

# Paediatric tuberculosis and advanced HIV disease

Irma Kruger

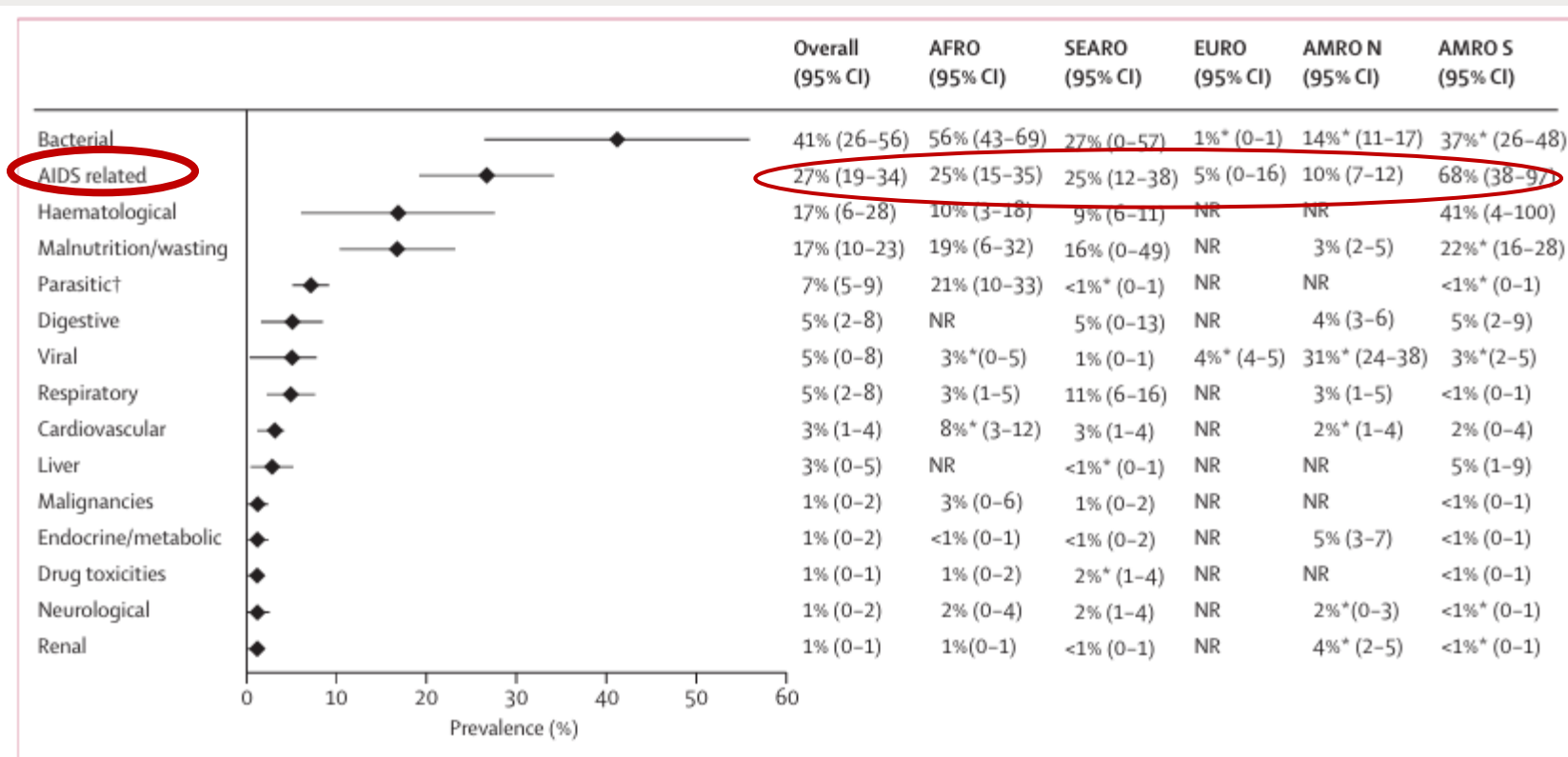
University of Cape Town

Red Cross War Memorial Children's Hospital

# Which of these children have **advanced** HIV disease?

- a) 3-month-old with severe pneumonia and CD4 count  $> 25 \%$
  - b) 6 weeks old growing well on  $+1$  z-score, CD4  $> 30 \%$ , asymptomatic, diagnosed during a PMTCT visit
  - c) 2-year-old with moderate malnutrition and CD4  $> 25 \%$
  - d) 10-year-old with TB
- Your company name
- a) All the above

