Implementation of TB disease severity assessment & new TB short course treatment regimens in children in Kenya

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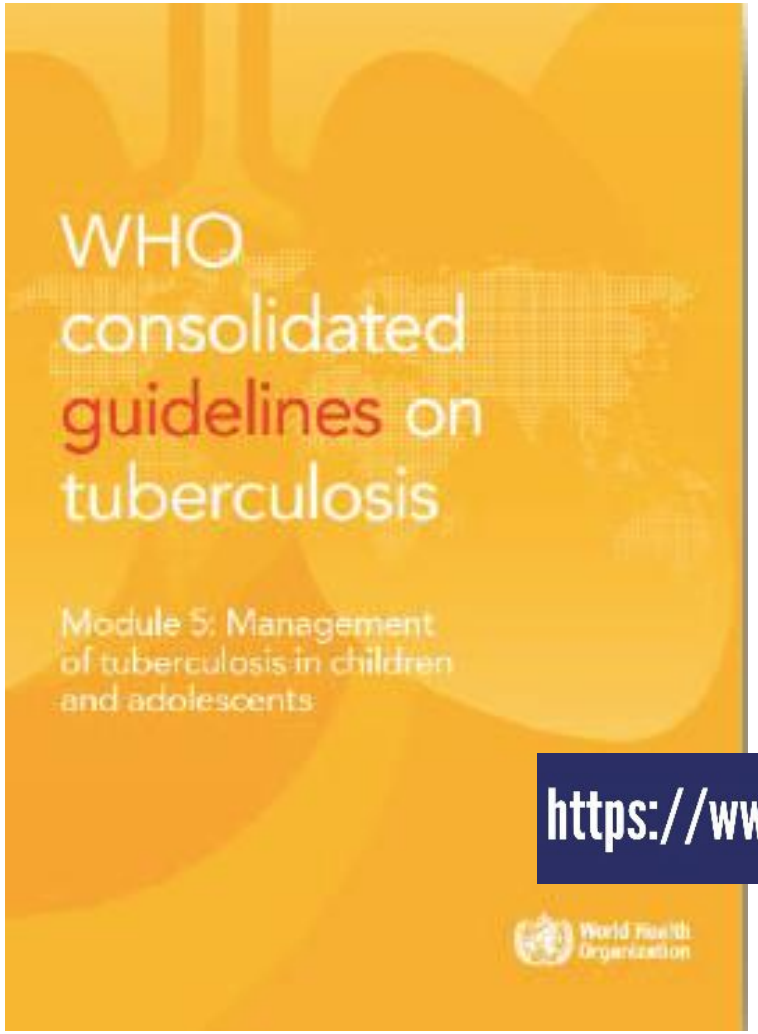
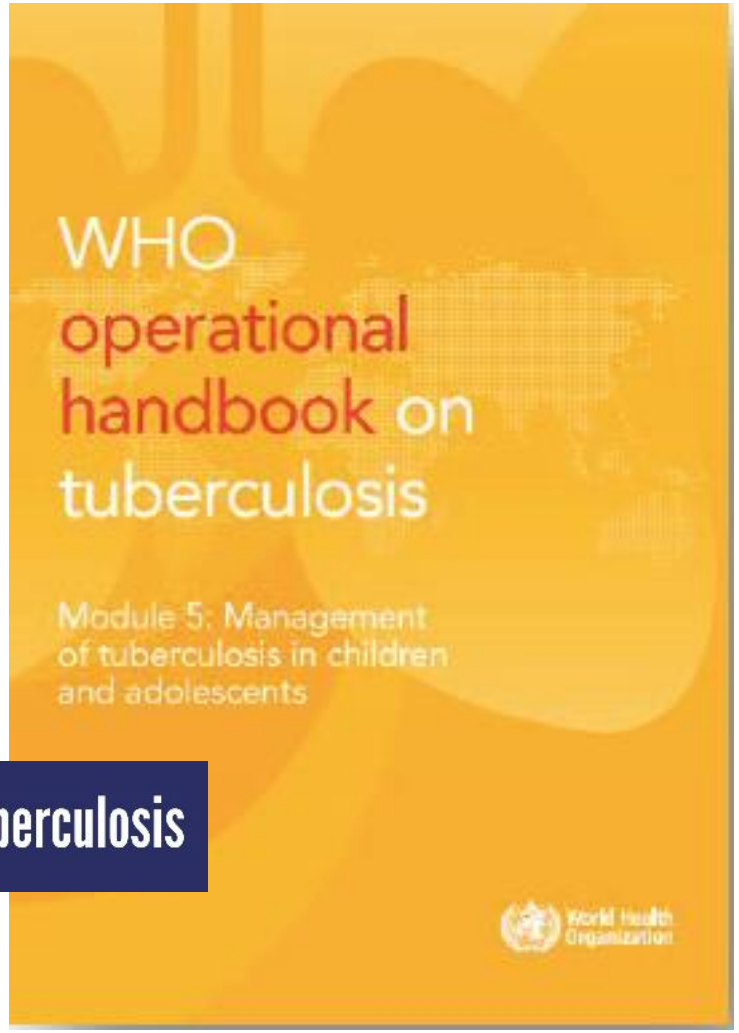
Annual meeting of the Child and Adolescent TB working group
Tuesday 29 November 2022

