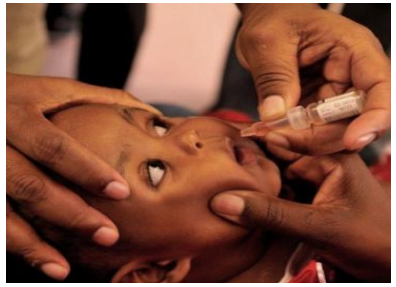

Webinar

TB in children and adolescents - what is new?
Overview of the 2024 guidelines

Date: 04 February 2025

Time: 13h00 – 15h00

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Health
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2030 NDP

30 YEARS OF FREEDOM
South Africa 1994 - 2024

Thank you for your interest in this webinar

- The chat has been disabled for the attendees.
- **Please use the Q&A box to post questions for our panel of experts.**
- The session is recorded and will be shared with all the presentations on the Knowledge Hub – www.knowledgehub.health.gov.za/lms

Programme Director: Prof N Ndjeka

Time	Duration	Topic	Presented by
13:00 - 13:05	5min	Opening and Welcome	Prof. Norbert Ndjeka
13:05 - 13:15	10min	Aims and objectives of webinar	Prof. Norbert Ndjeka
13:15 - 13:25	10min	Why we needed new guidelines	Dr Karen Du Preez
13:25 - 13:35	10min	Steps in decision making	Prof Helena Rabie
13:35 – 13:55	20min	Diagnosis of TB using the TB treatment decision algorithm	Dr Juaneta Luiz
13:55 - 14:15	20min	Treating children and adolescents with TB and deciding on short course	Prof Simon Schaaf
14:15 - 14:30	15min	Cases	Prof Helena Rabie/ Dr Juli Switala
14:30 – 14:55	25min	Discussion (Q&A)	Prof. Norbert Ndjeka
14:55 – 15:00	5min	Vote of thanks	Prof. Norbert Ndjeka

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Prof N Ndjeka

Prof Ndjeka serves as the Chief Director TB Control and Management, under the National Department of Health in South Africa.

Under his leadership, there has been a decline in the number of cases of DR - TB in South Africa and a remarkable improvement in proportion of patients successfully treated for DR- TB.

Dr K Du Preez

Dr du Preez is a clinician and senior researcher at the Desmond Tutu TB Centre, Stellenbosch University. Her work focuses on epidemiological and operational aspects of paediatric TB to allow a more effective response to the TB epidemic in children and adolescents.

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Prof H Rabie

Prof Rabie is a specialist in the field of paediatric infectious diseases and an associate professor of paediatrics at Tygerberg Hospital and the University of Stellenbosch. She has extensive experience in managing HIV-infected children and children with tuberculosis.

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Dr J Luiz

Dr Luiz is a clinical Researcher in the field of childhood TB diagnostics, with an interest in the high-risk groups; CLHIV, the malnourished and the very young. She manages a paediatric TB clinical research unit (est. 2017) with a strong local capacity development arm at Dora Nginza Hospital, Gqeberha.

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Prof S Schaaf

Prof Schaaf is an Emeritus Professor and Principal Researcher at the Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Stellenbosch University. He is a paediatrician and paediatric infectious diseases subspecialist and has a special interest in tuberculosis in children, especially drug-resistant tuberculosis

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Dr J Switala

Dr Switala is a Paediatrician who has worked in a variety of settings and countries but found her home in paediatric TB, which has been her focus for the last 7 years.

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Thank you for attending this webinar

The session recording and all the presentations will be shared on the Knowledge Hub – www.knowledgehub.health.gov.za

THANK YOU

Caring for children and adolescents with TB in South Africa

Why do we need new Child and Adolescent TB guidelines?

Dr Karen du Preez

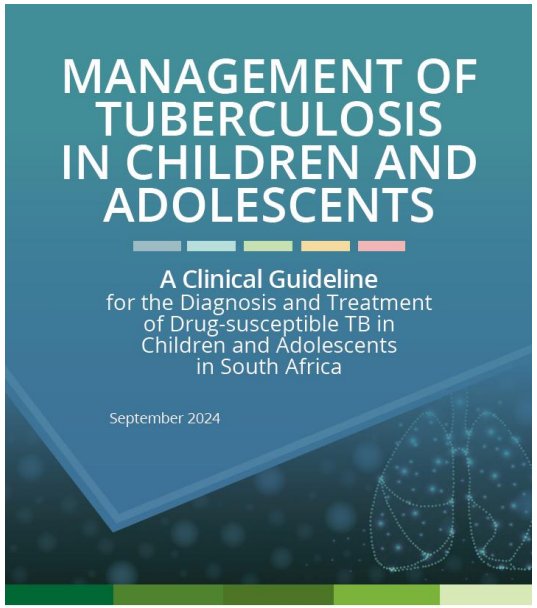
MBChB (UP), MSc Epidemiology (LSHTM), PhD (SU)

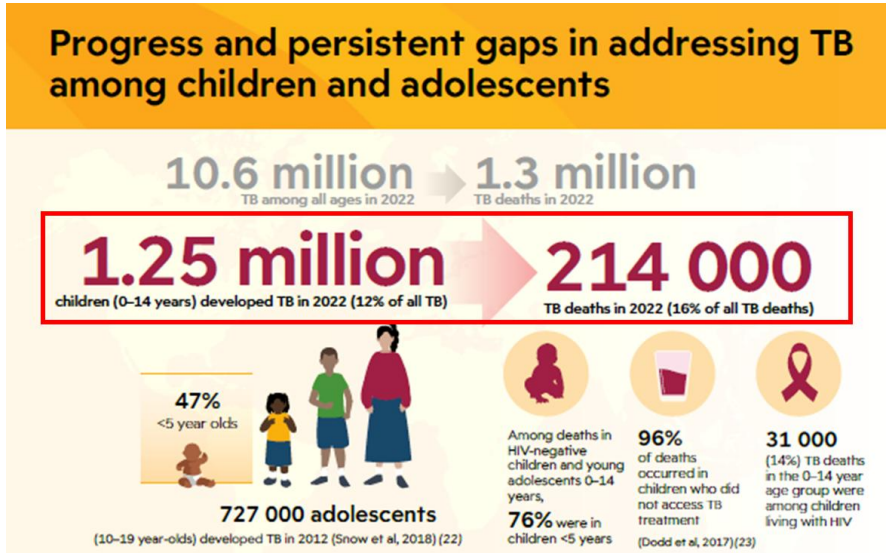
Senior researcher, Desmond Tutu TB Centre, Stellenbosch University

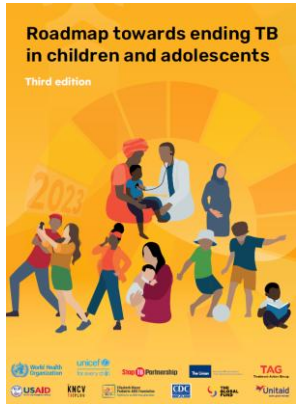
Chair: National Child, Adolescent and Maternal TB Working Group, SA TB Think Tank

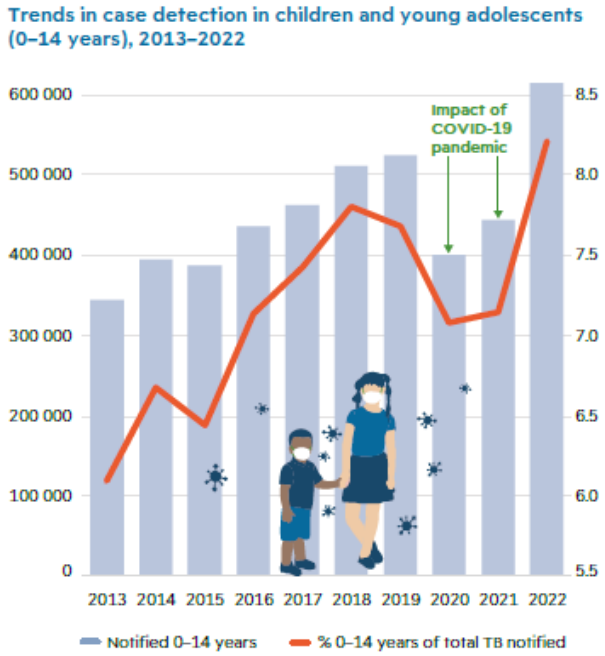
OUTLINE

- TB in children - Global and national burden
- WHO 2022 guideline – key updates
- Why SA needed new Child and Adolescent TB guidelines
- Guideline development process
- Guideline approval process
- Next steps





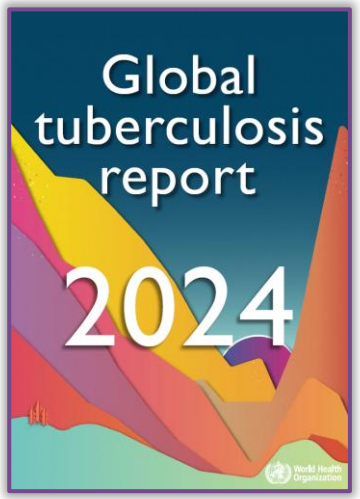




South Africa country summary: TB data		
	2022	**2023**
All TB cases		
Estimated total TB caseload	280 000	270 000
New and relapse TB case notifications	224 621	211 800
Treatment coverage (all)	80%	78%
Paediatric cases		
Estimated paeds(0-14) caseload	27 000	23 100
New and relapse (0-14) case notificatio	16 534	14 900
% Paediatric notifications	7,4%	7,0%
Treatment coverage (0-14)	61%	65%

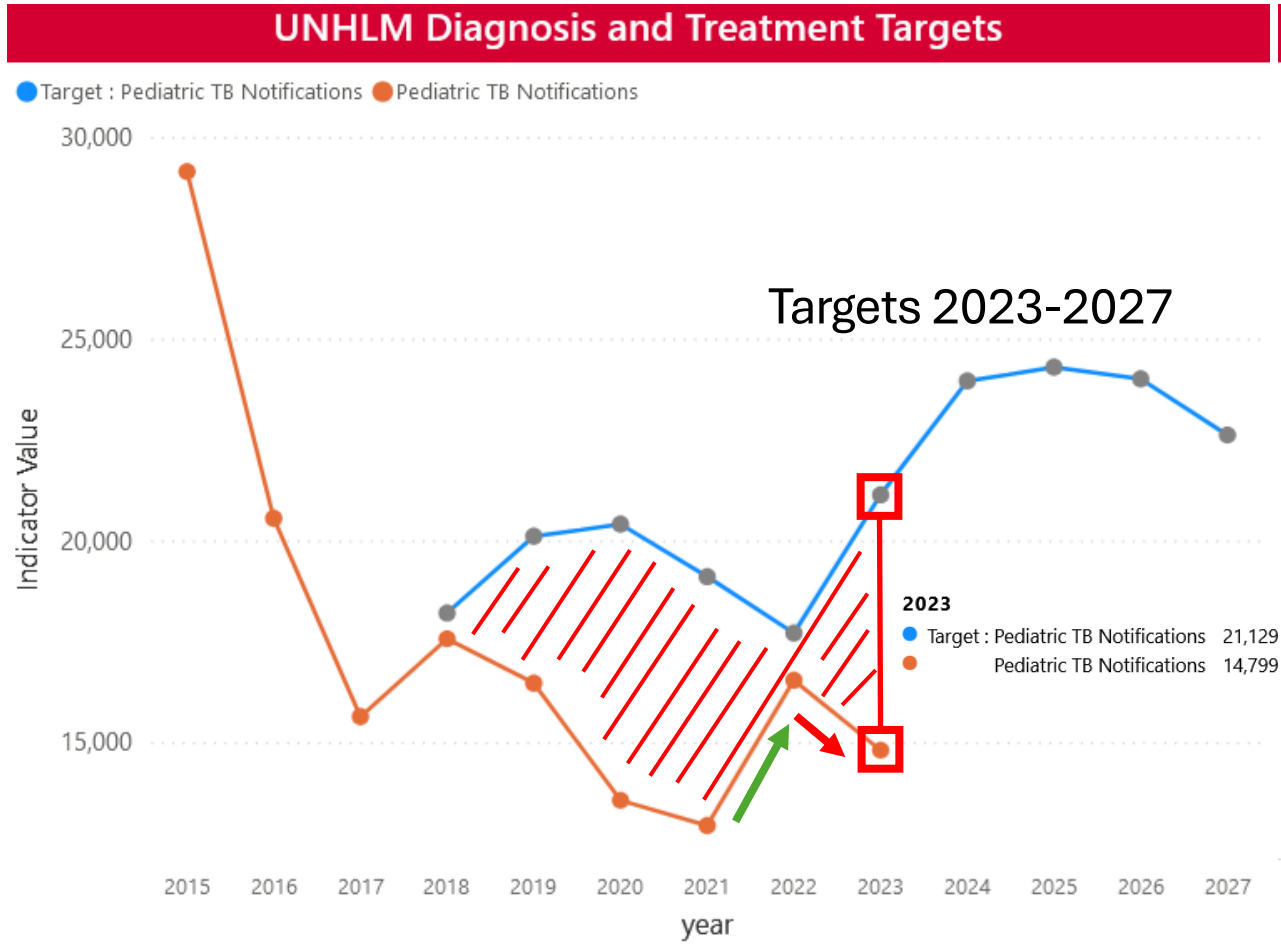
WHO TB estimates obtained from the WHO Global TB report 2024
Case notification data obtained from WHO global TB database
Available at: https://www.who.int/teams/global-tuberculosis-programme/data

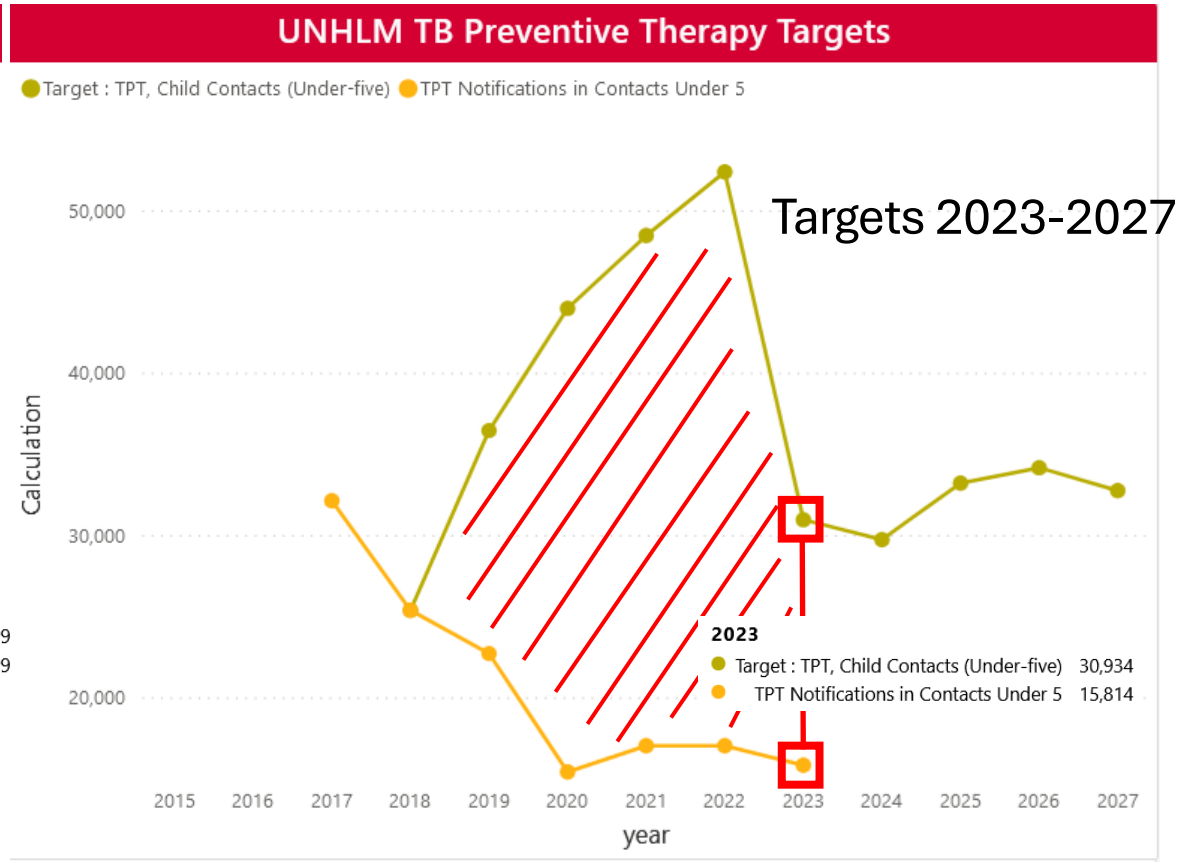
WHO's global TB database is updated regularly as countries notify WHO of corrections to previously submitted data. Therefore country data downloaded to CSV files may differ slightly from the data available at the time the Global Tuberculosis Report is written.



PROGRESS TOWARDS REACHING UNHLM TARGETS FOR PAEDIATRIC TB NOTIFICATIONS AND TPT FOR CHILD CONTACTS <5

SOUTH AFRICA





https://www.stoptb.org/resources/interactive-tb-data

Development of updated WHO guidelines
on the management of TB in children and adolescents

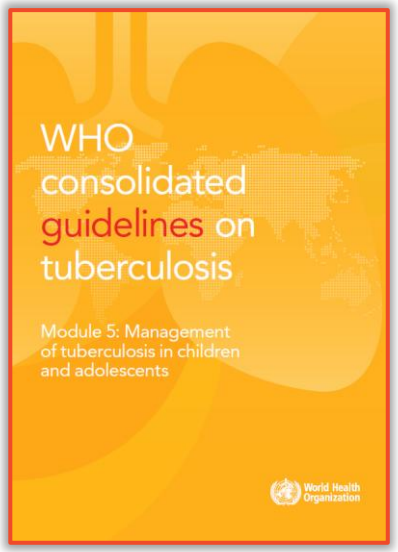
- Evidence reviewed on the following PICO questions

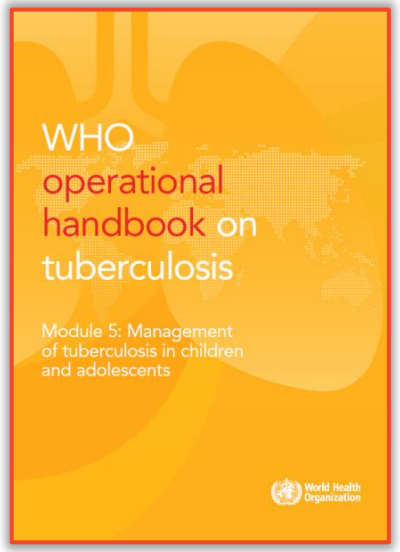
  (GRADE* methodology):

DIAGNOSIS
- → Use of Xpert Ultra in gastric aspirate and stool specimens
- → Integrated treatment decision algorithms

TREATMENT
- → Treatment shortening in children with non-severe TB
- → In children with MDR/RR-TB: Use of bedaquiline and delamanid
- → Short intensive treatment regimen for TBM

IMPLEMENTATION
- → Decentralized and family-centered models of care for case detection and provision of TPT





- Consolidated guidelines with operational handbook (March 22)

Guidelines: https://www.who.int/publications/i/item/9789240046764
Handbook: https://www.who.int/publications/i/item/9789240046832

*GRADE: Grading of Recommendations, Assessment Development and Evaluation

Slide used with courtesy of Dr Sabine Verkuijl, Kerri Viney, Tiziana Masini and Annemieke Brands

New recommendation: use of Xpert Ultra for diagnosis of PTB in children

In children with signs and symptoms of pulmonary TB, Xpert Ultra should be used as the initial diagnostic test for TB and detection of rifampicin resistance on sputum, nasopharyngeal aspirate, gastric aspirate or stool, rather than smear microscopy/culture and phenotypic DST

*(**UPDATED**: strong recommendation, moderate certainty of evidence for test accuracy in stool and gastric aspirate; low certainty of evidence for test accuracy in sputum; very low certainty of evidence for test accuracy in NPA)*

Remarks:

- *Although no evidence was available on the accuracy of the detection of rifampicin resistance, the previous recommendation on the use of Xpert Ultra for the detection of rifampicin resistance in sputum samples and NPA was extrapolated to stool and gastric aspirate.*
- *Considerations regarding the acceptability and feasibility of implementation of both stool and gastric aspirate specimens need to be taken into account.*

Slide used with courtesy of Dr Sabine Verkuijl, Kerri Viney, Tiziana Masini and Annemieke Brands

New recommendation: Use of integrated treatment decision algorithms

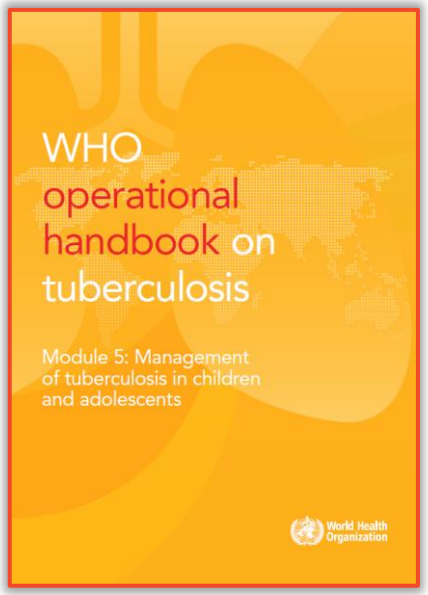
In children with presumptive pulmonary TB attending health care facilities, integrated treatment decision algorithms may be used to diagnose pulmonary TB

*(**INTERIM RECOMMENDATION** - conditional recommendation, very low certainty of evidence)*

Remarks:

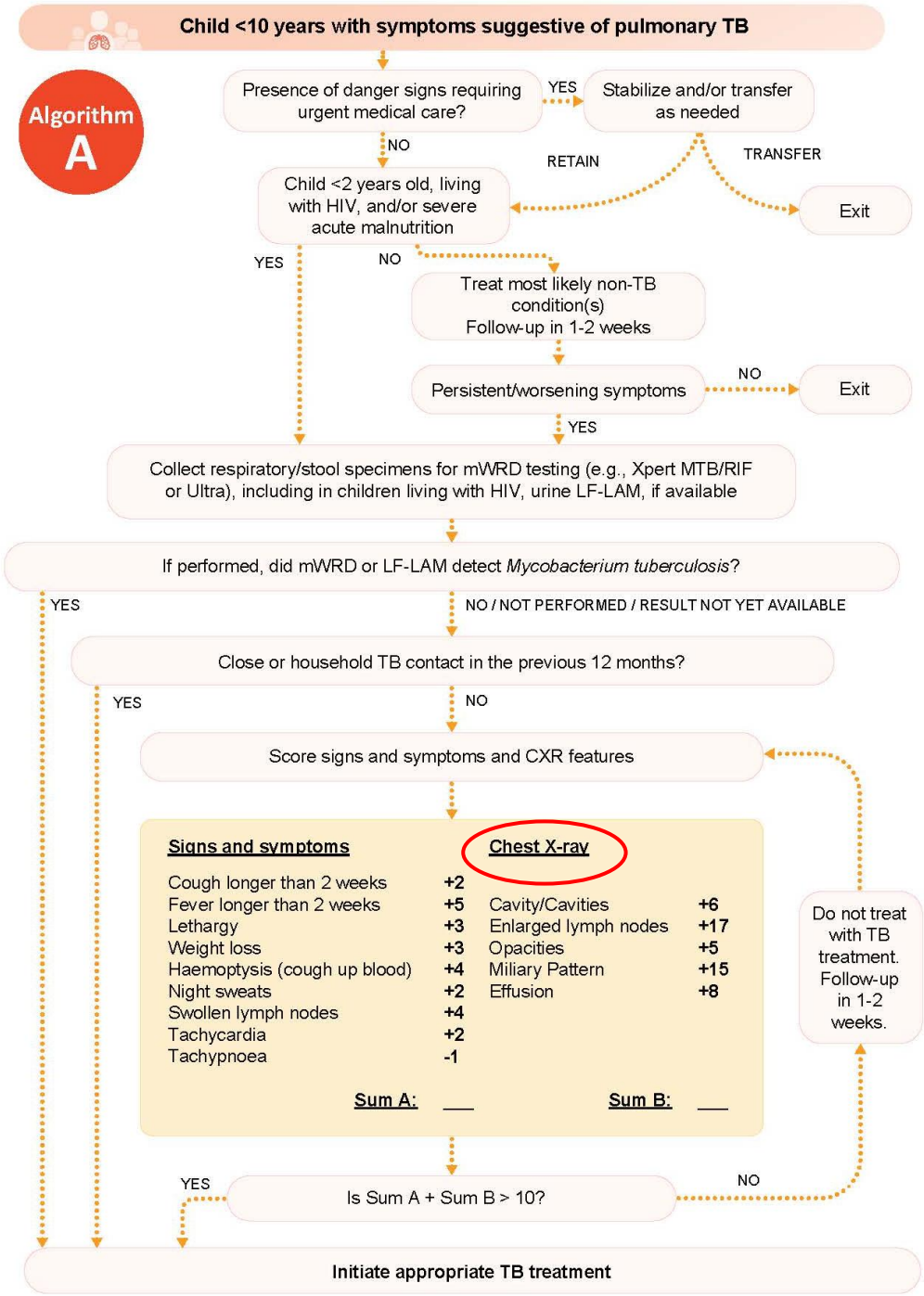
- *Bacteriological confirmation needs to be sought whenever possible, using available and recommended diagnostic tests and appropriate paediatric specimens – especially in children with a high likelihood of DR-TB*
- *Newly developed treatment decision algorithms for different settings with detailed practical guidance on there are included in the operational handbook. Use of these evidence-based algorithms is encouraged.*
- *Interim recommendation: valid for 24 months, after which new evidence will be reviewed*

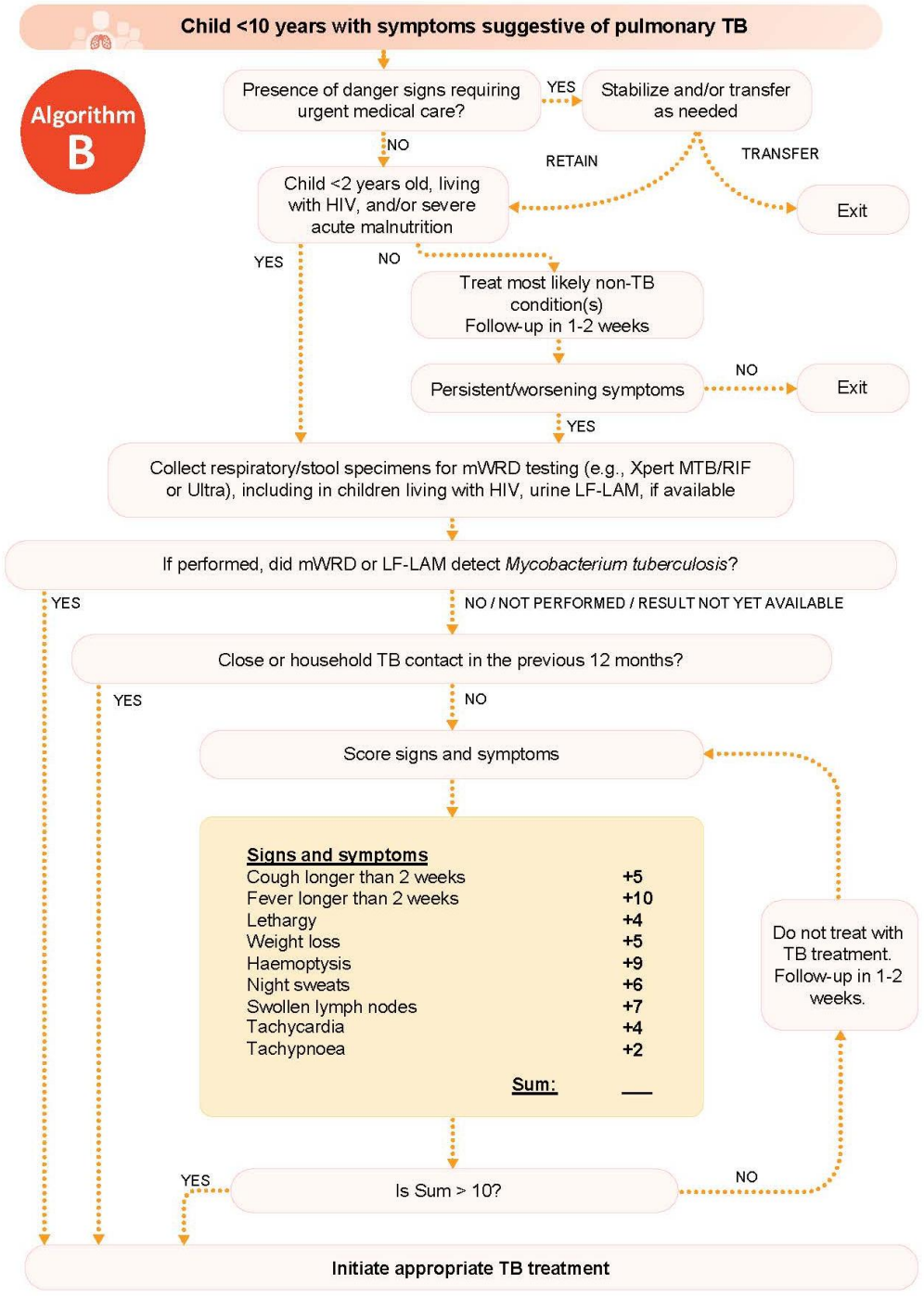
Slide used with courtesy of Dr Sabine Verkuijl, Kerri Viney, Tiziana Masini and Annemieke Brands