# Hospital admissions in children

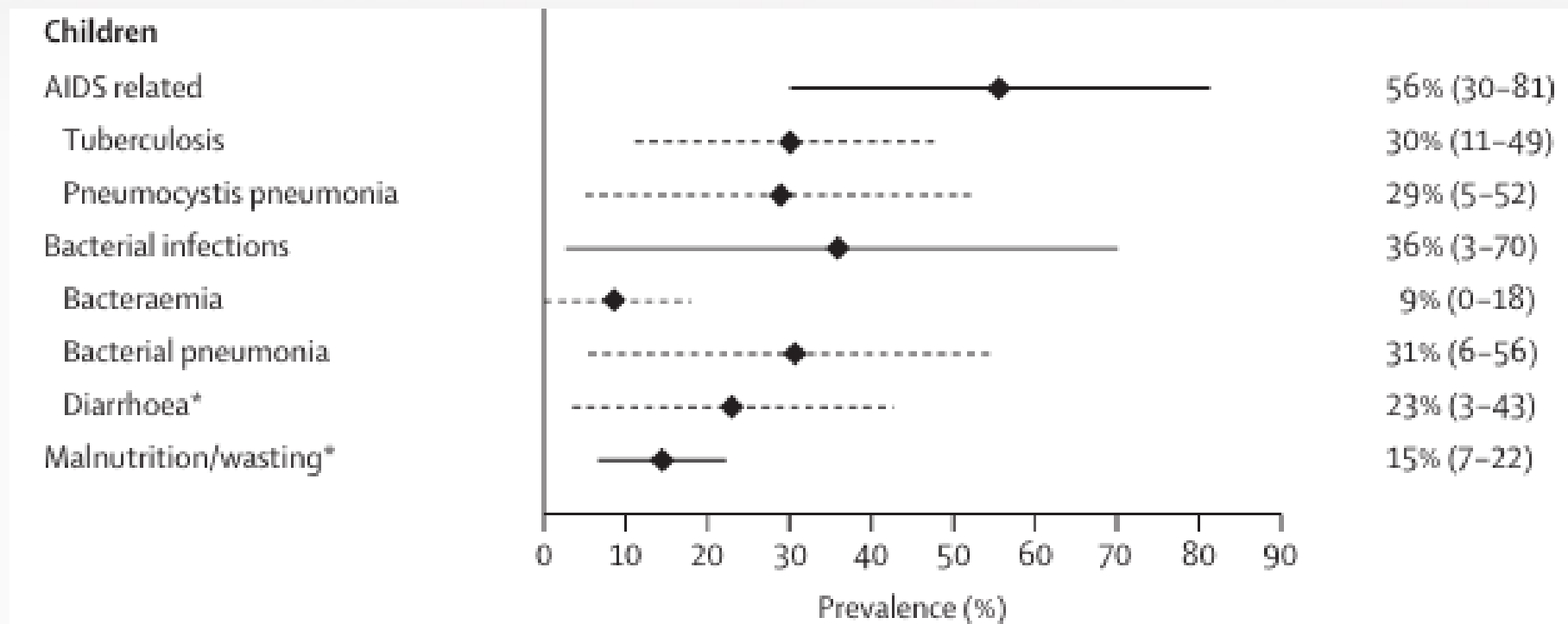


**Figure 3: Causes of hospital admission in children**

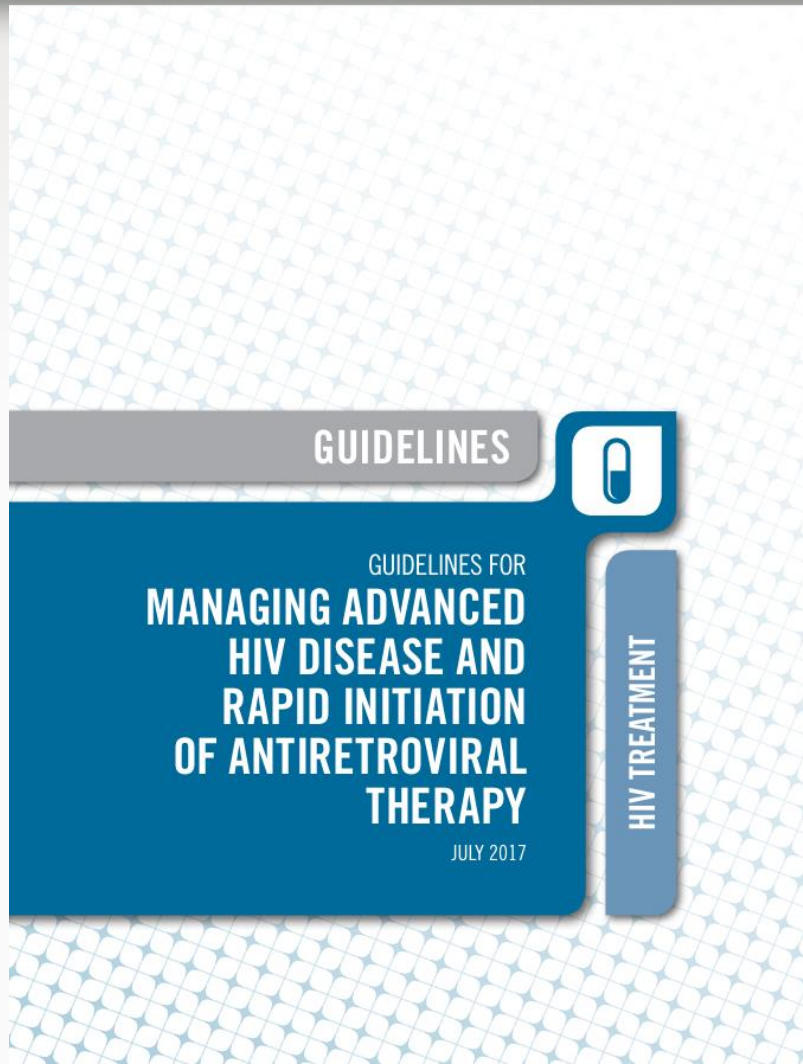
AFRO=African region. AMRO N=region of the Americas (North). AMRO S=region of the Americas (South and Central). EURO=European region. EMRO=eastern Mediterranean region. NR=not reported. SEARO=southeast Asia region. WPRO=western Pacific region. \*Only one study contributed to the estimate. †Mainly malaria.

# Mortality in hospital

## Causes of mortality in HIV + children admitted to hospital



# The WHO plan 2017



## Recommendations

### Management of advanced HIV disease

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease.

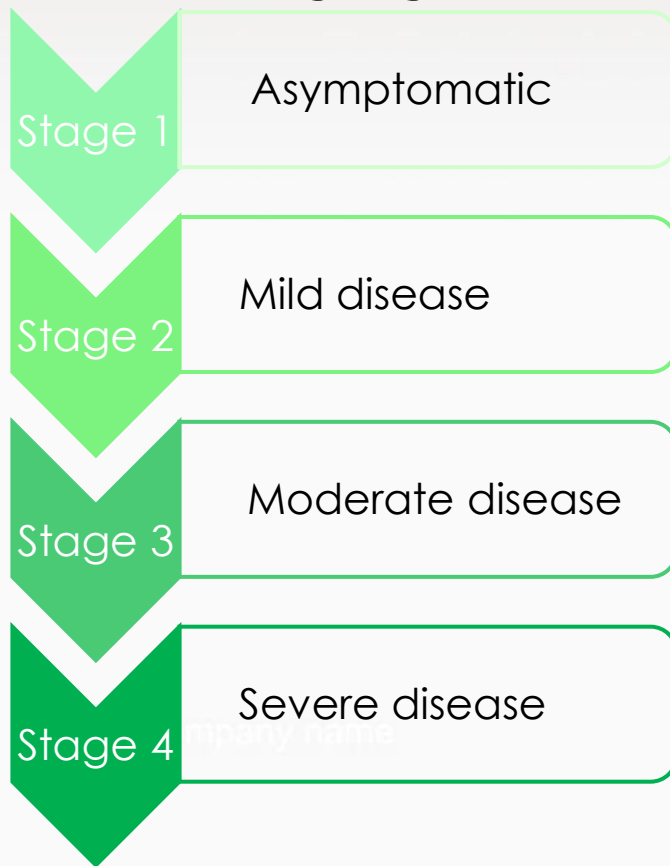
*(Strong recommendation, moderate-quality evidence)*

# The definition of advanced HIV disease in children is:

- a) Any child with HIV less than 5 years old and any child older than five years with CD4 < 200 or WHO Stage 3 or 4 disease
- b) All children less than 10 years regardless of CD4 count
- c) All children less than 5 years and must have CD4 count less than 200
- d) Any child older than 5 years with a CD4 count of less than 500
- e) All the above

# A quick reminder...

## WHO staging



## Immunological classification

Severity	< 12 months	13 – 59 months	> 5 years
None	> 35 %	> 25 %	> 500 cells/ml
Mild	25 -34 %	20 – 24 %	350 -499 cells/ml
Advanced	20 – 24 %	15 – 19 %	200 – 359 cells/ml
Severe	< 20 %	< 15 %	< 200 cells/ml

# Advanced HIV disease in children and adolescents

- Children 5 years and older
  - WHO stage 3 or 4
  - or
  - CD4 cell count  $<200$  cells/mm<sup>3</sup>
- All children younger than five years
  - Considered to have advanced disease