University of Nairobi

University of Nairobi

Updated Guidelines on Management of TB in Children & Adolescents. W.H.O. *Launched in March 2022*





https://www.who.int/health-topics/tuberculosis

Treatment for drug-susceptible TB in children 3 mth – 16 yrs
SHORTER 4 MONTH REGIMEN FOR NON-SEVERE TB (WHO 2022 update)

- Evidence from the SHINE trial reviewed by the GDG:
  - Main finding: 4-month treatment non-inferior to the 6-month regimen (consistent across all key analyses - including age groups, HIV status, type of TB and adherence)

SHINE: Shorter Treatment for Minimal Tuberculosis in Children

SHINE

TBTC Tuberculosis Trials Consortium

- In children and adolescents (3 months to 16 years) with **non-severe, presumed drug-susceptible TB**, a **4-month regimen 2RHZ (E) /2RH** should be used [rather than the standard 6-month regimen (2RHZ(E)/4HR)].
  - Important implementation considerations were noted to determine eligibility for the shorter treatment regimen and will be described in the consolidated guidelines and in the operational handbook.

END TB

Rapid communications:
Child and adolescent TB: *https://apps.who.int/iris/bitstream/handle/10665/344382/9789240033450-eng.pdf*
Drug-susceptible TB: *https://apps.who.int/iris/rest/bitstreams/1350979/retrieve*

World Health Organization

SHORTER 6 MONTH REGIMENS FOR TB MENINGITIS (WHO 2022 update)

- Current recommendation: 2 months HRZE followed by 10 months HR
  - (Based on 2009 literature review, non-randomized, non-comparative studies, not entered into GRADE)

- Systematic review and meta-analysis to compare the effectiveness of a shorter intensive regimen (6HRZEto, with slightly higher H and R dosing) vs WHO recommended regimen
  - Shorter intensive regimen: lower death rates, and higher successful treatment rates….

    ……but a high proportion of survivors with neurological sequelae

- Key update: In children and adolescents with bacteriologically confirmed or clinically diagnosed **TB meningitis** (without suspicion or evidence of MDR/RR-TB), **a 6-month intensive regimen (6RHZ + Ethionamide) may be used**
  - [as an alternative option to the **12-month regimen (2HRZE/10HR)**.]

World Health Organization

Kenya - process to review and implement new shorter course TB treatment for children & adolescents

Steps taken in adoption of the new guidelines in Kenya

Paediatric TB Committee of Experts (COE) series of meetings.

