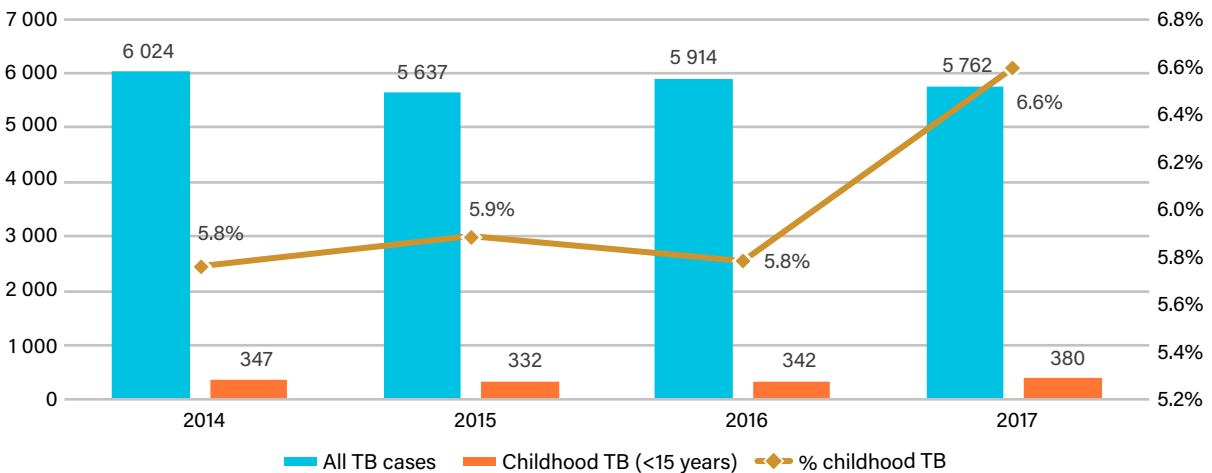
IPT coverage increased from 56% in 2013 to 94% in 2017. IPT completion increased from 73% to 98% over the same period (see Figure 7.1). The high IPT coverage was associated with home visits and contact tracing by healthcare providers in collaboration with community health workers.

FIGURE 7.1: IPT DATA FOR 2013 TO 2017



The use of TB integrated tools in the management of IMCI increased from 62% to 79% between 2015/2016 and 2016/2017. The number of childhood TB cases under 15 years of age increased from 347 in 2014 to 380 (6.6% of all cases) in 2017. Figure 7.2 summarizes childhood TB notification data from 2014 through 2017.

FIGURE 7.2: CHILDHOOD TB NOTIFICATIONS IN RWANDA, 2014-2017



The integration has helped Rwanda to reduce implementation related costs. Surveillance data up to 2017 included data on childhood TB for ages 0–14 combined, with data collection in separate age bands (0–4 and 5–14 years) starting from 2017.



Lessons learned

Strong political commitment and effective programme management were critical for successful TB contact tracing and integration of TB into IMCI. The high rate of IPT uptake was the result of close collaboration between the central and district levels and the community. This experience demonstrated that if maternal and child health and TB programmes work together and have a good understanding of critical issues and plan accordingly, integration is possible without additional cost.

Sustainability/scale-up

Rwanda has invested in a decentralized and integrated healthcare system with an effective community health system that contributed to reduce under-five and maternal mortality rates. The country will take advantage of the high universal coverage rate to provide access to health and strengthen community activities. Based on the experience of IMCI integration, Rwanda plans to scale up integration of childhood TB into iCCM.

Challenges/outstanding issues to be addressed

Despite sustained efforts to improve childhood TB case finding, the programme still has missing TB cases and the confirmation of active TB among children remains a challenge that needs innovative solutions. Therefore, capacity building is needed for health care providers. In addition, innovative diagnostic tools that are appropriate for TB diagnosis among children are needed.

7.5. Childhood TB integration into IMNCl in health facilities of Addis Ababa

Country: Ethiopia

Contributors: Lemma Ketema;¹ Dawit Assefa;¹ Eveline Klinkenberg;¹ Zewdu Gashu;¹ Zerihun Yaregal;¹ Getachew Wondimagegn;¹ Ahmed Bedru;¹ Sentayehu Tsegaye;¹ Tilaye Gudina;² Anteneh Kassa;² Taye Letta;² Blen Ayele;² Lissanu Tadesse;³ Yared Tadesse;³ Kassa Hailu;⁴ Ismael Hassen;⁴ Ben Tegegn;⁵ Kidist Abayneh;⁵ Hailemariam Legesse⁶

¹ USAID/ChallengeTB; ² FMOH/NTP Ethiopia; ³ FMOH/Child Health, Ethiopia; ⁴ Addis Ababa City Administration Health Bureau; ⁵ WHO Ethiopia; ⁶ UNICEF Ethiopia

Background

Ethiopia is one of the 14 countries that appear in all three high-burden country lists for TB, TB/HIV and MDR-TB. The estimated burden of TB in children (0–14 years) was 24 000 in 2016, with 15 806 TB child cases notified in 2016/17 (65.9% of estimated cases).

The National Health Management Information System TB performance report for 2007 (July 2014 to June 2015) showed that children aged below 15 years comprised 13.6% (18 444 out of 135 951) of all forms of reported TB. In Addis Ababa, this was only 6% (541/9401), due to a variety of reasons, including poor implementation of contact investigation, difficulty of obtaining sputum samples for bacteriological testing, inadequate identification of children with presumptive TB, as well as inadequate clinical skills and knowledge of clinicians to diagnose TB in children.

In July 2015, the national TB and leprosy programme in Ethiopia launched the “National Roadmap for Prevention and Control of Childhood TB in Ethiopia”, which calls for integrated childhood TB screening, evaluation and diagnostic services into the primary healthcare level through collaboration with the national



child health survival strategy. IMNCI and other relevant child health services provide delivery points to improve national notification of TB in young children and coverage of preventive treatment.

This demonstration study is designed to evaluate the feasibility of the integration model and assess the contribution of intervention packages towards childhood TB control.

Description

A demonstration research project on the integration of childhood TB to IMNCI was initiated in September 2016, as a collaboration between the Addis Ababa City Administration Health Bureau, the Federal MoH/NTP and the USAID funded Challenge TB project.

The demonstration study had the following objectives:

- To increase by 50% the proportion of identified presumptive TB cases among children under five years of age visiting health centres
- To increase by 50% the number and proportion of childhood TB cases among all detected TB cases
- To ensure that all sick children visiting IMNCI clinics are screened for symptoms of TB during the roll out of the intervention
- To increase by 75% the proportion of under-five TB contacts, for whom contact investigation is conducted
- To increase by 50% the uptake of IPT among eligible children under five years of age
- To increase IPT completion rates to 75% for all children started on IPT
- To assess the feasibility of integration of childhood TB into IMNCI/iCCM at the selected health facilities during the study period.

A total of 30 health centres were randomly selected from health centres with high paediatric patient loads. A phased approach was implemented, whereby 10 health centres were made part of the study in blocks. Training was conducted between August 2016 and December 2017.

The intervention package included the incorporation of a TB case management flowchart in the national IMNCI chart booklet, the addition of a TB screening column in the IMNCI treatment register, and sensitization training on paediatric TB for child health and TB programme officers, health extension supervisors and facility administrators from the 30 selected health facilities. A paediatric TB desk reference, contact investigation and IPT registers, and an updated IMNCI register were supplied. On-site coaching was provided on specimen collection using nasogastric aspiration techniques. Monitoring of implementation was conducted monthly and quarterly, and periodic performance review meetings were held.

Outcomes/successes

IMNCI/TB integration

TB screening at under-five clinics increased to 98% from 28.3% at baseline. The proportion of identified presumptive TB cases increased six fold (from 0.06% to 0.33%, although it is still low at less than 1%). Trained health care workers for the first time performed 81 nasogastric aspiration procedures during the intervention. Although all health facilities were provided with nasogastric tubes, the nasogastric aspiration procedure was done only for one third of children with TB symptoms. From September 2016 to November 2017, 50 TB cases in children under the age of five years were identified, 30 through IMNCI and eight through contact tracing (20% were bacteriological positive, and the others were clinically diagnosed). Before the intervention only one TB case among under-five children was diagnosed (July to August 2016). An additional nine TB cases were referred from other facilities. HIV testing was done for 97% of the child TB cases, with a positivity rate of 7%.



Table 7.3: Presumptive TB, TB case identification and nasogastric aspiration procedure

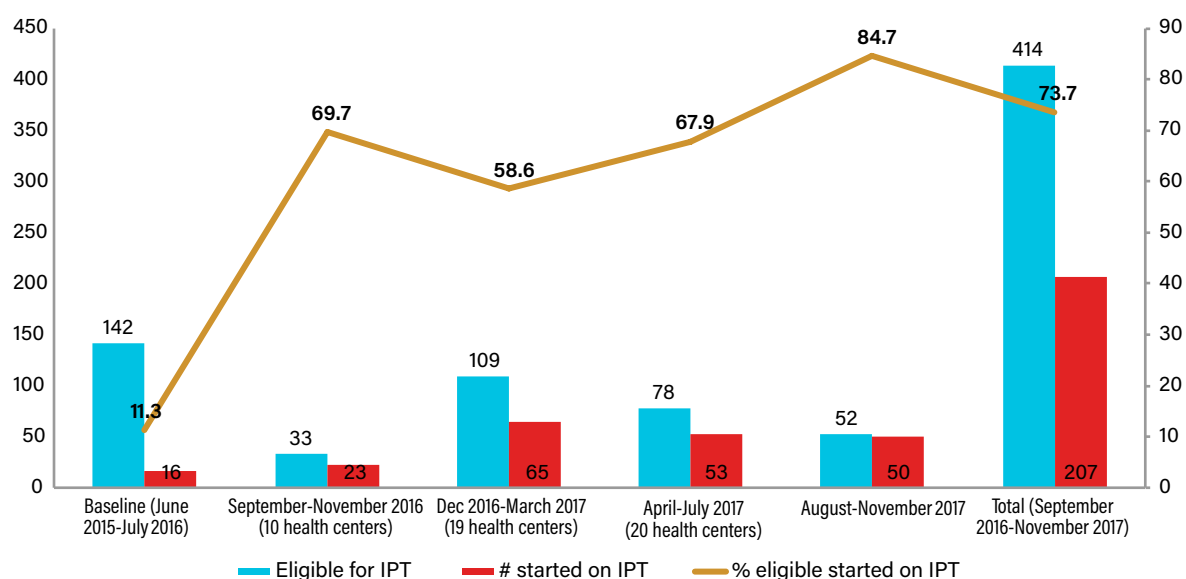
Period of implementation	Total children seen at IMNCI	Screened for TB (%)	Presumptive TB cases (% of screened)	Nasogastric aspiration done and tested for acid-fast bacilli/ Xpert MTB/RIF	TB case (% of presumptive TB)
Baseline (June-August 2016)	16 996	4 812 (28.3)	3 (0.06)	0	1 (33.3)
Sept-Nov, 2016	18 835	16 370 (96.3)	48 (0.29)	16	6 (12.4)
Dec 2016- March 2017	39 611	39 611 (100)	130 (0.33)	38	14 (10.8)
April-July 2017	35 665	34 941 (98)	66 (0.20)	27	18 (27.3)
August-Nov, 2017	31 666	31 590 (99.8)	257 (0.8)	28	12 (11)
Total (Sept 2016-Nov 2017)	125 777	122 512 (97.4)	501 (0.4)	109	50 (10)

September 2016-November 2017

Contact investigation

TB screening of contacts improved from 46% at baseline to 100% at the end of November 2017. Nine TB cases were identified through contact investigation. IPT coverage increased from 11.3% to 96.2% (see Figure 7.3 for details on IPT coverage from June 2015 to November 2017).

FIGURE 7.3: IPT COVERAGE AMONG CHILDREN UNDER FIVE YEARS OF AGE



Qualitative aspects

Clients (N=190), service providers (N=23) and programme coordinators (N=21) were satisfied with the availability of TB services at the same place as IMNCI services (95.0, 95.7 and 95.2%, respectively). They also found it appropriate to integrate TB services with IMNCI services (94.7, 90.9 and 100.0%, respectively).

Box 7.1 summarizes findings of the qualitative part of the study.



Box 7.1: Qualitative findings

Improving contact tracing:

Health care workers

- Work with health extension workers (HEWs) on community TB interventions so that they are supported to provide continuous health education.
- Gather full contact details including phone numbers and communicate these to HEWs to help trace most contacts.
- Give comprehensive information about TB Index cases and contacts to improve contact tracing.
- Strong collaboration with urban HEWs was emphasized.
- Good communication skills are important, for health education and health promotion for clients, awareness creation on TB transmission, benefits and risks of contact tracing, impact of TB such as severity of TB disease.
- Close follow-up for all families of TB cases is important.

Clients

- Clients suggested that education (using community health workers) about TB and awareness creation on the problem of TB transmission can help with contact tracing.
- Counselling and contact tracing need to be of good quality.
- HEWs can give health education during home visits regarding the importance of contact investigation, and can also assist with adherence to medications and advice on room ventilation.

Improving IPT uptake:

Healthcare providers

- Proper identification and screening of contacts to identify all children eligible for IPT.
- Continuous and good quality counselling to patients about the importance of IPT.
- *"... we need to be committed and avoid any reason as an obstacle for IPT initiation"*
- Initiation of IPT to be followed by routine provision of medication.
- Sound communication between healthcare providers and patients will enhance IPT completion.
- Health education and awareness creation about IPT for under-five children should include information on the minimal side effects of INH, follow-up of children on IPT every month and the need for adherence to IPT.
- Uninterrupted supplies of INH and pyridoxine need to be ensured.

Clients:

- Stressed the importance of education on IPT.
- Reminder to take TB medication using an alarm is more important than initiation of IPT.
- Completion of IPT could be guaranteed with child-friendly formulations: *"If the medication is a syrup the child can take it"*
- Parents or guardians need to monitor children on IPT daily.