# The definition of advanced HIV disease in children is:

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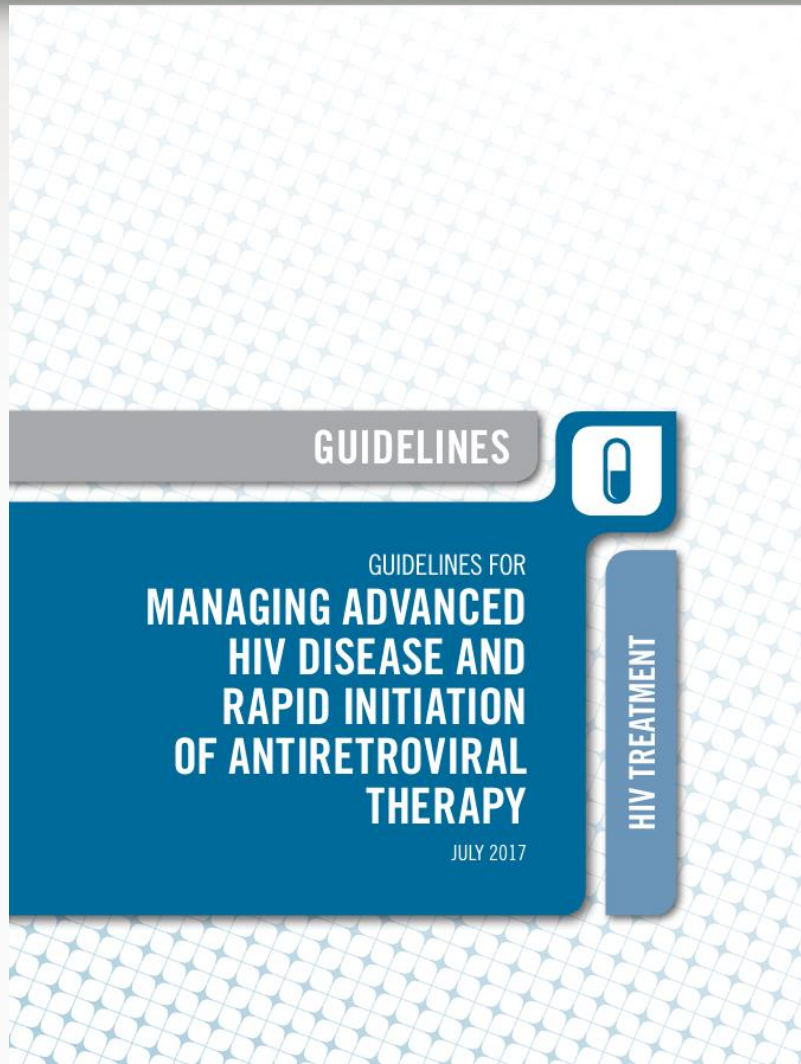
# Which of these children have **advanced** HIV disease?

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- b) 6 weeks old growing well on  $+1$  z-score, CD4  $> 30 \%$ , asymptomatic, diagnosed during a PMTCT visit
- c) 2-year-old with moderate malnutrition and CD4  $> 25 \%$
- d) 10-year-old with TB

Your company name

**a) All the above**

# The WHO plan 2017



## Recommendations

### Management of advanced HIV disease

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease.

*(Strong recommendation, moderate-quality evidence)*

# Mortality on ART

- Children living with HIV **< 1 year** of age on ART
  - More likely to die compared to PLHIV on ART 5 -14 years of age (CMR 7.6)
- Children living with HIV **1 - 4 years** of age on ART
  - More likely to die compared to those 5 -14 years of age (CMR 4.2)

# WHO guidelines for children



TECHNICAL BRIEF – JULY 2020

## PACKAGE OF CARE FOR CHILDREN AND ADOLESCENTS WITH ADVANCED HIV DISEASE: **STOP AIDS**



# STOP AIDS

## Screen\*

### TB

- Screen for TB using a clinical algorithm<sup>b</sup> followed by X-ray when indicated and if available
- Use the following diagnostic tests to confirm TB as applicable:<sup>c</sup>
  - Rapid molecular diagnostic (Xpert® MTB/RIF or Ultra) on (induced) sputum, stool, gastric aspirate or nasopharyngeal aspirate or other extrapulmonary samples if relevant
  - Lateral flow urine lipoarabinomannan (LF-LAM) assay<sup>d</sup>

### Cryptococcal infection among adolescents

- Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic

### Malnutrition

- Weight-for-height
- Height-for-age
- Mid-upper arm circumference among children 2-5 years old

## Treat

TB, severe pneumonia, severe bacterial infections, cryptococcal meningitis and severe acute malnutrition according to WHO guidelines

Your company name

# Screen, Treat, Optimize and Prevent AIDS

## Optimize

Rapid antiretroviral therapy start – within seven days with optimal regimens\*  
Antiretroviral therapy counselling

## Prevent

Bacterial infections and *Pneumocystis pneumonia*

- Co-trimoxazole prophylaxis

### TB

- TB preventive treatment

Cryptococcal meningitis among adolescents

- Fluconazole pre-emptive therapy

### Vaccinations

- Pneumococcal vaccine
- Human papillomavirus
- Measles
- BCG



# What does this mean in practice....

18 month old boy

- Presents with chronic diarrhoea

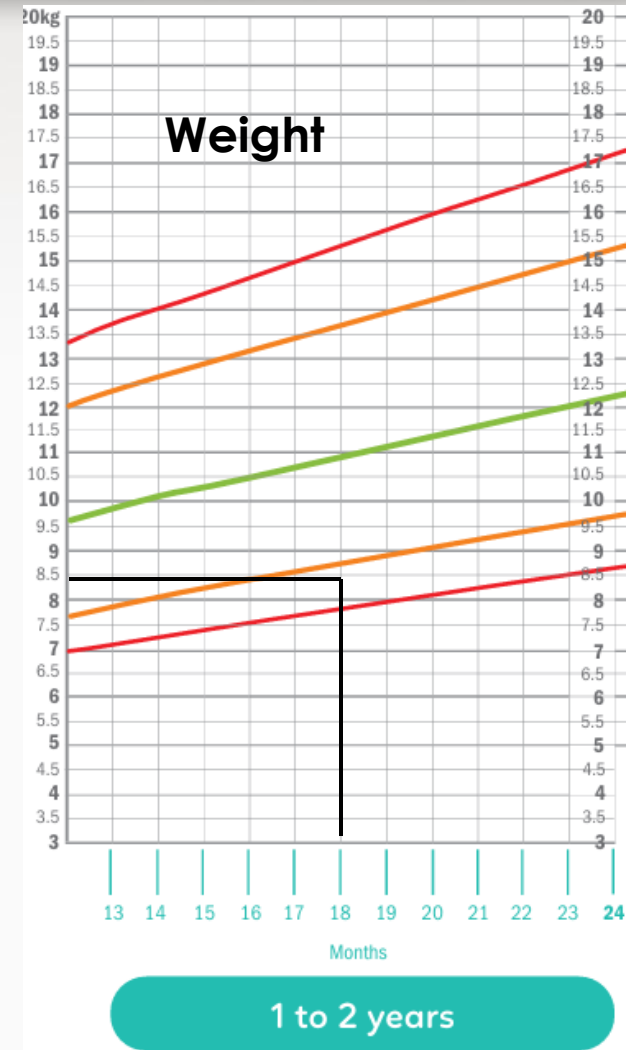
His mom also reports

- Skin lesions
- “He is just not happy”
- Not wanting to play
- Never really wants to eat