WHO TDAs based on IPD from >4500 children

Aimed at PHC level to build confidence and capacity to make decisions on starting TB treatment

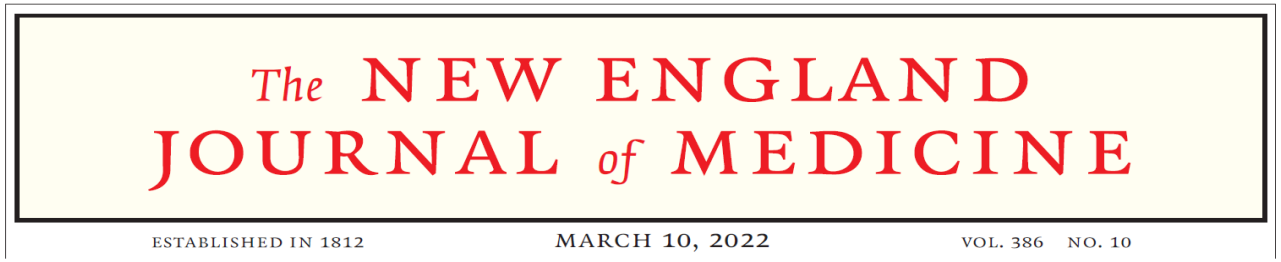




Shorter treatment duration in children with non-severe TB

- **In children and adolescents between 3 months and 16 years of age with non-severe TB (without suspicion or evidence of MDR/RR-TB), a 4-month treatment regimen (2HRZ(E)/2HR) should be used.**

  *(**NEW**: Strong recommendation, moderate certainty of evidence)*



SHINE: Shorter Treatment for Minimal Tuberculosis in Children

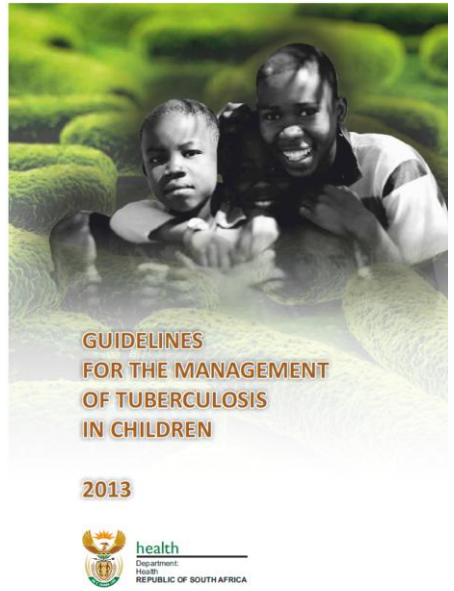
SHINE

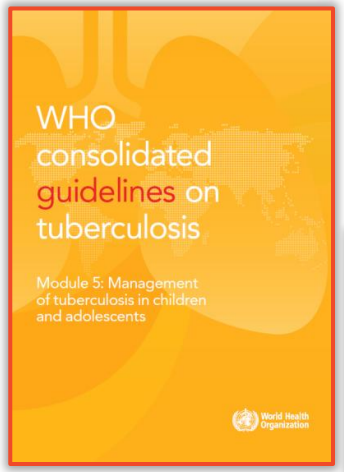
- Multi-centre, open-label, parallel-group, non-inferiority, randomized, controlled, two-arm trial comparing 4-month versus the standard 6-month treatment durations in children under 16 years of age with symptomatic non-severe TB
- South Africa, Uganda, Zambia and India
- Enrolled 1,204 children and adolescents
- Non-inferiority of the 4-month regimen consistent across all intention-to-treat, per-protocol and key secondary analyses

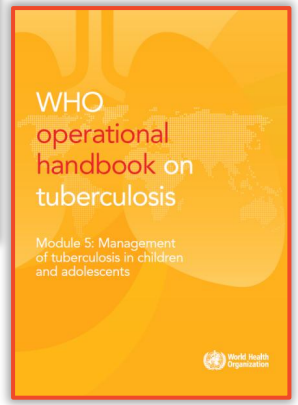
Slide used with courtesy of Dr Sabine Verkuijl, Kerri Viney, Tiziana Masini and Annemieke Brands

WHY DID WE NEED NEW SA TB GUIDELINES FOR CHILDREN AND ADOLESCENTS?

- High burden of TB in children and adolescents in SA
- Large treatment coverage gap (children > adults)
- Previous guidelines (2013), but WHO released important updates in 2022

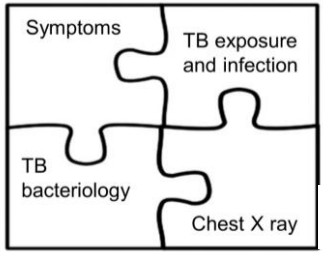






Important new updates:

- **Xpert MTB/RIF and Ultra (NAAT) testing of stool and other specimens** in children - allows for broader access to bacteriological testing (non-invasive)
  - **bacteriological testing** in children should be encouraged and facilitated – **clinical diagnosis** remains important if bacteriological tests are negative, not available or cannot be done
- use of **evidence-based treatment decision algorithms** in children <10 years
- **Treatment shortening** for children and adolescents with non-severe disease



Courtesy Liz Walters

NATIONAL CHILD, ADOLESCENT AND MATERNAL TB WORKING GROUP

Aim: To harmonize efforts to measure and improve TB care to children, adolescents and pregnant women along the continuum of care in South Africa

- Established Oct 2022
- 40 members
- Represented 5 provinces
- Tertiary, secondary, district, PHC
- Urban and rural clinicians
- FIDSSA, SASPID, HIV clinician society, RUDASA, EML, NCAC, Union, WHO

THINKTANK

SA TB Think Tank - Child, Adolescent and Maternal TB working group

Titel	Name (alphabetical order)	Academic	DOH	Other
Dr	Abeda Williams			J&J Global public Health
Dr	Anja Reuter			Sentinel Project of Pediatric TB
yes	Anneke Hesseling	Stellenbosch University		WHO Child and Adolescent TB working group
Prof	Brian Eley	University of Cape Town	Red Cross War Memorial Children's Hospital	
Dr	Buhle Makongwana	Walter Sisulu University	Nelson Mandela Academic Hospital	
Prof	David Moore	University of the Witwatersrand	Chris Hani Baragwanath Academic Hospital	
Dr	Denise Evans	University of the Witwatersrand		
Prof	Gary Reubenson	University of the Witwatersrand	Rahima Moosa Mother & Child Hospital	National EML Committee, FIDSSA, SASPID
Prof	Graeme Hoddinott	Stellenbosch University; University of Sydney		
Prof	Heather Zar	University of Cape Town	Red Cross War Memorial Children's Hospital	
Prof	Helena Rabie	Stellenbosch University	Tygerberg Academic Hospital	SASPID, HIV Cliniciens Society
Prof	James Nuttall	University of Cape Town	Red Cross War Memorial Children's Hospital	SA HIV Clinicians Society, SASPID
Prof	James Seddon	Stellenbosch University, Imperial College London		WHO Child and Adolescent TB working group, Sentinel Project on Pediatric
Dr	John-D Lotz	Walter Sisulu University	Madwaleni Hospital	RUDASA
Dr	Jenny Hughes	Stellenbosch University		WHO Child and Adolescent TB working group
Dr	Joseph Alt	University of Cape Town	George Hospital	
Dr	Juaneta Luiz	University of Cape Town	Dora Nginza Hospital	WHO Child and Adolescent TB working group
Dr	Juli Switala		The Aurum Institute	WHO Child and Adolescent TB Working group
Dr	Karen Du Preez	Stellenbosch University		WHO Child and Adolescent TB working group
Dr	Karl le Roux		Zithulele Hospital	
Prof	Lee Fairly	University of the Witwatersrand		WHRI
Dr	Lenny Naidoo		Cape Town City Health	
Dr	Lindiwe Mvusi		National Department of Health	
Prof	Lisa Frigati	Stellenbosch University	Tygerberg Academic Hospital	FIDSSA,FAMCRU
Dr	Marian Loveday	SA Medical Research Council		
Prof	Marieke van der Zalm	Stellenbosch University		WHO Child and Adolescent TB working group
Prof	Mark Hatherill	University of Cape Town		
Dr	Megan Palmer	Stellenbosch University		WHO Child and Adolescent TB working group
Prof	Mohemdran Archary	University of KwaZulu Natal/AHRI	Victoria Mxenge Hospital	SA HIV Clinicians Society, SASPID
Prof	Nicolette Du Plessis	University of Pretoria	Kalafong Provincial Tertiary Hospital	FIDSSA, SASPID
Dr	Nkateko Mhkondo		World Health Organization	
Dr	Nosisa Sipambo	University of the Witwatersrand	Chris Hani Baragwanath Academic Hospital	SA HIV Clinicians Society, SASPID
Prof	Regan Solomons	Stellenbosch University	Tygerberg Academic Hospital	
Prof	Ronald van Toorn	Stellenbosch University	Tygerberg Academic Hospital	
Prof	H. Simon Schaaf	Stellenbosch University	Tygerberg Academic Hospital	WHO Child and Adolescent TB working group
Mr	Sipho Nyathi	Nelson Mandela University	AQUITY Innovations	
Ms	Sue-Ann Meehan	Stellenbosch University		UNION Maternal and Child Health working group
Dr	Taryn Gaunt		Zithulele Hospital	
Prof	Anthony Figaji	University of Cape Town	Red Cross War Memorial Children's Hospital	
Prof	Ute Hallbauer	University of the Free State	Pelonomi and Universitas Hospital	

THE DEVELOPMENT PROCESS …

THINKTANK

First task of the new working group

- 18 months process:
  Oct 2022 – March 2024

<u>Considered global guidelines:</u>

Aligned with WHO Guidelines and Union Desk guide

<u>Considered national guidelines:</u>

- IMCI / SA-EPI / ART / TPT
- Paeds and PHC STG & EML

<u>Wide consultation and input:</u>

- Clinical experts (TB and HIV)
- Rural clinicians
- Laboratory (NICD)
- NDOH/NTP
- Provincial health and TB managers
- Other program managers (MCWH)

THE APPROVAL PROCESS …

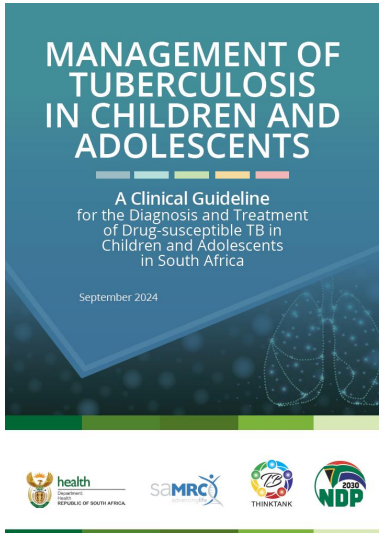
- Final draft document shared with the NTP on 25 March 2024
- Presented at NEMLC meetings in May and June 2024
  - Treatment shortening (already approved – practical guidance)
  - Including EMB in the intensive phase of TB Rx for children <8 with non-severe TB
  - Increased dosing of Rif in children Rx for TBM, other CNS-TB and miliary TB
- Presented to NAGI TB vaccine WG (June 2024) and at NAGI meeting (Aug 2024)
  - Provide BCG to all infants at discharge irrespective of TB exposure
  - For infants who started TPT or TB treatment in the first 6 weeks of life, repeat BCG
  - Catch-up BCG can be provided up to 10 years of age

THINKTANK

NEXT STEPS …

- SAMWG/Think Tank will continue supporting NDOH and provinces with implementation
  - Quick reference guide
  - EMB resources
  - HCW and caregiver education material
- Ensure alignment between other guidelines
  - EML PHC
  - EML Paeds hospital
  - IMCI
  - EPI

THANK YOU!



Acknowledgements

TB Think Tank Child, Adolescent and Maternal TB working group members

Prof H. Simon Schaaf
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Prof James Nuttall
Dr Juli Switala
Prof Anneke Hesseling
Dr John-D Lotz
Dr Juaneta Luiz
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Dr Nosisa Sipambo
Dr Taryn Gaunt
Prof Ute Hallbauer
Dr Nkateko Mhkondo
Dr Sipho Nyathi
Dr Denise Evans
Dr Marian Loveday
Dr Joseph Alt
Dr Jenny Hughes
Prof Graeme Hoddinott
Ms Sue-Ann Meehan
Dr Abeda Williams

Subject experts

Dr Farzana Ismail
Dr Shaheed Vally Omar
Prof Adrie Bekker

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National Department of Health

Dr Lindiwe Mvusi
Dr Lesley Bamford
Ms Nokwazi Madhlala
Mr Khathutshelo Nemukombame
Mr Mokete Phungwayo
Ms Nobesuthu Ramawela

Other Organisations

World Health Organisation
The Union Against Tuberculosis and Lung Disease
SA TB Think Tank
The Aurum Institute
Desmond Tutu TB Centre, Stellenbosch University
SA HIV clinicians society

Funder

South African Medical Research Council

Graphic Design

Tharina du Preez

Lead knowledge translaters and project coordinators

Dr Karen Du Preez
Dr Jeannette Wessels

Steps in tuberculosis treatment decision making

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Department of Pediatrics and Child Health
Family Research Centre with Ubuntu, Desmond Tutu TB Centre
Stellenbosch University
Tygerberg Hospital Department of Health Western Cape

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Western Cape Government

How do children present to the health system

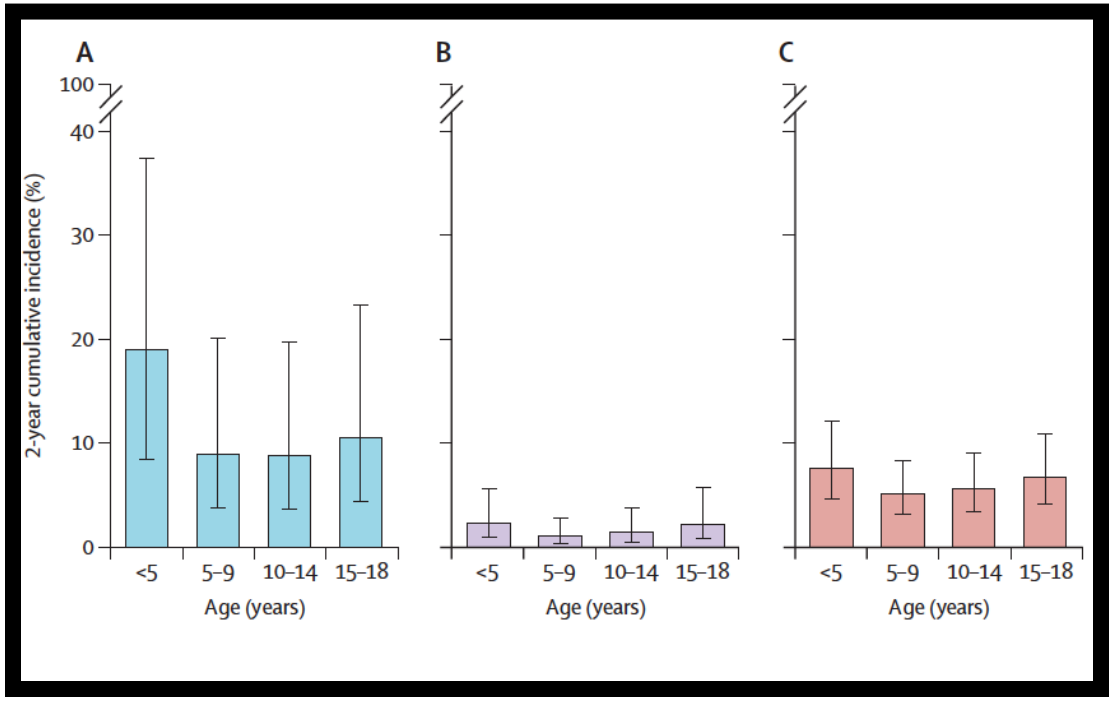
Active

- Presenting with illness
- Case finding / contact tracing

Passive

- Exposure / symptoms at each contact including well children

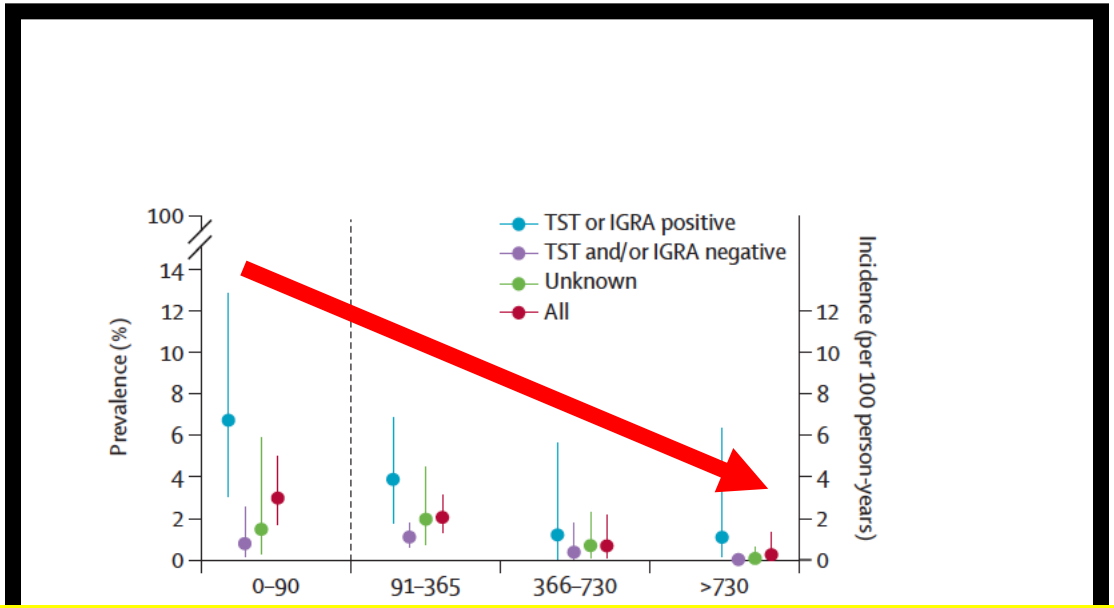
Adolescents and Children Exposed to TB

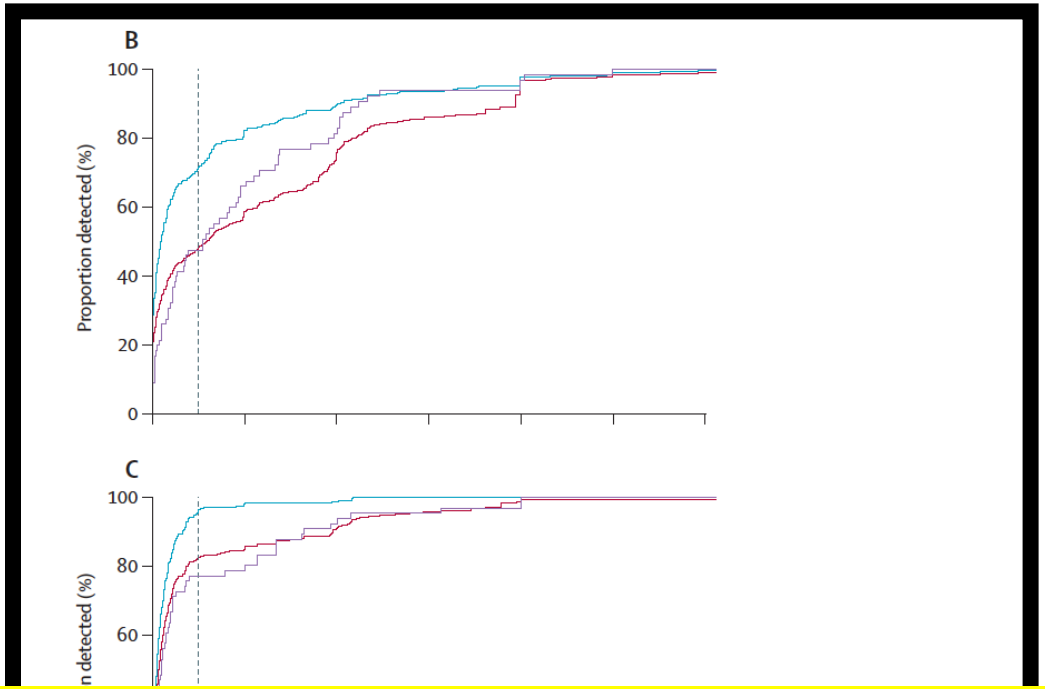


Age	Cumulative risk at 2 years
< 5	7.6%
5-9	5.2%
10-14	5.6%
15-18	6.7%

Martinez Lancet 2020

Adolescents and Children Exposed to TB

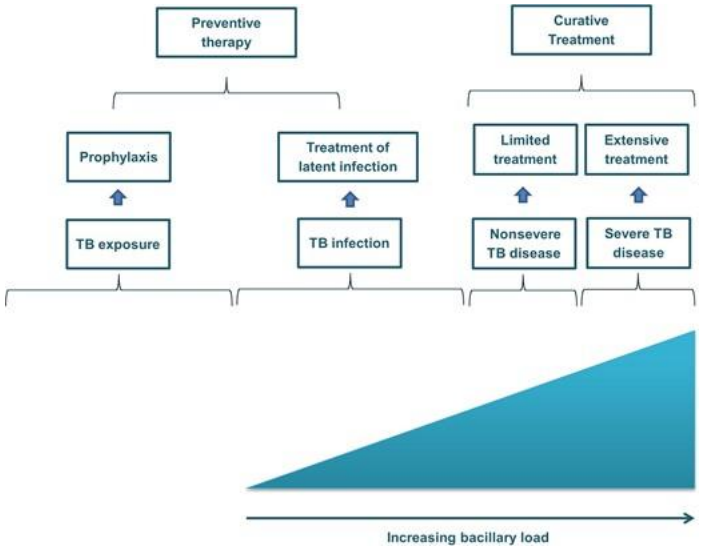




- 586 (61%) of TB cases were diagnosed in the first 90 days
- 292 /353 (83%) children < 5 years of age were diagnosed within 90 days

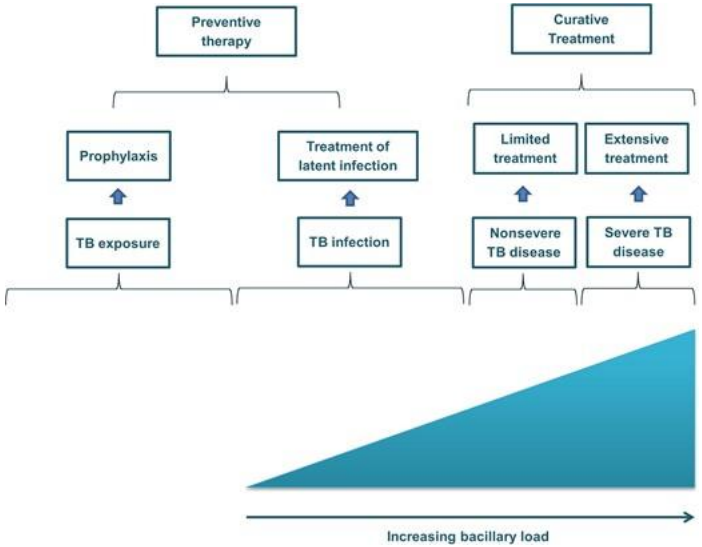
Martinez Lancet 2020

Very narrow line between infection and non-severe disease

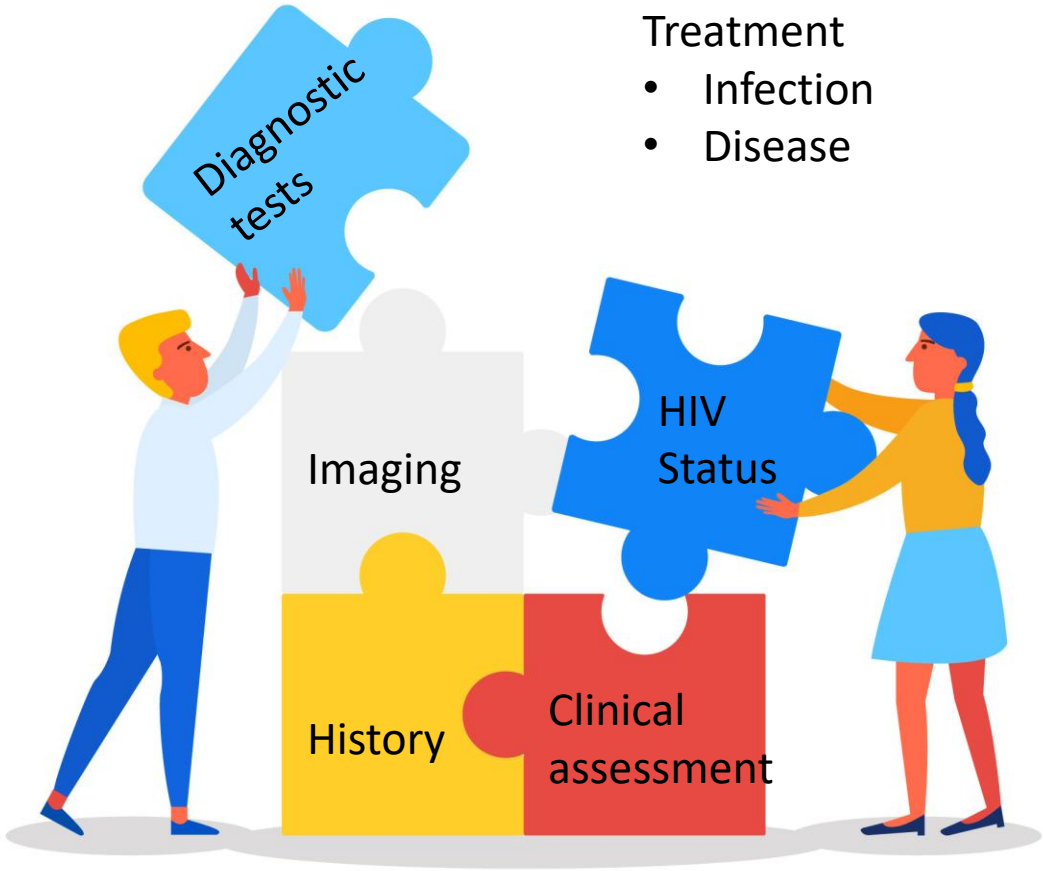


Seddon JA, et al. Recent developments and future opportunities in the treatment of tuberculosis in children. CID 2015

Very narrow line between infection and non-severe disease



Seddon JA, et al. Recent developments and future opportunities in the treatment of tuberculosis in children. CID 2015

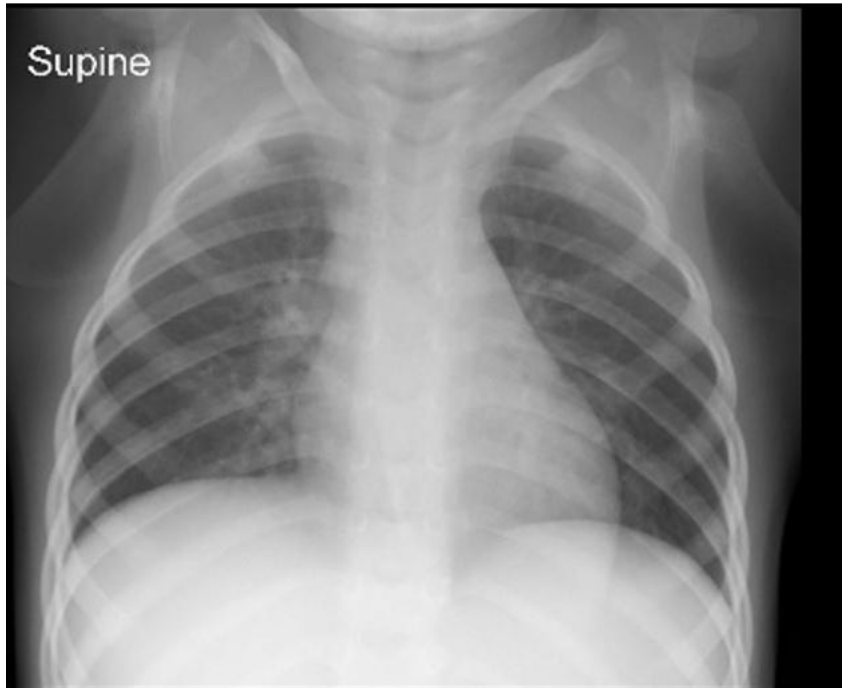


Treatment
- Infection
- Disease

Question 1: What are we treating infection or disease?