Lessons learned

- Childhood TB services can be decentralized to the primary healthcare unit using IMNCI platforms with additional interventions packages.
- Building skills of health care workers on the use of nasogastric aspiration for sputum sample collection is feasible for bacteriological examinations.
- Using Xpert MTB/RIF as the initial diagnostic test for children with presumptive TB ensures early diagnosis and initiation of treatment, and can contribute to reducing early mortality.
- Creating awareness and counselling on the benefits of IPT, and management of drug side effects can help increase IPT uptake.
- Strengthening linkages between health facilities and the community through existing platforms is crucial for awareness creation on TB, contact investigation, tracing treatment interrupters, and adherence counselling.

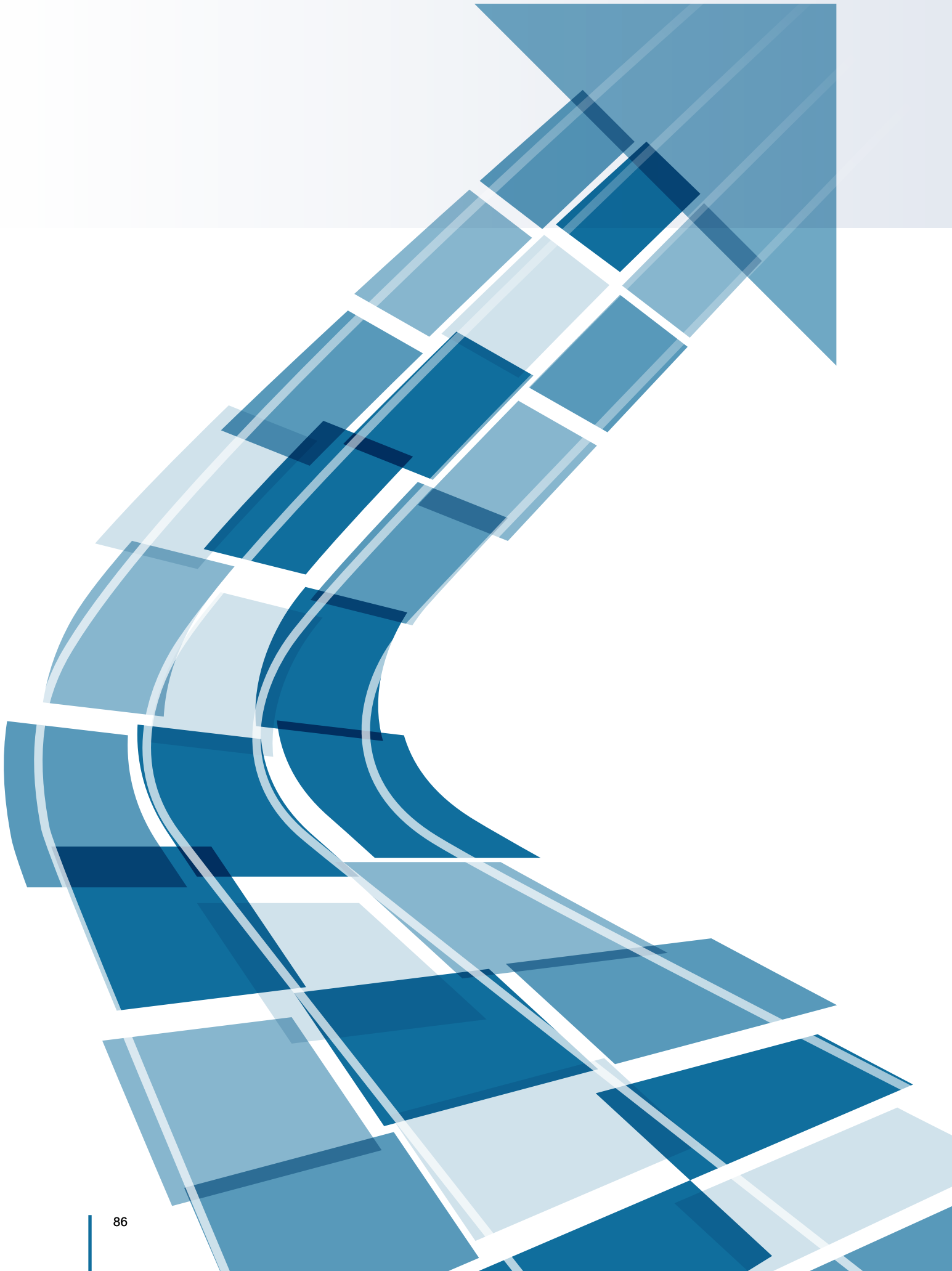
Sustainability/scale-up

- Strong commitment from the Government and development partners expressed through the stand-alone national childhood TB roadmap, with improved attention to childhood TB in the national TB and child health programmes.
- Wide roll out of IMNCI implementation in the country.
- Rapid scale-up of the national Xpert MTB/RIF service capacity with access at the primary care level through the specimen referral system.
- A large pool of private and public hospitals to provide referral service for children who need further evaluation.
- Establishing functional health facility TB/reproductive, maternal, newborn, child and adolescent health (RMNCAH) task forces to jointly plan, monitor and evaluate childhood TB case detection, linkage to treatment, care and prevention.
- Working with HEWs to integrate childhood TB with iCCM, and strengthen referral of presumptive TB cases among children from the community to the health centres.

Challenges/outstanding issues to be addressed

- High turnover of trained staff during project implementation.
- Variable collaboration and implementation of the integrated service model at lower levels.
- Low yield of presumptive TB cases among children, as symptoms overlap with other acute illnesses.
- Children who are given antibiotics for one week are often not given an appointment for review, which may lead to prescription of antibiotics at different centres.
- Recommended preventive treatment regimen for TB exposed children is not child-friendly.







8 Address research gaps

2013 Roadmap for childhood tuberculosis:

Research priorities with a special focus on TB in children:

- ▶ Epidemiology: burden of disease; recording and reporting; understanding of variations in TB dynamics in different settings; epidemiology of TB and TB/HIV in adolescents.
.....
- ▶ Fundamental research: biochemical, clinical and epidemiological approaches; host-pathogen interactions; identification of biomarkers.
.....
- ▶ Development of new diagnostics: usefulness of diagnostics in children; diagnostics suitable for use with paediatric samples; point-of-care diagnostics for children.
.....
- ▶ Development of new anti-TB medicines: optimal doses for children; optimal treatment duration; clinical trials; safety/toxicity of TB medicines in children.
.....
- ▶ Development of new vaccines: suitable clinical end-points for vaccine trials in children; pre-vaccine epidemiological studies; improved vaccines to prevent TB in children.
.....
- ▶ Operational and public health research: approaches to provide preventive treatment.
.....

8.1. Child-friendly formulations

8.1.1. Development and roll out of child-friendly paediatric FDCs

Global

Contributors: Brian Kaiser;¹ Thomas Lynch;² Shelly Malhotra;² Yamuna Mundade;³ Irina Usherenko;² Brenda Waning¹

¹ Stop TB Partnership's Global Drug Facility; ² TB Alliance; ³ Unitaid

Background

WHO's revised dosing guidelines for paediatric TB treatment in 2010 was based on evidence indicating a need for higher doses of first-line TB medicines for children. WHO subsequently invited expressions of interest from suppliers for appropriately dosed, quality medicines in a child-friendly format. No responses were received, given the perception of the paediatric TB market as commercially unviable. Various commodity access issues contributed to this perception, including low demand for existing products, a dependence on donor funding for paediatric TB drug procurement in high burden countries, and challenging regulatory pathways. In addition, several public health factors contributed to low uptake of paediatric TB medicines. Many countries did not have sufficient data on the burden of TB in children and did not have systems in place to identify children with TB. Because the majority of children with TB are not infectious, this key population was not a focus for TB programmes that are largely structured around curbing transmission. Challenges with confirming the diagnosis of TB in children contributed to gaps in case detection and under-reporting of childhood TB.

Without properly formulated TB medicines, country programmes, clinicians and caregivers continued to rely on treatment practices that included splitting or crushing multiple, bitter-tasting pills or combining old fixed dose paediatric combinations⁹ to try and achieve the recommended new dosing for children (19).

Description

STEP-TB – an initiative led by the TB Alliance and WHO (Essential Medicines and Health Products department and the Global TB Programme), and funded by Unitaid and USAID – was launched in August 2013 (see also section 10.1).

Project partners spanning the public and private sectors were instrumental in ensuring that the FDCs were rapidly taken up and made widely available, including:

- NTPs in target countries.
- Stop TB Partnership's GDF.
- Funding partners, such as the Global Fund, USAID and Global Affairs Canada.
- Child health stakeholders, such as UNICEF, Stop TB Partnership's Child and Adolescent TB Working Group, paediatric associations in several high burden countries.
- Technical partners, such as Management Sciences for Health (MSH), KNCV, The Union, CHAI, Mapping Health, TESS Development Advisors, and RTI International.
- Commercial partners, such as Macleods, Janssen and Lupin.
- Academic partners, such as Baylor University College of Medicine Global Childhood TB Program, Imperial College London, the University of Sheffield, University of Stellenbosch Desmond Tutu TB Centre, National Institute of Tuberculosis and Respiratory Diseases (India), and Yale University (USA).

⁹ A three-drug FDC for the intensive phase (rifampicin/isoniazid/pyrazinamide 60mg/30mg/150mg) and two, two-drug FDCs for the continuation phase (rifampicin/isoniazid 60mg/30mg for daily use and rifampicin/isoniazid 60mg/60mg for three-times weekly dosing).



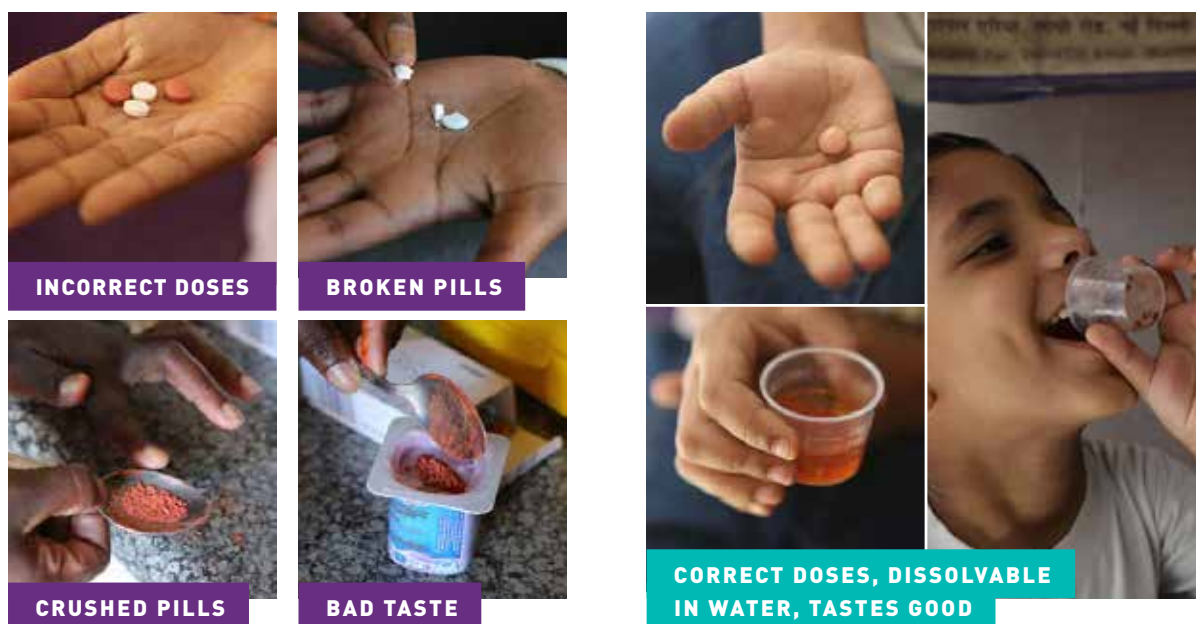
- Advocacy partners, such as MSF Access Campaign and Treatment Action Group (TAG).
- The TB Procurement and Market Shaping Action Team (TPMAT), which involves partners listed above as well as other partners, including procurers of TB commodities.
- Other teams within the Stop TB Partnership.

Project goals included: (i) driving the availability of appropriately dosed, properly formulated, affordable, high-quality paediatric TB medicines; and (ii) establishing a sustainable market for these products.

The project catalysed commercial entrance of the first supplier of child-friendly FDCs ahead of schedule, and the FDCs were launched in December 2015 during the 46th Union Conference on Lung Health in Cape Town. The available formulations include (20):

- For the intensive phase (first two months) of treatment: three-drug FDC – rifampicin 75 mg + isoniazid 50 mg + pyrazinamide 150 mg.
- For the continuation phase of treatment: two-drug FDC – rifampicin 75 mg + isoniazid 50 mg.

Inadequate Pediatric Treatment → Now Available



Paediatric TB treatment before and after the availability of the child-friendly FDCs (Source: New pathways for childhood TB treatment. Lessons from the STEP-TB Project. TB Alliance and Unitaaid; 2017 (https://www.tballiance.org/sites/default/files/child-resources/New_Pathways_for_Childhood_TB_Treatment.pdf, accessed 18 August 2018).

These FDCs are fruit flavoured and water-dispersible, so tablets no longer need to be cut or crushed to achieve an appropriate dose. They offer the opportunity to simplify and improve treatment for children around the world, enhance adherence, promote completion of treatment, and help prevent the development of drug resistance. The FDCs are available through the Stop TB/GDF at a median price for a course of treatment of approximately US\$ 15.