# Anthropometry

- Weight: 8.4 kg / Height: 73 cm

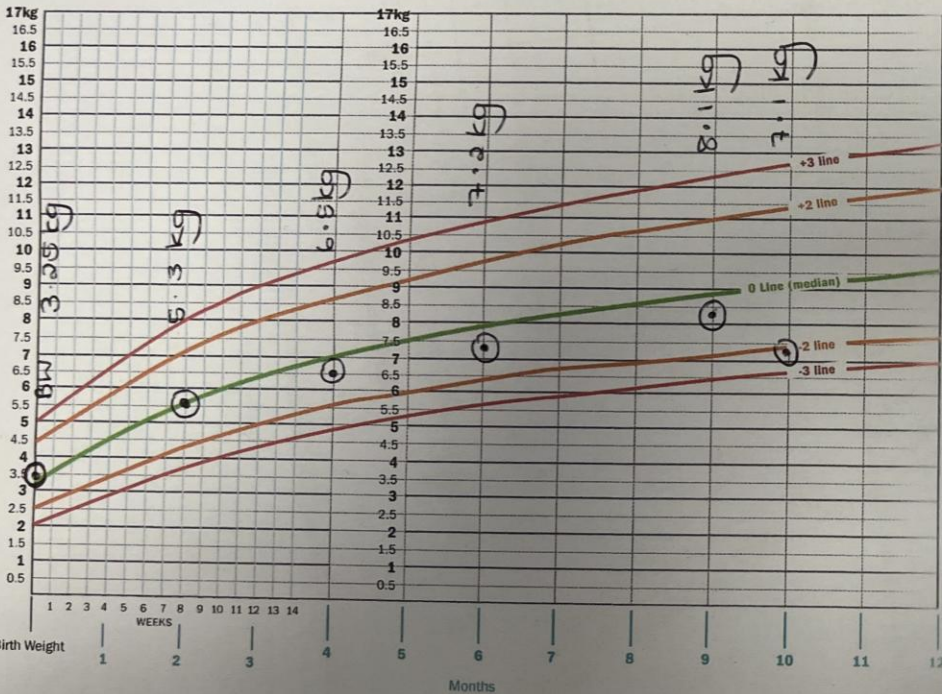
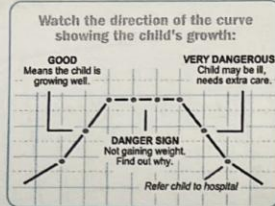
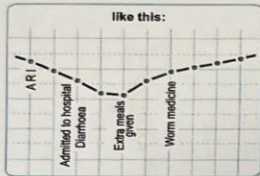


# Weight-for-age

## BOYS: Weight-for-age charts

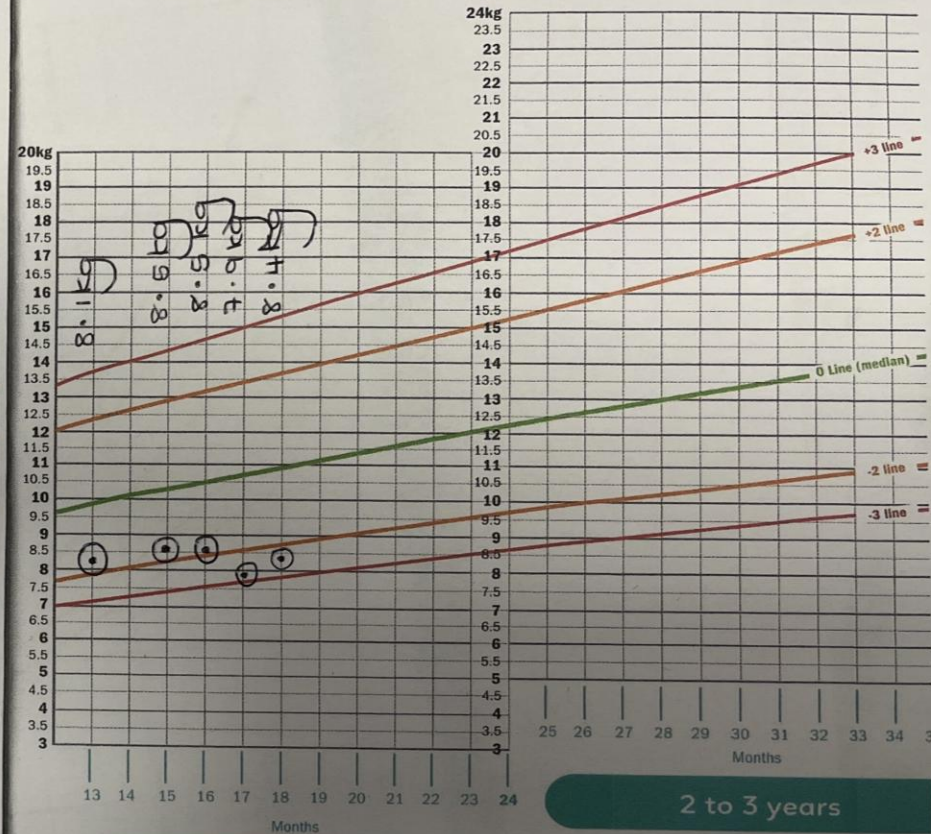
### Write on the chart

- Any illness e.g. diarrhoea, ARI, etc.
- Admission to hospital,
- Solids introduced,
- Breastfeeding stopped,
- Birth of next child, etc.