- Symptoms
- Tests of infection
  - IGRA
  - TST
- CXR
- Microbiological tests

A 4 year old boy on ART since birth



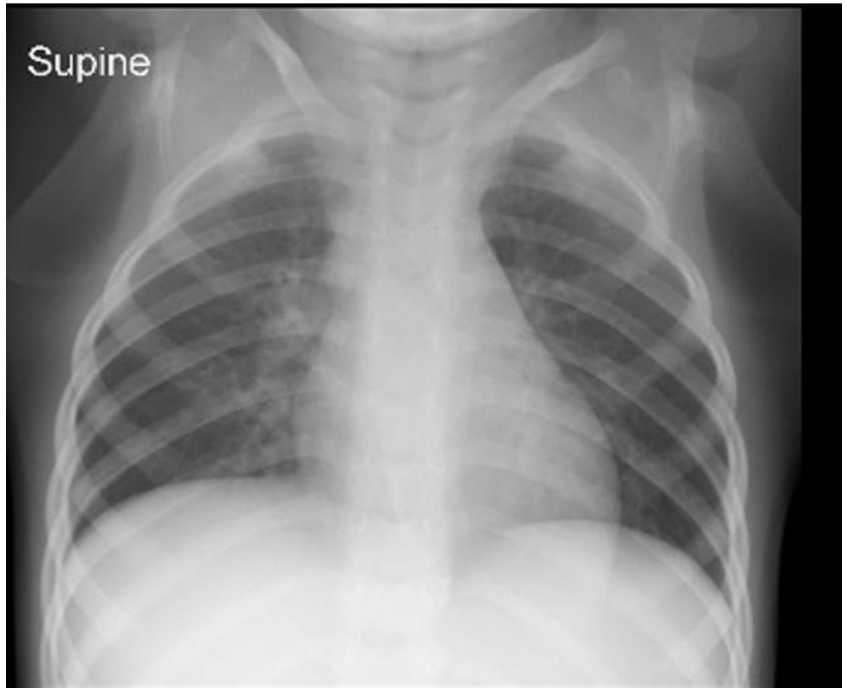
- TB contact
- No symptoms
- Negative TB-NAAT X1

- Looks like TB exposure / Infection

What is the most appropriate therapy

- INH – 6 months
- INH/RIF – 3 Months
- RIF – 4 Months
- Don’t treat infection treat disease
- I Need more data

Who is the contact?



Auramine O Stain:

Result (concentrated)	Positive ++ (1-10 AFB/immersion field)

TB Culture:

Culture result	Culture positive. AFBs observed.
Incubation time	11 days

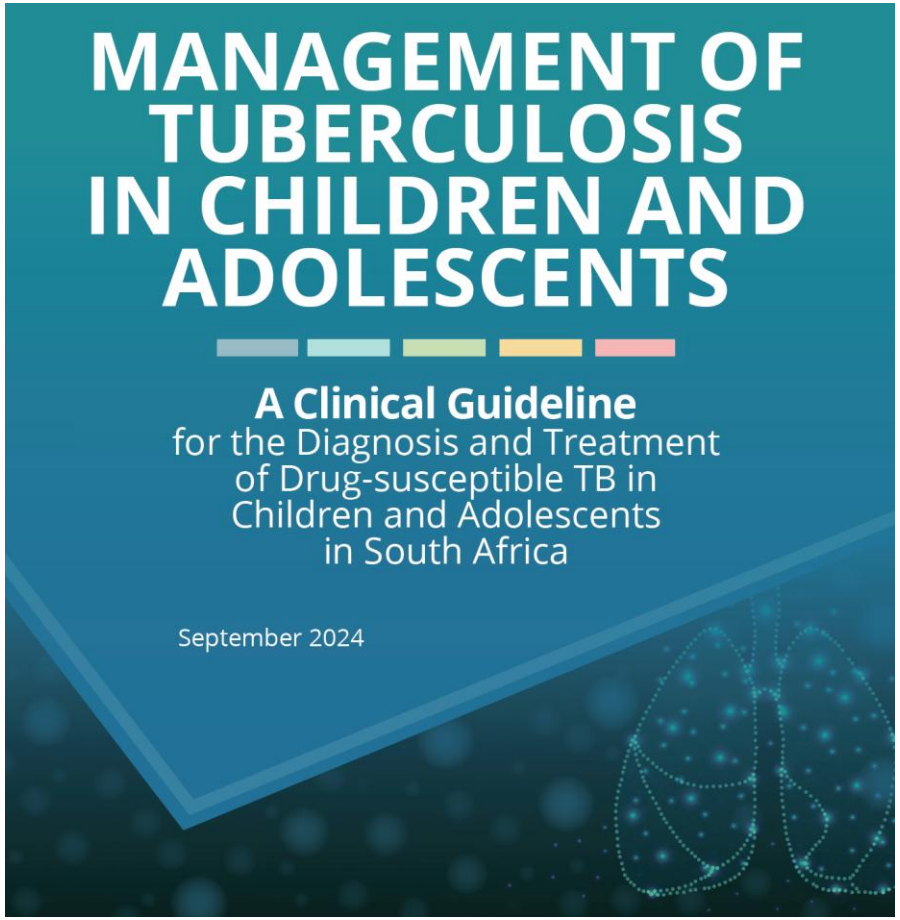
Molecular resistance testing for first line agents for TB:

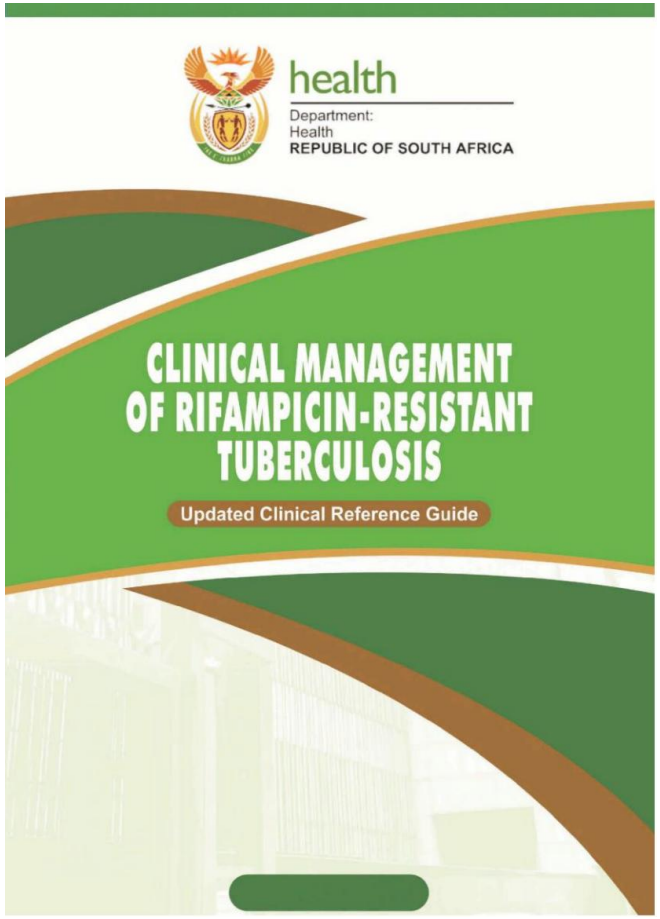
Test performed on:	Cultured isolate
PCR/Line Probe Assay Result	Mycobacterium tuberculosis complex
Isoniazid (INH)	Resistant
Rifampicin	Sensitive

This isolate is resistant to INH, and susceptible to rifampicin.

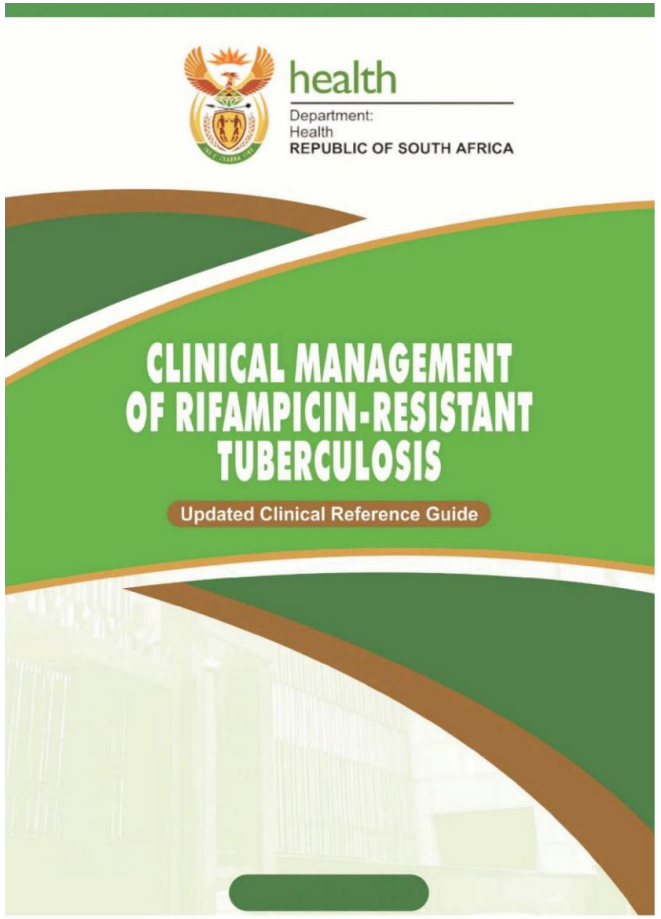
This isolate has a mutation in the inhA gene, which has been shown to correlate with ethionamide resistance. This may also represent low-level INH resistance, and addition of INH in high doses may be useful.

Question 2: What is the confirm or suspected resistance profile



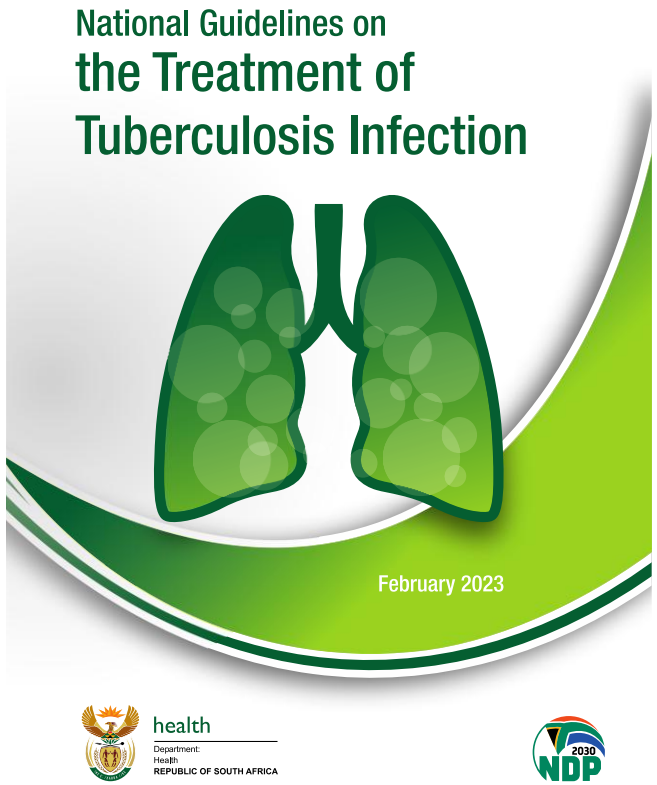


If rifampicin resistance is known



- Next question is … FLUROQUINELONE
- Remember increasing BDQ resistance and fluroquinolone susceptible BDQ resistance

Question 2: What is the confirmed and or suspected resistance profile



- Isoniazid
- Isoniazid and rifampicin
- Rifampicin
- Rifapentine / Isoniazid

- Fluroquinolone

Question 3: If you are treating disease - Which sites are affected?

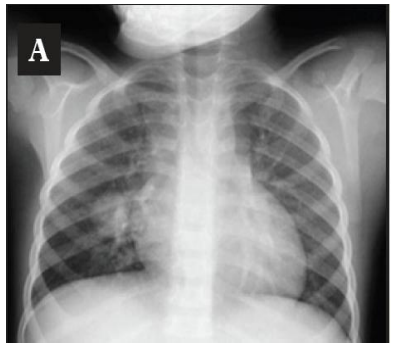
Pulmonary Tuberculosis

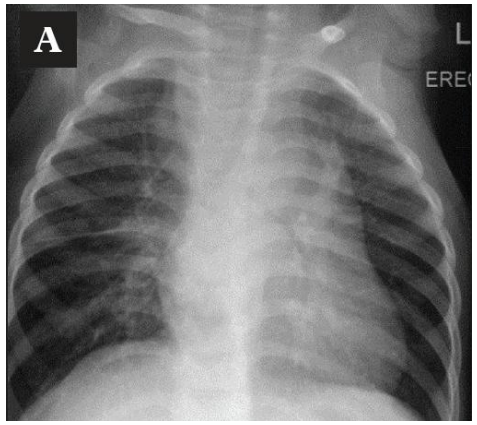
- Age
- Clinical presentation
- CXR
- “Sputum smear”

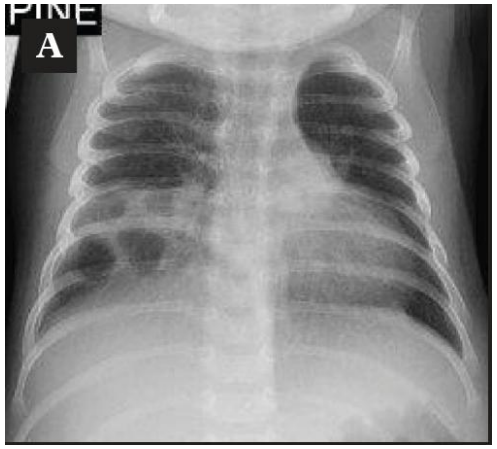
Extrapulmonary Tuberculosis

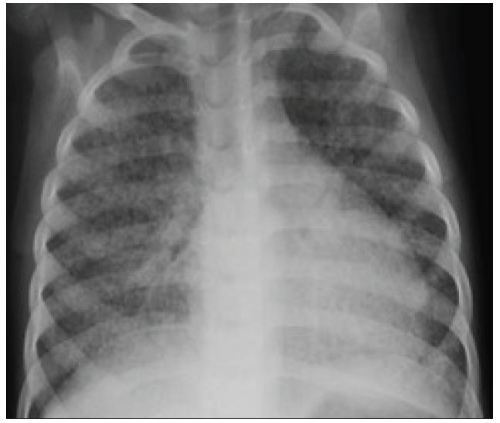
- Neck nodes
- Other extrapulmonary sites
- Meningitis/ Milary Tuberculosis

Question 4:Treating pulmonary TB
Does the patient have severe disease?









Question 4: Are there other considerations?

HIV

- Ensure ART access
- Ensure viral suppression
- Ensure appropriate adaptation of dosing ad drugs

Ensuring wholistic care and family conversations

Question 5: What are the follow-up needs ?

- More severe disease and drug resistance
- Ensure clinical recovery
- Dose adjustments with weight gain

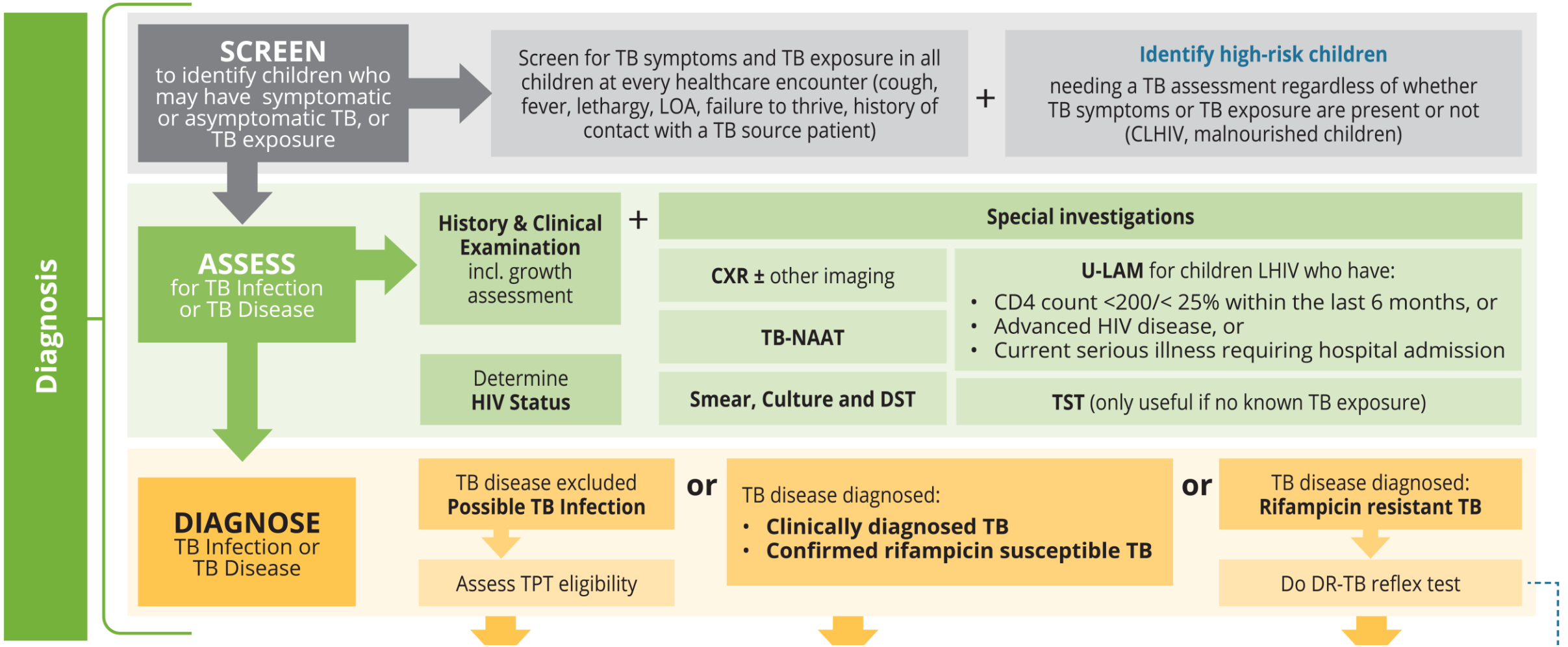
TB Diagnostics

Juaneta Luiz

University of Cape Town | SAMRC Unit for Child and Adolescent Health |

National Child, Adolescent & Maternal TB Working Group, SA TB Think Tank

Dora Nginza Hospital, Gqeberha


Diagnosis
SCREEN
to identify children who may have symptomatic or asymptomatic TB, or TB exposure
Screen for TB symptoms and TB exposure in all children at every healthcare encounter (cough, fever, lethargy, LOA, failure to thrive, history of contact with a TB source patient)
+
Identify high-risk children
needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not (CLHIV, malnourished children)
ASSESS
for TB Infection or TB Disease
History & Clinical Examination
incl. growth assessment
Determine HIV Status
+
Special investigations
CXR ± other imaging
TB-NAAT
Smear, Culture and DST
U-LAM for children LHIV who have:
• CD4 count <200/< 25% within the last 6 months, or
• Advanced HIV disease, or
• Current serious illness requiring hospital admission
TST (only useful if no known TB exposure)
DIAGNOSE
TB Infection or TB Disease
TB disease excluded
Possible TB Infection
Assess TPT eligibility
or
TB disease diagnosed:
• Clinically diagnosed TB
• Confirmed rifampicin susceptible TB
or
TB disease diagnosed:
Rifampicin resistant TB
Do DR-TB reflex test

The Diagnostic Puzzle

CXR – If available

+TB exposure (known or symptomatic),

Symptoms

Dx testing:

TB-NAAT, Culture, DST

Other (EPTB): Abdo US, Neuroimaging etc.

:CSF, Aspirates: LN, pleural fluid etc.

HIV test:

If last test neg / unknown

+Growth

TB should be considered part of the differential diagnosis in ANY ill child, especially if no alternative cause for symptoms is found or if there is a history of TB exposure.

First, TRIAGE: Does the child need to be admitted?

Box 1 Danger signs needing urgent attention

Give urgent attention to the child with possible:

- Fitting/seizures
- Breathing problem: difficulty breathing, increased respiratory rate (see *Section 6.3 on page 11*), chest indrawing, nasal flaring, grunting, wheezing, blue lips/tongue
- Breathless at rest or while talking
- Coughs up ≥ 1 tablespoon of fresh blood
- Drowsy/confused/loss of consciousness
- Difficulty feeding/eating
- Neck stiffness
- Persistent vomiting/headache
- New weakness of arm/leg
- Pupils of different sizes
- Swollen abdomen
- Abnormal spine
- Not moving or sitting properly

TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

- **Screen for TB symptoms and TB exposure** in all children at every healthcare encounter
- **Identify high-risk children** needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not e.g. CLHIV

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]

Cough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, lethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care. Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition. Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR** ± any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

Interpretation

CXR or imaging suggestive of TB and/or Positive result on any diagnostic test

Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.

Follow-up on results of any culture and DST, as applicable. **Ensure response to treatment,** especially if TB was clinically diagnosed.
Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.
4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
5. A decision to start TB treatment should not be delayed if the necessary investigations are not available, particularly in children at higher risk of developing severe disease, such as young children, malnourished children or those living with HIV.

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]	Score
Cough > 2 weeks	+ 5
Fever > 2 weeks	+ 10
Reduced playfulness/energy	+ 4
Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

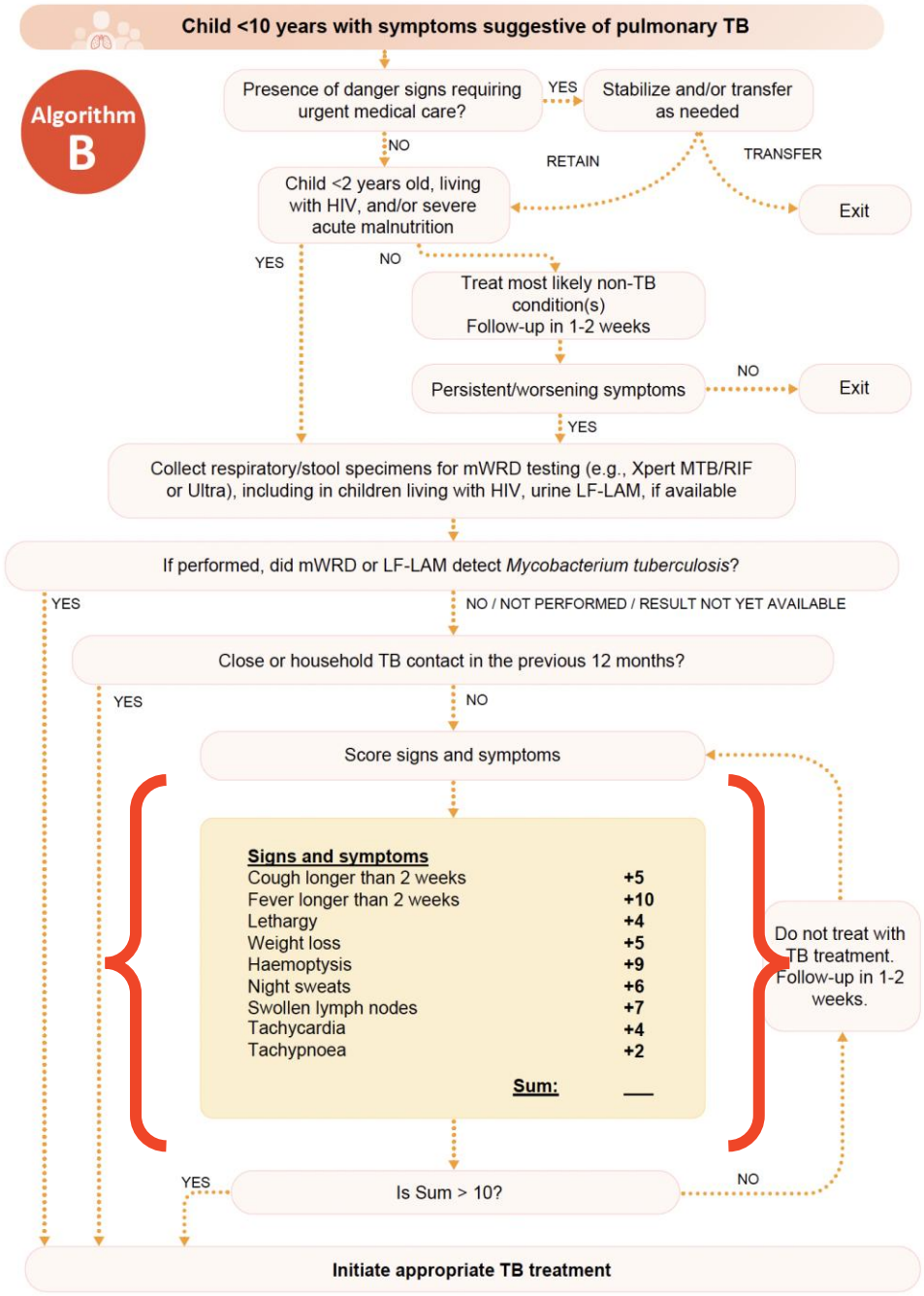
Treatment Decision Algorithms – Why?

- Large burden of undiagnosed TB in children (>65%), esp. <5yr

- Barriers: Sample collection in young children, access to CXR, lack of confidence in diagnosing / initiating TB Tx

- If sufficient Clinical ±Radiological evidence for TB
  - Do not delay TB Treatment if TB-NAAT/Culture pending/unavailable
  - Especially in the HIGH RISK (<2 yr, CLHIV, severely malnourished)

Figure 4.5. Algorithm B



WHO Integrated Treatment Decision Algorithms

- Based on meta-analysis using prediction modelling

Development of treatment-decision algorithms for children evaluated for pulmonary tuberculosis: an individual participant data meta-analysis

Kenneth S Gunasekera, Olivier Marcy, Johanna Muñoz, Elisa Lopez-Varela, Moorine P Sekadde, Molly F Franke, Maryline Bonnet, Shakil Ahmed, Farhana Amanullah, Aliya Anwar, Orvalho Augusto, Rafaela Baroni Aurilio, Sayera Banu, Iraj Batool, Annemieke Brands, Kevin P Cain, Lucía Carratalá-Castro, Maxine Caws, Eleanor S Click, Lisa M Cranmer, Alberto L García-Basteiro, Anneke C Hesseling, Julie Huynh, Senjuti Kabir, Leonid Lecca, Anna Mandalakas, Farai Mavhunga, Aye Aye Myint, Kyaw Myo, Dorah Nampijja, Mark P Nicol, Patrick Orikiriza, Megan Palmer, Clemax Couto Sant'Anna, Sara Ahmed Siddiqui, Jonathan P Smith, Rinn Song, Nguyen Thuy Thuong Thuong, Vibol Ung, Marieke M van der Zalm, Sabine Verkuijl, Kerri Viney, Elisabetta G Walters, Joshua L Warren, Heather J Zar, Ben J Marais, Stephen M Graham, Thomas P A Debray, Ted Cohen, James A Seddon

Algorithm A

With Chest X-ray (CXR)

Sensitivity 86%[2]
Specificity 37%[2]

Algorithm B

Without CXR

Sensitivity 84%[2]
Specificity 30%[2]

TB Treatment Decision Algorithm

Evaluate For TB

Screen

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YES

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STABILISED

NO

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1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

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YES

YES

Investigations

If possible, **perform CXR** ± any other imaging as indicated for possible extrapulmonary TB

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YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
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Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

HIGH RISK = Immune-compromised or Immune immature:

- CLHIV
- <2 years
- Severely malnourished
- Other reasons for immunosuppression…
- Children with TB in the past 2 years

What is a TB Exposure?