Despite the new, higher estimates of TB disease burden in children and the history of programmes procuring old FDCs for children, by mid-2016 it was clear that new FDCs were not being introduced or scaled-up in many countries. Based on discussions between Stop TB/GDF and programmes and implementers, there were some clear themes that emerged around barriers and challenges to implementing the new FDCs. At the global level, there was a lack of clear guidance for programmes to move to the new FDCs as soon as possible. There was also a risk that a second supplier of the FDCs would be delayed that could cause supply insecurity. At the country level, programmes were concerned about wastage of current stocks of old FDCs, particularly those that were ordering larger quantities less frequently. Additionally, programmes



required assistance in developing accelerated, but realistic, transition plans between the old and new FDCs. In some instances, programmes, particularly those without access to donor funding for first-line drugs, required grants to cover the initial procurement of new FDCs as their domestic financing and procurement processes prevented access to these small volume products.

The approach to addressing the challenges around introduction and scale-up of the new FDCs fell into three areas of work: (i) an initial area of work devoted to **shaping the market for the new FDCs right at product launch**; (ii) **in-country support around procurement and supply chain management** to develop phase-in and phase-out plans (including estimates of wastage); (iii) work developed from the in-country work package which identified **global policy barriers** to implementing the new FDCs as quickly as possible. These were addressed via partner coordination, particularly via the TPMAT.

Market-shaping during development and launch of new paediatric FDCs

25% price reduction

Stop TB/GDF successfully facilitated a 25% reduction compared to the originally negotiated launch prices. The GDF conducted a critical assessment of originally suggested launch prices and determined that the launch prices were too high and would limit the number of children accessing treatment. Partners convened to identify and implement additional means to further reduce prices prior to product launch.

Market consolidation around two formulations

Stop TB/GDF was instrumental in reducing the number of formulations and consolidating the market around two formulations to avoid fragmenting the small market, higher prices, longer lead times, increased chances of stock-outs, and substantial wastage at supplier and country levels.

Minimum order quantity reversal

The high minimum order quantity requirement initially agreed with the manufacturer was reversed, to avoid delays in the introduction and scale-up, the risk of stock-outs and treatment interruptions.

Global Fund ad-hoc Expert Review Panel (ERP)

The Global Fund's ERP is a key mechanism to facilitate the use of products that are under review by WHO's Prequalification Programme (PQP). An ERP approval is an endorsement of the quality of a product, enabling it to be procured in a time limited manner, generally until the product is prequalified. ERP submissions and reviews are generally launched twice a year. However, products can be ready for submission outside of the regular review schedule; and for products that address significant supply security risks, it would be necessary to review them as quickly as possible. Stop TB/ GDF and partners worked closely with the Global Fund to define the criteria on what constitutes a significant supply security risk. TPMAT has developed and maintains a prioritized list of the products that are most urgently needed to address supply security risks, including paediatric FDCs. When a product on the prioritized list is ready for submission, GDF and partners notify the Global Fund and an ad-hoc review process is launched. The overall goal is to ensure that quality products become eligible for procurement as soon as possible and decrease the risks for supply insecurity.

Introduction and scale-up of new paediatric FDCs into national programmes

National transition plans developed and implemented

Direct technical assistance and capacity building to almost forty countries was provided by the GDF for the development and implementation of NSPs to facilitate rapid uptake of new medicines and regimens, including new child-friendly TB medicines. Technical assistance was concentrated in the areas of medicines forecasting and quantification; supply planning; plans to phase out old medicines and phase in new medicines; supply chain data collection; and development of early warning systems to prevent stock-outs.



Identification and development of global policies to address barriers to use of new paediatric FDCs

Global Fund agreement to allow wasting of older, non-optimized medicines

Primary stakeholders convened to discuss and agree on an approach that would allow Global Fund Principle Recipients to waste the existing stock of older, non-optimized medicines to expedite the introduction of the new, optimized paediatric TB medicines. Many countries were delaying introduction of new medicines as they felt the need to use their existing stock before converting to newer medicines. This practice was delaying introduction of new medicines by up to 18 months and resulting in suboptimal treatment of children with TB. Given that the value of existing stock was typically less than US\$ 20 000, all stakeholders agreed this was a small loss to incur to ensure all children had immediate access to optimized medicines that delivered accurate dosing. At the request of the Global Fund, Stop TB/GDF developed a tool that systematically estimates the value of existing stock to be wasted and the value of new medicines to be purchased. This tool allowed for consistent and rapid reprogramming of Global Fund grants to expedite access to the new medicines. This approach with expedited introduction of child-friendly TB medicines set a new precedent and has since been replicated to accelerate the introduction of shorter regimens for MDR-TB.

WHO statement on the use of new paediatric medicines

In March 2017, WHO and UNICEF issued a joint statement endorsing the use of the child-friendly FDCs (21): "WHO and UNICEF advise against the continued use of the former suboptimally dosed FDCs or adult formulations (crushed tablets), which may lead to under- or over-dosing, unfavourable treatment outcomes, and increase the likelihood of developing drug resistance. WHO and UNICEF therefore urge all national TB programmes to discontinue and replace the previously used medicines for children weighing less than 25 kg with the child-friendly dispersible TB FDCs as soon as possible." The Stop TB Partnership, WHO and UNICEF strongly encouraged donor agencies to fund the procurement of new FDCs instead of older, improperly formulated medicines. This WHO guidance served several purposes: it helped the Global Fund to promote the use of new medicines and justify the development of the wastage agreement; and provided the written documentation needed to allow national policy makers to quickly update treatment guidelines.

Stop TB/GDF Statement on removing old paediatric FDCs from its catalogue

At the TPMAT meeting in December 2016, progress made on the implementation and scale-up of the new paediatric FDCs was reviewed and discussions were held to determine if there were any further challenges to be addressed. It was noted that most countries had developed accelerated phase-in and phase-out plans and had either ordered or were planning to order the new FDCs. It was suggested that GDF remove the old FDCs from its product catalogue, so they would no longer be available for procurement. This served to not only consolidate the market around only the new FDCs, but also acted as a public statement that transition to the new FDCs was nearly complete. The GDF published the statement in December 2016 and removed old FDCs from its catalogue effective 1 January 2017.¹⁰

Outcomes /successes

The market for paediatric TB medicines was reshaped by this innovative collaboration, which reduced barriers to entry, catalysed the launch of optimized child-friendly products, and mobilized unprecedented demand in this historically fragmented market.

Intermediate outcomes included:

- 25% initial price decrease.
- Improved supply terms with no minimum order quantities.
- Consolidation around a single flavoured formulation.
- Removal of the old product from the market.
- Policies to support accelerated introduction, including wastage of old products.

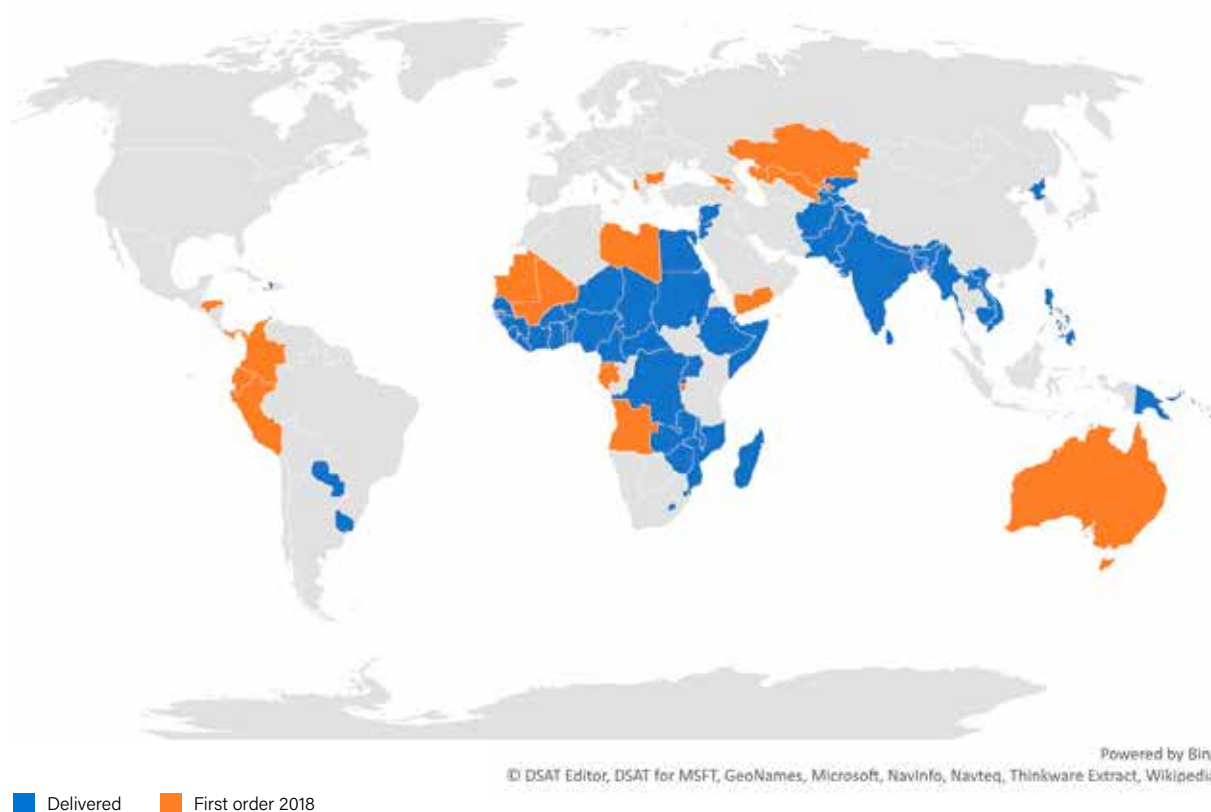
¹⁰ GDF information on paediatric formulations. Stop TB Partnership [website]. (<http://www.stoptb.org/gdf/drugsupply/paedforms.asp>, accessed 18 August 2018).



New products were made widely available at an affordable price, enabling broad access for children around the world to better TB medicines in the right doses. Kenya was the first country to order child-friendly FDCs and to launch nationally on 1 October 2016 (see section 5.1). The GDF has served a critical role as the primary platform for country access to FDCs. By mid-2018, 85 countries had ordered around 789 000 patient treatment courses through the GDF (treatment course calculated as three tablets of the paediatric formulations daily). This includes direct procurement support for 21 countries via grants provided by Stop TB/GDF on behalf of Global Affairs Canada (see Figure 8.1).

By increasing visibility of TB on the broader child survival agenda and leveraging partner networks, STEP-TB drew global attention to the long-neglected crisis of childhood TB. This process was facilitated by various awareness raising and communications efforts, including the launch of the “Louder than TB” campaign, several peer reviewed publications, a project web portal, global media coverage, civil society mobilization, and advocacy by key champions.¹¹

FIGURE 8.1: PROCUREMENT OF CHILD-FRIENDLY FDCS VIA THE GDF



Source: Global Drug Facility, June 2018

¹¹ Publications stemming from the project include: Dodd P, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health* 2014;2(8):e453–9.; Coghlan R, Gardiner E, Amanullah F, Ihekweazu C, Triasih R, Grzemska M, et al. Understanding market size and reporting gaps for paediatric TB in Indonesia, Nigeria and Pakistan. Supporting improved treatment of childhood TB in the advent of new medicines. *PLoS ONE* 10(10): e0138323; Malhotra S, Ursu I, Ghoneim R, Jodrey PP, Brown MS, Barr-DiChiara M. From availability to uptake: planning for the introduction of new, child-friendly anti-tuberculosis formulations. *Int J Tuberc Lung Dis*. 2015 Dec;19 Suppl 1:32–38; Scott C, Gardiner E, de Lucia A. The procurement landscape of pediatric tuberculosis treatment: a Global Drug Facility perspective. *Int J Tuberc Lung Dis* 2015;19(12):S17–S22; Usherenko I, Basu Roy U, Mazlish S, Liu S, Benkoscki L, Coutts D, et al. Pediatric tuberculosis drug market: an insider perspective on challenges and solutions. *Int J Tuberc Lung Dis* 2015;19(12):S23–S31; New pathways for childhood TB treatment. Lessons from the STEP-TB Project. TB Alliance and Unitaaid; 2017; and others in the following pediatric supplement: <http://www.ingentaconnect.com/content/iatld/ijtld/2015/00000019/a00112s1> (accessed 18 August 2018).

Lessons learned

The successful launch and roll out of paediatric FDCs yielded several key learnings.

Importance of building evidence base to inform strategies and raise market visibility

The STEP-TB initiative invested in a partnership with the University of Sheffield to refine the methodology for estimating childhood TB burden. This effort contributed to the recognition that incidence of TB in children is almost two times higher than what was previously estimated. Improved understanding of disease burden raised visibility about TB's contribution to overall childhood morbidity and mortality and built awareness about the critical need for broader representation of TB within the child health agenda. This evidence helped enhance understanding of market size and strengthened commercial confidence in the paediatric TB market.

Inventory studies of paediatric TB treatment channels in the private sector and analyses of procurement processes, policy change drivers, and regulatory pathways helped to steer introduction planning efforts. As important as these landscaping assessments, were investments in clinical evidence to support understanding of dosing requirements, particularly for vulnerable under-five kilogram populations.

Catalysing commercial investment and driving availability

Perceptions of potential conflicts of interest often inhibit commercial suppliers from directly engaging with public sector stakeholders to mobilize demand for new treatments. TB Alliance's position as a product development partner enabled them to bridge across commercial and public health stakeholders to drive progress towards jointly established goals in the areas of clinical development, formulation, registration strategy, evidence building, demand generation and product launch. De-risking commercial involvement by defraying reformulation and regulatory costs and mobilizing demand for the products was critical in incentivizing commercial participation.

The project's supply strategy sought to foster generic competition for the new paediatric FDCs to drive affordability, while at the same time avoiding excessive fragmentation in this already modest commercial market. While attracting investments in this historically neglected space with a sustainable number of generic competitors was successful, delays in timelines for the second generic entrant led to a period of supply monopoly. Leveraging the collective influence of funders and procurers proved important in negotiating affordable pricing during this period.