Birth to 1 year

## BOYS: Weight-for-age charts



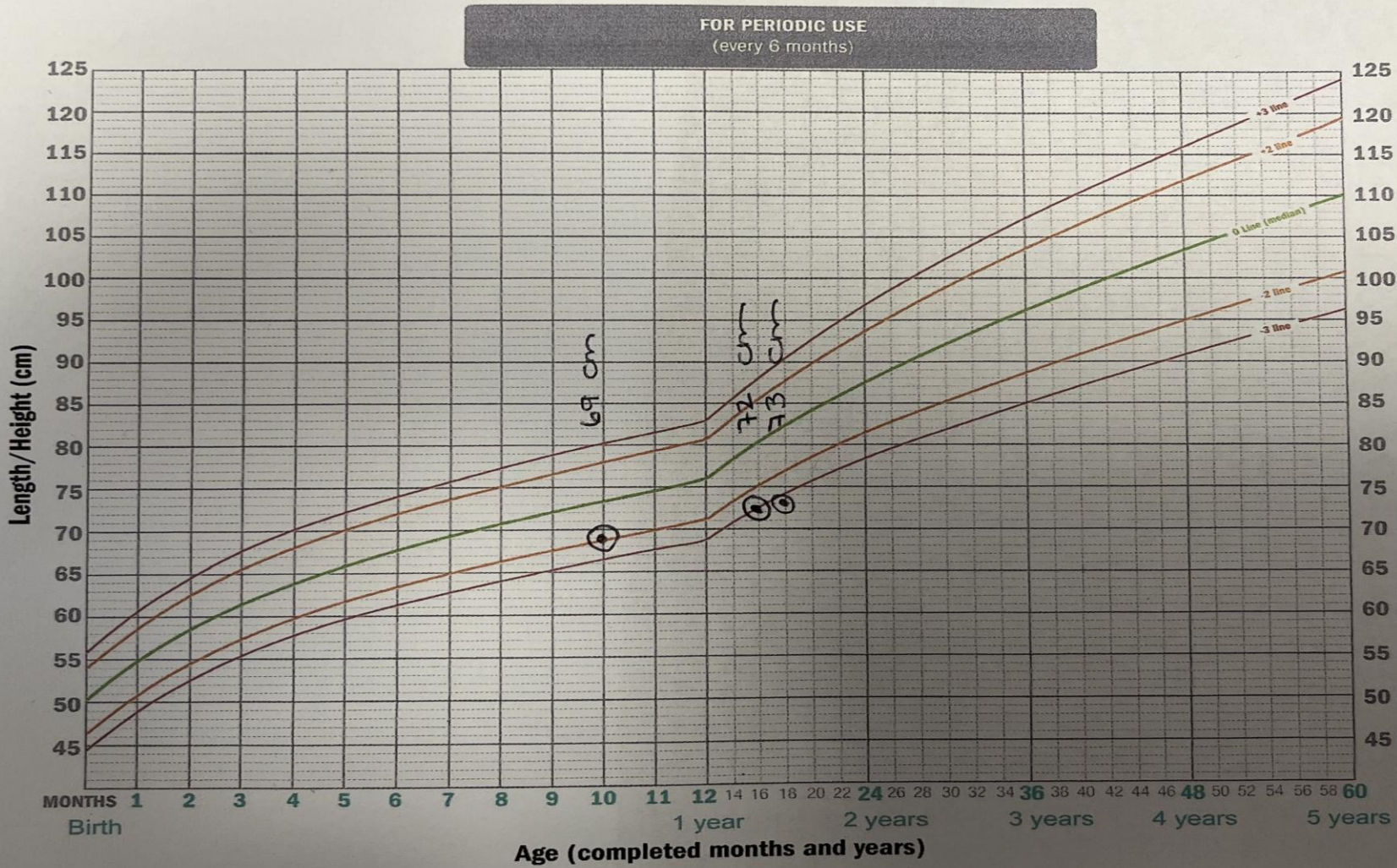
1 to 2 years

2 to 3 years

### Interpretation of lines:

- This Weight-for-Age Chart shows body-weight relative to age in comparison to the Median (green

# Height-for-age

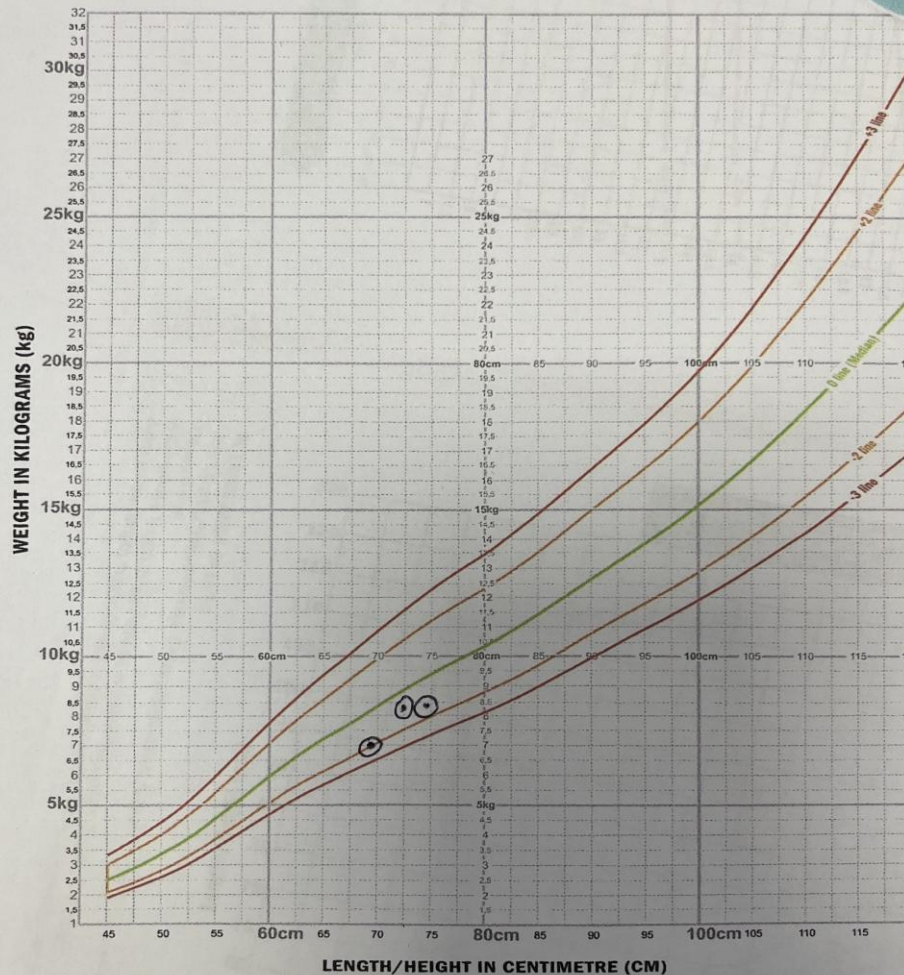


birth to 5 years

**BOYS:** Height-for-age charts

# Weight-for-height

**BOYS:** Weight-for-height charts



## Summary of findings

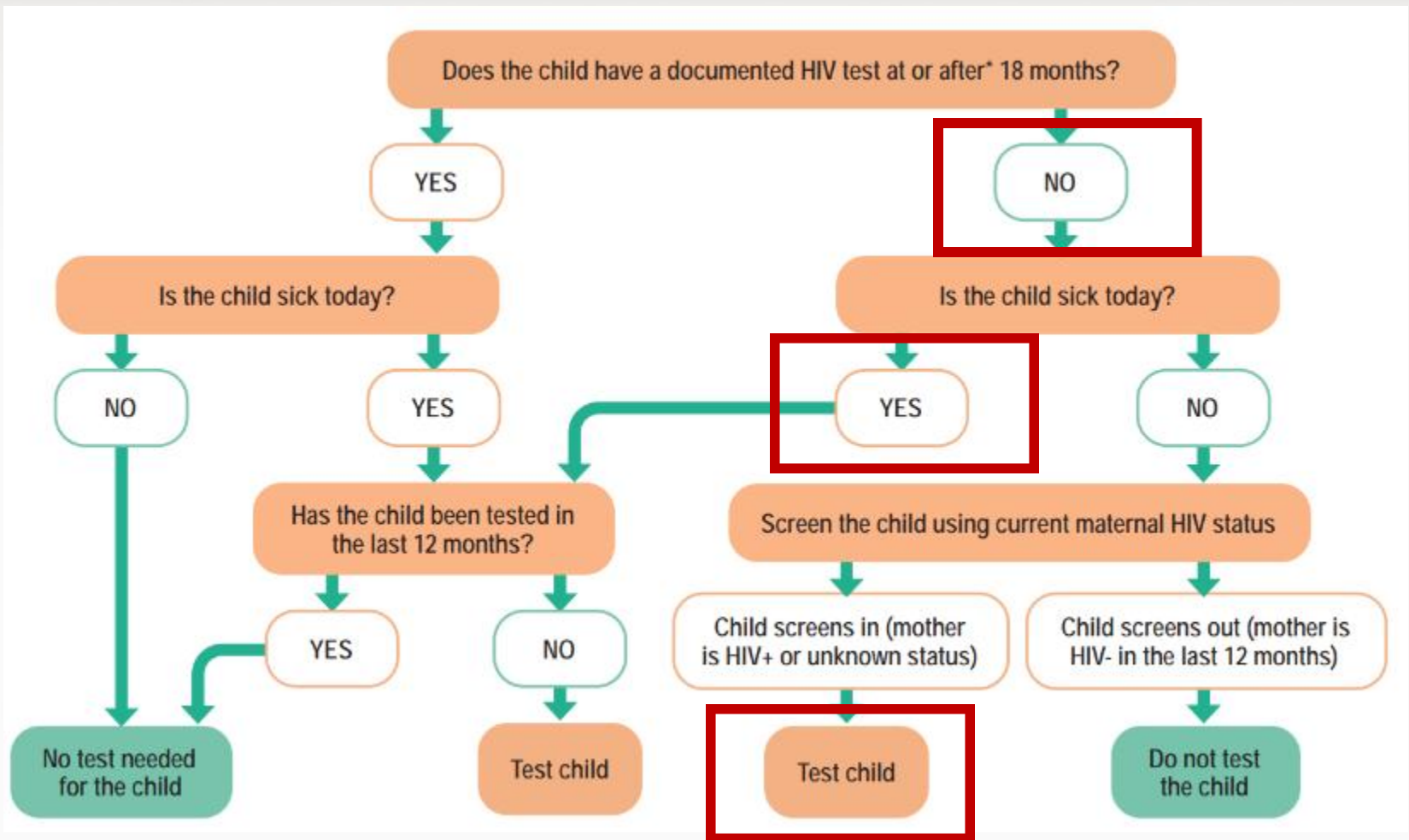
Parameter	Z-score
Weight	Between - 2 and - 3
Height	< - 3
Weight-for-height	Just above - 2