- Past 12 months
- To an adult/adolescent with PTB
- For ≥1 night OR frequent extended daytime periods
- Household / creche / school / neighbours / transport

Ask about contacts with TB symptoms

Screen all adults / children with symptoms

If +TB exposure:

- Use NHLS Labtrak for drug susceptibility
- This will guide child's treatment regimen

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]

Cough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, lethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO

If asymptoma… TPT if eligible …line for details See the 2023 T…

TPT

YES

Cough can be:

- **Persistent**/unremitting (>2 weeks), esp if not responding to Antibiotics
- **Acute** (e.g. Acute pneumonia) – infants, immunocompromised

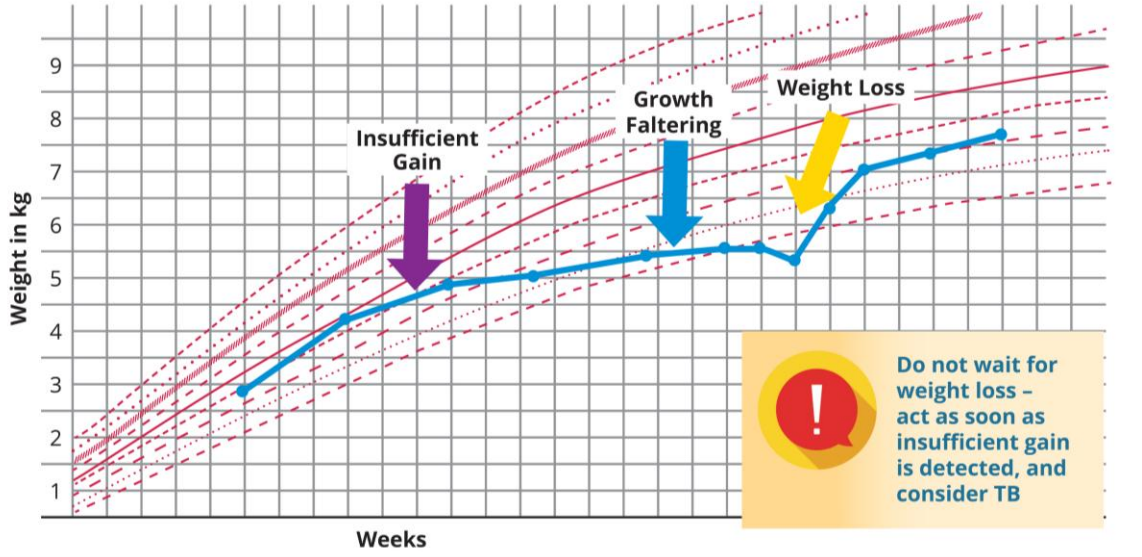
Wheeze/noisy breathing (non-responsive to nebs)**:** Can be lymph nodes compressing airways

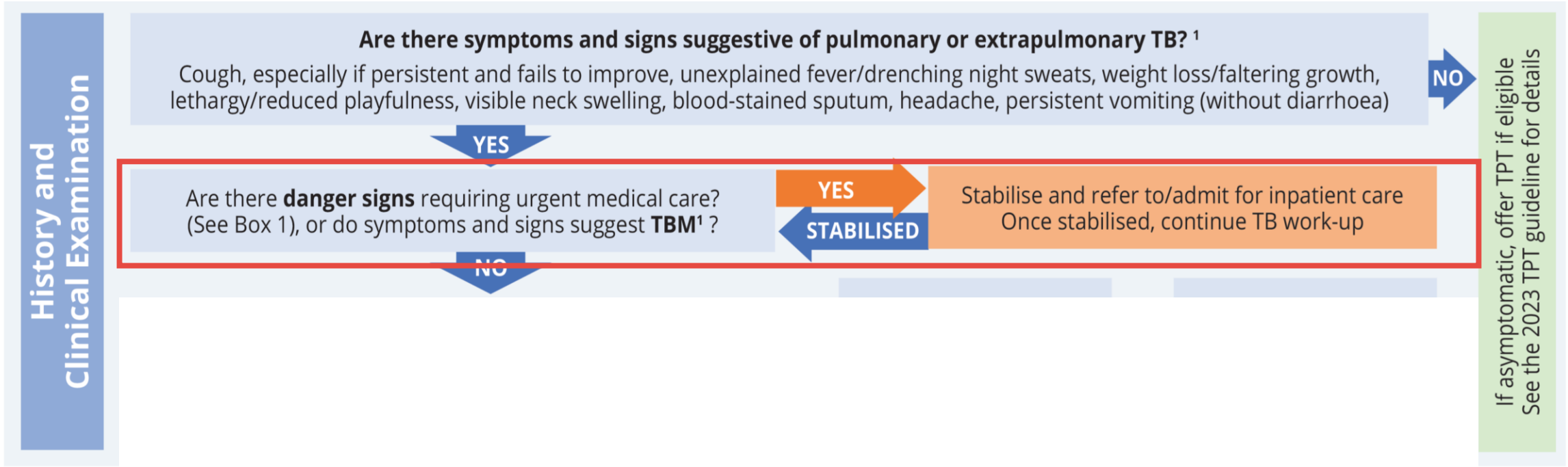
TB symptoms can be vague/non-specific: Have a high index of suspicion

Assess Growth

- Failure to thrive
  - **Insufficient Gain** : clear deviation from previous growth trajectory
  - **Growth Faltering** : flattening of the growth curve / crossing percentiles in past 3/12
  - If no previous/recent growth trajectory: W4A <-2 OR WFH <-2

- Documented **Weight Loss**
- Any malnutrition, not responding to nutritional intervention &deworming
- CLHIV not responding to ART




History and Clinical Examination
Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]
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NO
If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details
YES
Are there danger signs requiring urgent medical care? (See Box 1), or do symptoms and signs suggest TBM[1] ?
YES
STABILISED
Stabilise and refer to/admit for inpatient care Once stabilised, continue TB work-up
NO

EPTB Symptoms – Head to toe

TBM

Early = non-specific

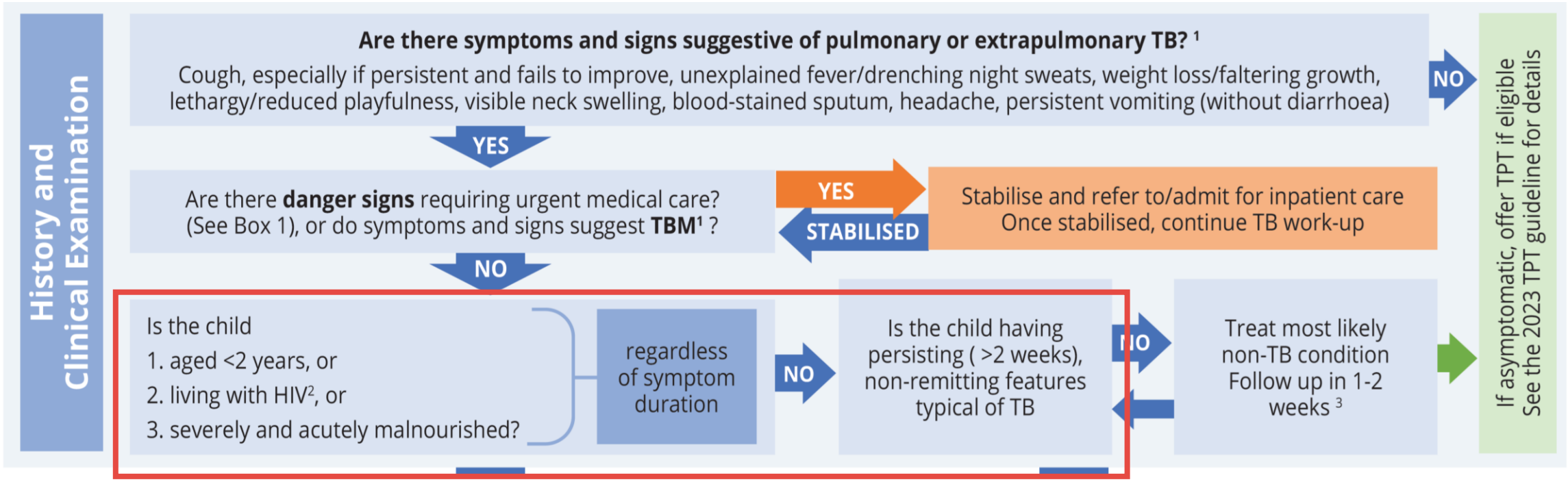
- Low-grade fever
- Vomiting (w/out diarrhoea)
- Cough
- LOW/FTT
- Decreased playfulness

- Headache
- Neck stiffness
- Irritability / Abnormal behaviour
- Regression of milestones
- Unilateral weakness/Cranial Nerve palsies
- Seizures
- Confusion
- Lethargy / ↓LOC

N.B. Younger children/malnourished/CLHIV = high risk for severe disease / sudden deterioration!

N.B. Miliary TB on CXR – treat as TBM (even if Normal CSF)

Site of EPTB	Typical clinical presentation	Comment
TB Meningitis	• Headache, irritability/abnormal behaviour, vomiting without diarrhoea • lethargic/reduced level of consciousness • convulsions • neck stiffness • bulging fontanelle • cranial nerve palsies	• Usually young (<5 years) with disseminated disease and severely ill • Children with miliary tuberculosis should all be considered to have meningitis, even if no symptoms or neurological signs are present and even if CSF has a normal result
Miliary TB	• Non-specific symptoms, reduced activity/playfulness, persistent fever, loss of weight	
TB Adenitis	• Asymmetrical, painless, non-tender lymph node enlargement for > 2 weeks ± discharging sinus • Most commonly in the neck	• Most common form of EPTB in children • If axillary node enlargement on the same side as the BCG in an infant, consider BCG disease
Pleural TB	• Dullness on percussion and reduced breath sounds ± chest pain • No acute illness • If pus in pleural tap, consider empyema and refer	
Abdominal TB	• Abdominal distension with ascites or abdominal masses	
Pericardial TB	• Cardiac failure • Distant heart sounds • Apex beat difficult to palpate	
Spinal TB	• Chronic back pain in a child • May have lower limb weakness/paralysis/unable to walk • Bulge on the back of the spine	
TB of Bone and Joint	• Swelling end of long bones with limitation of movement • Unilateral effusion or chronic pain of usually the knee or hip, often following injury	



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History and Clinical Examination

...If diagnosis uncertain and no danger signs:

Follow-up in 1-2 weeks

- Depending on - likelihood that child can return
- Return earlier if any worsening of symptoms / danger signs

Treat most likely non-TB condition Follow up in 1-2 weeks [3]

If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

- 'Treat most likely non-TB condition':
  - Antibiotics for cough/fever
  - Nutritional rehabilitation
  - Rehydrate for AGE etc.

Reassess weight, persistence/improvement of symptoms

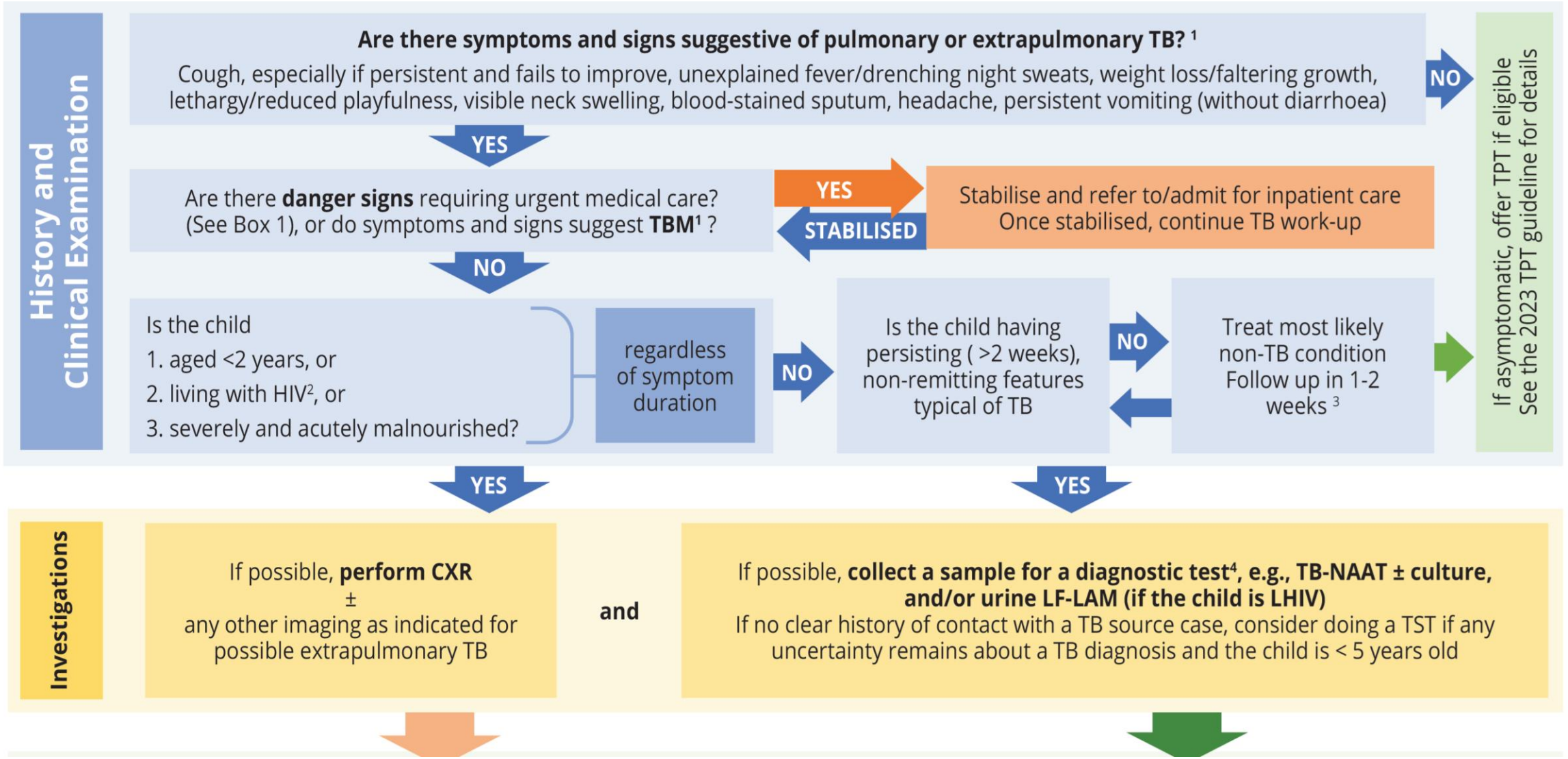

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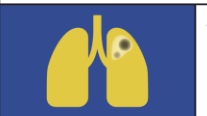
Table 6.1: Classification of radiological disease severity on CXR	
Non-Severe	**Severe**
Uncomplicated lymph node disease	Complicated lymph node disease
	
Primary (Ghon) focus	Primary (Ghon) focus with cavitation
	
Simple pleural effusion	Complicated pleural effusion
	
Alveolar opacification: < 1 lobe	Alveolar opacification: involving a whole lobe or multiple lobes
	
Other:	Other:
 - Interstitial pneumonia	 - All cavitary disease
 - Perihilar infiltrates	 - Expansile pneumonia
	 - Miliary TB
	 - TB bronchopneumonia

1. **CXR, if possible:**

- AP/PA and lateral (to see LN)
- Assess severity of disease* to determine treatment duration

CXR AND OTHER IMAGING

health
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If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

2. Should I take respiratory samples?

- **YES – make every effort! It is possible at all levels of care.**
- **Especially for:**
  - **Young children**
  - **Exposed to RRTB**
  - **Complicated or severe disease**

If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

2. Samples (always attempt to collect):

- Respiratory samples: Induced sputum, gastric washing, NPA, ETA (stool) etc.

- EPTB – CSF, Aspirates: lymph node, pleural fluid, pericardial, pus, joint etc., biopsies etc.

TAKE RESPIRATORY SAMPLES IN CHILDREN AT YOUR FACILITY

"Induced…

1. **Salbutamol using mask and spacer OR Nebulised**
   Opens lower airways, prevents bronchoconstriction
2. **5% Hypertonic saline – nebulisation (2-4ml)**
   Draws sputum into large airways + stimulates cough to mobilise secretions upwards

Sputum"

- **Children <6yr OR >6yr that cannot expectorate –** Aspiration using mucus extractor (similar to NPA)
- **Children > 6 yr –** Expectoration

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

DIAGNOSTIC TESTING

If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

2. Testing: TB-NAAT
: RIF ±INH resistance

- **GeneXpert Ultra**
- **BD Max TB PCR**
- **Roche TB PCR**

: TB culture (take extra volume)
- Especially if ?DRTB for DST
- Remember to trace results!

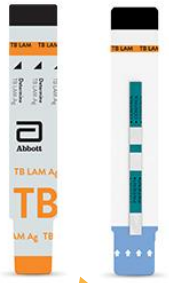
Diagnostic test – not repeated for treatment monitoring unless ongoing symptoms / concern for resistance

A negative TB-NAAT does not rule out TB disease!

: Smear – Often negative in younger children
- If positive, suggests cavitatory (severe) disease
- If negative at baseline, DO NOT repeat at follow-up, unless deteriorating clinically

If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

2. Testing: URINE LAM



- ONLY for CLHIV/ALHIV admitted to hospital
- Symptomatic out-patient CLHIV with:
  - CD4% <25% (<5 years) OR CD4 count <200 (>5 years) in the last 6 months
  - 'Advanced HIV disease' (stage 3 or stage 4)

- False positives – especially if bag specimen
  (clean catch / in-and-out catheter gives better results)

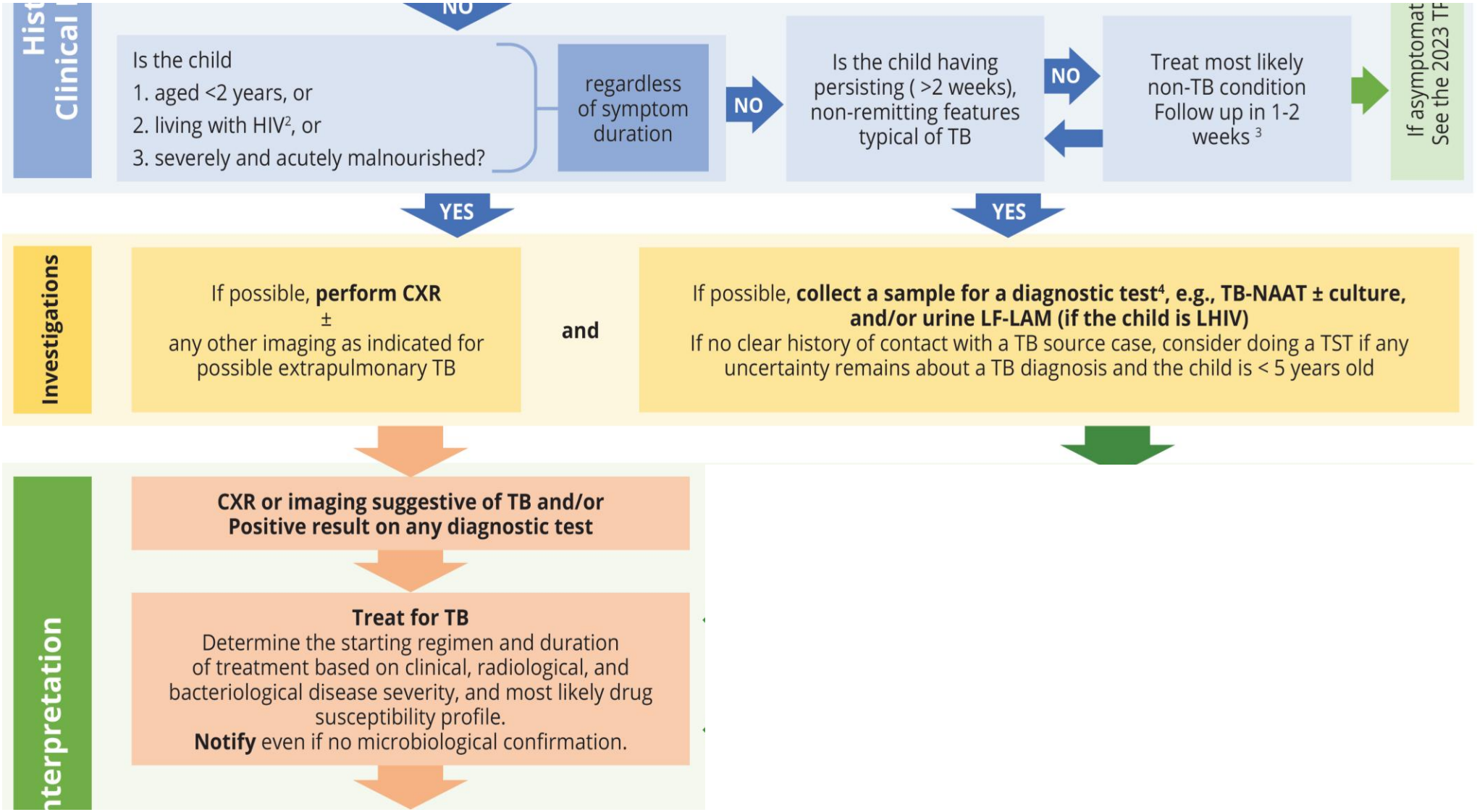
N.B. Time to result e.g. 25 mins

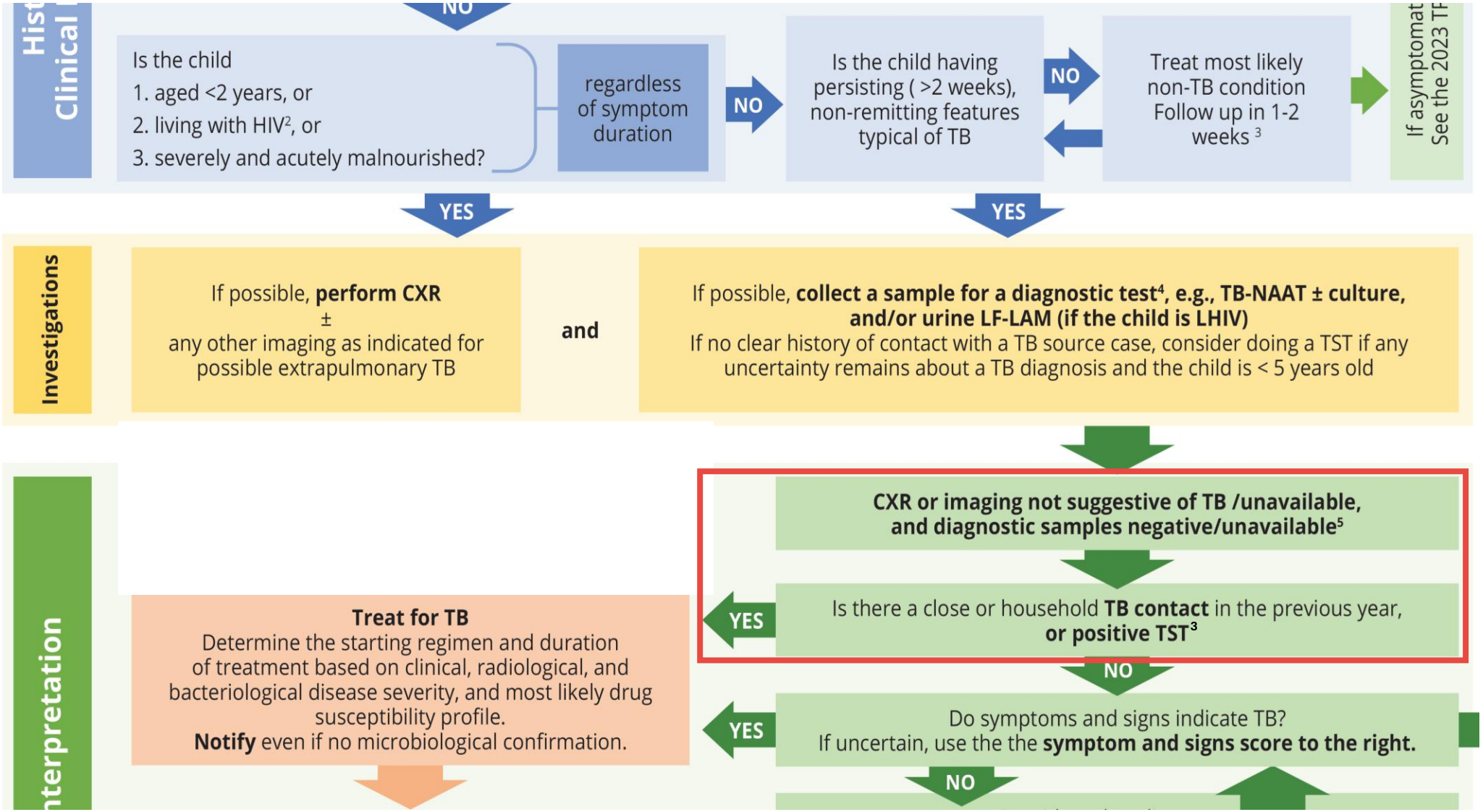
If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

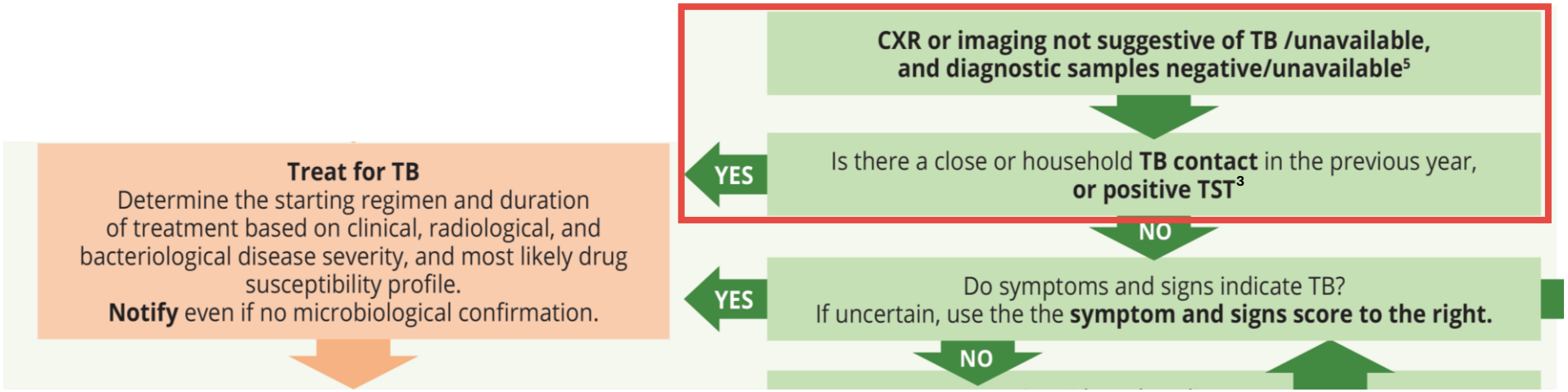
2. Testing: TST ('Mantoux')

- NOT when TB exposure is known
- Can use where **+TB symptoms, but no known contact**

- Positive = TB infection (does not confirm disease)
- Negative = Does not exclude TB infection/disease
- Requires a functional immune system, and > 2 weeks post exposure
- ≥ 10mm for all EXCEPT CLHIV and those severely malnourished (≥5mm)


Clinical
NO
Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?
regardless of symptom duration
NO
Is the child having persisting (>2 weeks), non-remitting features typical of TB
NO
Treat most likely non-TB condition Follow up in 1-2 weeks [3]
If asymptomat
See the 2023 TF
YES
YES
Investigations
If possible, perform CXR
±
any other imaging as indicated for possible extrapulmonary TB
and
If possible, collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old
nterpretation
CXR or imaging suggestive of TB and/or
Positive result on any diagnostic test
Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.


Clinical
Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?
regardless of symptom duration
NO
Is the child having persisting (>2 weeks), non-remitting features typical of TB
NO
Treat most likely non-TB condition Follow up in 1-2 weeks [3]
If asymptomat
See the 2023 TF
YES
YES
Investigations
If possible, perform CXR
±
any other imaging as indicated for possible extrapulmonary TB
and
If possible, collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old
nterpretation
CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]
YES
Is there a close or household TB contact in the previous year, or positive TST[3]
NO
YES
Do symptoms and signs indicate TB?
If uncertain, use the the symptom and signs score to the right.
NO
Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.



3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

Clinical feature [1]		
Cough > 2 weeks	+ 5	Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB
Fever > 2 weeks	+ 10	
Reduced playfulness/energy	+ 4	
Weight loss	+ 5	
Haemoptysis	+ 9	
Night sweats	+ 6	
Enlarged typical lymph nodes	+ 7	
Tachycardia	+ 4	
Tachypnoea/fast breathing	+ 2	
Total score	?	

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Symptom Scoring tool

Primarily for **PHC level - Where CXR and bacteriological testing may not be available**

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]		
Cough > 2 weeks	+ 5	Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB
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Weight loss	+ 5	
Haemoptysis	+ 9	
Night sweats	+ 6	
Enlarged typical lymph nodes	+ 7	
Tachycardia	+ 4	
Tachypnoea/fast breathing	+ 2	
Total score	?	

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

- **Screen for TB symptoms and TB exposure** in all children at every healthcare encounter
- **Identify high-risk children** needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not e.g. CLHIV

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]

Cough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, lethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care. Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition. Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR** ± any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

Interpretation

CXR or imaging suggestive of TB and/or Positive result on any diagnostic test

Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.

Follow-up on results of any culture and DST, as applicable. **Ensure response to treatment,** especially if TB was clinically diagnosed.
Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.
4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
5. A decision to start TB treatment should not be delayed if the necessary investigations are not available, particularly in children at higher risk of developing severe disease, such as young children, malnourished children or those living with HIV.