Market preparation and demand mobilization are critical to success

Market preparation was critical in ensuring country demand and readiness at the time of product availability. In partnership with Management Sciences for Health/Systems for Improved Access to Pharmaceuticals and Services Program (SIAPS) countries' early transition planning in key areas was supported, including sensitization, consensus building, supply chain transition, inclusion in the Essential Medicine List for children, policy updates and training. In addition, regional and national level meetings – bringing together WHO regional focal points, NTP managers, child health actors, and civil society representatives to create national roadmaps and targets for measuring countries' childhood TB responses – were also critical in generating a sense of shared accountability in addressing childhood TB and planning for FDC adoption. Leveraging the broad country networks and technical support platforms of additional partners, such as KNCV, the Global Childhood TB Program at Baylor University, The Union, and national paediatric societies helped to support countries' planning as well.

Procurement and supply management

Despite supporting the development of products, making them commercially available, and developing the evidence base and supportive tools needed to implement them programmatically, there was still a need for active intervention around procurement and supply chain management (PSM) – from the



country implementation level up to the global policy level – to get these products into programmes at sustainable prices. For future projects looking to implement new products, particularly for replacing an older product, PSM activities and planning should be a core component in the project's scope. PSM activities should include broad stakeholder consultation to specifically identify and proactively address global policy bottlenecks prior to products being commercially available. Addressing PSM challenges from the very beginning of a project should help enable faster and more equitable scale-up of new products.

Sustainability/scale-up

- For small and fragmented markets with public health needs, global mechanisms such as the GDF are critical in consolidating demand and accelerating access to products pending national registration. Expanding the target market for the project to include a strong focus on middle income, high burden countries also proved imperative in creating adequate scale for this low volume product. A key learning was that procurement pathways and adoption drivers are distinct in middle-income settings, requiring targeted strategies. Given the strong role that national experts play in either enabling or blocking adoption of new treatments, empowering local opinion leaders with the knowledge and tools they needed to mobilize new treatments proved critical in ensuring both early adoption and uptake. Generating visibility around early adopter countries was also helpful in catalysing subsequent waves of adoption.
- Based on Stop TB/GDF historic procurement data, only 89 countries had ever procured the old paediatric FDCs. Between 2016 and mid-2018, 85 countries had procured the new paediatric FDCs. Based on these numbers it would appear that the new FDCs are now nearly at scale. However, the number of countries that are procuring has changed significantly over time. More analysis and discussions are needed to determine why some countries are no longer procuring paediatric FDCs through Stop TB/GDF and other internationally recognized quality-assured sources and what could be done to make these products available in those programmes. For countries that are interested in re-introducing paediatric FDCs, there will likely be a need for technical assistance, trainings and perhaps some grant support for initial procurement(s). These activities will all need funding support. There will also be a benefit to determining why some countries that had not previously procured paediatric FDCs through the GDF or quality-assured sources have decided to do so now and if there are any best practices that can be derived from these programmes.

Challenges/outstanding issues to be addressed

Finding the missing cases

Gaps remain between the estimated disease burden and the number of children started on treatment (40%; (7)). Efforts to roll out improved treatment options for children will be insufficient if significant progress is not made in diagnosis, notification and treatment initiation for children with TB.

Budget allocation

Budget allocation for new commodities is typically not possible until products are commercially available. In addition, funding and procurement cycles are often not aligned. These factors may contribute to delays in ordering new treatments. Opportunities to influence budget allocations for new tools early in the process and build in flexibility to reprogramme funds mid-cycle to respond to innovations are critical to enabling timely access to improved products.

Avoiding delays in stock transition

Significant stocks of existing, suboptimal paediatric products and perceived negative consequences related to wastage of products (either from donors or governments) can delay phase-in and phase out plans. This problem is likely to increase in frequency and severity as more research results become available and guidelines and recommendations are updated more frequently and with more significant changes.



Efforts are needed to increase visibility into the pipeline, strengthen forecasting, and subsidize the cost of wastage and supply replenishment for countries transitioning to new products. Programmes should consider procuring products more frequently (twice a year) to minimize stocks in country and thus minimize potential waste when phasing out old products.

Mitigating against transition fatigue

Countries often lack capacity or have competing priorities that need to be considered if product introduction and uptake is to be successful. Moreover, fatigue can result from the frequency of policy recommendations countries receive and from poor coordination of technical assistance provision. Efforts are needed to support prioritization of interventions, align planning and harmonize technical support for mitigating against country transition fatigue.

Adequate resources needed

The success of the initiative was due in large part to the shared responsibility and important resources that were committed by donors and national governments to support the launch. Ongoing resource support is needed to facilitate scale up of additional commodities for the treatment and prevention of TB in children, including:

- Child-friendly medicines for preventive treatment, comprising dispersible isoniazid 100 mg and a dispersible FDC of isoniazid plus rifapentine; dispersible levofloxacin (for MDR-TB infection).
- Child-friendly second-line drugs to treat drug-resistant TB (see section 8.1.2).
- Ongoing efforts to improve visibility in the paediatric TB market would help raise awareness and support prioritization of market interventions to drive uptake of these additional medicines.

Limited financing for the procurement of first-line TB medicines for drug-sensitive TB

Fewer countries will receive Global Fund support over the next grant period (2018–2020) for purchase of the new, paediatric TB medicines. Similarly, fewer countries will receive Global Fund financing for the procurement of adult medicines for drug-sensitive TB. Global Fund's newly revised Sustainability, Transition and Co-financing Policy requires that all countries, regardless of income level, to consider co-financing procurement of medicines.

Countries wishing to purchase new, paediatric TB medicines directly from suppliers with their own funds will face many challenges

Given the small volume and value of sales for paediatric TB medicines, manufacturers will be reluctant to respond to national tenders. These countries may revert to using adult medicines of incorrect doses and formulations that must be split multiple times and/or crushed for paediatric administration. If manufacturers do respond to national tenders, it could lead to increased prices and long lead times causing stock-outs and treatment interruptions. Manufacturers have not yet registered these products outside of India and most countries require registration in order to purchase via national tenders. Suppliers will be reluctant to register these medicines in most countries given the real and opportunity costs. Most countries wishing to purchase new, child-friendly TB medicines with domestic funds will need to purchase via an entity like Stop TB/Global Drug Facility.

Technical assistance on procurement and supply chain management, including early warning systems

A confluence of factors is making procurement and supply chain management of TB medicines increasingly complicated. In addition to the risks around financing availability, challenges with decentralized procurement and changing guidelines and recommendations noted above, all of which create risks of stock-outs and



new products with short shelf lives that can increase the risk of expiry are being introduced. There is, and will continue to be, a need for ongoing technical assistance and capacity building around procurement and supply chain management, including implementing, maintaining and responding to early warning systems that detect the potential for stock-outs and treatment interruptions.

8.1.2. Child-friendly formulations for drug-resistant TB

Global

Contributors: Brenda Waning and Brian Kaiser

Stop TB Partnership's Global Drug Facility

Background

The incidence of paediatric (defined as children less than 15 years of age) drug-resistant TB is estimated to be between 25 000 and 32 000 annually (7, 22). Of these, less than 1000 are reported as having received treatment each year, globally (23). Despite the low treatment numbers, medicines suppliers have developed and received internationally recognized quality assurance status for several paediatric-friendly formulations of medicines used to treat drug-resistant TB (see Table 8.1).

There remains a mismatch between supply and demand for these new formulations. From a demand perspective, these products are intended for younger children (generally below five years of age or less than 25 kg) who are unable to swallow the adult tablets. The current estimates are for children less than 15 years of age, meaning only a portion of the 1000 children treated each year for drug-resistant TB would benefit from the new formulations. Additionally, demand is fragmented as treatment is often individualized for children, while rapidly emerging evidence and recommendations mean treatment approaches are often changing.

From a supply perspective, the minimum order quantities (MOQ) for these products are far larger than the amount required for any single programme or country. The products also have a relatively short shelf life (24 months), which would necessitate more frequent ordering to minimize wastage due to expiry, making it even more difficult for a single programme to reach a MOQ.

Table 8.1: Products developed and quality assured (either WHO Prequalification or Global Fund Expert Review Panel)

Medicine	Strength	Formulation
Ethambutol	100 mg	Dispersible tablet
Ethionamide	125 mg	Dispersible tablet
Cycloserine	125 mg	Mini-capsule
Levofloxacin	100 mg	Dispersible tablet
Moxifloxacin	100 mg	Dispersible tablet
Pyrazinamide	150 mg	Dispersible tablet

Description

The Stop TB Partnership's GDF recognizes the need to get these new formulations into programmes as soon as possible. GDF has developed a two-pronged approach to facilitate introduction: (i) improve visibility on demand; and (ii) minimize supply side barriers.

To begin to quantify the demand, the GDF has enlisted the Sentinel Project (a broad network of clinicians and activists in paediatric drug-resistant TB), to provide a link to country programmes. The Sentinel Project is identifying programmes that could absorb these products quickly, listing the clinical needs for treatment (such as weight-based doses, frequency of administration and duration of treatment) and capturing historical and planned patient enrollment based on age and weight. KNCV has provided significant support to the project in identifying programmes and facilitating data collection. The GDF team of procurement and supply chain experts are using this information and their extensive experience



while introducing paediatric FDC products (see section 8.1.1) to develop a forecasting and quantification approach for these new drug-resistant TB products.

Simultaneously, GDF is engaging with the suppliers to address multiple supply side obstacles including, batch sizes, MOQs, lead times and price. Based on initial demand estimates, GDF has been able to negotiate a smaller batch size for most products to better align with expected volumes. GDF has also been able to use its role as a pooled procurement mechanism to agree to buy products by the batch. This allowed for a nearly 20% reduction in the price from the initial offer as it decreased the risk of wastage and write-offs for the supplier.

Outcomes/successes

This intervention is ongoing. Intermediate results include:

- Decrease in batch sizes that more closely aligned with identified demand.
- Nearly 20% decrease in price from initial offer.
- Initial quantification approach developed for children with drug-resistant TB.

Lessons learned

While the intervention remains ongoing, some initial lessons learned include:

Demand

- There are likely more children being treated for drug-resistant TB than estimates would indicate.
- Quantifying and forecasting for these medicines is difficult because:
 - Children tend to receive individualized regimens based on DST rather than a “standard” regimen
 - Children tend to gain weight quickly once on treatment, moving to different weight bands and using more product
 - Clinicians are more likely to switch medicines in children experiencing side effects
 - Most country data systems are not designed to disaggregate between children that would benefit from paediatric-friendly formulations (those less than five years of age or less than 25 kg) and older children.

Supply

- Mechanisms like the GDF can serve as leverage points for supplier negotiations and result in meaningful improvements in MOQs, lead times and price.
- Aligning the supply of these new formulations with the relatively low demand takes significant coordination at the global level and has only been possible because of a pooled procurement mechanism. As countries take on more ownership of their TB programmes, including procuring TB commodities using domestic resources, they will likely need to continue to access a pooled procurement mechanism to maintain availability of these small demand products.

Sustainability/scale-up

The Sentinel Project is working on the tools, job aides and trainings needed to implement the new drug-resistant TB formulations once they are available in countries’ TB programmes. Both the Sentinel Project and KNCV will help support the programmatic use of these new formulations and to collect actual product consumption data. The GDF will use consumption data to refine the quantification and forecasting approach, which along with other tools and job aides, should facilitate other programmes to implement these products.



Challenges/outstanding issues to be addressed

- Further work remains to find and treat the children with drug-resistant TB that are not currently accessing care.
- The acceptability of these products still needs to be assessed under programmatic conditions.
- Country-level consumption data should be tracked to refine the quantification approach.
- Country-level data systems should be adapted to disaggregate between younger (<5 years) and older children (5–14 years).
- Outcome data with the new formulations should be tracked.
- Recommendations on treatment of drug-resistant TB should be updated to include the most current weight-based dosing for these products.
- Pooled/coordinated procurement approaches will be required to maintain this market.

8.2. Accelerating access to quality TB care for presumptive paediatric TB patients through improved diagnostic strategies

Country: India

Contributors: Sanjay Sarin;¹ Debadutta Parija;¹ Aakshi Kalra;¹ Neeraj Raizada²

Foundation for Innovative New Diagnostics (FIND) India; Independent consultant

Background

India has close to 400 million children in the 0–14 years age group, who constitute about one third of the total population.¹² The incidence of childhood TB in India was estimated at 227 000 or 8.1% of the estimated adult incidence for 2016 (1).

Children run the risk of progressing from infection to disease within one year. The diagnosis of TB in children is challenging, because children are often unable to produce sputum, and TB can mimic many other common childhood diseases. The sensitivity of smear microscopy for the diagnosis of childhood TB remains low; therefore the diagnosis of childhood TB is primarily based on clinical criteria, with potential for both under- and over-diagnosis. Delayed diagnosis of TB in children, which presents an obstacle to effective management of TB, has been flagged in many studies in India and other countries (24).

Though MDR-TB and XDR-TB are documented in the paediatric age group (25), there are no representative estimates of the overall burden because of diagnostic difficulties and the exclusion of children in most drug resistance surveys.

Moreover, limited availability of highly sensitive rapid diagnostic tests that can be applied with a quick turnaround time often leads to microbiological confirmation not being attempted. These diagnostic challenges and over-reliance on clinical diagnosis limit the possibility of diagnosis of rifampicin-resistant TB among presumptive paediatric TB patients.

Using Xpert MTB/RIF as an initial rapid test, offers a promising solution to achieve the global objective of early and accurate detection of TB and rifampicin-resistant TB. Xpert MTB/RIF diagnoses TB and resistance to rifampicin, a first-line drug that is an accepted predictor for MDR-TB, in just two hours. The standard culture approach can take two to six weeks, and further three weeks that conventional drug resistance

¹² Population ages 0–14 (% of total). The World Bank [website] (<https://data.worldbank.org/indicator/SP.POP.0014.TO.ZS>, accessed 18 August 2018).



tests can take. Xpert MTB/RIF also delivers reliable results with regards to paediatric TB diagnosis, because samples other than sputum can be used.