# Interpretation of growth parameters

<b>Parameter</b>	<b>Z-score</b>	<b>Interpretation</b>
Weight	Between - 2 and - 3	Moderately underweight for age
Height	< - 3	Severely stunted
Weight-for-height	Just above - 2	Not wasted

Your company name

# First things first



# Now...

- 18 months old
- HIV infected
- Moderately underweight
- Stunted
- Chronic diarrhoea

## **ADVANCED HIV DISEASE**

(Any child with HIV less than 5 years old)

# In this case...

## Screen

- TB
- Malnutrition

## Treat

- Malnutrition: WHO 10 steps
- Bacterial infection
- Diarrhoea

## Optimize

- Early ART and counselling

## Prevent

- Immunisations
- PJP



# But what if...

11 year old boy

- ELISA positive
- CD4 count 220 cells/mm<sup>3</sup>
- Chronic diarrhoea > 14 days
- Does this child have advanced disease?



# In this case...

## Screen

- TB
- Malnutrition

## Treat

- Malnutrition: WHO 10 steps
- Bacterial infection
- Diarrhoea

## Optimize

- Early ART and counselling

## Prevent

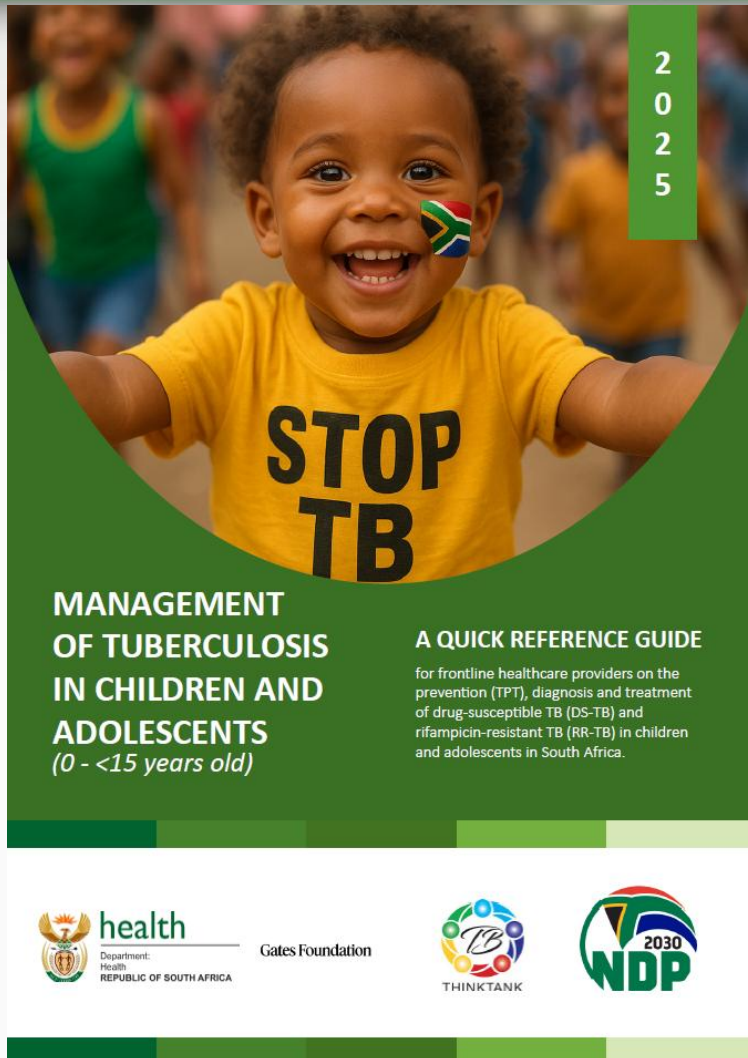
- Immunisations
- PJP



# Remember...

- Advanced HIV disease in children is more than just PJP, CMV and cryptococcal infection
- Children living with HIV remains at risk – even if they are on ART
- ART saves lives – but more is needed
- A comprehensive package of care is needed to STOP AIDS (**S**creen, **T**reat, **O**ptimize and **P**revent)

# Tuberculosis in children



This quick reference guide has been designed to supply all the definitions and basic ‘how to’ tools to support frontline health workers to navigate through a TB consultation with a child or adolescent.

**According to updated South African TB preventive therapy (TPT) guidance, which of the following individuals is MOST appropriately eligible for TPT?**

- a) Only children younger than 5 years and people living with HIV (PLHIV)
- b) Any person with confirmed pulmonary TB disease
- c) Persons with significant TB exposure or those at high risk of progression to TB disease
- d) Only healthcare workers with occupational TB exposure
- e) Adults older than 65 years regardless of TB exposure risk

# TB preventative therapy (TPT) update

People eligible for TPT include all persons who:

- Have had a significant TB exposure or,
- Have a high risk of TB disease progression

Your company name

According to updated South African TB preventive therapy (TPT) guidance, which of the following individuals is **MOST** appropriately eligible for TPT?

- a) Only children younger than 5 years and people living with HIV (PLHIV)
- b) Any person with confirmed pulmonary TB disease
- c) Persons with significant TB exposure or those at high risk of progression to TB disease**
- d) Only healthcare workers with occupational TB exposure
- Your company name  
e) Adults older than 65 years regardless of TB exposure risk

# Another important update... BCG

**Old news:** deferring BCG in newborns with TB exposure

**New news:** *All healthy newborn infants being discharged home are to receive BCG at discharge, regardless of HIV status or TB exposure status.*

*BCG should be repeated in the well child once TB medication is completed (TPT or TB treatment)*

## According to the updated South African childhood TB guidelines, which statement BEST reflects the new recommendations regarding treatment duration?