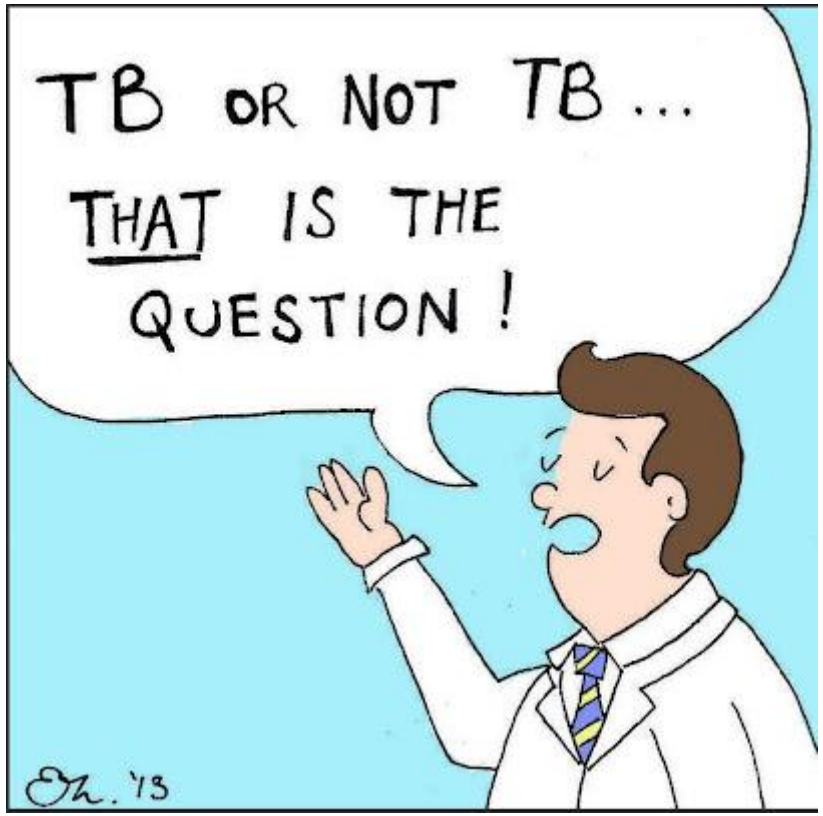
Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]	Score
Cough > 2 weeks	+ 5
Fever > 2 weeks	+ 10
Reduced playfulness/energy	+ 4
Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.



HELPLINE

If in doubt about any aspect of HIV or TB management, contact one of the following resources:

National HIV & TB Health Care Worker Hotline:
0800 212 506

Right to Care Paediatric Adolescent and Adult HIV Helpline:
082 352 6642

KZN Paediatric Hotline:
082 352 6642

ONE CALL AWAY

REFERENCES

(INCLUDING PHOTOS AND GRAPHICS)

1 Screenshots from *MANAGEMENT OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS: A Clinical Guideline for the Diagnosis and Treatment of Drug-susceptible TB in Children and Adolescents in South Africa - September 2024,* throughout the presentation

2 Gunasekera K, Marcy O, Munoz J, et al. Development of treatment-decision algorithms for children evaluated for pulmonary tuberculosis: an individual participant data meta-analysis. Lancet Child Adolesc Health 2023; 7(5): 336-46.

3 World Health Organization. WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva, 2022.

3 Photo of child receiving hypertonic saline nebulization: Taken with permission at the Red Cross War Memorial Children's Hospital, Cape Town, South Africa. Photographic release statements signed by caregivers and participants (if assent required).

4 Photo of child having nasopharyngeal aspiration performed: Taken with permission at the Red Cross War Memorial Children's Hospital, Cape Town, South Africa. Photographic release statements signed by caregivers and participants (if assent required).

TB guidelines children & adolescents
What is new in treatment?

H. Simon Schaaf

Desmond Tutu TB Centre, Dept of Paediatrics and Child Health,

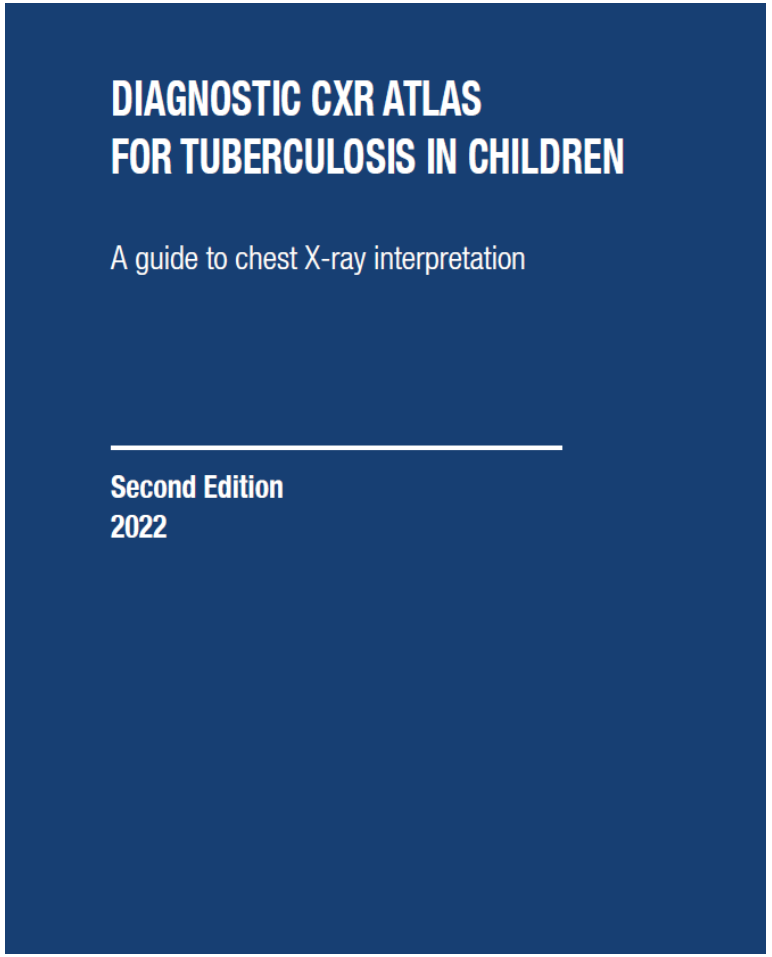
Stellenbosch University

What is new in DS-TB treatment in children and adolescents

- Shorter 4-month regimen for children with non-severe pulmonary TB and/or peripheral lymph node TB. What is non-severe vs severe pulmonary TB?
- Ethambutol included as a fourth drug in all children with DS-TB for intensive phase treatment.
- New dosing charts DS-TB.
- TBM/Miliary TB – new FDC dosing.
- Some RR/MDR-TB update.

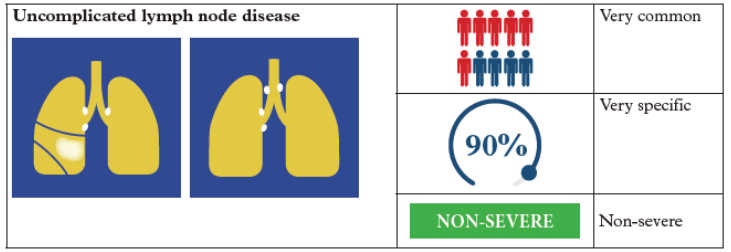
Updated Union CXR Reading Atlas

Includes guidance regarding disease severity of pulmonary TB



Enlargement of mediastinal lymph nodes is the radiological hallmark of paediatric pulmonary TB.

Uncomplicated lymph node disease



Uncomplicated lymph node disease refers to the presence of enlarged mediastinal lymph nodes with:

1. NO significant airway compression AND
2. Either minimal (<1 lobe) or no parenchymal involvement.

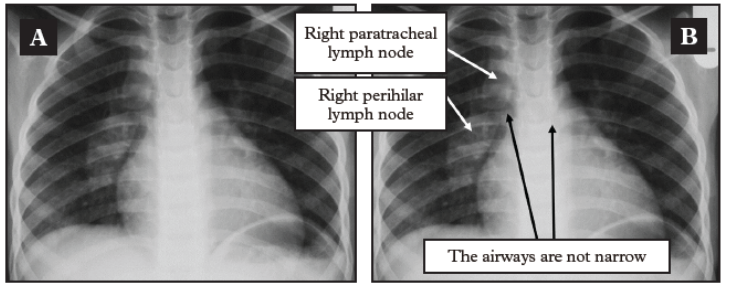
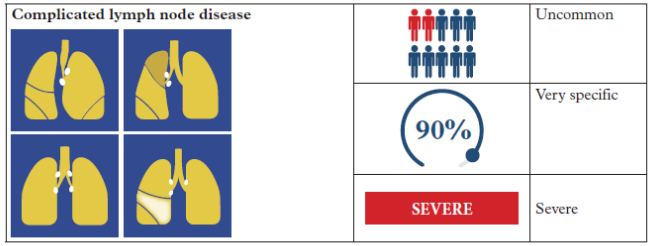


Figure 5.15: CXR B is an annotated version of CXR A which was taken from a 3-year-old child. This CXR shows an enlarged paratracheal and perihilar lymph nodes on the right, with no airway or parenchymal involvement. This is radiologically non-severe disease.

Airway involvement is more commonly seen in younger children because they have more compressible airways.



Large airway compression

In young children, compression or deviation of the large airways can indicate enlargement of mediastinal lymph nodes, even if the lymph nodes cannot be seen.

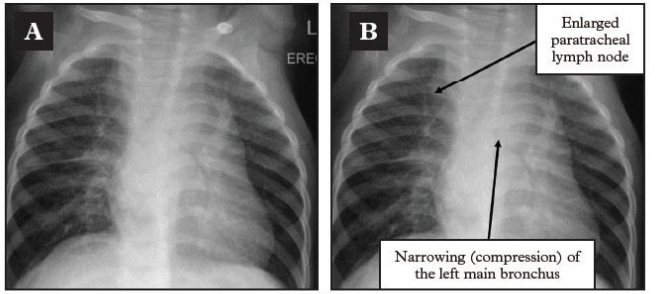
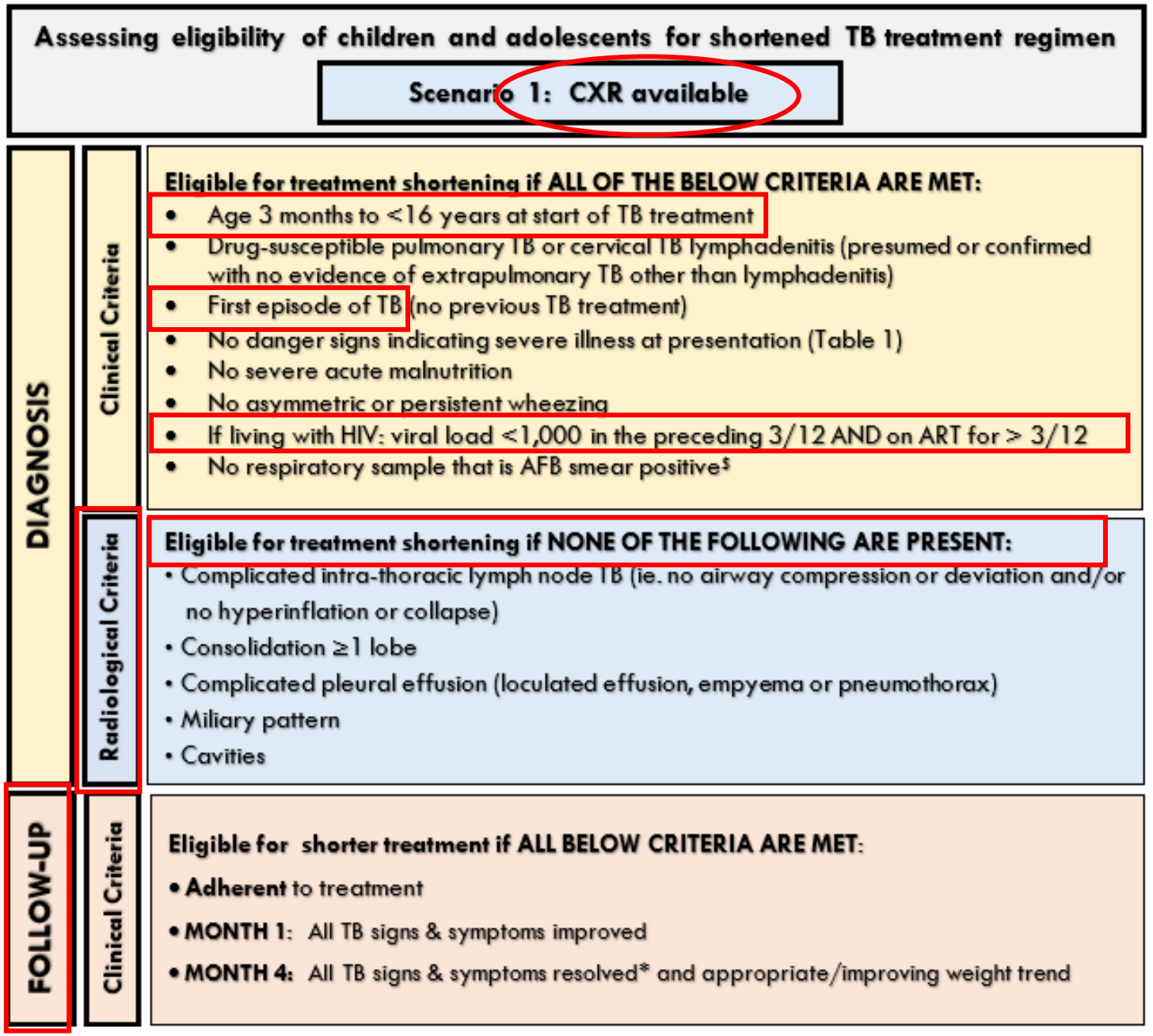


Figure 5.22 CXR B is an annotated version of CXR A, an AP CXR taken from a 3-year-old child. There is an enlarged right paratracheal lymph node that has caused the trachea to shift to the left. There is also narrowing of the left main bronchus – this is caused by enlarged hilar (including sub-carinal) lymph nodes compressing the airway. The lymph nodes themselves are not always easy to see (as is the case with the perihilar lymph nodes in this CXR).

https://theunion.org/technical-publications/diagnostic-cxr-atlas-for-tuberculosis-in-children

Assessing non-severe tuberculosis to decide on shorter 4-month regimen

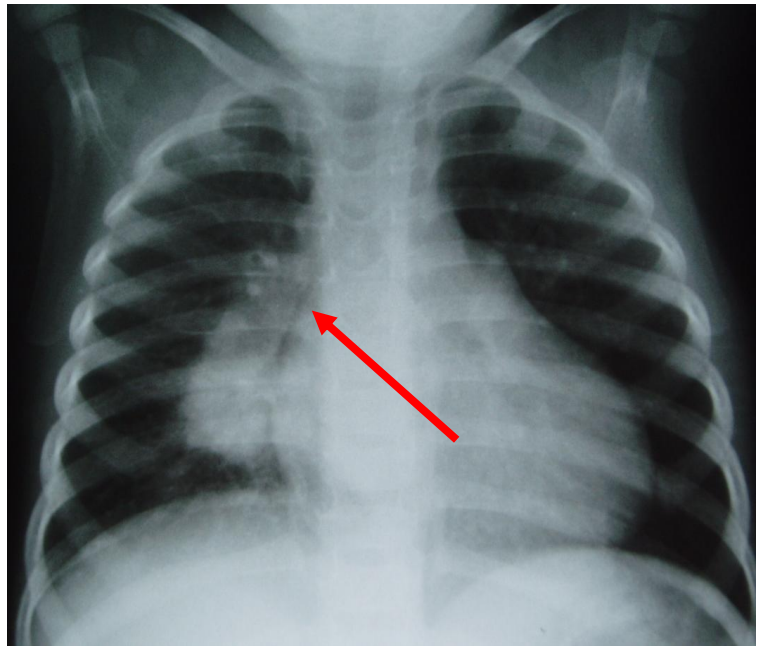


Radiological Criteria

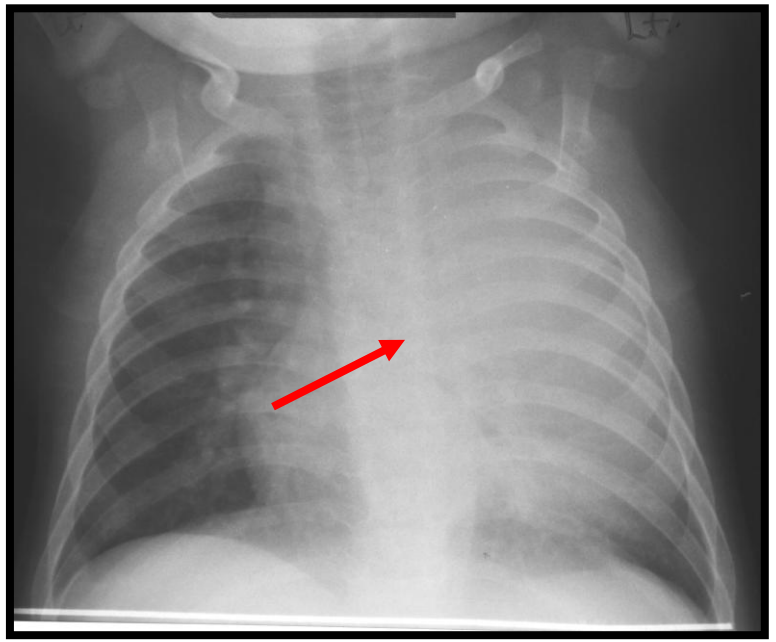
Eligible for treatment shortening if NONE OF THE FOLLOWING ARE PRESENT:

- Complicated intra-thoracic lymph node TB (ie. no airway compression or deviation and/or no hyperinflation or collapse)
- Consolidation ≥1 lobe
- Complicated pleural effusion (loculated effusion, empyema or pneumothorax)
- Miliary pattern
- Cavities

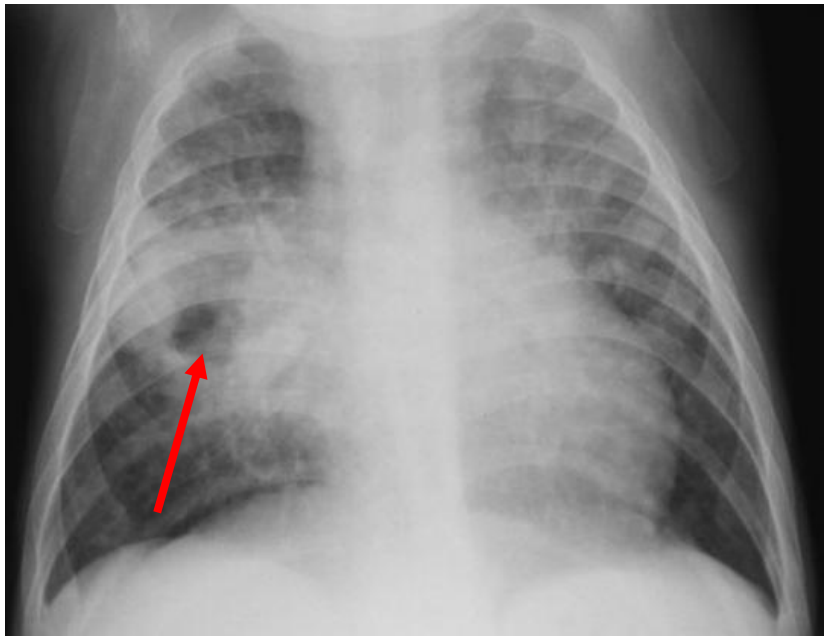
Airway compression nodes



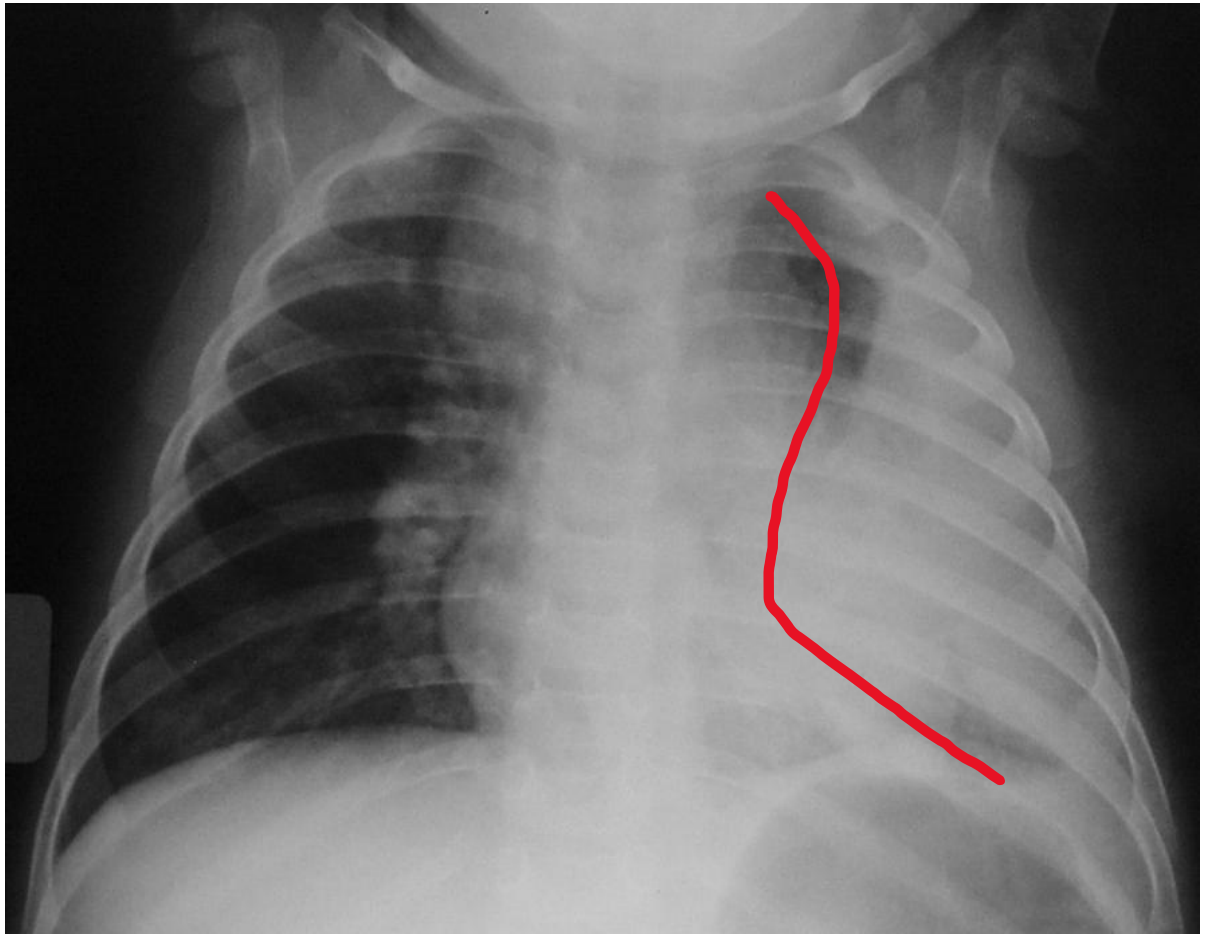
Opacification ≥1 lobe



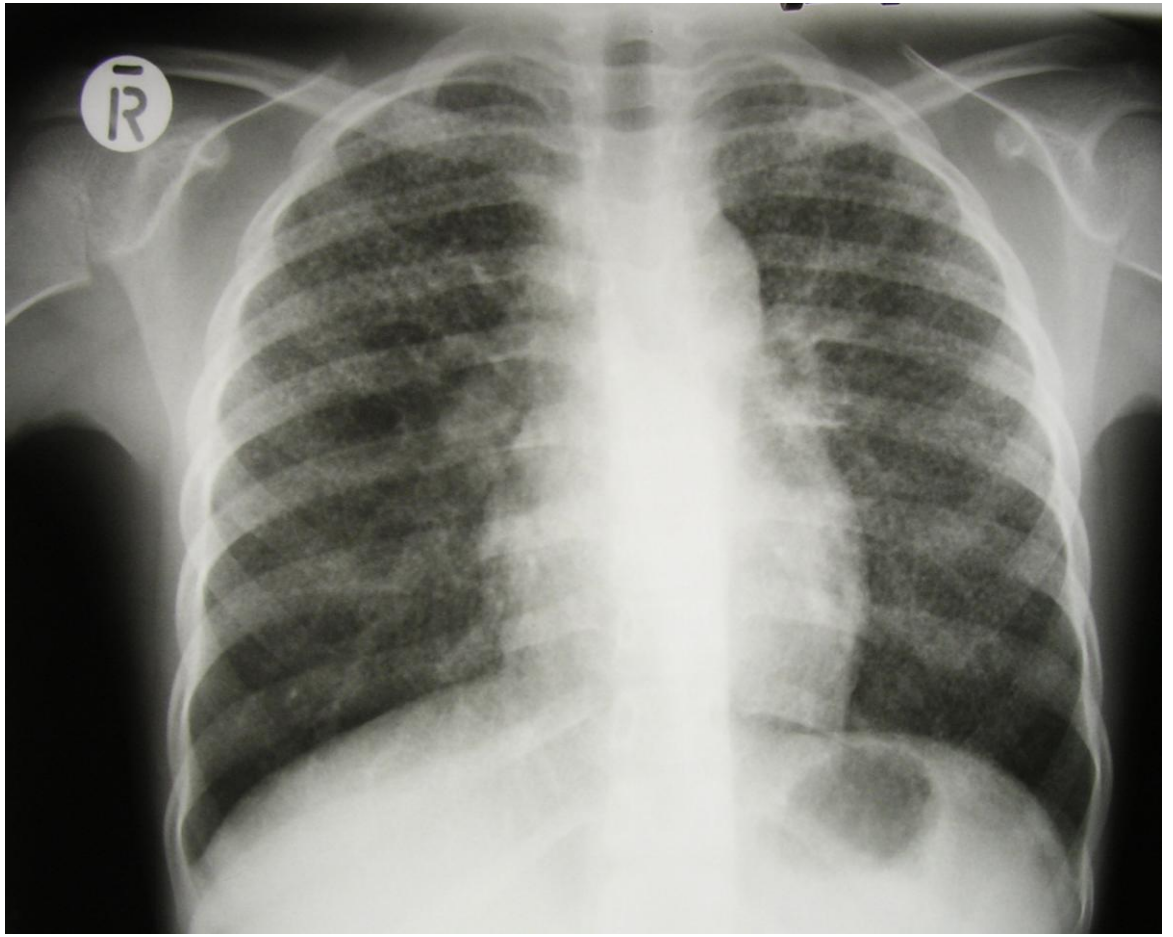
Cavity (+ >1 lobe/nodal compression)