WHO has recommended that Xpert MTB/RIF be used instead of conventional microscopy and culture as the initial diagnostic test for all children presumed to have TB. Against this backdrop, the current project was conceptualized and implemented by the Foundation of Innovative New Diagnostics (FIND) in India to address TB diagnostic challenges in the paediatric population. The project offered free, upfront Xpert MTB/RIF testing to paediatric presumptive TB cases through providers in both public and private sectors.

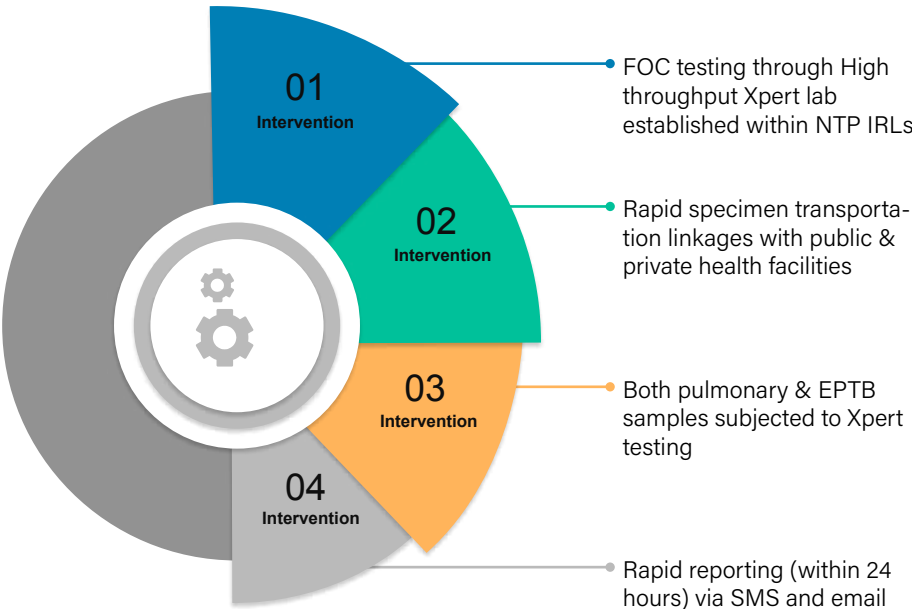
Description

Process of development of intervention/action

FIND, in consultation with the Revised National TB Control Programme of India (RNTCP) and with funding support from USAID, CDC and PATH, began implementing this novel paediatric initiative in April 2014 in Chennai, Delhi, Hyderabad and Kolkata.

High-throughput Xpert MTB/RIF laboratories (two Xpert MTB/RIF machines per laboratory) were established at RNTCP sites in each of the above-mentioned cities. In each location, potential referral institutions (public and private) were mapped and health care providers were engaged via sensitization workshops and advocacy meetings. A hub and spoke model was established with laboratories acting as hubs and engaged providers as spokes. Free, upfront Xpert MTB/RIF-based diagnosis was offered to all children showing symptoms of pulmonary and extra-pulmonary TB who sought care with these referral institutions, and those that accepted had their samples sent in for analysis. Linkage to testing was conducted, free-of-charge, via rapid specimen transport networks and results were delivered via electronic reporting (e-mail/SMS) (see figure below). Based on notable impact seen over just two years, the project was scaled up to include five more Indian cities (Bangalore, Guwahati, Nagpur, Surat and Vizag) in 2016 and a tenth city (Indore) was added in mid-2017.

FIGURE 8.2: PAEDIATRIC PROJECT OVERVIEW



The project has been unique in several ways:

1. This was **the first time** that Xpert MTB/RIF was offered as an upfront test for TB diagnosis of paediatric populations in India.



2. From the beginning, there was a specific focus on **public-private mix** activities targeting paediatric populations in key cities which helped build paediatric diagnostic capacity not only in the public sector but also the private sector, where a large proportion of patients go for medical care, at least as a first point of contact.
3. For the first time a large proportion of **extra-pulmonary specimens** were routinely tested using Xpert MTB/RIF.

Stakeholders

The project was carried out in close coordination with the national TB programme and their state and district teams (state TB officers and district TB officers including their staff). Key stakeholders were also involved in the project, including the Indian Academy of Paediatrics, Indian Medical Association, hospitals (public and private sector including corporate and charitable facilities), chemists and medical representatives of pharmaceutical companies and local private practitioner associations.

Monitoring and evaluation

Given the wide geographic spread of the sites in this study, the project staff relied heavily on the use of a number of widely available, free information technology tools for remote access and web-based sharing of folders, including team viewer, Skype, web-transfer, drop box, and Microsoft excel, etc. The study technical team was able to effectively solve majority of the technical issues in Xpert MTB/RIF testing through remote technical assistance and supplemented this with need-based on-site visits by Cepheid. The day-to-day performance of the Xpert MTB/RIF laboratories was supervised remotely and through on-site visits by the FIND paediatric project technical team.

Case study 1

Sabir is 14 years old and lives in Surat, India. He loves studying and competed in the national Science Olympiad. One day, Sabir remembers, "I started feeling giddy and then I had fever, I lost my appetite and I was coughing a lot." He went to a private physician, who gave him medicine that didn't help, and subsequently saw four other doctors – but no one mentioned TB. "We thought that he was suffering from chikungunya. We thought he may have dengue or malaria or something similar," his aunt explained. Finally, Sabir said, "doctors visited our school and said that if you have these symptoms then you should get a test done for TB" – and after 22 days of suffering and uncertainty, Sabir tested positive for TB and is now being treated. He is looking forward to going back to school.

Sabir's diagnosis was made using WHO-endorsed Xpert MTB/RIF. This device, co-developed by FIND, Rutgers University and Cepheid, is able to diagnose TB in children with high sensitivity through testing samples other than sputum – as children cannot produce it. FIND's paediatric TB programme provides a free-of-charge diagnostic solution for children with suspected TB, engaging providers in both public and private sectors for referrals and trainings. Over 88 280 children have now been tested using Xpert MTB/RIF across ten cities, and more than 5980 TB cases detected.¹³

Case study 2: Tackling paediatric TB in india: a story of hope

Seven-year-old Suhana is one of the many children who have benefited from this initiative. When she developed severe pain in her lower abdomen, her parents immediately took her to the nearest hospital. The doctor examined the child and advised an ultrasound. The prescribing paediatrician suspected that it could be TB. The facility was engaged with the project and sent a pus sample to the project laboratory for testing. The test results came back the very same day confirming that Suhana did indeed have TB that was rifampicin resistant. She was put on standardized treatment for MDR-TB immediately. She is currently on treatment and is recovering well. She is determined and well on her way towards achieving her dream of becoming a doctor one day.

¹³ Link to case study: Sabir's long road to TB diagnosis. (<https://www.finddx.org/news/sabirs-tb-diagnosis/>, accessed 18 August 2018).

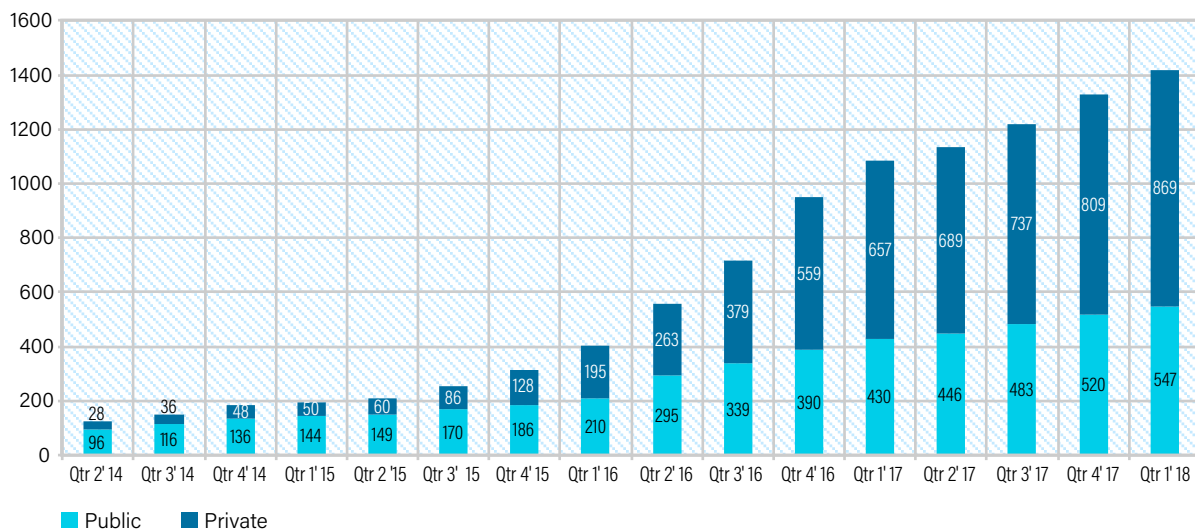


Outcomes/successes

Key findings

- Overall (April 2014–March 2018), 94 415 presumptive paediatric patients were tested by Xpert MTB/RIF
- Sensitization workshops, continued medical education sessions for clinicians, and outreach activities were held across project sites, engaging 1416 facilities/providers (61% private sector) (see Figure 8.3 below).
- For the first time under RNTCP, both sputum and extra-pulmonary specimens were tested on Xpert MTB/RIF. The type of samples tested included gastric aspirate, gastric lavage, broncho-alveolar lavage, cerebrospinal fluid, pleural fluid and pus.
- Overall the project was highly successful in increasing detection rates. Xpert MTB/RIF positivity under the project was close to 7% compared to a positivity rate of around 2% with smear microscopy, which was the only laboratory test used before the start of the project. The microbiological detection of paediatric TB increased more than threefold under the project.
- Of the total TB cases detected on Xpert MTB/RIF, around 9% were diagnosed as rifampicin resistant TB. This highlights the additional benefit of using Xpert MTB/RIF.
- For 94 415 patients, 103 045 specimens were tested on Xpert MTB/RIF of which around half were non-sputum.
- The project facilitated prompt access to quality diagnostic services. Average turnaround time for Xpert MTB/RIF testing was one day including specimen collection, transportation, testing and reporting.
- Of the total diagnosed TB cases, around 89% have been confirmed to be accessing treatment.

FIGURE 8.3: PROVIDER ENGAGEMENT UNDER THE PROJECT: CLASSIFIED BY TYPE OF PROVIDERS/FACILITIES ENGAGED



Lessons learned

- City specific handouts and flyers in the local language were useful in demand generation via providers and direct engagement of patients
- A simplified provider involvement process was successful in engaging private sector providers. This consisted of:
 - an abridged referral form;
 - a streamlined sample transport, testing and reporting pathway helped in building confidence of the providers; and



- maintaining operational efficiency by timely reporting of results helped in building a rapport with the providers.
- Minimizing stock-outs of cartridges and other consumables helped in ensuring rapid turnaround time and consequently gaining the provider's trust. Preventing stock-outs required estimation of cartridges needs based on historic data. Based on these estimates, one month running stock and a minimum of three months buffer stock was provided to the sites. Other laboratory consumables, as identified during the site assessment visits, were also provided and stock was monitored in the same manner as for cartridges.
- Regular follow-up with potential providers to seek and implement their feedback helped further fine-tune the intervention.
- Qualitative research was carried out as part of the project, including:
 - understanding how national guidelines on TB diagnosis and Xpert MTB/RIF technology have been integrated into paediatric TB care practices of different health providers;
 - documenting pathways to microbiological confirmation for paediatric TB patients; and
 - enabling researchers to understand current practices and identify gaps which paved the way for future corrective steps.

Sustainability/scale-up

This intervention has facilitated a policy decision by the RNTCP mandating the use of Xpert MTB/RIF as a primary diagnostic tool for diagnosis of TB in children. Because of this, the intervention is now being scaled up across the country under the aegis of RNTCP by leveraging learnings from the intervention.

Challenges/outstanding issues to be addressed

- Lack of facilities for extra-pulmonary sample collection at most private clinics/providers
 - The providers were linked to existing tertiary care centres with sample extraction facilities
- Competing interests with private laboratories in the project cities providing diagnosis by Xpert MTB/RIF
- Perception of public sector (delays, red tape, loss of patient to the private sector)
 - Mitigated during one-to-one meetings and continuing medical education
- Providers are encouraged to refer samples to nearby Xpert MTB/RIF sites under the NTP for testing.

Funding

The project was funded by USAID under the Challenge TB project, CDC and PATH. FIND was responsible for implementation, training, coordination, monitoring, data analysis and writing of the report in close coordination with the Central TB Division, Ministry of Health and Family Welfare, Government of India.