*A 7-year-old child is diagnosed with smear-negative, non-severe drug-sensitive tuberculosis (DS-TB).*

- a) All children with DS-TB should still receive a standard 6-month regimen regardless of disease severity.
- b) A 4-month regimen may be used for eligible children with non-severe, smear-negative DS-TB.
- c) The shortened 4-month regimen is recommended only for children living with HIV.
- d) Ethambutol should not be included in young children because of optic toxicity risk.
- e) Treatment shortening applies only to children younger than 5 years old.

# SHINE trial



The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE



## Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

**Authors:** Anna Turkova, M.R.C.P.C.H., Genevieve H. Wills, M.Sc., Eric Wobudeya, M.Med., Chishala Chabala, M.Med., Megan Palmer, M.B., Ch.B., M.Med., Aarti Kinikar, M.D., Syed Hissar, M.D., M.P.H., [+22](#), for the SHINE Trial Team\* [Author Info & Affiliations](#)

Published March 9, 2022 | N Engl J Med 2022;386:911-922 | DOI: 10.1056/NEJMoa2104535 | [VOL. 386 NO. 10](#)

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# TB treatment duration

New shortened **4-month** TB regimen for *eligible* children.

Your company name

## According to the updated South African childhood TB guidelines, which statement BEST reflects the new recommendations regarding treatment duration?

*A 7-year-old child is diagnosed with smear-negative, non-severe drug-sensitive tuberculosis (DS-TB).*

- a) All children with DS-TB should still receive a standard 6-month regimen regardless of disease severity.
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- c) The shortened 4-month regimen is recommended only for children living with HIV.
- d) Ethambutol should not be included in young children because of optic toxicity risk.
- e) Treatment shortening applies only to children younger than 5 years old.

Ethambutol is back for everyone!



Your company



## According to updated South African RR-TB guidelines, which of the following statements is MOST accurate?

*A 10-year-old child is diagnosed with fluoroquinolone-susceptible rifampicin-resistant tuberculosis (RR-TB).*

- a) Children younger than 15 years should still routinely receive 18 months of RR-TB treatment.*
- b) Bedaquiline and delamanid remain contraindicated in young children.*
- c) Non-severe RR-TB in children may be treated with a standardised 6-month regimen.*
- d) The terms “short” and “long” regimens are still the preferred classification in current guidelines.*
- e) Delamanid should only be used in adults with severe RR-TB.*

# Back to the case...

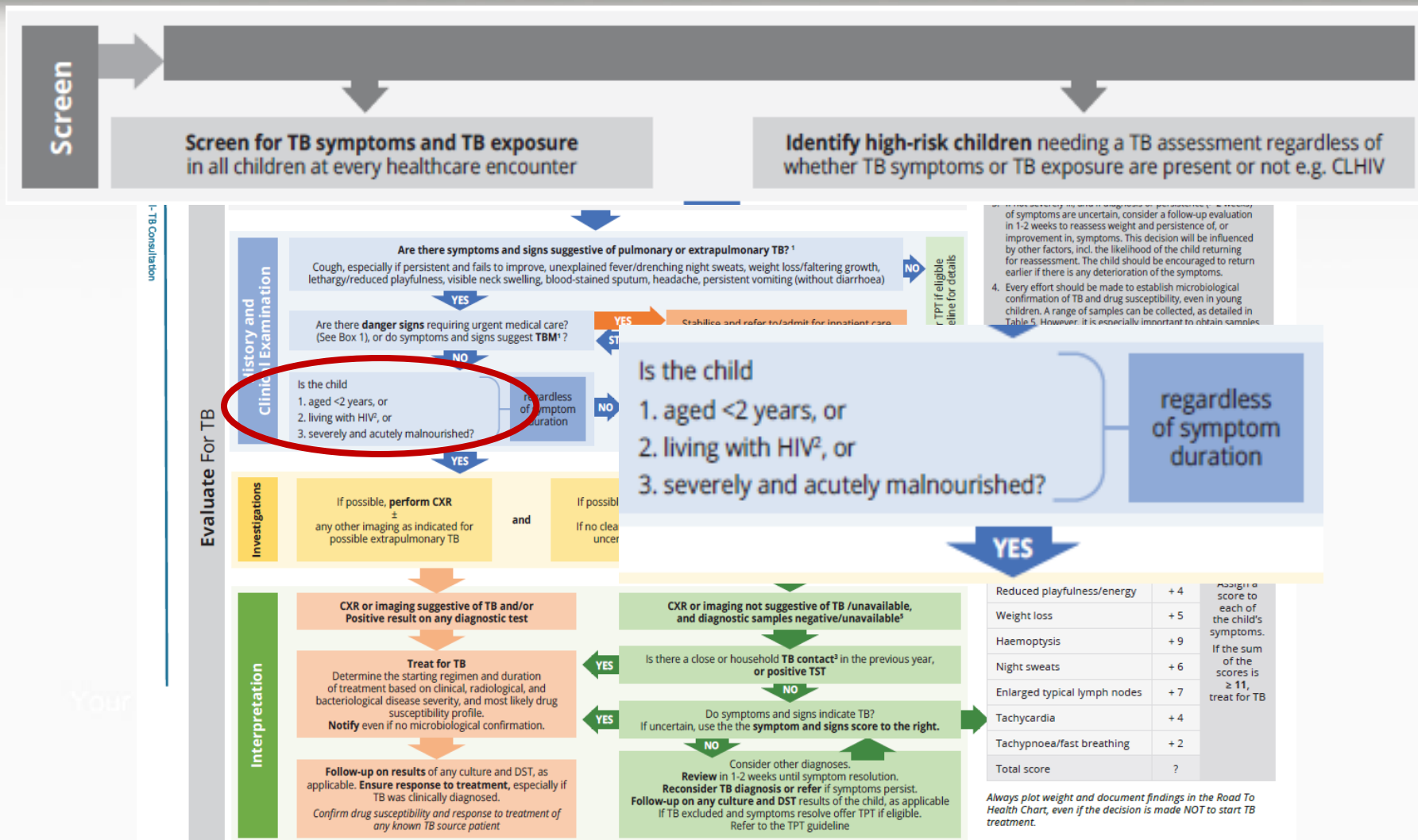
- 18 months old
- HIV infected
- Moderately underweight
- Stunted
- Chronic diarrhoea



## **ADVANCED HIV DISEASE**

(Any child with HIV less than 5 years old)