Loculated pleural effusion

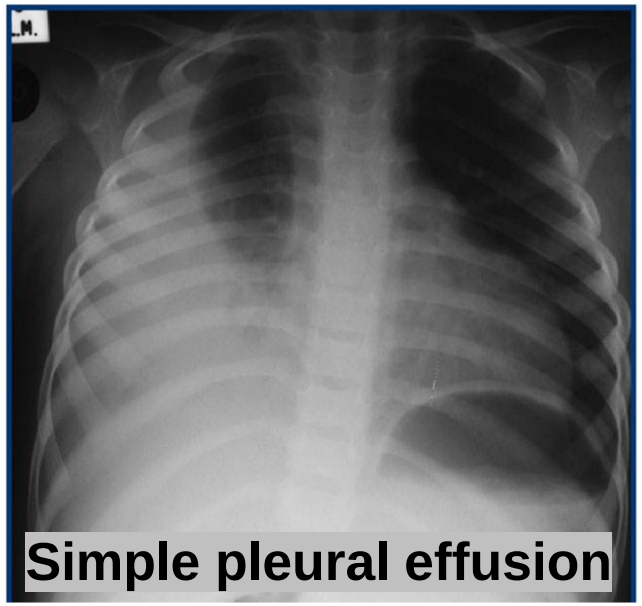


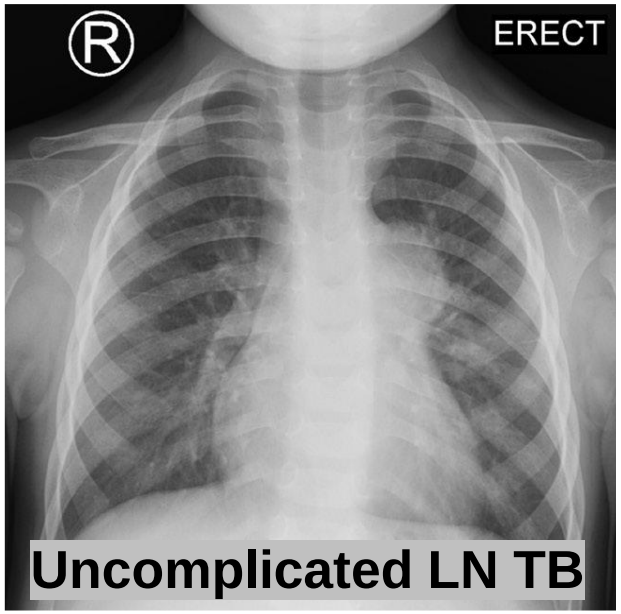
Miliary TB

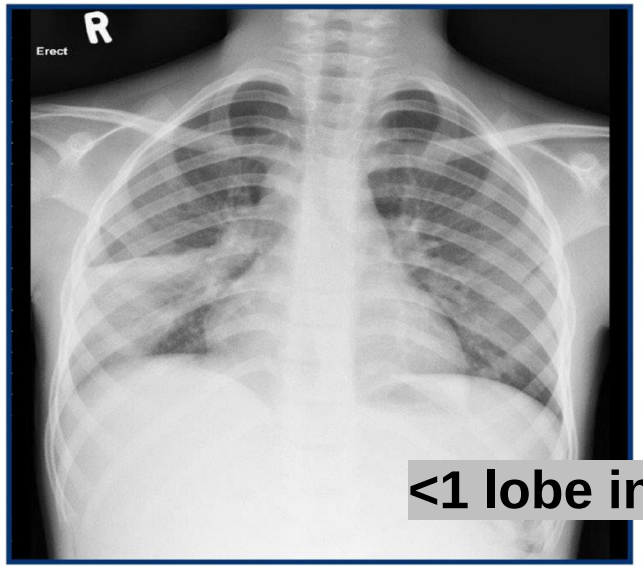


SEVERE PULMONARY TB FORMS

Non-severe Pulmonary TB







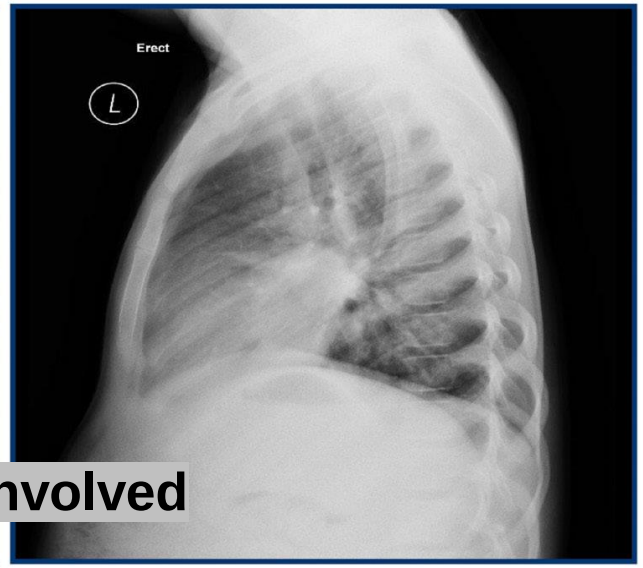
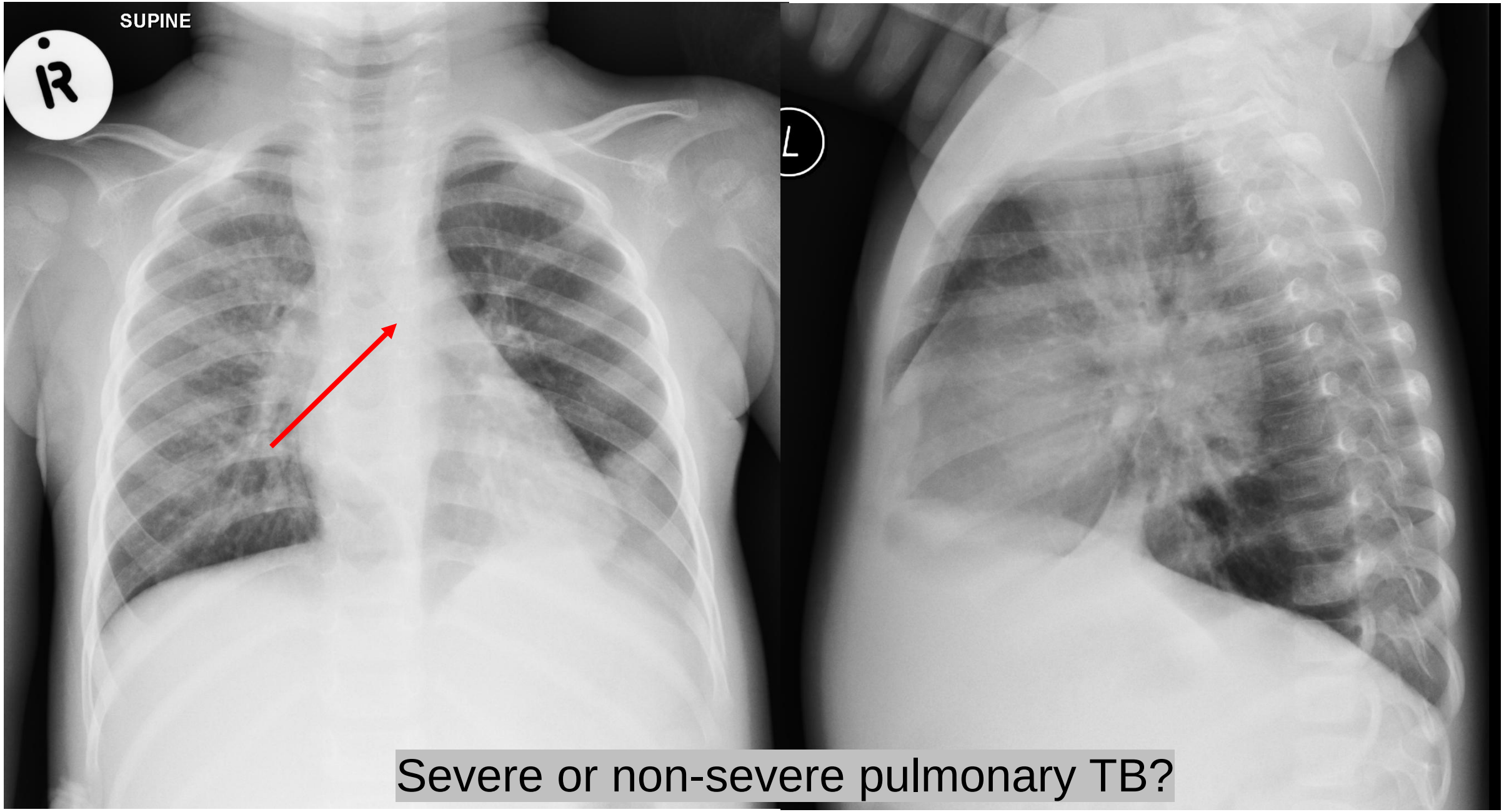


Table 6.1: Classification of radiological disease severity on CXR

Non-Severe	Severe
Uncomplicated lymph node disease	Complicated lymph node disease
Primary (Ghon) focus	Primary (Ghon) focus with cavitation
Simple pleural effusion	Complicated pleural effusion
Alveolar opacification: < 1 lobe	Alveolar opacification: involving a whole lobe or multiple lobes
Other:	Other:
- Interstitial pneumonia	- All cavitary disease
- Perihilar infiltrates	- Expansile pneumonia
	- Miliary TB
	- TB bronchopneumonia

Case for decision

- A 7-month-old infant presents with cough for 2 weeks, has flattening of weight-for-age on growth chart and fever at night. The child received 5 days of antibiotics but did not improve much.
- On further history, the infant was in the care of an aunt for a few weeks, but she was recently diagnosed with rifampicin-susceptible TB on sputum.
- The infant was then considered to have presumed pulmonary TB. On clinical examination, there was slight wheezing, breathing rate was 45/min, there was no peripheral lymphadenopathy, and the child was awake and alert.
- A CXR was done – see CXR.



Severe or non-severe pulmonary TB?

Assessing eligibility of children and adolescents for shortened TB treatment regimen

Scenario 2: NO CXR available

DIAGNOSIS

Clinical Criteria

Eligible for treatment shortening if ALL OF THE BELOW CRITERIA ARE MET:

- Age 3 months to **<8 years** at start of TB treatment
- Drug-susceptible pulmonary TB or cervical TB lymphadenitis (presumed or confirmed with no evidence of extrapulmonary TB other than lymphadenitis)
- First episode of TB (no previous TB treatment)
- No danger signs indicating severe illness at presentation (Table 1)
- No severe acute malnutrition
- No asymmetric or persistent wheezing
- **Not living with HIV (HIV negative)**
- No respiratory sample that is AFB smear positive[$]

FOLLOW-UP

Clinical Criteria

Eligible for shorter treatment if ALL BELOW CRITERIA ARE MET:

- **Adherent** to treatment
- **MONTH 1:** All TB signs & symptoms improved
- **MONTH 4:** All TB signs & symptoms resolved* and appropriate/improving weight trend

If <u>not eligible</u> for the shortened treatment regimen, treat for standard duration (Table 2)

[$]Routine smears for AFB are not recommended as part of the diagnostic work-up. However, if there is an AFB smear positive result on any respiratory sample, the child is not eligible for treatment shortening. (FNA smear positivity is not an exclusion.)

**If cervical peripheral lymph nodes did not decrease in size at month 4, continue to 6 months of treatment. If there was not a significant reduction in size of the lymph nodes, enlargement or complications, especially if TB was not bacteriologically confirmed, refer for further investigation (biopsy or aspiration) to exclude other diagnoses.*

2023 TB Drug Dosing Chart for Children / Adolescents <16 years

With Drug-Susceptible Non-severe TB, Severe Pulmonary TB and Extrapulmonary TB

excluding TB meningitis / central nervous system (CNS) TB / miliary TB)

	Intensive phase Once daily, 7 days a week		Continuation phase Once daily, 7 days a week			
	Duration: 2 months		Non-severe TB: Duration: 2 months	Severe PTB & most EPTB: Duration: 4 months	Bone & joint TB: Duration: 10 months	
Target dose (dose range) (mg/kg/day)	Isoniazid (H): 10 (7-15), Rifampicin (R): 15 (10-20), Pyrazinamide (Z): 35 (30-40), Ethambutol (E): 20 (15-25)					Target dose (dose range) (mg/kg/day)
Formulation Body weight (kg)	HRZ 50/75/150 mg dispersible tablet (scored) OR 50/75/150 mg/4 ml suspension [5]	E 400 mg tablet (not scored) OR 400 mg/8 ml suspension [#]	HR 50/75 mg dispersible tablet (scored) OR 50/75 mg/4 ml suspension [5]			Formulation Body weight (kg)
<2	Obtain expert advice					<2
2 - 2.9	½ tab	1 ml	½ tab			2 - 2.9
3 - 3.9	¾ tab (3 ml) [5]	1.5 ml	¾ tab (3 ml) [5]			3 - 3.9
4 – 7.9	1 tab	2.5 ml	1 tab			4 – 7.9
8 - 11.9	2 tabs	½ tab or 4 ml	2 tabs			8 - 11.9
12 - 15.9	3 tabs	¾ tab or 6 ml	3 tabs			12 - 15.9
16 - 24.9	4 tabs	1 tab or 8 ml	4 tabs			16 - 24.9
≥ 25	HRZE 75/150/400/275 mg tablet		Choose one of below options			≥ 25
			HR 75/150 mg tablet	HR 150/300 mg tablet		
25 – 29.9	2 tabs		2 tabs	1 tab		25-29.9
30 – 34.9	3 tabs		3 tabs	-		30 – 34.9
35 – 64.9	4 tabs		4 tabs	2 tabs		35 – 64.9
≥65	5 tabs		5 tabs	-		≥65

Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication

[5] To make an oral suspension, for weight band 3 – 3.9 kg, for each dose, disperse 1 x HRZ 50/75/150 mg tablet (2 months intensive phase) or 1 x HR 50/75 mg tablet (continuation phase) in **4 ml** of water, administer 3 ml, discard unused suspension. For other weight bands, an oral suspension can be made by dispersing the required number of tablets & fractions of tablets in a small amount of water (5-10 ml) and administering all of the the suspension to the child orally or via nasogastric tube.

[#] If oral suspension required, for each dose, crush 1 x Ethambutol 400 mg tablet to a fine powder, disperse in **8 ml** of water to prepare a concentration of 400 mg/8 ml (50 mg/ml), administer required dose as indicated in above chart, discard unused suspension.

Adapted from World Health Organisation Operational Handbook on Tuberculosis Module 5: Management of tuberculosis in children and adolescents (2022)

2023 TB Drug Dosing Chart for Children / Adolescents <16 years

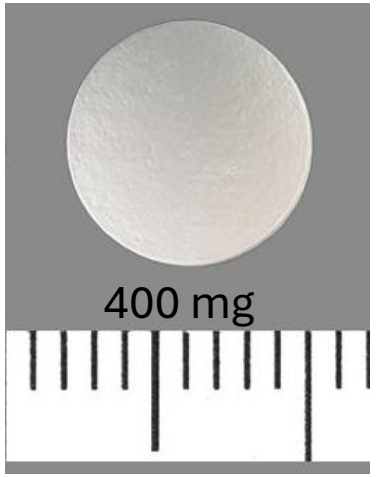
With Drug-Susceptible Non-severe TB, Severe Pulmonary TB and Extrapulmonary TB

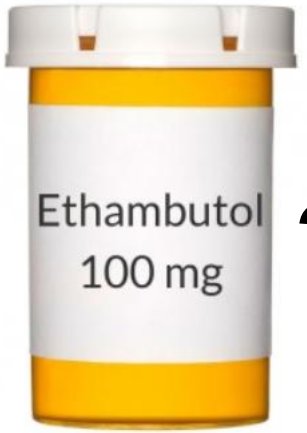
excluding TB meningitis / central nervous system (CNS) TB / miliary TB)

	Intensive phase Once daily, 7 days a week		Continuation phase Once daily, 7 days a week			
	Duration: 2 months		Non-severe TB: Duration: 2 months	Severe PTB & most EPTB: Duration: 4 months	Bone & joint TB: Duration: 10 months	
Target dose (dose range) (mg/kg/day)	Isoniazid (H): 10 (7-15), Rifampicin (R): 15 (10-20), Pyrazinamide (Z): 35 (30-40), Ethambutol (E): 20 (15-25)					Target dose (dose range) (mg/kg/day)
Formulation Body weight (kg)	HRZ 50/75/150 mg dispersible tablet (scored) OR 50/75/150 mg/4 ml suspension [δ]	E 400 mg tablet (not scored) OR 400 mg/8 ml suspension [#]	HR 50/75 mg dispersible tablet (scored) OR 50/75 mg/4 ml suspension [δ]			Formulation Body weight (kg)
<2	Obtain expert advice					<2
2 - 2.9	½ tab	1 ml	½ tab			2 - 2.9

Motivation for including ethambutol as fourth drug

- Ethambutol was always included in first-line anti-TB regimens for all children ≥ 8 years of age (settings with >4% INH resistance)
- Also included in first-line regimens for all children with severe PTB, TB/HIV and severe EPTB (except TBM/miliary TB)
- Ethambutol was usually not included in children treated for non-severe DS-TB; **however,** with the shorter 4-month treatment +/- 70% of the children in the SHINE trial received ethambutol in the intensive phase therefore it is now recommended for all children receiving the shorter regimen as well.
- This makes practical implementation for first-line TB treatment easier – no selecting of who gets EMB – all children now receive EMB in their intensive phase DS-TB treatment regimen





?

TB meningitis, central nervous system TB (e.g. tuberculomas) and for all children with miliary TB: Treat with 6(-9) HRZEto

2023 TB Drug Dosing Chart for Children / Adolescents <16 years
With Drug-Susceptible/Presumed Drug-Susceptible TB Meningitis / Central Nervous System TB / Miliary TB

	Single phase of treatment: 6-9 months Once daily, 7 days a week			
Target dose range & maximum doses	Isoniazid (H): 15-20 mg/kg, maximum dose 450 mg Rifampicin (R): 22.5-30 mg/kg, maximum dose 900 mg	Pyrazinamide (Z): 35-45 mg/kg, maximum dose 2 g	Ethionamide (Eto): 17.5-22.5 mg/kg, maximum dose 1 g	Target dose range & maximum doses
Formulation Body weight (kg)	HR 50/75 mg dispersible tablet (scored) OR 50/75 mg/4 ml suspension *	Z 500 mg tablet (scored) OR 500 mg/8 ml suspension *	Eto 250 mg tablet (scored) OR 250 mg/8 ml suspension *	Formulation Body weight (kg)
<2	Obtain expert advice			<2
2 – 2.9	¾ tab or 3 ml	1 ml	1.5 ml	2 – 2.9

While Eto was out of stock, levofloxacin at 20-25mg/kg/day was used as alternative

Criteria for discharge of children with TBM/CNS TB

- Good **tolerance of anti-TB treatment** and child **clinically stable**
- A **reliable caregiver**(s) who can and will administer & adhere to giving the child's treatment
- **A named clinician** to care for the patient post-discharge
- A **follow-up facility that can provide all medication** and **detect missed appointments** and **will recall patients who do not arrive**

- TBM (and miliary TB – as almost all children with miliary TB have CNS TB) is a fatal disease (almost 100% if not treated) or can rapidly progress and cause severe neurological sequelae or death if treatment is not properly supplied and administered correctly.

What's new in treating RR/MDR-TB disease in children and adolescents?

- New **shorter all-oral** regimens for children with RR/MDR-TB **– mainly 9 months**, but **non-severe RR/MDR-TB** (as in DS-TB definition) can be treated for **6 months** (with good post treatment completion follow-up for at least a year)
- Both bedaquiline and delamanid can be used in children of all ages
- **Pretomanid** only to be used in specific regimens (BPaL or BPaL-L) and only in adolescents 14 years or older.
- **Dosing and safety of pretomanid has not been established in children <14 years of age;** currently not recommended in this age group.
- Most children/adolescents with RR/MDR-TB should be **managed as outpatients (clinic-based)**. Essential to identify a **reliable caregiver** AND **all oral RR/MDR-TB drugs should be available** at primary healthcare level and the necessary toxicity/safety screening during treatment should also be available at PHC level.

Figure 3.1: Approach to treatment of RR-TB in children < 15 years

Child (< 15 yrs) with confirmed / presumptive RR-TB

If resistance to BDQ / LZD / CFZ identified or suspected at any point – **discuss with specialist regarding both treatment regimen and treatment duration**

PCAC/NCAC!!!

Non-severe disease
Treat for 6 months

FLQ-susceptible:
BDQ / LFX / CFZ / TRD / LZD (2m)

FLQ-resistant:
BDQ / CFZ / TRD / DLM / LZD (2m+)

Severe disease
Treat for 9 months

FLQ-susceptible:
BDQ / LFX / CFZ / TRD / LZD (2m+)

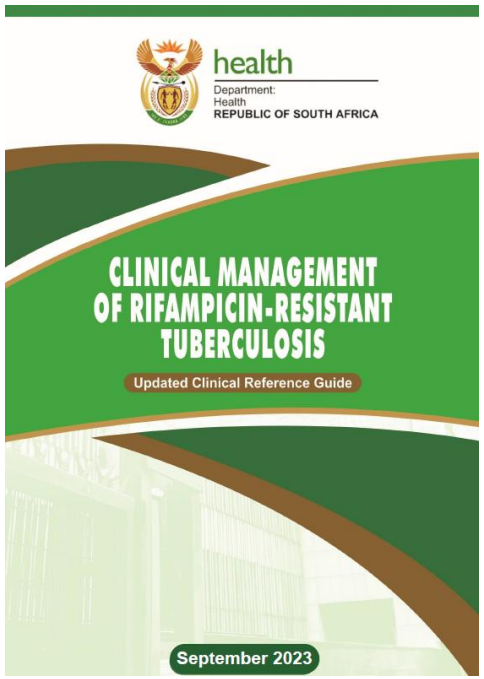
FLQ-resistant:
BDQ / CFZ / TRD / DLM / LZD

CNS / miliary / bone / pericardial
Treat for minimum 12 months

BDQ / (LFX) / LZD / CFZ / TRD / DLM

Note that LZD is very toxic in children and often poorly tolerated, therefore will require close and regular monitoring for adverse effects including myelosuppression (FBC and diff WCC two-weekly in first month then monthly; risk especially high in the first 2 months of exposure), peripheral neuropathy (especially beyond 2 months of exposure) and optic neuritis (any time during treatment). Drug substitution may be required if LZD is relied upon as one of the effective drugs in any regimen.

BDQ and DLM are usually given for only 6 months regardless of the total treatment duration, however, duration of BDQ and DLM may be extended beyond 6 months with appropriate monitoring if considered necessary in some cases.



Department of Health SA. Clinical management of rifampicin-resistant tuberculosis. Updated clinical reference guide 2023.

BEAT-Tuberculosis regimen

- Study completed in SA – presented at UNION meeting in Bali and WHO RR-TB guideline development group
- WHO issued a Rapid Communication in June 2024: **Key updates to the treatment of drug-resistant tuberculosis**
- WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid, levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance (conditional recommendation, very low certainty of evidence).
- In this study and recommendation, LZD is given for full 6 months.
- Either Cfz (if Lfx-susceptible) or Lfx (if Lfx-resistant) may be stopped when Lfx DST known
- Very important to follow up on source patient/child's isolate BDQ DST, as BDQ resistance is rapidly increasing - these cases to be discussed with PCAC and/or NCAC

Western Cape Government FOR YOU

Drug-resistant-TB Treatment Dosing Table for Children 2024

(< 46 kg and < 15 years)

MEDICINES INFORMATION CENTRE

	WHO Group A									WHO Group B			
	Levofloxacin (LFX) (preferred quinolone)		Moxifloxacin (MFX)	Bedaquiline (BDQ)		Linezolid (LZD)				Terizidone (TRD)#	Clofazimine (CFZ)		
Available formulations	100 mg DT** OR 10 mg/mL	250 mg tablet OR 500 mg tablet OR 25 mg/mL	400 mg tablet	20 mg DT	100 mg tab OR 10 mg/mL solution	20 mg/mL suspension	150 mg DT** OR 15 mg/mL solution	600 mg tablet OR 60 mg/mL solution		250 mg capsule	50 mg DT**	100 mg capsule	Available formulations
Target dose	15-20 mg/kg/day		10 - 15 mg/kg/day	Once daily loading dose for 14 days then thrice weekly (TIW) dosing M/W/F		1 - 15 kg: 15 mg/kg per day; ≥ 15 kg: 10-12 mg/kg daily				7 - 29.9 kg: 15 - 20 mg/kg; ≥ 30 kg: 10 - 15 mg/kg	2 - 5 mg/kg when given daily		Target dose
MDD	1.5g		400 - 800 mg	Loading dose: 400 mg daily; Maintenance dose: 200 mg M/W/F		600 mg				750 mg	100 mg		MDD
Practical advice	In general, for older children able to swallow tablets/capsules whole, avoid crushing and mixing tablets/capsules with water, as this may reduce palatability (tastes worse than swallowing tablets whole). Discard any unused portion of a non-commercial solution. Dispersible tablets (DT) can either be dispersed in a liquid or mixed with a soft or semi-soft food such as yoghurt or porridge												Practical advice
	For a 10 mg/mL suspension: crush and disperse 1 x 100 mg DT in 10 mL water	For a 25 mg/mL suspension: crush and disperse 1 x 250 mg tablet in 10 mL water	For 40 mg/mL suspension: crush and disperse 1 x 400 mg tablet in 10 mL water	A daily loading dose for 2 weeks, followed by a maintenance dose given three times a week for 22 weeks. If treatment is interrupted see Table on Bedaquiline interruptions on next page for guidance on reloading. For 10 mg/mL suspension: Crush and disperse 1 x 100 mg tablet in 10 mL water. Vigorous stirring/shaking is needed prior to administrating the 100 mg tablet crushed and suspended in water		Once reconstituted, must be used within 21 days	For 15 mg/mL suspension: crush and disperse 1 x 150 mg DT in 10 mL water	For 60 mg/mL suspension: crush and disperse 1 x 600 mg tablet in 10 mL water	For 25 mg/mL suspension: Open capsule and mix contents with 10 mL water	The 50 mg DT is preferred for children < 24 kg. For 5 mg/mL suspension: crush and disperse 1 x 50 mg DT in 10 mL water	Dosing interval changes as weight of child increases. Soften 1 capsule in water or yoghurt and administer entire volume‡	
Wt. (kg)	Consult with a clinician experienced with DR-TB prescribing for children weighing < 5 kg. Refer to adult guidelines in children > 46 kg and > 15 years of age												Wt. (kg)
3 - 4.9	5 mL OR 0.5 x 100 mg DT daily	2 mL daily	1 mL daily	20 mg DT: Loading dose daily for 2 weeks: < 3 months: 1.5 x 20 mg DT daily; ≥ 3 months: 3 x 20 mg DT daily	20 mg DT: Maintenance dose M/W/F for 22 weeks: < 3 months: 0.5 x 20 mg DT M/W/F; ≥ 3 months: 1 x 20 mg DT M/W/F	100 mg tab OR 10 mg/mL solution: Loading dose daily for 2 weeks: < 3 months: 3 mL daily; ≥ 3 months: 6 mL daily	100 mg tab OR 10 mg/mL solution: Maintenance dose M/W/F for 22 weeks: < 3 months: 1 mL M/W/F; ≥ 3 months: 2 mL M/W/F	2 mL daily	2.5 mL daily		1 mL daily	2-4 mL daily		3 - 4.9
5 - 6.9	1 x 100 mg DT daily	5 mL OR 0.5 x 250 mg tab daily	2 mL daily					4 mL daily	5 mL OR 0.5 x 150 mg DT daily	1.25 mL daily	2 mL daily	5 mL daily	1 x 100 mg cap M/F	5 - 6.9
7 - 9.9	1.5 x 100 mg DT daily		3 mL daily	< 3 months: 1.5 x 20 mg DT daily; ≥ 3 - 6 months: 3 x 20 mg DT daily; ≥ 6 months: 4 x 20 mg DT daily	< 3 months: 0.5 x 20 mg DT M/W/F; ≥ 3 - 6 months: 1 x 20 mg DT M/W/F; ≥ 6 months: 2 x 20 mg DT M/W/F	< 3 months: 3 mL daily; ≥ 3 - 6 months: 6 mL daily; ≥ 6 months: 8 mL daily	< 3 months: 1 mL M/W/F; ≥ 3 - 6 months: 2 mL M/W/F; ≥ 6 months: 4 mL M/W/F	6 mL daily	1 x 150 mg DT daily	2.5 mL daily	5 mL daily			7 - 9.9
10 - 15.9	2 x 100 mg DT daily	1 x 250 mg tab daily	5 mL daily OR 0.5 x 400 mg tab	≥ 3 - 6 months: 3 x 20 mg DT daily; ≥ 6 months: 6 x 20 mg DT daily	≥ 3 - 6 months: 1 x 20 mg DT M/W/F; ≥ 6 months: 3 x 20 mg DT M/W/F	≥ 3 - 6 months: 6 mL daily; ≥ 6 months: 12 mL daily^Δ	≥ 3 - 6 months: 2 mL M/W/F; ≥ 6 months: 6 mL M/W/F	8 mL daily			1 x 250 mg cap daily	1 x 50 mg DT daily OR 10 mL daily	1 x 100 mg cap M/W/F	10 - 15.9
16 - 23.9	3 x 100 mg DT daily	1.5 x 250 mg tab daily	7.5 mL daily OR 0.75 x 400 mg tab	10 x 20 mg DT daily	5 x 20 mg DT M/W/F	2 x 100 mg tabs daily	1 x 100 mg tab M/W/F	11 mL daily	2 x 150 mg DT daily=	5 mL daily OR 0.5 x 600 mg tab daily	2 x 250 mg caps daily			16 - 23.9
24 - 29.9	5 x 100 mg DT daily	2 x 250 mg tab daily OR 1 x 500 mg tab daily	1 x 400 mg tab daily	20 x 20 mg DT daily	10 x 20 mg DT M/W/F			14 mL daily				2 x 50 mg DT daily	1 x 100 mg cap daily	24 - 29.9
30 - 35.9						4 x 100 mg tabs daily	2 x 100 mg tabs M/W/F	15 mL daily						30 - 35.9
36 - 45.9		1.5 x 500 mg tab OR 3 x 250 mg tabs daily						20 mL daily	3 x 150 mg DT daily	7.5 mL daily OR 0.75 x 600 mg tab daily				36 - 45.9

**Only available via Section 21. Not available at all facilities; ‡If there are any administration difficulties, consult with a TB hospital; ^Δ Use 2 x 100 mg tabs in 20 mL water, and give 12 mL. Discard the rest; #hdINH and TZD: Only to be co-used after consultation with an expert; =For weight band 16 - 23.9 kg: Clinicians may opt to administer 1.5 x 150 mg DT or 4 mL of the 60 mg/mL solution to ensure the dose does not exceed 10 - 12 mg/kg; cap = capsule; DT = dispersible tablet; M/W/F = administer medicines three times a week on a Monday, Wednesday and Friday; tab = tablet; MDD = maximum daily dose