For more information:

Recently published project data

- <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193656>, accessed 18 August 2018
- <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193194>, accessed 18 August 2018
- <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193341>, accessed 18 August 2018

Manuscripts under review

1. Pediatric pathways in four Indian cities: a mixed method study of pathways to microbiological confirmation for pediatric tuberculosis patients

Authors: Neeraj Raizada¹, Andrew McDowell², Sunil D. Khaparde³, Aakshi Kalra¹, Raghuram Rao³, T.N. Pavani¹, S Sudha¹, Himshweta Tyagi¹, Y Mary Rebecca¹, Sophie Huddart⁴, Virender Singh Salhotra³, Sreenivas Achuthan Nair⁵, Catharina Boehme⁶, Claudia M Denkinge⁶, Sanjay Sarin^{1*}

¹ Foundation for Innovative New Diagnostics, New Delhi, India ² Institut national de la santé et recherche médicale, Paris, France ³ Central TB Division, Government of India, New Delhi, India, ⁴ McGill University, Montreal, Canada ⁵ World Health Organization, Country Office for India, New Delhi, India ⁶ Foundation for Innovative New Diagnostics, Geneva, Switzerland

1. Upfront Xpert MTB/RIF testing on various specimen types for presumptive infant TB cases for early and appropriate treatment initiation

Authors: Neeraj Raizada¹, Sunil D. Khaparde², Raghuram Rao², Aakshi Kalra¹, Sanjay Sarin¹, V.S. Salhotra², Soumya Swaminathan³, Ashwani Khanna⁴, Kamal Kishore Chopra⁵, M. Hanif⁶, Varinder Singh⁶, K R Umadevi⁷, Sreenivas Achuthan Nair⁸, Sophie Huddart⁹, Rajneesh Tripathi¹, CH. Surya Prakash¹⁰, B K Saha¹¹, Claudia M Denkinge^{12*}, Catharina Boehme¹²

¹ Foundation for Innovative New Diagnostics, New Delhi, India ² Central TB Division, Government of India, New Delhi, India ³ Indian Council of Medical Research, New Delhi, India ⁴ State TB office, Govt of NCT, New Delhi, India ⁵ New Delhi TB Centre, New Delhi, India ⁶ Lady Hardinge Medical College and assoc Kalawati Saran Children's Hospital, New Delhi, India ⁷ National Institute of research in Tuberculosis, Chennai, India ⁸ World Health Organization, Country Office for India, New Delhi ⁹ McGill University, Montreal, Canada, ¹⁰ Intermediate Reference Laboratory, Hyderabad, India ¹¹ Intermediate Reference Laboratory, Kolkata, India ¹² Foundation for Innovative New Diagnostics, Geneva

8.3. Improving TB diagnosis in children below five years of age

Country: Kenya

Contributors: Ellie Click;¹ Rinn Song;^{2,3} Kimberly McCarthy;¹ Kevin Cain¹

¹ Centers for Disease Control; ² University of Oxford; ³ Harvard Medical School

Background

Globally, the majority of children with TB disease are not diagnosed or treated. One of the challenges to case detection in children is that it is difficult to confirm TB disease by bacteriological testing. Gold standard specimens (gastric aspirate and induced sputum) are invasive, challenging to obtain, and rarely used in high TB burden settings. Many studies have compared one specimen type to another but there is limited evidence on a broad range of specimens and tests and combinations of them.



Description

In a collaboration between the CDC, the Kenya Medical Research Institute, and Harvard University, a prospective cohort study was conducted in Kisumu, Kenya to determine the best specimen or combination of specimens for diagnosis of TB in children. A total of 300 children under 5 years of age with and without HIV were enrolled from inpatient and outpatient settings as well as through TB contact tracing activities from October, 2013–August, 2015. Participants had prolonged symptoms suggestive of TB (cough, fever, malnutrition or lymphadenopathy) and parenchymal abnormalities on chest radiographs despite treatment for alternative causes. For each child, up to two specimens each of nasopharyngeal aspirate, early morning gastric aspirate, string test, induced sputum, lymph node aspirate, stool, urine, blood, were collected from each participant and tested by smear microscopy, liquid TB culture (BACTEC™ MGIT™ (Becton Dickinson Microbiology Systems, Cockeysville, MD)) and Xpert® MTB/RIF (Cepheid, Sunnyvale, USA). Participants were evaluated at 2 weeks, 2 months, and 6 months. TB treatment was provided based on bacteriologic or clinical diagnosis, and preventive treatment was provided, where indicated, if TB disease was ruled out on the basis of laboratory testing and clinical evaluation.

Outcomes/successes

Preliminary results indicated that a combination of more easily obtainable specimens (nasopharyngeal aspirate + stool) have a diagnostic yield comparable to commonly accepted gold standard specimens (Tables 8.2 and 8.3).

Table 8.2: Diagnostic yield (number of children diagnosed) of specimen types among children with bacteriologically-confirmed TB (n=32) by type of diagnostic test. Yields of diagnostic tests are not mutually exclusive

Specimen	Smear microscopy	Xpert or MGIT
Gastric aspirate	5	22
Nasopharyngeal aspirate	6	22
Induced sputum	4	15
String test	2	13
Stool	4	14
LNA		3
Urine	1	4
Blood		1

Table 8.3: Diagnostic yield of specimen combinations among children with bacteriologically-confirmed TB (n=32)

	Specimen type	Yield
Reference standard	2 IS	20
	1 GA +1 IS	24
	2 GA	24
Minimally invasive	1 NPA	22
	2 NPA	24
	1 NPA + 1 stool	25
Invasive	1 NPA + 1 GA	27
	2 NPA + 2 GA	29
	1 NPA + 2 GA + 1 stool	30

NPA = nasopharyngeal aspirate, IS = induced sputum, GA = gastric aspirate

Lessons learned

- The combination of one NPA and one stool had the same yield and as invasive gold-standard specimens (induced sputum or gastric aspirate), suggesting this combination of readily-obtainable specimens may be adequate for diagnosis in routine circumstances.
- Bacteriologic diagnosis of TB in children may be improved by using a combination of invasive and non-invasive specimens, when needed. Such approaches may be particularly relevant when isolation of bacteria is especially important (e.g. when there is concern for drug resistance), or when diagnostic accuracy and sensitivity are critical (e.g. clinical trials).
- Despite extensive sampling, laboratory confirmation of TB using currently available diagnostic tools remains challenging in children <5 years of age.



Sustainability/scale-up

- Diagnostic yield under programmatic conditions using nasopharyngeal aspirates and stool will be further investigated in large multi-country studies with the goal of subsequent implementation and scale-up based on findings.
- Collection of nasopharyngeal aspirates and stool is being piloted as part of TB household contact tracing in Mozambique, Uganda and as part of paediatric hospital care in Mexico.

Challenges/outstanding issues to be addressed

- Nasopharyngeal aspiration uses an electronic suction device. Even simpler methods of obtaining nasopharyngeal specimens (such as field aspirator, nasopharyngeal swab) merit evaluation.
- Current stool processing protocols require use of appropriate laboratory standard operating procedures (SOPs); efforts are underway to develop more simple processing protocols and devices.
- More research is needed to develop and evaluate biomarker-based tests that do not rely on direct mycobacterial detection.

This study was reviewed and approved by the CDC and Kenya Medical Research Institute IRBs (CDC Protocol #6334). The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the funding agencies.

8.4. New drug regimens for the treatment of multi- and extensively-drug resistant TB in children and adolescents

Country: Belarus

Contributors: Alena Skrahina;¹ Irina Babchonak;¹ Dzmitry Klimuk;¹ Aliaksandr Skrahin;² Henadz Hurevich¹

¹ Republican Research and Practical Centre for Pulmonology and Tuberculosis, Minsk, Belarus; ² Belarusian State Medical University, Minsk, Belarus

Background

The epidemiological situation on TB in Belarus is characterized by a decrease in the number of notified TB cases: from 5324 in 2012 to 3057 in 2017. The incidence of all forms of TB has decreased substantially from 56.3 (2012) to 32.2 (2017) per 100 000 population. At the same time Belarus has one of highest MDR-TB proportions among TB cases in the world: 34.8% among new and 65.2% among previously treated TB cases in 2017.

Similar epidemiological trends are evident in child and adolescent TB: the number of TB cases has gradually decreased from 54 in 2012 to 38 in 2016. The greatest number of cases was found among adolescents (aged 15–17 years): 33 (2012) and 25 (2017). In 2012, seven cases of MDR-TB were notified among adolescents; no such cases have been notified among younger children (0–14 years of age). A total of 18 cases of MDR-TB were notified among adolescents and four among children aged 0–14 years in 2016. Of the 22 MDR-TB child and adolescent patients registered in 2016, seven had additional resistance to fluoroquinolones or SLI drugs (pre-XDR-TB), and five had XDR-TB.



Description

Rapid uptake of new drugs is one of the key directions of the NSP. In Belarus, new drugs, bedaquiline (BDQ) and delamanid (DLM), became available in June 2015 and June 2016, respectively. Repurposed drugs, including linezolid (LZD), clofazimine (CFZ), and carbapenems were introduced earlier.

New drugs were implemented under programmatic conditions with assistance and support of the Global Fund, WHO and MSF. Up to now, BDQ, DLM and CFZ have not been registered in the country, but the drugs were included in the national guidelines. The drugs were made available through an "Import waiver". By the MoH order new drugs can only be used under close clinical monitoring under active TB drug safety monitoring and management of adverse events (aDSM).

The use of BDQ among children and adolescents began in September 2015, followed by the use of DLM in December 2016. Each MDR-TB case considered for the new drug-containing regimen was discussed at the MDR-TB expert committee. Regimen design was based on DST results, history (including drug tolerability), co-morbidity, and severity of the disease. The backbone of new regimens is a combination of BDQ or DLM, LZD, CFZ in the intensive phase and LZD, CFZ in the continuation phase. Other MDR-TB drugs were added to build an effective regimen: fluoroquinolones, SLIs, pyrazinamide, ethionamide/prothionamide, carbapenems (imipenem, meropenem), ethambutol, cycloserine/terizidone, and amoxicillin/clavulanate. Cohort event monitoring was used to assess the safety and effectiveness of the new regimens. Paper-based forms are completed during each patient visit, after which the information is summarized in a review form. Data are then captured in the electronic national TB register (including a newly developed pharmacovigilance component), and to the national database of adverse drug reactions.

Outcomes/successes

By 31 March 2018, the cohort of child and adolescent MDR-TB patients on new TB drug-containing regimens included 33 patients of both sexes, aged 10–17 years (median 15 years): 16 were on BDQ and 17 on DLM; 31 with pulmonary and two with extra-pulmonary disease; two MDR-TB cases, 12 pre-XDR-TB cases (six with additional resistance to fluoroquinolones, and six to SLI), 19 XDR-TB cases.

Intermediate results have been promising. There were no cases with treatment failure, loss to follow-up and death. Eight patients successfully completed the course of treatment: six patients with the outcome of "cure" and two patients "treatment completed" (the others are still on treatment). Sputum culture conversion occurred within a period of three months. Despite all patients experiencing adverse events, they were mild and moderate, resolved spontaneously or with minimal interventions.

Lessons learned

Interim results on safety and effectiveness of new TB drugs (BDQ, DLM) used for the treatment of M/XDR-TB in children and adolescents are promising. Before the start of a new drug-containing regimen, careful patient selection and discussion at the MDR-TB expert committee is important. For patients on new drugs close clinical and aDSM of adverse events is critical.

Sustainability/scale-up

In view of the relatively small number of cases of MDR-TB among children and adolescents registered annually in the country, they are expected to have uninterrupted access to new TB drugs and regimens due to the social and ethical priority accorded in the treatment of such patients.

Challenges/outstanding issues to be addressed

BDQ and DLM, despite having been used since 2015 and 2016 respectively, have still not been registered in Belarus. The registration of new drugs needs to be simplified to reach eligible patients quickly to help improve treatment outcomes.







9 Meet funding needs for childhood TB

2013 Roadmap for childhood tuberculosis:

- ▶ New tools for prevention, diagnosis and treatment.
.....
- ▶ Implementation of interventions addressing childhood TB.
.....
- ▶ Analysis based on seven high-burden countries (estimates):
 - US\$ 80 million per year required to address childhood TB.
 - US\$ 40 million per year for antiretroviral treatment/cotrimoxazole prophylaxis therapy for TB/HIV co-infected children.
.....

9.1. Funding for childhood TB through the Global Fund to Fight AIDS, Tuberculosis and Malaria

Global

Contributors: Anna Scardigli; Nnamdi Nwaneri; Erin Ferenchick; Nicholas Furtado

The Global Fund

Background

Founded in 2002, the Global Fund is a partnership between governments, civil society, the private sector and affected people, designed to accelerate the end of HIV/AIDS, TB and malaria as epidemics. The Global Fund raises and invests nearly US\$ 4 billion per year to support programmes run by local experts in countries and communities most in need.

The Global Fund's strategy for 2017–2022 has four synergistic objectives that represent a comprehensive approach of “investing to end epidemics”: (i) maximize impact against HIV, TB and malaria; (ii) build resilient and sustainable systems for health (RSSH); (iii) promote and protect human rights and gender equality; and (iv) mobilize increased resources.

Each strategic objective is underpinned by a number of subobjectives and supported by two strategic enablers. These objectives provide a critical path, outlining how the Global Fund will work with partners to ensure that their response globally and at country level is inclusive, impactful and sustainable. Innovation and differentiation along the development continuum and mutually accountable partnerships will help drive the new strategy forward.

General description of funding opportunities

The Global Fund's main investments to address childhood TB include the following approaches:

Country allocation for TB

- In their funding requests, countries most frequently use the TB modules to support the following childhood TB activities:
- Expanding diagnostics, including the most sensitive molecular testing and digital radiography tools for sample collection in children
- Switching to new paediatric formulations
- Scaling-up short regimens for MDR-TB in adults and children
- Exploring opportunities for integrated service delivery of TB services with other health services at primary care level, including facility and community-based diagnosis and treatment
- Leveraging the antenatal care and iCCM platforms to include maternal and child TB prevention and care
- Training and capacity building of health care workers on childhood TB diagnostics and treatment
- Other interventions relevant to prevent, detect and treat TB in children (such as TB/HIV integrated models of care).

Additional interventions addressing children and adolescents are included in modules of other diseases.



Catalytic funding

Three categories of catalytic investments exist:

1. Additional matching funds: A matching pool available to selected countries at the time of allocation to incentivize funding request with focus on key strategic priorities
2. Multi-country/regional funds: Used for selected cross-border initiatives, which are critical for the global response to HIV, TB and malaria
3. Strategic initiatives: Strategic areas that cannot be addressed through country allocations.

"Catalytic funding" countries:

Bangladesh, Democratic Republic of the Congo, Indonesia, India, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, Philippines, South Africa, Tanzania, Ukraine

Specific special initiatives

Programme quality and improvement, Western and Central African collaborative initiative, multi-country requests for proposals, among others.

Cross-cutting RSSH investments

Weak health systems are critical barriers to scaling-up the global response to TB, including childhood TB. As such, RSSH has a central place within the Global Fund strategy for 2017–2022, and the Fund has outlined seven priority areas for RSSH support that underpin its disease-specific investments. These priorities include: (i) strengthening community responses and systems; (ii) supporting RMNCAH and platforms for integrated service delivery; (iii) strengthening global and in-country procurement and supply chain systems; (iv) leveraging critical investments in human resources for health; (v) strengthening data systems for health and countries' capacity for analysis and use; (vi) strengthening and aligning to robust national health strategies and national disease-specific strategic plans; and (vii) strengthening financial management. While all are essential to supporting the TB response more broadly, there are three areas of focused investment in the health system that facilitate key steps in the pathway of prevention and care in childhood and adolescent TB: (i) strengthening community systems along the pathway of care; (ii) investing in human resources for health (HRH) for the delivery of comprehensive TB services through integrated platforms; and (iii) laboratory system strengthening for the use of appropriate diagnostics.