# Decision making algorithm



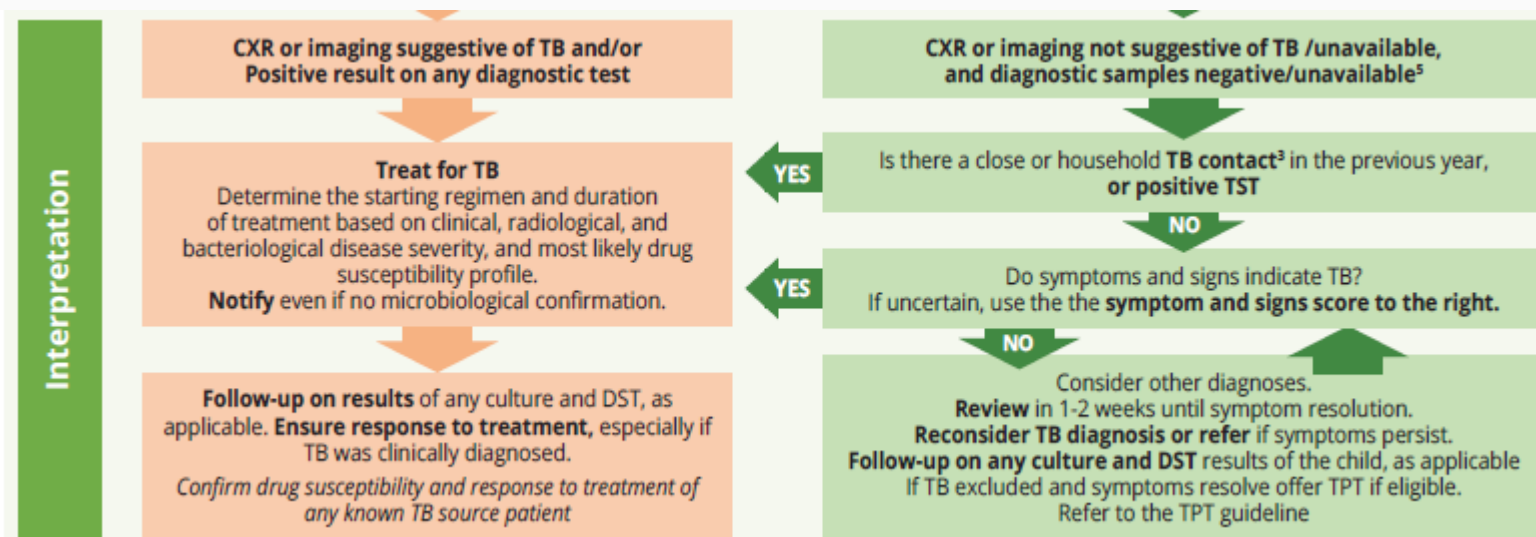
# Decision making algorithm

## Investigations

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

and

If possible, **collect a sample for a diagnostic test<sup>4</sup>**, 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



# Interpret results...

## How to interpret TB culture results:

### If results say:

**TB Culture:**  
**Mycobacterial Culture Liquid Medium:**  
**Culture result:** Culture positive. AFBs observed.  
**Incubation time:** 27 days

Consider this a **POSITIVE** result for TB.  
Diagnose TB and check DST results.

### If results say:

**TB Culture:**  
**Mycobacterial Culture Liquid Medium:**  
**Growth result:** Negative  
**Incubation time:** 42 days  
**Culture result:** No growth after 42 days

Consider this a **NEGATIVE** result for TB

## How to interpret DST results

### If results say:

#### **TB-NAAT: GeneXpert MTB/Rif Ultra (Sediment)**

**PCR M. tuberculosis result:** Mycobacterium tuberculosis complex detected  
**Rifampicin (molecular)** Sensitive

#### **TB-NAAT DR-TB: GeneXpert MTB/XDR (Cultured Isolate)**

**PCR M. tuberculosis result:** Mycobacterium tuberculosis complex detected  
**Isoniazid, INH (molecular)** Sensitive  
**Fluoroquinolone, FQ (molecular)** Sensitive  
**Amikacin, AMK (molecular)** Sensitive  
**Ethionamide, ETH (molecular)** Sensitive

Consider this **DRUG-SUSCEPTIBLE TB (DS-TB)**.

# 2024 TB DRUG DOSING CHART FOR CHILDREN / ADOLESCENTS <15 YEARS

WITH CONFIRMED/CLINICALLY DIAGNOSED DRUG-SUSCEPTIBLE/PRESUMED DRUG-SUSCEPTIBLE NON-SEVERE TB, SEVERE PULMONARY TB AND EXTRAPULMONARY TB (EPTB) excluding TB meningitis / central nervous system (CNS) TB / miliary TB (refer to chart on next page)

**\*Non-severe TB** = intrathoracic lymph node TB without airway obstruction, simple TB pleural effusion (i.e. NOT loculated effusion/empyema/associated pneumothorax), isolated perihilar opacities, consolidation involving less than an entire lobe with no cavities or miliary pattern, or isolated cervical lymph node TB  
**Severe pulmonary TB** = children & adolescents <15 years who do not meet the criteria for non-severe TB

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

## \*ELIGIBILITY CRITERIA FOR SHORTER 2 MONTHS CONTINUATION PHASE: ALL CRITERIA SHOULD BE MET

### AT DIAGNOSIS

#### Clinical

- 3 months - <16 years at start of TB treatment
- Drug-susceptible pulmonary TB or cervical TB lymphadenitis (& no other extrapulmonary TB)
- First episode of TB treatment
- No danger signs\* indicating severe illness at presentation
- No severe acute malnutrition
- No asymmetric or persistent wheezing
- If living with HIV, must be on ART for at least 3 months with viral load <1000 at TB diagnosis or in the previous 3 months
- If no CXR available at start of TB treatment, must be 3 months - <8 years, HIV negative and no acid-fast bacilli smear positive respiratory samples (if done)

### Radiological - NONE of the following should be present

- Complicated intra-thoracic lymph node TB (airway compression/deviation and/or hyperinflation/collapse)
- Consolidation involving ≥1 lobe
- Complicated pleural effusion (loculated effusion, empyema, pneumothorax)
- Miliary pattern
- Cavities

### AT FOLLOW-UP

#### Clinical

- Adherent to treatment
- Month 1: all TB symptoms & signs improved including weight
- Month 4: all TB symptoms and signs resolved & improving weight trend

Those not meeting the eligibility criteria should receive 4 months continuation phase (or 10 months for bone & joint TB)

\* Refer to Table on next page

<sup>1</sup> 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 suspension to the child orally or via nasogastric tube.

<sup>2</sup> 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.

**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**

## NEED HELP?

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

0800 212 506 / 021 406 6782

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

www.mic.uct.ac.za



MEDICINES  
INFORMATION  
CENTRE

Based on the 2024 NDoH 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

# Remember...

- We need to screen for and think about TB
- Not only in children living with HIV, but in all children accessing healthcare facilities
- Stop, think and ask the right questions
- If you are not sure... ask

# Summary

## **Advanced HIV disease in children and adolescents**

- Children 5 years and older
  - WHO stage 3 or 4
  - or
  - CD4 cell count  $<200$  cells/mm<sup>3</sup>
- All children younger than five years
  - Considered to have advanced disease


# Summary

Provide a package of care



Your company name

# Summary




2  
0  
2  
5


**STOP  
TB**


**MANAGEMENT  
OF TUBERCULOSIS  
IN CHILDREN AND  
ADOLESCENTS**  
*(0 - <15 years old)*

**A QUICK REFERENCE GUIDE**  
for frontline healthcare providers on the prevention (TPT), diagnosis and treatment of drug-susceptible TB (DS-TB) and rifampicin-resistant TB (RR-TB) in children and adolescents in South Africa.

 **health**  
Department:  
Health  
REPUBLIC OF SOUTH AFRICA

 Gates Foundation

 **THINKTANK**

 **2030  
NDP**

Use resources wisely and don't forget about TB



Your company name