Summarizes dosing tables pages 47-52 in the SA RR-TB guidelines

	WHO Group C						Other medicines		
	Delamanid (Dlm)		Ethionamide (Eto)	Para-aminosalicylic acid (PAS)[##]	Meropenem[†]	Amoxicillin/clavulanate	High-dose isoniazid (hdINH)[#]		
Available formulations	25 mg DT[**]	50 mg tablet OR 5 mg/mL suspension	250 mg tablet	4 g sachet	500 mg per vial (10 mL) 1 g powder per vial (20 mL)	250 mg / 62,5 mg in 5 mL suspension 250/125 mg tablet	100 mg tablet	300 mg tablet	Available formulations
Target dose	3 - 4 mg/kg/day		15 - 20 mg/kg/day	200 - 300 mg/kg/d	20 - 40 mg/kg IV every 8h	To be used with meropenem	15 - 20 mg/kg/day		Target dose
MDD	100 mg twice daily		1 g	8 g	2 g twice daily	250/125 mg three times a day	600 mg		MDD
Practical advice	Discard any unused portion of a non-commercial solution. Dispersible tablets (DT) can either be dispersed in a liquid or mixed with a soft or semi-soft food such as yoghurt or porridge.								Practical advice
	≥ 3 months: twice daily dosing; For 2.5 mg/mL suspension: disperse 1 x 25 mg DT in 10 mL water	≥ 3 months: twice daily dosing; For 5 mg/mL suspension: disperse 1 x 50 mg DT in 10 mL water	For a 25 mg/mL suspension: Crush and disperse 1 tablet in 10 mL water	Ensure patient receives the special measuring spoon to measure the dose correctly. Administer with yoghurt or other soft food with low pH (e.g. apple puree, tomato or orange juice)	Intravenous administration (only to be used with clavulanic acid)	To be given with each dose of the carbapenem. Oral administration, 30 min before IV meropenem. Dosing expressed as clavulanate. Once reconstituted, must be used within 7 days (confirm with specific product information)	For 10 mg/mL suspension: crush and disperse 1 tablet in 10 mL water Pyridoxine (vitamin b6) is always given with high dose INH: < 5 years: 12.5 mg/d ≥ 5 year: 25 mg/d	Pyridoxine (1 - 2 mg/kg) is always given with high dose INH: < 5 years: 12.5 mg/d ≥ 5 year: 25 mg/d	
Wt. (kg)	Consult with a clinician experienced with DR-TB prescribing for children weighing < 5 kg. Refer to adult guidelines in children > 46 kg and > 15 years of age								Wt. (kg)
3 - 4.9	1 x 25 mg DT daily	5 mL OR 0.5 x 50 mg tab daily	Consult with experienced clinician	300 mg twice daily	50 mg (1 mL) three times a day	18,75 mg (1.5 mL) three times a day	5 mL daily OR 0.5 x 100 mg tab daily		3 - 4.9
5 - 6.9	< 3 months: 1 x 25mg DT daily; ≥ 3 months: 1 x 25 mg DT twice daily	< 3 months: 5 mL OR 0.5 x 50 mg tab daily; ≥ 3 months: 5 mL OR 0.5 x 50 mg tab twice daily	3 mL daily	750 mg twice daily	100 mg (2 mL) three times a day	25 mg (2 mL) three times a day	1 x 100 mg tab daily		5 - 6.9
7 - 9.9			5 mL daily OR 0.5 x 250 mg tab daily	1 g twice daily	200 mg (4 mL) three times a day	37.5 mg (3 mL) three times a day	1.5 x 100 mg tabs daily		7 - 9.9
10 - 15.9	1 x 25 mg DT twice daily	5 mL OR 0.5 x 50 mg tab twice daily	1 x 250 mg tab OR 10 mL daily	2 g twice daily	300 mg (6 mL) three times a day	62.5 mg (5mL) three times a day	2 x 100 mg tabs daily		10 - 15.9
16 - 23.9	2 x 25 mg DT in the morning and 1 x 25 mg DT at night	10 mL in the morning and 5 mL at night OR 1 x 50 mg tab in the morning and 0.5 x 50 mg tab at night	2 x 250 mg tabs daily	3 g twice daily	450 mg (9 mL) three times a day	100 mg (8 mL) three times a day	3 x 100 mg tabs daily	1 x 300 mg tab daily	16 - 23.9
24 - 29.9				3.5 g twice daily	550 mg (11 mL) three times a day	250/125 mg tab three times a day[¶]	4 x 100 mg tabs daily	1.5 x 300 mg tabs daily	24 - 29.9
30 - 35.9	2 x 25 mg DT twice daily	1 x 50 mg tab twice daily		4 g twice daily	1 g (1 vial) three times a day OR 2 g twice a day	250/125 mg tab three times a day or twice a day according to meropenem dosing[¶]			30 - 35.9
36 - 45.9							4.5 x 100 mg tabs daily		36 - 45.9

[##]If sodium amino salicylate 1g tablets (Monopas®), accessed via section 21, is used, consult expert on administration; [†]In consultation with an experienced clinician, other carbapenems can be considered; [¶]Alternatively, use 10mL of the 250/62.5 mg/mL syrup two to three times day; [#]hdINH and TZD: Only to be co-used after consultation with an expert; MDD = maximum daily dose

MONITORING FOR ADVERSE REACTIONS TO DR-TB MEDICINES IN CHILDREN

TEST	FREQUENCY	COMMENT
FBC, neutrophil count and platelets	Baseline, at week 2, 4, 6 and 8, and then monthly	Hb < 8, neutrophils < $0.75x10^9$/L or platelets < $50x10^9$/L needs urgent intervention. Often caused by LZD
ECG	Baseline, at two weeks, at one month, and then monthly	QTcF > 500msec needs urgent intervention. Also repeat ECG after 2 weeks if >60msec difference from previous QTcF result. If still raised consult with specialist. Fridericia's formula: QTcF: QT/RR(0.33)
Peripheral neuropathy (PN)	Baseline, then monthly	Can be caused by LZD, hdINH and TZD and may be permanent. LZD induced neuropathy occurs mostly with long-term use and does not respond to pyridoxine. Consult with TB specialist
Visual acuity/optic neuritis	Baseline, then monthly	Possible culprits: Ethambutol, LZD, rifabutin
ALT	Baseline, repeat if symptomatic for liver dysfunction	Symptoms of liver toxicity include: nausea and vomiting, right upper quadrant pain and tender liver, visible jaundice. Stop all medicines if ALT > 5 x ULN or if ALT > 3 x ULN with symptoms of liver dysfunction and discuss with an expert
K+ and Mg2+	Baseline, repeat if QTcF is prolonged or vomiting/diarrhoea/clinically unwell	
TSH (if using PAS and/or ethionamide)	Baseline and every 2 - 3 months	If TSH is increased, do free T4

BEDAQUILINE INTERRUPTIONS > 30 KG

Duration of interruption	Instructions for reloading
< 2 weeks	No reloading needed
2 - 4 weeks	3 days 400 mg[†] bedaquiline daily
1 - 12 months	7 days 400 mg[†] bedaquiline daily
> 12 months	14 days 400 mg[†] bedaquiline daily

[†]If the patient weighs between 16 and 30 kg, reload with 200 mg daily. If patient < 16kg, consult with an expert

NEED HELP?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 /021 406 6782

Alternatively "WhatsApp" or send an SMSor "Please Call Me" to 071 840 1572

www.mictwct.ac.za

ALT = alanine transaminase; ECG = electrocardiogram; FBC = full blood count; K^+ = potassium; Mg^{2+} = magnesium; QTcF = corrected QT interval using the Fridericia formula

Largely based on the 2023 NDoH Clinical Management of Rifampicin-Resistant Tuberculosis—Updated Clinical Reference Guide. Additional references available on request

Published February 2024, Version 1

Thank you

Updated BCG guidelines

Juli Switala

Infectious Diseases Paediatrician

Paediatric TB Senior Technical specialist

The Aurum Institute

Updated BCG guidelines

- **Previous SA guidelines: up to 1 year of age**
- **Updated SA guidelines: All healthy infants at discharge or 'as soon after birth as possible' up to 10 years old**

Given as soon as possible after birth (time to efficacy ?+/- 6 weeks)

Benefits:

- 19% reduction in infection after exposure
- 50-60% protection against pulmonary TB disease
- >80% protection against severe forms of TB (eg: TB Meningitis)
- Some general benefits: associated with reduced 'all cause' mortality
- Safe to give with other vaccinations

No Benefit:

- NO evidence of efficacy as post exposure prophylaxis
- Protection wanes after 15 years
- No evidence for protection against COVID-19

THE AURUM INSTITUTE

Updated BCG guidelines

Considerations when deciding when to give the BCG vaccine

- All healthy newborns should receive the BCG vaccine at discharge from the delivery unit, regardless of TB exposure or HIV exposure status.
- For infants that are transferred to a neonatal unit, the timing of BCG vaccination will depend on the infant's clinical status. Neonatal units should have a policy to ensure vaccination occurs prior to hospital discharge
- If the infant initiates TPT or TB treatment in the first six weeks[18] of life, the effectiveness of the live, attenuated BCG vaccine may be negatively impacted. Therefore, the BCG vaccine should be repeated on completion of either TPT or TB treatment. Infants or children living with HIV should be 1) on ART, 2) clinically well, and 3) have a CD4 > 25%.
- Infants living with HIV may have an additional CD4 count to determine if the infant meets the criteria for receiving BCG. Do not wait for the routine annual CD4 count to be done for ART monitoring purposes, as this delay may result in many infants not receiving BCG at all.
- Regardless of the service point at which the child is receiving either TPT or TB treatment, a comprehensive package of services should be provided as per the RTHB, including routine HIV testing for the HIV-exposed infant, immunisations, and growth monitoring.
- Any infant who tests positive for HIV at birth or at any time during TPT or TB treatment should be initiated on ART.
- The BCG vaccine can be administered at any vaccination visit, with other routine vaccines.
- It is acceptable to open a BCG vial for just one infant.
- Children with suspected or confirmed inborn errors of immunity or other acquired immunodeficiency conditions should be discussed with an expert before giving BCG
- A 'catch-up' BCG should be administered to any child <10 years of age who did not get a BCG at birth. Infants or children living with HIV should be 1) on ART, 2) clinically well, and 3) have a CD4 > 25% (if ≤5 years of age) or >200 cells (if >5 years of age).
- Pharmacovigilance and reporting serious adverse events (SAE) remain important for all age groups.

THE AURUM INSTITUTE

Updated BCG guidelines

Considerations when deciding when to give the BCG vaccine.

- All healthy newborns should receive the BCG vaccine at discharge from the delivery unit, regardless of TB exposure or HIV exposure status.
- For infants that are transferred to a neonatal unit, the timing of BCG vaccination will depend on the infant's clinical status. Neonatal units should have a policy to ensure vaccination occurs prior to hospital discharge.
- If the infant initiates TPT or TB treatment in the first six weeks[18] of life, the effectiveness of the live, attenuated BCG vaccine may be negatively impacted. Therefore, the BCG vaccine should be repeated on completion of either TPT or TB treatment. Infants or children living with HIV should be 1) on ART, 2) clinically well, and 3) have a CD4 > 25%.
- Infants living with HIV may have an additional CD4 count to determine if the infant meets the criteria for receiving BCG. Do not wait for the routine annual CD4 count to be done for ART monitoring purposes, as this delay may result in many infants not receiving BCG at all.
- Regardless of the service point at which the child is receiving either TPT or TB treatment, a comprehensive package of services should be provided as per the RTHB, including routine HIV testing for the HIV-exposed infant, immunisations, and growth monitoring.
- Any infant who tests positive for HIV at birth or at any time during TPT or TB treatment should be initiated on ART.
- The BCG vaccine can be administered at any vaccination visit, with other routine vaccines.
- It is acceptable to open a BCG vial for just one infant.
- Children with suspected or confirmed inborn errors of immunity or other acquired immunodeficiency conditions should be discussed with an expert before giving BCG
- A 'catch-up' BCG should be administered to any child <10 years of age who did not get a BCG at birth. Infants or children living with HIV should be 1) on ART, 2) clinically well, and 3) have a CD4 > 25% (if ≤5 years of age) or >200 cells (if >5 years of age).
- Pharmacovigilance and reporting serious adverse events (SAE) remain important for all age groups.

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Updated BCG guidelines

Considerations when deciding when to give the BCG vaccine.

- All healthy newborns should receive the BCG vaccine at discharge from the delivery unit, regardless of TB exposure or HIV exposure status.
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- Pharmacovigilance and reporting serious adverse events (SAE) remain important for all age groups.

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Updated BCG guidelines

The recommendations for providing BCG are summarised in *Figure 13* below.

In delivery unit	When to repeat BCG in infants who initiated TPT or TB treatment in the first 6 weeks of life	
All newborns should receive BCG at discharge (regardless of HIV status or TB exposure status[1]) If living with HIV, initiate ART immediately	**Repeat BCG after completion of TPT or TB treatment [2]** If the infant is also LHIV, they should be on ART, clinically well, and have a CD4 > 25% [3] to be able to receive BCG**	** If the criteria to receive BCG are not met, i.e., the infant is - Not on ART, or - Unwell, or - CD4 < 25% **→ Delay BCG until on ART and immunologically stable (CD4 > 25%)** **→ Start/continue TPT until the child is eligible to receive BCG**

1. In the current data-free context, the recommendation to give all infants BCG at birth is based on operational considerations. The decision to give BCG or not and initiate TPT are often made by different people and sometimes in different facilities. When an intervention requires more than one service provider, more than one service location and multiple patient visits, the neonate may miss getting a BCG when indicated at birth, either because of a lapse in communication and continuity of care or because multiple visits become burdensome to the family.
2. **BCG vaccination should be done 24 hours after the last anti-TB treatment dose.** If the infant received rifapentine give BCG from 5 days after the last dose, and if the infant received bedaquiline or clofazamine give BCG vaccination two months after the last dose.
3. After TPT/TB treatment is completed, an additional CD4 count may be done to determine if the infant meets the criteria for receiving BCG.

Figure 13 When to give the BCG vaccine

- **All** well children get Birth BCG
- If miss birth BCG: give catchup
- If start TPT/TB treatment within 6 weeks after BCG-> repeat (once stable on ART)
- BCG can be given 24 hrs after last dose
- For CLHIV: repeat when on ART, well, CD4>25%

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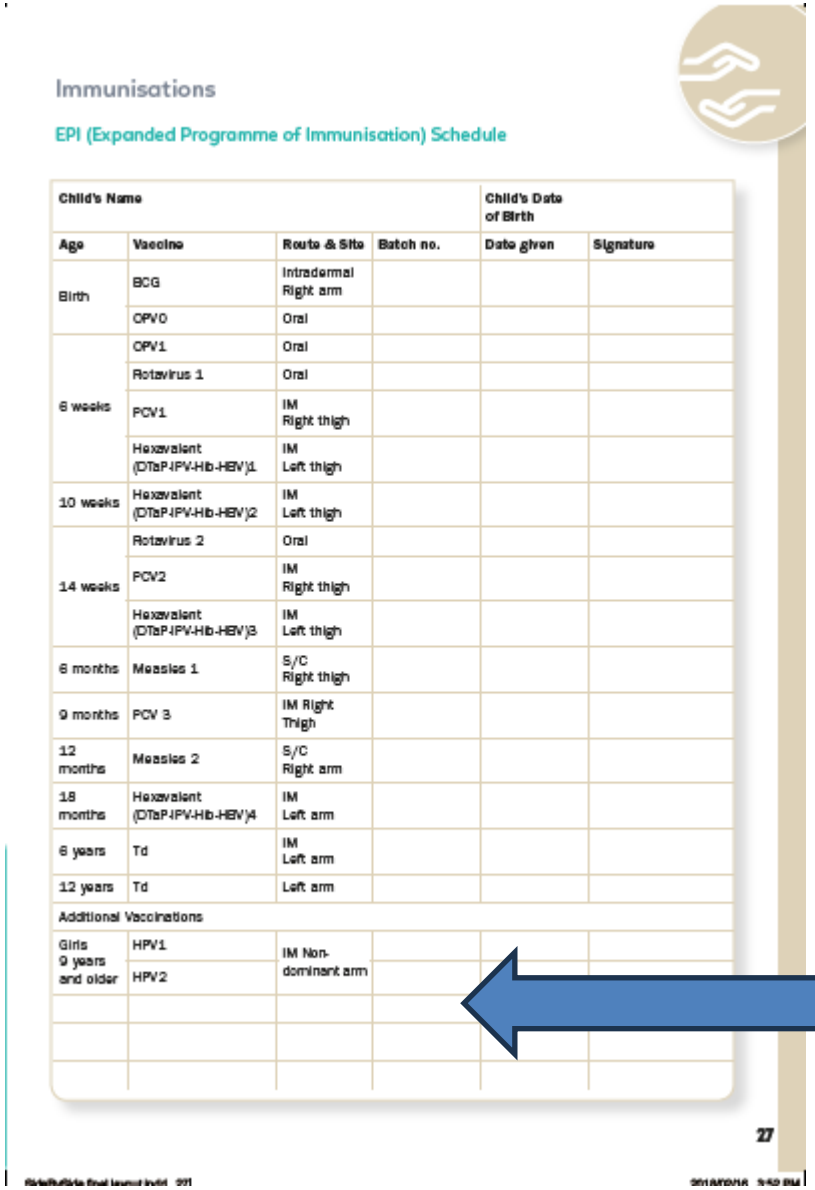
Updated BCG guidelines



Immunisations

EPI (Expanded Programme of Immunisation) Schedule

Child's Name				Child's Date of Birth	
Age	**Vaccine**	**Route & Site**	**Batch no.**	**Date given**	**Signature**
Birth	BCG	Intradermal Right arm			
	OPV0	Oral			
6 weeks	OPV1	Oral			
	Rotavirus 1	Oral			
	PCV1	IM Right thigh			
	Hexavalent (DTaP-IPV-Hib-HBV)1	IM Left thigh			
10 weeks	Hexavalent (DTaP-IPV-Hib-HBV)2	IM Left thigh			
14 weeks	Rotavirus 2	Oral			
	PCV2	IM Right thigh			
	Hexavalent (DTaP-IPV-Hib-HBV)3	IM Left thigh			
6 months	Measles 1	S/C Right thigh			
9 months	PCV 3	IM Right Thigh			
12 months	Measles 2	S/C Right arm			
18 months	Hexavalent (DTaP-IPV-Hib-HBV)4	IM Left arm			
6 years	Td	IM Left arm			
12 years	Td	Left arm			
Additional Vaccinations					
Girls 9 years and older	HPV1	IM Non-dominant arm			
	HPV2				

27

Repeat BCG can be captured here

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Childhood TB Case Studies

Juli Switala

Infectious Diseases Paediatrician

Paediatric TB Senior Technical specialist

The Aurum Institute

Patient NB

4 year old HIV unexposed child presents to the clinic with a 6 day history of fever and cough and is seen by a nurse who notes he has a fever of 37.8’C.
He has crepitations on the left side of his chest but is stable, has no features of respiratory distress.
He is miserable but fully awake and co-operates.
The mother is unaware of any contact with anyone with TB.

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Patient NB

- 4 years
- HIV unexposed – UNEXPOSED means nothing-> TEST him now (HIV Rapid: negative)
- No TB contact
- 6 day cough and documented fever
- Growing well
- L side crepitations – no other clinical concerns

What would you do next?

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Screening

Annexure 2: TB Screening Tool

health
Department: Health
REPUBLIC OF SOUTH AFRICA

NDP 2030

TB SYMPTOMS SCREENING TOOL FOR ADULTS AND CHILDREN

PATIENT DETAILS

Surname: _____ First Name: _____

Physical Address: _____ Age: _____

_____

Cell Phone number: _____ Patient Folder: _____

MEDICAL HISTORY

	Tick the appropriate answer (√)		
Close contact of a person with infectious TB	Yes	No	Unknown
Type of Index Case	DS-TB	Rif Resistant TB	MDR/XDR TB
Uncontrolled Diabetic	Yes	No	
HIV Status	Positive	Negative	Unknown
Mine worker/Ex-mine worker			
Other (Specify)			

TB SYMPTOMS

1.ADULTS

Symptoms (Tick √)	Yes	No
Current cough of any duration		
Persistent fever for 2 weeks or more		
Unexplained weight loss of >1.5kg in a month, or failure to gain weight in pregnant women		
Drenching night sweats		

2. CHILDREN

Symptoms (Tick √)	Yes	No
Current cough of any duration		
Persistent fever for 2 weeks or more		
Fatigue/less playful		
Weight loss or failure to thrive.		

If "yes" to one or more of these questions, consider TB

If the patient is coughing, collect sputum specimen and send it for TB-NAAT

If the patient is not coughing but has other symptoms, clinically assess the patient, or refer for further investigation.

Date of the last TB test: _____

2. CHILDREN

Symptoms (Tick √)	Yes	No
Current cough of any duration	✓	
Persistent fever for 2 weeks or more		
Fatigue/less playful		
Weight loss or failure to thrive.		

If "yes" to one or more of these questions, consider TB

If the patient is coughing, collect sputum specimen and send it for TB-NAAT

If the patient is not coughing but has other symptoms, clinically assess the patient, or refer for further investigation.

Date of the last TB test: _____

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TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

- **Screen for TB symptoms and TB exposure** in all children at every healthcare encounter
- **Identify high-risk children** needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not e.g. CLHIV

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]
Cough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, lethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care
Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition
Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR**
±
any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

Interpretation

CXR or imaging suggestive of TB and/or Positive result on any diagnostic test

Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.

Follow-up on results of any culture and DST, as applicable. **Ensure response to treatment,** especially if TB was clinically diagnosed.
Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.
4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
5. A decision to start TB treatment should not be delayed if the necessary investigations are not available, particularly in children at higher risk of developing severe disease, such as young children, malnourished children or those living with HIV.

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]	Score
Cough > 2 weeks	+ 5
Fever > 2 weeks	+ 10
Reduced playfulness/energy	+ 4
Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

When to go further

What if:

He returns in 2 weeks and still has a cough?
OR

Is living with HIV
OR
Is under 2 years ?
OR
-Has Severe Acute Malnutrition?

Prolonged symptoms

High Risk Group

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TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

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YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM[1]** ?

YES → Stabilise and refer to/admit for inpatient care
Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
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3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition
Follow up in 1-2 weeks [3]

Investigations

If possible, **perform CXR**
±
any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test[4], e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
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YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
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Total score	?

Assign a score to each of the child's symptoms.
If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

Adding puzzle pieces

Potential investigations:

- **TST** (if **no** known contact and <5 years)
- **U-LAM** (if qualifies)
- **CXR** (or other relevant imaging)
- **Microbiological tests**:

A) Samples	B) Request
Sputum	NAAT
Induced Sputum	Culture
Gastric Aspirate	+/- Resistance testing
Stool	
FNA	
Other	

Note: microscopy not usually recommended for young children

- **Other relevant tests**: HIV
  CSF , effusions etc

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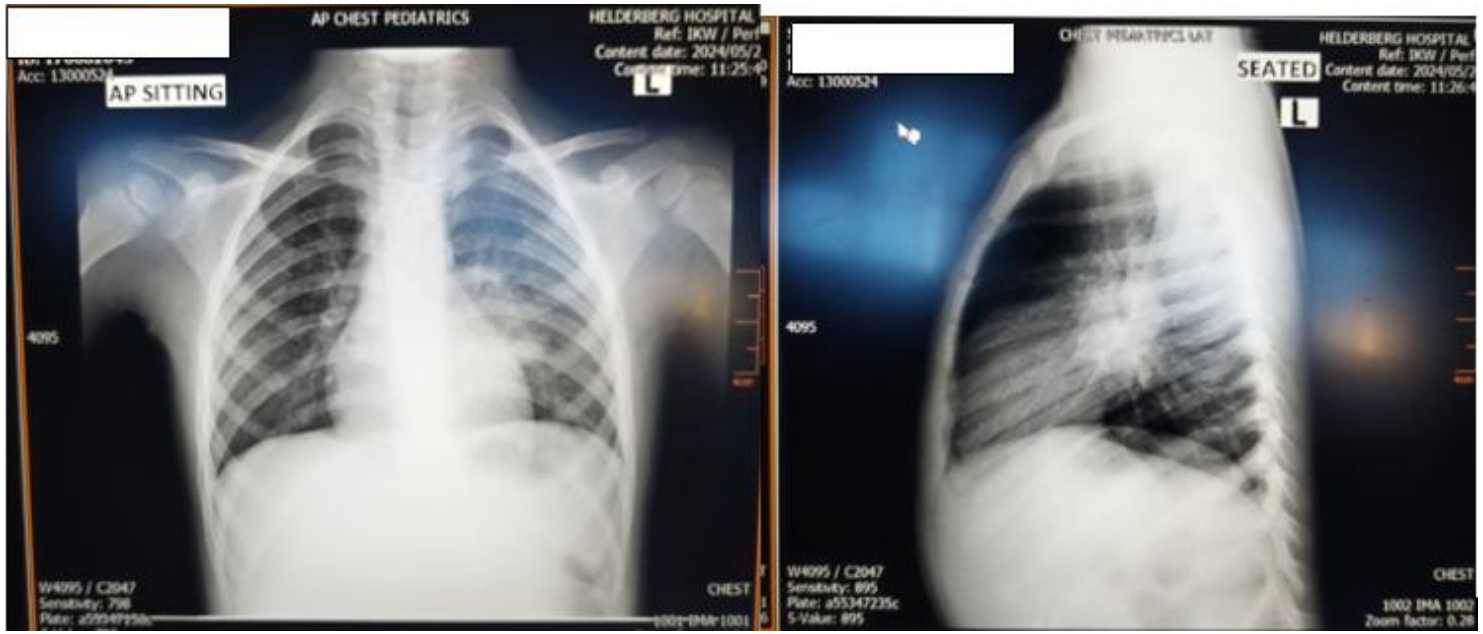
Adding puzzle pieces

Potential investigations:

- **TST** – Mantoux reaction 11mm
- **U-LAM** **-** not applicable
- **CXR** : hilar lymphadenopathy
- **Microbiological tests**: not possible at the PHC
- **Other relevant tests**: HIV : negative



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NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care
Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR**
±
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and

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Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

Pick a regimen

Pick a regimen based on:

- Known susceptibility (if no results for child – check any possible source case results)
- Pulmonary vs extra pulmonary vs TBM/miliary
- Severe vs non severe
- Short course eligibility
- Consider: previous drug exposure, other medications (HIV) , available formulations

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Assess for short course eligibility

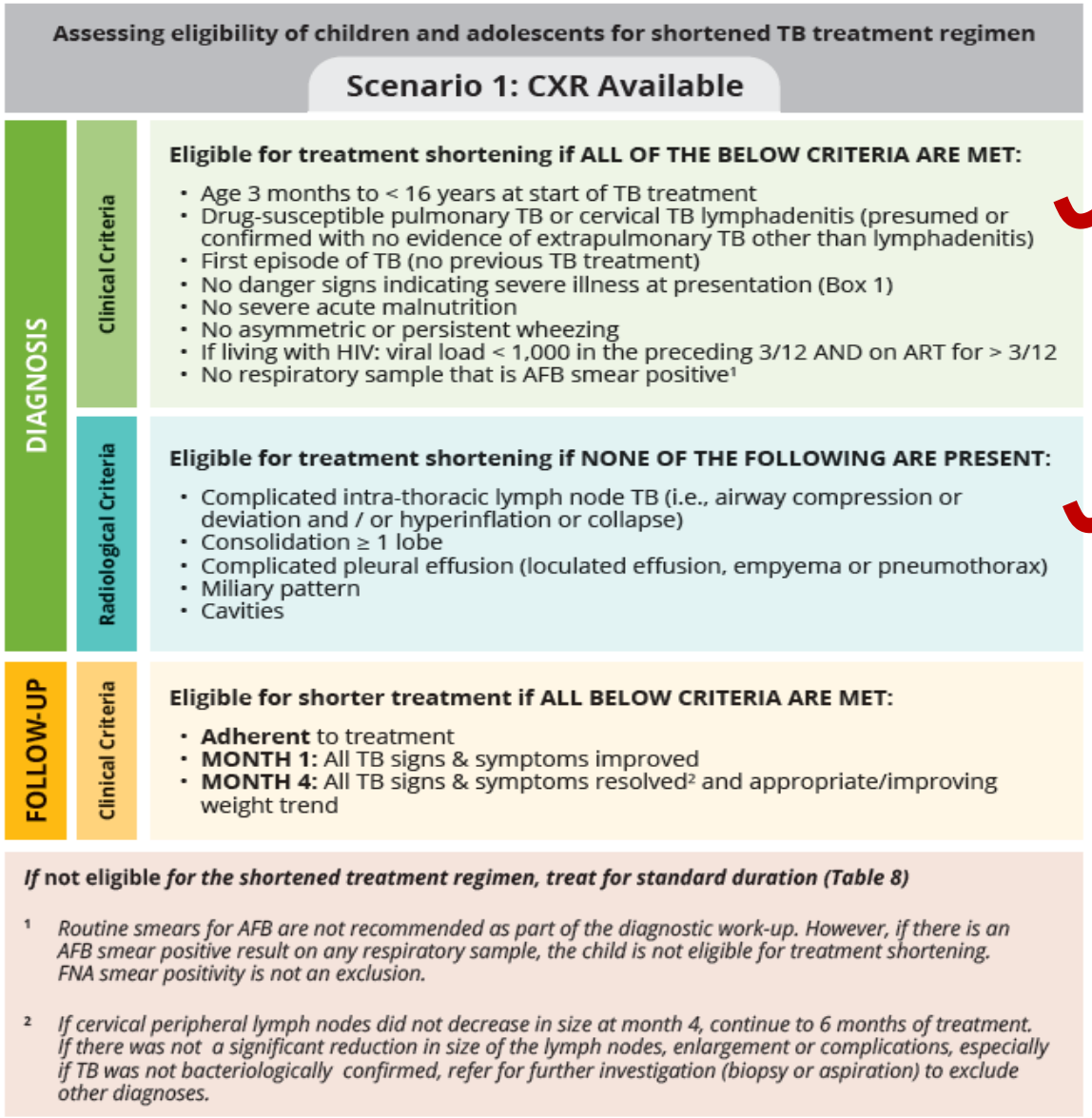

Figure 10 Assessing children and adolescents' eligibility for treatment shortening when CXR is available