Focus on specific investments

Catalytic funding

Catalytic investments for the period 2017–2019 include US\$ 190 million for TB (focusing on finding missing people with TB and drug-resistant TB, including children), with funding matched by the Global Fund following the submission of innovative and ambitious plans/targets to detect and treat additional TB cases; and to foster collaboration with other partner initiatives focusing on improving case detection (see Table 9.1).

Table 9.1: Summary of TB catalytic funding

TB catalytic funds modality	Total funding (US\$ million)	% of funding
Matching funds	115	60.5%
Multi-country proposals	65	34.2%
Strategic initiatives	10	5.3%
Total	190	

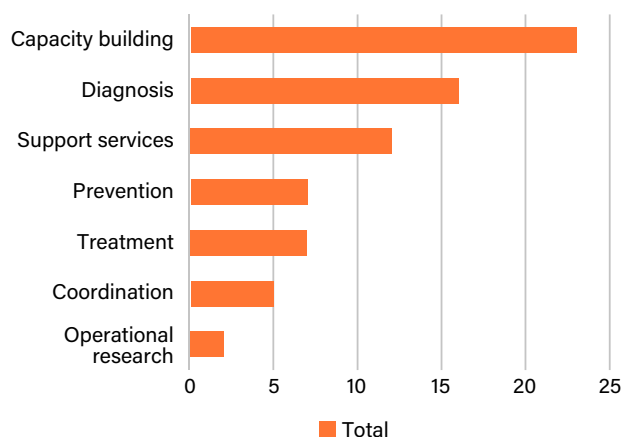


The 13 catalytic investment countries account for approximately 75% of all global missing cases (adults and children) and over 400 000 missing childhood TB cases.

A review of the childhood TB related activities as outlined in the matching funding requests submitted at the end of 2017 by 11 catalytic funding countries identified the following main areas of focus, with the following approximate distribution (frequency) of paediatric TB activities:

- Capacity building: childhood TB trainings, on-the-job training, sensitization campaigns, etc.
- Diagnosis: procurement of Xpert MTB/RIF machines and cartridges, chest radiography, CT scans, FNAC (fine needle aspiration), TB screening, FAST approach, etc.
- Prevention: procurement of isoniazid for IPT in children, contact tracing, etc.
- Treatment: procurement of anti-TB drugs for children (child-friendly FDCs).
- Support services: sputum transportation, patient support, printing of paediatric tools and guidelines.
- Coordination: Childhood TB Working Group meetings, meetings with paediatricians, joint monitoring missions, etc.
- Operational research: targeted at children (such as coverage of services on diagnosis and treatment of TB infection in children).

FIGURE 9.1: NUMBER OF CHILDHOOD TB ACTIVITIES IN COUNTRIES' GLOBAL FUND FUNDING REQUEST GROUPED ACCORDING TO AREAS OF FOCUS



The US\$ 10 million TB strategic initiative aims to support the global End TB Strategy by finding missing people with TB and improving case detection in the 13 countries listed above. The activities proposed in the TB strategic initiative that are being supported by WHO and STOP TB include: addressing barriers to find missing TB cases (including children); documentation, learning and experience sharing; support to the key priorities of the Global Fund strategy; support to the uptake and scale-up of tools and approaches; and development of tools and approaches for finding missing TB cases (including children).

Special initiatives

- Tanzania and Kenya programme quality and efficiency (PQE) to increase capacities to diagnose TB cases (including children). The initiative allowed an increase in TB notification in the implementation districts and is now scaled-up nationwide. A similar initiative is ongoing in Uganda.
- Western and Central Africa collaborative initiative to improve TB case finding and treatment outcomes in collaboration with partners. This included a workshop for best practices sharing in Benin, where 20 participant countries had the opportunity to share and learn from others experiences, and to start thinking on how to address TB case finding in their context in more innovative ways. Various experiences addressed paediatric TB, and included the following examples: pilot studies to find missing cases in children under five years of age through contact investigation and preventive treatment; strengthening health facility and community level health care delivery to improve childhood TB, case finding, treatment and prevention; evaluation of the feasibility of iCCM/TB/HIV/malnutrition integration; and implementation research on active case finding in children through the seasonal malaria chemoprevention mass campaign (see also section 7.3). One of the outcomes of the Western and Central Africa workshop was a TB declaration (Cotonou TB declaration – see figure below) where countries, among other issues, explicitly recognized that three quarters of paediatric TB cases are missed in their region, and called on governments and stakeholders to support a multi-sectorial response against TB to accelerate childhood TB interventions (i.e. preventive treatment, case finding and treatment) by at least 50% by 2020.
- Quality improvement of integrated antenatal and postnatal care to assess the integration of HIV, TB and malaria in the package of services provided to mothers and newborns accessing this platform and




the impact of facility level standards-based quality improvement in Afghanistan, Chad, Ghana, Niger, Nigeria and Togo.

COTONOU TB DECLARATION

Workshop to share best practices and lessons learned in tuberculosis case finding and treatment in Western and Central Africa

26 - 28 March 2018




Preamble

We note with concern that every year, the Western and Central Africa (WCA) Region is missing more than 50% of TB cases. Among children, three quarter of cases are missed. The estimated mortality in TB/HIV co-infected patients in WCA region is 50% higher than in the rest of Africa. Our national programs are currently diagnosing and treating only 20% of the patients suffering from DR-TB.


We, the National TB Programs of WCA region*, having come together with partners at the Regional Workshop in Benin, reaffirm our commitment to end TB as declared in the Sustainable Development Goals and require absolute commitment from our Governments.

We recognize that 2018 is a historical moment in the fight against TB, with the upcoming UN General Assembly (UNGA) High Level Meeting on TB in September.

We call on our Governments and stakeholders for a multi-sectoral response against TB and provide the needed **political** and **operational** leadership to end the TB epidemic and we affirm to do the following:




Reduce the proportion of missing TB cases by 50% by 2020 for DS and DR-TB



Reduce the TB/HIV mortality by half by 2020


* The West and Central African countries present at the workshop: Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Cote d'Ivoire, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Niger, Senegal and Sierra Leone, Nigeria, Sierra Leone and Togo.




Accelerate childhood TB interventions including preventive treatment, case finding, and treatment by at least 50% by 2020



Strengthen systematic use of implementation research to generate locally relevant evidence-based data for innovative interventions and scale up



Strengthen strategic partnerships with community and civil society to foster integrated, community-led, people-centered, rights-based and gender-transformative approaches to the TB response



Ensure adequate financing for TB, including following through on existing domestic government commitments to support essential TB drugs, human resources and services



Strengthen partnerships among stakeholders for elimination of TB, including accountability for the outcomes of this declaration at national, regional and global levels

Cotonou TB declaration

RSSH: focus on integrated services

The Global Fund strategy emphasizes the importance of evidence-based, integrated, people-centred care for women, newborns, children and adolescents. Four platforms of integrated service delivery are prioritized for co-investment: (i) antenatal care; (ii) iCCM; (iii) integrated sexual and reproductive health-HIV services; and (iv) adolescent health. Countries are encouraged to critically evaluate which packages of services and models of delivery are most appropriate and feasible.

In particular, three important opportunities – (i) during antenatal and postnatal care, (ii) during child immunizations, well-child visits and growth monitoring events and in nutrition centres, and (iii) during the case management of sick children including IMCI and iCCM – identified in RMNCAH service delivery for childhood TB-related activities should be included.

Lessons learned from countries' funding requests (TB modules)

- Coordination at country level is needed to enable integration and leveraging funding opportunities for childhood TB:
 - Engage in discussions on national health sector plans and disease strategies
 - Advocate for the integration of RMNCAH and disease specific policies
 - Reach out to Country Coordinating Mechanisms to participate in the country dialogue process and preparation of Global Fund support request and/or programme revision
 - Advocate that funding requests include – and prioritize – evidence-based interventions for RMNCAH and integrated service delivery
 - Encourage increased domestic financing to complement investments.
- Interventions to increase childhood TB notification in the funding request applications are often not exhaustive, and have little innovations (i.e. business as usual)
- In some settings there are concerns around alignment of private sector MDR-TB case management with public sector MDR-TB standards. Overall, targets for MDR-TB treatment success rates are modest.
- Overall coverage of preventive treatment for TB infection is low.
- Diagnostic algorithms frequently limit the optimal use of Xpert MTB/RIF: restrictive algorithms do not include it as the initial or recommended test for all presumptive child TB cases. Access gaps remain: geographical coverage, private versus public availability of Xpert MTB/RIF machines, weak sample



transport system, etc. There is a need to consider Xpert MTB/RIF as a package, not just as a diagnostic test in isolation.

- Most country applications do not prioritize aDSM.
- Private service delivery models in the funding request applications are not detailed enough and adoption of innovative approaches is missing (rapid diagnostics, digital tools, e-notification).
- Specifics on the operationalization of TB/HIV activities are often limited.
- Countries often do not differentiate between adult and childhood TB activities in their funding requests, and therefore the proportion of Global Fund support to countries for childhood TB is difficult to trace and may be under-estimated.

Sustainability and scale-up

- The Global Fund encourages countries to be more ambitious in scaling up innovative approaches, tools and strategies to find missing TB cases (including children and adolescents). Applicants should engage with country teams, NTPs/principal recipients and partners during funding requests, grant making and implementation. The global move to find missing cases should be sustained, and for finding missing paediatric cases, contact investigations and preventive treatment should be scaled up.
- Countries should swiftly switch and accelerate the transition in all ongoing grants and ensure that future applications and funding requests do not include old formulations. The Global Fund teams coordinate with technical partners to support countries to accelerate transition from old formulations to the new child-friendly FDCs taking into account the recommendations, quantity and cost of new formulations and wastage of old drugs which will not be used. The Global Fund works with partners to support the transition to child-friendly FDCs (as well as to shorter MDR-TB regimens) in a coherent manner, taking into account countries' preparedness, procurement processes and timelines to ensure the best possible health outcomes for patients and to maximize impact. This also includes rapid uptake of new diagnostics and new MDR-TB drugs.
- RSSH investments for childhood and adolescent TB should be leveraged. The successful prevention, detection and management of TB, particularly for children and adolescents, requires strong health systems with a robust community response for empowerment and social mobilization as well as delivery of integrated services. The primary care platform, both at community and facility level, is ideally placed to address key steps along the pathway of care, and should be strengthened overall as articulated in the SDGs and aligned with the achievement of universal health coverage. Sustainability is central to ensuring that such investments are strategic and work towards achieving universal health coverage. While Global Fund's Sustainability, Transition and Co-financing Policy aims to support NSPs for the sustainability of TB programming, it also works to ensure alignment with national health sector programmatic strategies and health financing strategies that promote the principles of universal health coverage.

Challenges and outstanding issues

Investments in childhood TB still appear suboptimal, and there is often limited definition of TB interventions for children and adolescents.

9.2. Recent childhood TB projects funded through Unitaid

Regions: AFRO, PAHO, SEARO and WPRO

Contributor: Yamuna Mundade

Unitaid



9.2.1. TB prevention for high-risk groups (IMPAACT4TB)

The IMPAACT4TB Consortium, led by the Aurum Institute, aims to reduce TB incidence and deaths among under-five child contacts and people living with HIV (PLHIV) in low and middle-income countries by contributing to the sustainable scale up of affordable, quality-assured 3HP (isoniazid plus rifapentine taken weekly for three months). 3HP has been recommended by WHO as an alternative to six months of IPT for both adults and children in countries with a high TB incidence. The project targets starting 400 000 people on 3HP in 12 project countries, to catalyse an increase in supply and demand for and uptake of 3HP in these countries.

Expected outcomes of the IMPAACT4TB project are to:

- Increase the number of child contacts and PLHIV (all ages) started on 3HP.
- Contribute to the revision of WHO guidance on the programmatic management of LTBI based on evidence generated from the IMPAACT4TB grant.

Proposed outputs and related activities include:

- Determining the safety and pharmacokinetics of rifapentine (RPT) in PLHIV on dolutegravir (DTG) by conducting a pharmacokinetic study in South Africa.
- Reducing the price of RPT by inclusion of 3HP in the national guidelines for TB preventive treatment; anchoring pricing to a large middle-income purchaser like South Africa; leveraging Global Fund and PEPFAR funding; and using GDF's large procurement power across 10 of the IMPAACT4TB project countries.
- Accelerating development and filing of rifapentine as a single drug by generic suppliers
- Supporting initial scale up of 3HP by providing technical assistance to project countries to address barriers to the scale up of 3HP, incorporating revision of TB preventive treatment guidelines to include 3HP, advocacy for 3HP, inclusion of RPT onto the essential medicines list, strengthening quantification, forecasting and supply chain management.
- Generating and disseminating evidence for optimal use of 3HP and scalable models of delivery.

Other members of the IMPAACT4TB consortium are: KNCV, CHAI, Johns Hopkins University, GDF and TAG.

IMPAACT4TB project countries

AFRO

Ethiopia, Ghana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zimbabwe

PAHO WPRO

Brazil Cambodia

SEARO

India, Indonesia

9.2.2. Catalysing Paediatric TB innovations (CaP TB)

Led by the Elizabeth Glaser Pediatric AIDS Foundation, the CaP TB project will be implemented in nine sub-Saharan African countries and India. The goal of the project is to reduce morbidity and mortality associated with paediatric TB. This will be achieved by reducing the paediatric TB diagnostic and treatment gap, increasing coverage of the new paediatric FDCs, as well as scaling up of treatment of TB infection through innovative models of care for paediatric TB management and prevention that focuses on integration and decentralization.

Specific targets include:

- Increase childhood TB case detection two fold overall (over 16 000 additional children with TB), including over 12 000 to be treated with the child-friendly FDCs.
- 90% treatment initiation.
- 90% successful treatment.

CaP TB project countries

AFRO

Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Kenya, Lesotho, Malawi, Tanzania, Uganda, Zimbabwe

SEARO

India



- Increase preventive treatment coverage four fold (over 52 000 additional children).
- The estimated years of life saved by the end of the project is over 100 000 and the estimated cost savings amount to US\$ 1.8 million.

The project proposes the following activities to achieve its goal:

- Develop, document and facilitate uptake of innovative models of care that support integration and decentralization to strengthen:
 - *case-finding approaches for childhood TB* through the integration of TB screening, diagnosis, and treatment initiation into maternal, newborn and child health; paediatric inpatient and outpatient departments; nutrition programmes; and HIV care and treatment entry points. In India, efforts will be focused on integrating paediatric TB care in the private sector.
 - *contact tracing* at community and household level.
- Improve the screening and clinical diagnostic capacity of health care providers.
- Increase the uptake of molecular diagnostics, such as Xpert MTB/RIF ultra and Omni, for paediatric TB.
- Support the integration of TB care in non-TB health care facilities (such as HIV, nutrition and maternal, newborn and child health facilities).
- Conduct intensive monitoring and dedicated research:
 - Routine patient and process-level monitoring and evaluation.
 - A multi-centric longitudinal prospective cohort study in three countries.
 - Cluster-randomized controlled studies in two or three countries.
 - Costing data and cost-effectiveness analysis.

9.2.3. Strengthening paediatric TB services for enhanced early detection

Strengthen Paediatric TB services for Enhanced Early Detection (TB-SPEED) is a four-year project implemented in seven countries, led by the University of Bordeaux. The project's goal is to contribute to the reduction in childhood mortality from TB by delivering an available, feasible, cost-effective and decentralized childhood TB diagnostic approach to enhance case finding and access to treatment. The project is expected to generate evidence on the most appropriate decentralization strategy for TB diagnosis and the improvement of TB diagnosis in high-risk children (HIV-infected, malnourished children and children with severe pneumonia).

TB-SPEED project countries

AFRO

Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, Uganda, Zambia

WPRO

Cambodia

The project's outputs and activities are:

- Test new decentralized childhood TB diagnostic approaches at the district health system level.

This is an operational research study that will use an innovative diagnostic approach based on Xpert MTB/RIF (using Xpert Ultra and battery-operated Xpert MTB/RIF Omni platform), performed on a combination of easy to collect samples (nasopharyngeal aspiration and stool), using standardized symptoms screening and chest radiograph interpretation.
- Evaluate an early TB detection strategy in children with severe pneumonia.

This is a pragmatic cluster-randomized clinical trial to evaluate the impact of adding systematic early detection of TB by Xpert MTB/RIF Ultra on mortality and case detection (performed on nasopharyngeal aspiration and stools) to the WHO recommended standard of care for children with severe pneumonia.
- Validate diagnostic tools and algorithms in highly vulnerable groups with presumptive TB, specifically HIV-infected and severely malnourished children.

This will be a diagnostic cohort study enrolling HIV-infected children and hospitalized severely malnourished children. The study will validate a recently proposed algorithm for diagnosis of TB in HIV-infected children and the evaluation of several diagnostic tests in hospitalized severely malnourished children.



- Identify optimized, suitable and affordable specimen processing and collection methods for childhood TB diagnosis in resource-limited countries.

This involves microbiological and technological optimization work to identify and test simple and affordable specimen processing and collection methods for childhood TB diagnosis that can be deployed at the low healthcare level in resource-limited countries.

- Evaluate cost-effectiveness of the proposed diagnostic approaches.
- Disseminate, communicate and engage stakeholders.

Other members of the TB-SPEED consortium are: University of Montpellier (Research Institute for Development), Makerere University – Johns Hopkins University Research Collaboration (Uganda), Institut Pasteur (Cambodia), Programme PAC-CI (Côte d’Ivoire), Instituto Nacional de Saude (National Institute of Health, Mozambique), Therapeutic Solidarity and Initiatives for Health (Sierra Leone) and the University of Zambia.

9.3. Funding for paediatric TB research

Global

Contributors: Mike Frick and Lindsay McKenna

Treatment Action Group (TAG)

In 2016, funding for paediatric TB research amounted to US\$ 29.1 million, which was only slightly higher than the US\$ 25–26 million spent annually between 2013 and 2015. Nearly half of this money supported paediatric TB drug research and development.

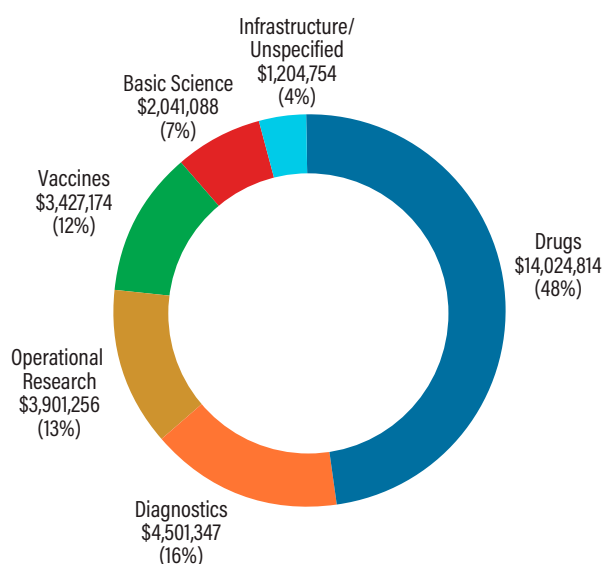
Although children represent around 10% of the TB caseload globally, funding for paediatric research represented only 3% of total TB research funding available in 2016 (US\$ 726 million). The improved understanding of the burden of child and adolescent TB (see chapter 2) has strengthened the case for increased research into paediatric TB (26).

Gaps in diagnosis and treatment of children with TB reflect both the inadequacy of existing tools and suboptimal implementation by TB and child health programmes. Less than half of the estimated one million children who fall ill with TB every year, and less than 10% of the estimated 32 000 children with MDR-TB, are diagnosed and put on treatment.

Child-friendly FDCs were introduced in 2015 (see section 8.1.1). This is a major milestone in paediatric TB research, given the resulting improvement in the ability of care providers to administer appropriate doses of TB medicines to children. Similar second-line products have since been developed and pre-qualified (see section 8.1.2). Yet over 96% of the quarter million children dying of TB never receive appropriate treatment.

FIGURE 9.2: PAEDIATRIC TB RESEARCH AND DEVELOPMENT FUNDING

Paediatric TB R&D Funding by Research Category, 2016
Total: \$29,100,432



Source: The ascent begins: tuberculosis research funding trends, 2005–2016. New York: Treatment Action Group; 2017 (http://www.treatmentactiongroup.org/sites/default/files/TB_FUNDING_2017_final.pdf, accessed 17 August 2018).



Great progress has been made in recent years towards the development of improved tools for TB, including rapid molecular diagnostic tests, child-friendly first-line formulations, new drugs and shortened regimens for the prevention of TB and the treatment of drug-resistant TB. However, the benefits of this scientific progress have yet to reach most children.

Improving prevention, diagnosis and management of children and adolescents affected by TB will require increased investments in paediatric-specific research and development.

Priority areas for investment include developing a vaccine with better and lasting protective efficacy; less invasive and more sensitive diagnostic tests designed for children; and shorter, safer and child-friendly regimens for TB prevention and treatment. A comprehensive list of research priorities is available as an accompanying document to the 2018 Roadmap.¹⁴

“There will be no end to the TB epidemic without an end to TB among the groups most threatened by the disease. Funders must commit to supporting a TB research agenda that includes children, pregnant women, and other vulnerable groups.”

Source: The ascent begins: tuberculosis research funding trends, 2005–2016. New York: Treatment Action Group; 2017 (http://www.treatmentactiongroup.org/sites/default/files/TB_FUNDING_2017_final.pdf, accessed 17 August 2018).

The TB research agenda on paediatric TB represents a commitment to equity in TB research that moves beyond children to address the needs of other vulnerable populations, including pregnant women. In recent years, there has been a move to appropriately include more pregnant women in TB drug trials. This is an example of how advocates and researchers can apply the lessons learned in paediatric research and development to advance research relevant to other vulnerable populations.

¹⁴ The brochure “Research Priorities for paediatric tuberculosis” will be available on the Treatment Action Group (TAG) website: <http://www.treatmentactiongroup.org/>



Notes

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10 Form coalitions and partnerships to study and evaluate the best strategies for preventing and managing childhood TB, and for improving tools used for diagnosis and treatment

2013 Roadmap for childhood tuberculosis:

- ▶ Collaboration with industry, academia, major agencies, NGOs and other organizations involved in development and evaluation of diagnostics and therapeutics.

Examples:

- Earlier pharmacokinetic studies for children.
 - Collaboration and partnerships to pool data and information.
 - Multi-site collaboration to achieve larger numbers of confirmed paediatric TB cases.
-

10.1. Value of partnerships and coalitions for the STEP-TB Project

Global

Contributors: Irina Usherenko;¹ Shelly Malhotra;¹ Anne Detjen;² Yamuna Mundade³

¹ *Global Alliance for TB Drug Development*; ² *UNICEF*; ³ *Unitaid*

Background

STEP-TB, an initiative led by the TB Alliance and WHO (Essential Medicines and Health Products department and the Global TB Programme), and funded by Unitaid and USAID, was launched in August 2013. STEP-TB aimed to drive the availability of appropriately dosed, properly formulated, affordable, high-quality paediatric TB medicines and establish a sustainable market for these products (see section 8.1.1).

At the core of STEP-TB was a collaboration between two organizations with complimentary roles: TB Alliance and the WHO. The partnership between these two organizations was vital to the success of the project. TB Alliance was well positioned to leverage a global network of public and private partners to effectively advance the development of the child-friendly FDCs. The WHO, with operations in 147 countries, leveraged its normative function, establishing and working with countries to implement policy and best practices. Its global reputation and technical expertise were essential for bringing global experts, countries, key opinion leaders, and other stakeholders into the work of STEP-TB. In addition, formal and informal partnerships with other entities across the work streams of the project were critical to success. These partners included the scientific and academic community, clinicians, international technical and donor agencies, the pharmaceutical and manufacturing sector, non-profit organizations, governments, policy makers and regulatory authorities.

Outcomes/successes

Active collaboration with pharmaceutical partners was key to success. The TB Alliance and pharmaceutical partner(s) contributed their expertise towards jointly established goals in clinical development, registration strategy, market research, demand generation and product launch, resulting in delivering FDCs ahead of schedule. In addition, through focused efforts to collaborate with high TB burden countries early in the project, high volume countries such as India and the Philippines purchased child-friendly FDCs for the first time.

Engaging child health champions in TB endemic countries (including paediatric associations, civil society, and patient representatives) helped to place TB on the child health agenda at the national level. Improved linkages and specific strategies for supply of products to healthcare providers in the child health and primary care sectors, were critical in affording treatment access. The creation of the “Louder than TB”¹⁵ advocacy platform (a coalition of more than 50 partner organizations spanning the maternal and child health, TB and HIV sectors) helped to amplify the collective voice, draw necessary attention to the issue of childhood TB, and mobilize demand for improved TB treatments.

Lessons learned

Bringing the TB agenda to other health sectors

One reason for the low uptake of paediatric TB treatment historically has been poor linkages between care-seeking channels for children and TB diagnostic and treatment sites. The project’s strategic partnership with UNICEF helped to break down barriers between child health and TB disease approaches and proved

¹⁵ <http://www.louderthantb.org/>, accessed 26 August 2018.



critical in advancing a more integrated and patient-centred approach to addressing childhood TB. The project also ensured participation of partners outside of the TB sector including HIV, maternal and child health, and nutrition. Leveraging partner networks helped draw much needed global attention to the neglected issue of childhood TB.

Partner engagement for driving demand

The project partners worked closely with stakeholders and countries to drive demand for the introduction of new paediatric products and ensure global availability. In partnership with the TB Alliance, WHO organized a series of regional, interregional and national meetings bringing together WHO regional focal points, NTP managers, child health actors, members of the Stop TB Partnership's Child and Adolescent TB Working Group and civil society representatives to create national roadmaps and targets for measuring countries' childhood TB responses. These were critical in generating a sense of shared accountability in addressing childhood TB and planning for FDC adoption. Leveraging the broad country networks and technical support platforms of additional partners, such as KNCV, the Global TB Programme at Baylor University, The Union, and national paediatric societies helped to support country planning. Broad stakeholder involvement at the national level was needed to drive guideline and adoption decisions. As a result of this preparation, more than 80 countries, many of whom were engaged by the project, adopted the new paediatric products within just two years of availability.

Collaboration with donors and global partners

Collaboration with donors, such as the Global Fund, Unitaaid and USAID, was important to ensuring timely reprogramming of funds for FDC procurement and scale up. A global mechanism, such as the Stop TB Partnership's GDF, served as an effective means to accelerate access to products, and early engagement with the GDF was instrumental in ensuring accessibility and affordability of the new medicines.

Challenges/outstanding issues

Maintaining sustained interest from partners is a challenge. Partner engagement requires continuous time and funding to ensure that progress towards shared deliverables continues after the finite project period. All regional meetings and coalition-based activities required funding to bring partners together.

Lastly, integrating TB into maternal and child health, and other health sectors can be difficult with partners having conflicting agendas and goals with the additional need for increased commitment, leadership and coordination across all stakeholders. Leveraging partner networks helped draw much needed global attention to the neglected issue of childhood TB, but maintaining the momentum remains a challenge. Ongoing efforts are needed to bring together a wide range of partners for sustaining the momentum required to address the issue of paediatric TB.



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Notes

A series of 20 horizontal dotted lines for writing notes.