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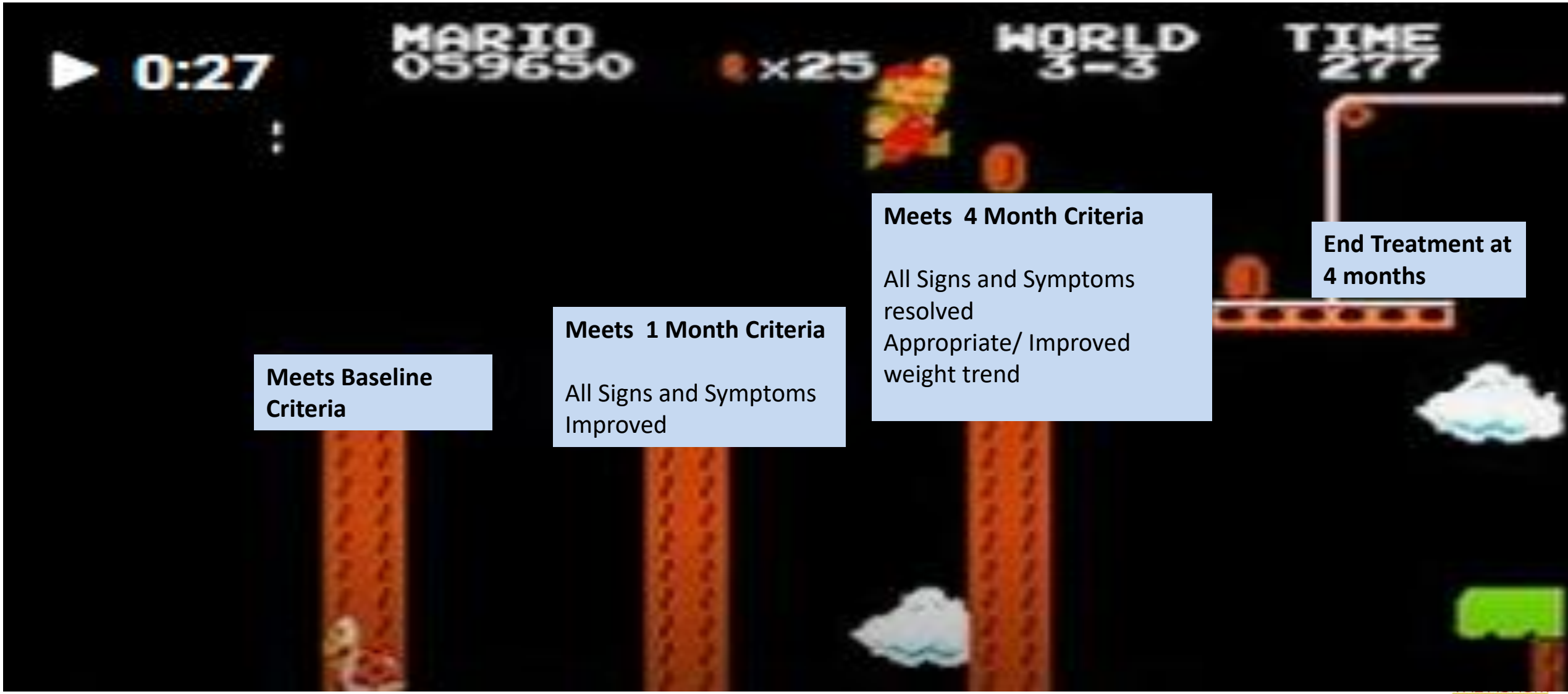
Short course eligibility – 3 checks

Short course eligibility



DS-TB Regimens

	Intensive phase Once daily, 7 days a week		Continuation phase Once daily, 7 days a week		
	Duration 2 months		Non-severe TB Duration: 2 months	Severe PTB & most EPTB: Duration: 4 months	Bone & joint TB: Duration: 10 months
Target dose (dose range) (mg/kg/day)	Isoniazid (H): 10 (7-15), Rifampicin (R): 15 (10-20), Pyrazinamide (Z): 35 (30-40), Ethambutol (E): 20 (15-25)				
Formulation Body weight (kg)	HRZ 50/75/150 mg dispersible tablet (scored) OR 50/75/150 mg/4 ml suspension *	E 400 mg tablet (not scored) OR 400 mg/8 ml suspension *	HR 50/75 mg dispersible tablet (scored) OR 50/75 mg/4 ml suspension *		

2RHZE/2RH

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It’s not just about medication

You are not done yet:

- Notify as **Clinically Diagnosed Pulmonary TB** (only Confirmed if NAAT/microscopy/culture positive)
- Reverse tracing to find adult/adolescent source
- Write a note in RTHC and plot weight
- Explain medication to caregivers and what to expect
- Follow up/ Linkage plans

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TB is a family disease

Patient NB's mother is also noted to be coughing, and she provides a sputum which returns a result:

TB-NAAT: MTB Complex Detected
Rifampicin : Sensitive.
Smear: 2+ AFB

She is managed according to adult guidelines, but contact history reveals that there are 2 other children in the home: her 8 year old son (SB)and her sister's 1 month old baby (KL). Both are tested for HIV and are negative.

Because of their contact history both children need to get SOMETHING – either TPT or treatment – but how would you decide which?

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Patient SB

8 year old:

History and examination reveals that the 8 year old is asymptomatic, eats ‘everything in the house’ and has no clinical findings of concern.

2. CHILDREN

Symptoms (Tick √)	Yes	No
Current cough of any duration		
Persistent fever for 2 weeks or more		
Fatigue/less playful		
Weight loss or failure to thrive.		

If "yes" to one or more of these questions, consider TB

If the patient is coughing, collect sputum specimen and send it for TB-NAAT

If the patient is not coughing but has other symptoms, clinically assess the patient, or refer for further investigation.

Date of the last TB test: _____

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TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

Screen for TB symptoms and TB exposure in all children at every healthcare encounter

Identify high-risk children needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not e.g. CLHIV

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]

Cough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, lethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care Once stabilised, continue TB work-up

STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR** ± any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

Interpretation

CXR or imaging suggestive of TB and/or Positive result on any diagnostic test

Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.

Follow-up on results of any culture and DST, as applicable. **Ensure response to treatment,** especially if TB was clinically diagnosed.
Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

YES

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.
4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
5. A decision to start TB treatment should not be delayed if the necessary investigations are not available, particularly in children at higher risk of developing severe disease, such as young children, malnourished children or those living with HIV.

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]	Score
Cough > 2 weeks	+ 5
Fever > 2 weeks	+ 10
Reduced playfulness/energy	+ 4
Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

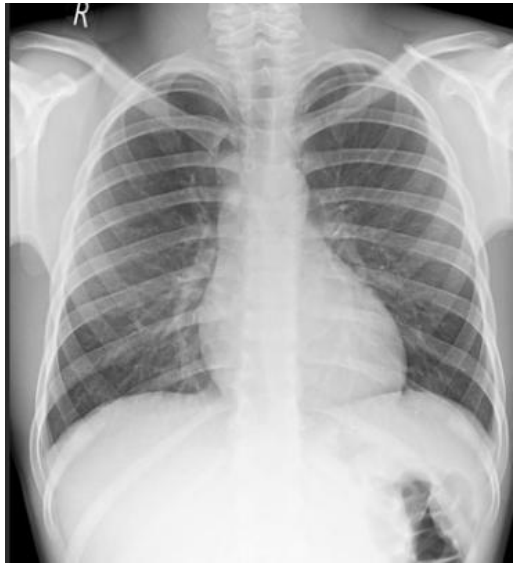
Adding puzzle pieces

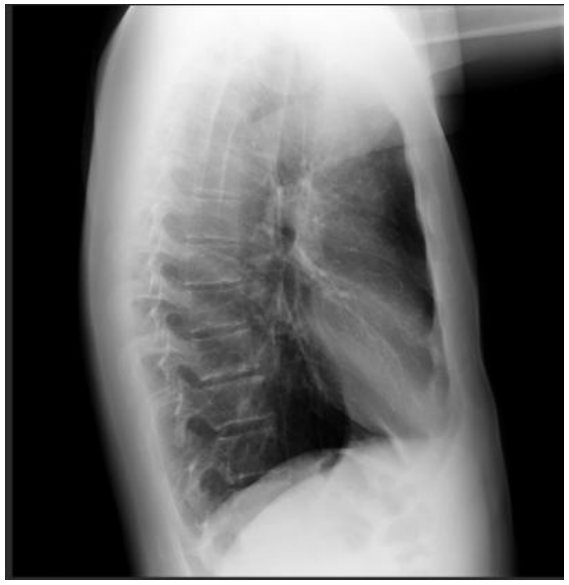
Potential investigations :

- **TST** – not helpful if known contact
- **U-LAM –** not eligible
- **CXR** – if easily available, perform CXR (if unavailable: not a barrier to TPT if asymptomatic)
- **Microbiological tests**:

  If < 25kg: pulmonary sample can be taken if symptomatic (if unavailable: not a barrier to TB treatment)

Other relevant tests: HIV negative





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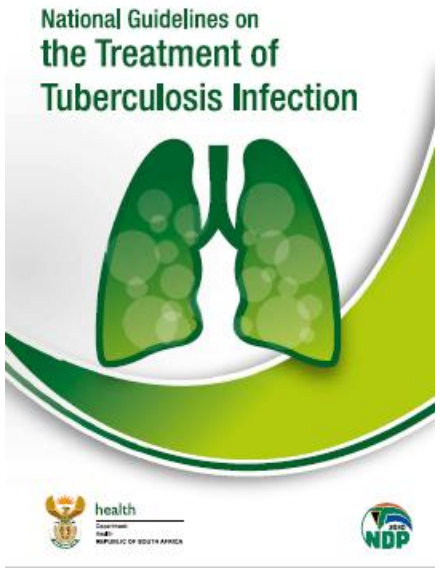
Pick a regimen…

Pick a TPT regimen based on:

- Known susceptibility of source
- Weight (>25kg considered ‘adult’)
- HIV status (ART and TPT interactions)
- Short course eligibility (3HP)
- Consider: previous drug exposure, other medications (HIV) , available formulations



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Pick a regimen…

TPT options:

HIV neg (<25kg)
3RH

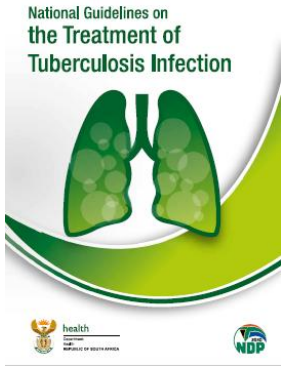
HIV pos (<25kg)
6H

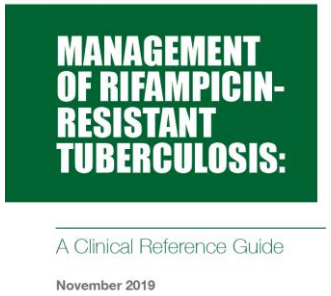
HIV neg (>25kg)
3HP

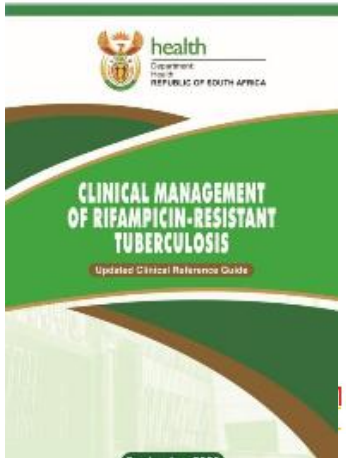
HIV pos (>25kg)
-not on DTG OR suppressed 3HP
- on DTG OR not suppressed 12H

INH monoR: 4R
Rif monoR: 6H (if confirmed)
FQN R: discuss with expert

MDR: 6Lfx (or 6Lfx/H/E)







It’s not just about medication

You are not done yet:

- Notify in TPT register
- Write a note in RTHC and plot weight
- Explain medication to caregivers and what to expect
- Follow up/ Linkage plans
- Follow up results if specimens taken

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Patient KL

1 month old:

Her mother says she is ok. She has had a fever twice this week and once the previous week, but is currently apyrexial. She doesn't cough but her mom says she snores a bit for the last week and is a bit fussy so her mother and is trying different formulas because she isn't drinking breastmilk well. She is stable on examination, and apart from a very subtle wheeze, has no symptoms of concern.

2. CHILDREN

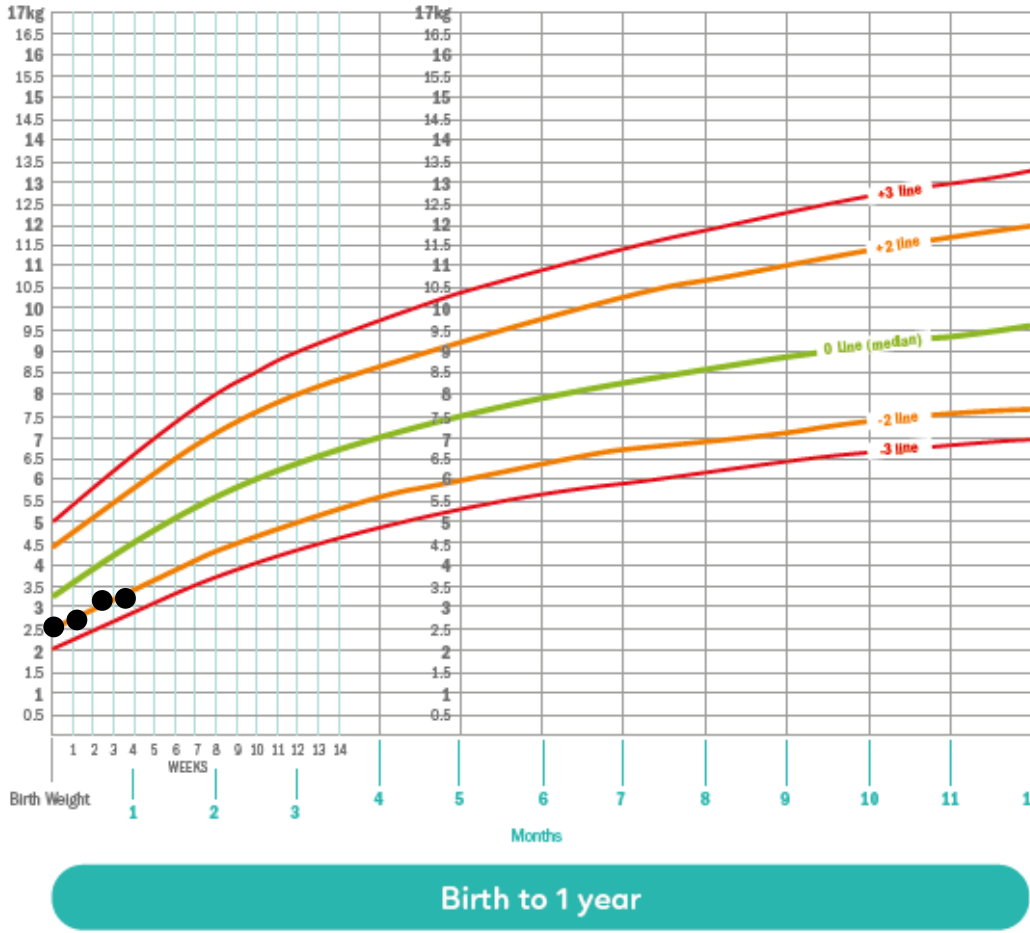
Symptoms (Tick √)	Yes	No
Current cough of any duration		
Persistent fever for 2 weeks or more		
Fatigue/less playful		
Weight loss or failure to thrive.		

If "yes" to one or more of these questions, consider TB

If the patient is coughing, collect sputum specimen and send it for TB-NAAT

If the patient is not coughing but has other symptoms, clinically assess the patient, or refer for further investigation.

Date of the last TB test: _____



TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

- **Screen for TB symptoms and TB exposure** in all children at every healthcare encounter
- **Identify high-risk children** needing a TB assessment regardless of whether TB symptoms or TB exposure are present or not e.g. CLHIV

History and Clinical Examination

Are there symptoms and signs suggestive of pulmonary or extrapulmonary TB? [1]

…ough, especially if persistent and fails to improve, unexplained fever/drenching night sweats, weight loss/faltering growth, …ethargy/reduced playfulness, visible neck swelling, blood-stained sputum, headache, persistent vomiting (without diarrhoea)

NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger si…ns** requiring urgent medical care? (See Box 1), or do s…mptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care Once stabilised, continue TB work-up

STABILISED

NO

…s the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR** ± any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
If no clear history of contact with a TB source case, consider doing a TST if any uncertainty remains about a TB diagnosis and the child is < 5 years old

Interpretation

CXR or imaging suggestive of TB and/or Positive result on any diagnostic test

Treat for TB
Determine the starting regimen and duration of treatment based on clinical, radiological, and bacteriological disease severity, and most likely drug susceptibility profile.
Notify even if no microbiological confirmation.

Follow-up on results of any culture and DST, as applicable. **Ensure response to treatment,** especially if TB was clinically diagnosed.
Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

YES ← Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

NO

YES ← Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
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4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
5. A decision to start TB treatment should not be delayed if the necessary investigations are not available, particularly in children at higher risk of developing severe disease, such as young children, malnourished children or those living with HIV.

Note: The TB Treatment Decision Algorithm does not replace sound clinical judgement.

A clinician could still choose to start TB treatment, even if the symptom score is less than 11, or consider other childhood illnesses to be present, even if the symptom score is ≥ 11

Clinical feature [1]	Score
Cough > 2 weeks	+ 5
Fever > 2 weeks	+ 10
Reduced playfulness/energy	+ 4
Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

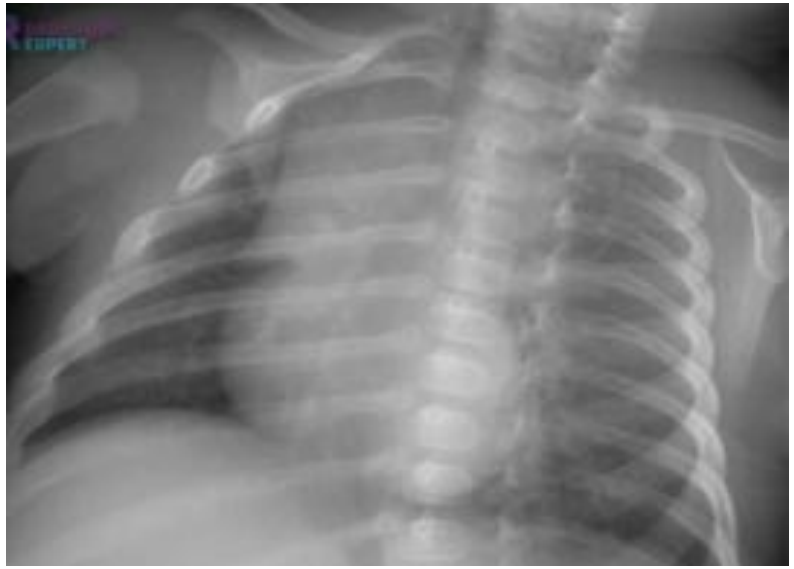
Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

Adding puzzle pieces

Potential investigations:

- **TST** – not helpful if known contact
- **U-LAM –** not eligible
- **CXR** – very helpful in this child
- **Microbiological tests**: Gastric Aspirate – request : NAAT, culture
- **Other relevant tests**: HIV test



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TB Treatment Decision Algorithm

Evaluate For TB

Screen

Identify children who may have TB or TB exposure

- **Screen for TB symptoms and TB exposure** in all children at every healthcare encounter
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NO → If asymptomatic, offer TPT if eligible See the 2023 TPT guideline for details

YES

Are there **danger signs** requiring urgent medical care? (See Box 1), or do symptoms and signs suggest **TBM**[1] ?

YES → Stabilise and refer to/admit for inpatient care
Once stabilised, continue TB work-up
STABILISED

NO

Is the child
1. aged <2 years, or
2. living with HIV[2], or
3. severely and acutely malnourished?

regardless of symptom duration

NO → Is the child having persisting (>2 weeks), non-remitting features typical of TB

NO → Treat most likely non-TB condition
Follow up in 1-2 weeks [3]

YES

YES

Investigations

If possible, **perform CXR**
±
any other imaging as indicated for possible extrapulmonary TB

and

If possible, **collect a sample for a diagnostic test**[4], **e.g., TB-NAAT ± culture, and/or urine LF-LAM (if the child is LHIV)**
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Confirm drug susceptibility and response to treatment of any known TB source patient

CXR or imaging not suggestive of TB /unavailable, and diagnostic samples negative/unavailable[5]

Is there a close or household **TB contact**[3] in the previous year, **or positive TST**

YES → **Treat for TB**

NO

Do symptoms and signs indicate TB?
If uncertain, use the the **symptom and signs score to the right.**

YES → **Treat for TB**

NO

Consider other diagnoses.
Review in 1-2 weeks until symptom resolution.
Reconsider TB diagnosis or refer if symptoms persist.
Follow-up on any culture and DST results of the child, as applicable
If TB excluded and symptoms resolve offer TPT if eligible.
Refer to the TPT guideline

1. Please see Table 2 and Table 3 for additional details on the clinical features of TB.
2. Ensure HIV status has been established and managed appropriately.
3. If not severely ill, and if diagnosis or persistence (> 2 weeks) of symptoms are uncertain, consider a follow-up evaluation in 1-2 weeks to reassess weight and persistence of, or improvement in, symptoms. This decision will be influenced by other factors, incl. the likelihood of the child returning for reassessment. The child should be encouraged to return earlier if there is any deterioration of the symptoms.
4. Every effort should be made to establish microbiological confirmation of TB and drug susceptibility, even in young children. A range of samples can be collected, as detailed in Table 5. However, it is especially important to obtain samples for children exposed to a RR-TB source case and those with complicated or severe disease.
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Weight loss	+ 5
Haemoptysis	+ 9
Night sweats	+ 6
Enlarged typical lymph nodes	+ 7
Tachycardia	+ 4
Tachypnoea/fast breathing	+ 2
Total score	?

Assign a score to each of the child's symptoms. If the sum of the scores is **≥ 11**, treat for TB

Always plot weight and document findings in the Road To Health Chart, even if the decision is made NOT to start TB treatment.

Figure 6 TB Treatment Decision Algorithm

Pick a regimen…

Pick a regimen based on:

- Known susceptibility (if no results for child – check any possible source case results)
- Pulmonary vs extra pulmonary vs TBM/miliary
- Severe vs non severe
- Short course eligibility
- Consider: previous drug exposure, other medications (HIV) , available formulations

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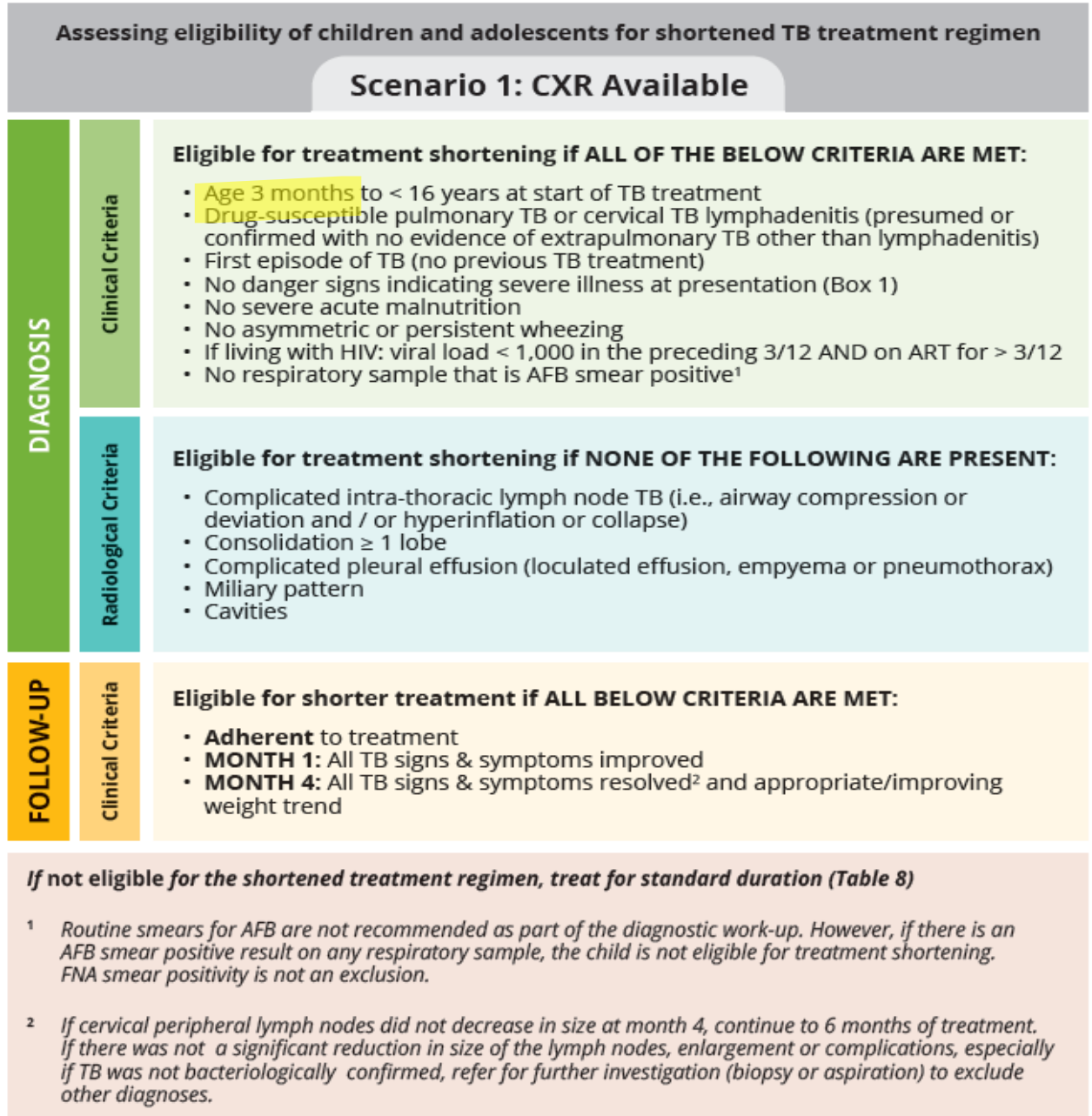

Figure 10 Assessing children and adolescents' eligibility for treatment shortening when CXR is available

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DS-TB Regimens

	Intensive phase Once daily, 7 days a week		Continuation phase Once daily, 7 days a week		
	Duration 2 months		Non-severe TB Duration: 2 months	Severe PTB & most EPTB: Duration: 4 months	Bone & joint TB: Duration: 10 months
Target dose (dose range) (mg/kg/day)	Isoniazid (H): 10 (7-15), Rifampicin (R): 15 (10-20), Pyrazinamide (Z): 35 (30-40), Ethambutol (E): 20 (15-25)				
Formulation Body weight (kg)	HRZ 50/75/150 mg dispersible tablet (scored) OR 50/75/150 mg/4 ml suspension *	E 400 mg tablet (not scored) OR 400 mg/8 ml suspension *	HR 50/75 mg dispersible tablet (scored) OR 50/75 mg/4 ml suspension *		

2RHZE★/4RH

★ May substitute Ethionamide

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It’s not just about medication

You are not done yet:

- Notify as **‘Clinically Diagnosed TB’**
- Write a note in RTHC and plot weight
- Explain medication to caregivers and what to expect
- Follow up/ Linkage plans
- Follow up results of culture
- Increase doses according to weight
- Repeat BCG after TB treatment

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Repeat BCG

The recommendations for providing BCG are summarised in *Figure 13* below.

In delivery unit	When to repeat BCG in infants who initiated TPT or TB treatment in the first 6 weeks of life	
All newborns should receive BCG at discharge (regardless of HIV status or TB exposure status[1]) If living with HIV, initiate ART immediately	Repeat BCG after completion of TPT or TB treatment [2] If the infant is also LHIV, they should be on ART, clinically well, and have a CD4 > 25% [3] to be able to receive BCG**	** If the criteria to receive BCG are not met, i.e., the infant is - Not on ART, or - Unwell, or - CD4 < 25% **→ Delay BCG until on ART and immunologically stable (CD4 > 25%)** **→ Start/continue TPT until the child is eligible to receive BCG**

1. In the current data-free context, the recommendation to give all infants BCG at birth is based on operational considerations. The decision to give BCG or not and initiate TPT are often made by different people and sometimes in different facilities. When an intervention requires more than one service provider, more than one service location and multiple patient visits, the neonate may miss getting a BCG when indicated at birth, either because of a lapse in communication and continuity of care or because multiple visits become burdensome to the family.
2. **BCG vaccination should be done** 24 hours after the last anti-TB treatment dose. If the infant received rifapentine give BCG from 5 days after the last dose, and if the infant received bedaquiline or clofazamine give BCG vaccination two months after the last dose.
3. After TPT/TB treatment is completed, an additional CD4 count may be done to determine if the infant meets the criteria for receiving BCG.

Figure 13 When to give the BCG vaccine

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Thank You

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