Examined each new recommendation

July 2022

Data synthesis and review of WHO 2022 recommendations workshop.

Drafted new guideline

Min of Health (NTLP, child health division) Academia, Implementors, funding & implementing partners

September 2022

Presented revised guideline to all stakeholders

[Technical experts Professional associations

Patient communities, CSOs]

Piloted in selected counties

October 2022

Data synthesis and review of WHO 2022 child & adolescent TB recommendations workshop

- ❑ Detailed review of the WHO guidelines
- ❑ Review of the evidence
- ❑ Review of the current and past Kenya guidelines- TB, Basic paediatric protocols
- ❑ Lecture on childhood TB
- ❑ Heated plenary discussions in country context, low access to CXR for children, bacteriologic test low yield and contribution to delay in child TB Rx decisions

Criteria for 4-month TB regimen WHO 2022

Box 5.3 Eligibility criteria for the 4-month regimen (2HRZ(E)/2HR) in children and adolescents aged between 3 months and 16 years with non-severe pulmonary or peripheral lymph node TB in various settings

In children and adolescents who have undergone bacteriological testing and CXR, a 4-month treatment regimen should be started in children and adolescents meeting all of the following three criteria:

- CXR findings consistent with non-severe TB (
  it can be performed at any point during the
  - intrathoracic lymph node TB without signif
  - PTB confined to one lobe with no cavities
  - uncomplicated pleural effusion (without pr
- TB that is negative, trace, very low or low usin
  negative (if Xpert MTB/RIF or Ultra not availa
- the child or adolescent has mild TB symptom

In settings without access to CXR, a 4-month tre
children and adolescents meeting all of the follov

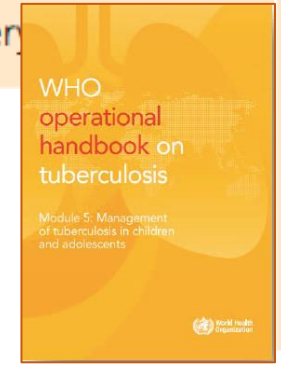
- TB that is negative, trace, ver
- the child or adolescent has mild TB symptoms that do not require hospitalization; [a]
- TB symptoms resolved completely within 1 month of treatment initiation and the child is completely well, including a normal nutritional status, at 4 months of treatment.

In the absence of bacteriological testing and CXR, a 4-month treatment regimen may also be started in children and adolescents meeting any of the following two criteria:

- isolated extrathoracic (peripheral) lymph node TB, without involvement of other extrapulmonary sites of disease;
- the child or adolescent has mild TB symptoms that do not require hospitalization. [a]

[a] Mild symptoms that do not require hospitalization means:

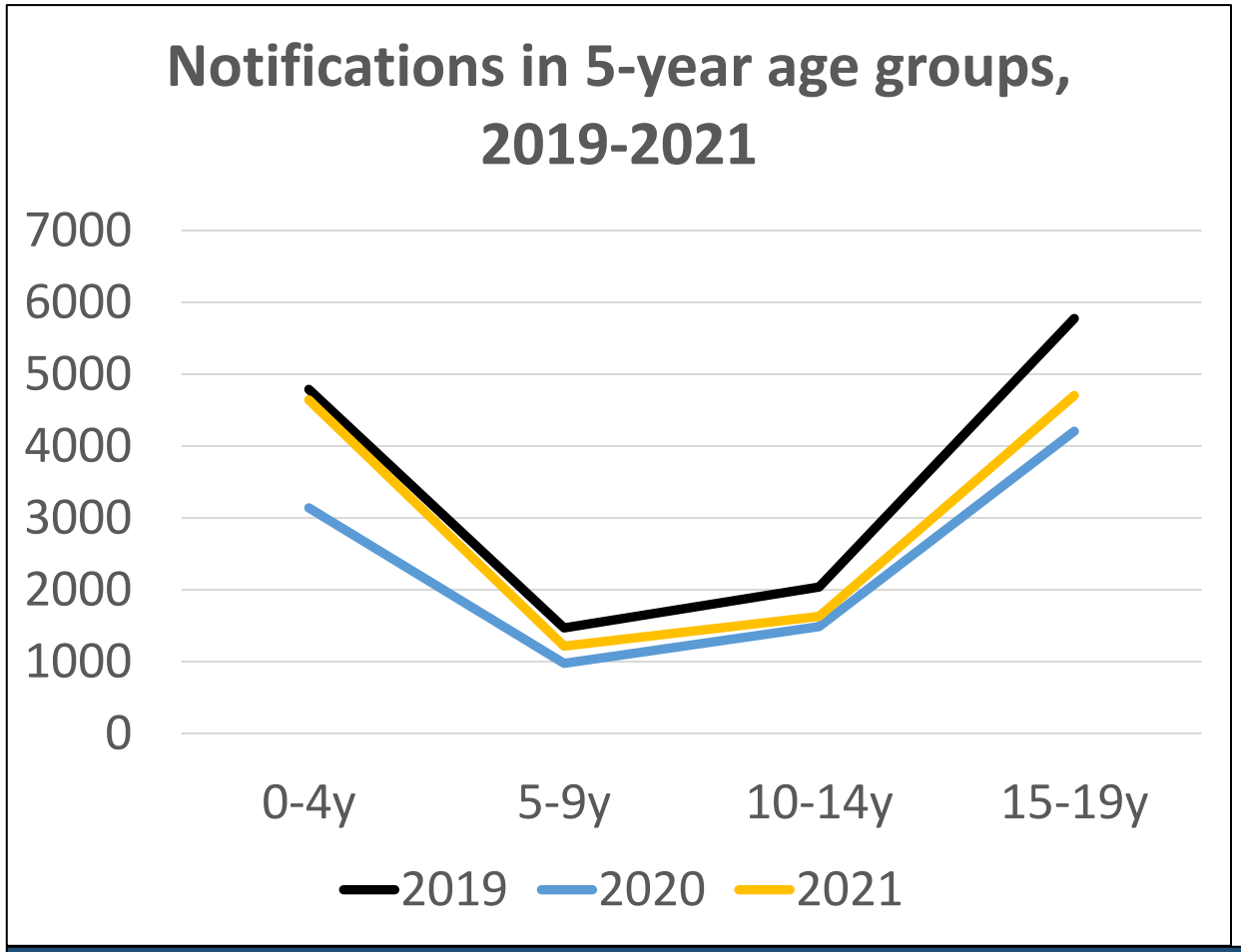
- none of the danger or high-priority signs listed in Table 4.5;
- no asymmetrical and persistent wheezing;
- no signs of EPTB other than peripheral lymph node TB;
- none of the following: SAM, respiratory distress, high fever (over 39 °C), severe pallor, restlessness, irritability or lethargy.



To define severe versus non-severe TB Disease WHO 2022 - with chest x-ray and/or bacteriologic tests

	Detail	Severe	Non-severe
Pulmonary TB			
Chest x-ray	Hilar LN	Compressing bronchi	No compression
	Parenchyma	Lesions in >1 lobe	=< 1 lobe
		Miliary	-
		Cavitation	-
	Pleura	Complicated effusion	Uncomplicated effusion
Microbiologic tests	Bacillary load	High bacillary load	Paucibacillary, trace or negative
Extrapulmonary TB			
	Location EPTB	TB meningitis, bone-joint	Cervical LN TB
	Dissemination	Any miliary	Other peripheral LN TB

TB in children & adolescents in Kenya 2019 - 2021



Percent of all cases diagnosed:

0-4y: 52.2%
(incidence 2020: 8,900)

5-14y: 36.9%
(incidence 2020: 7,700)

All children <15y:

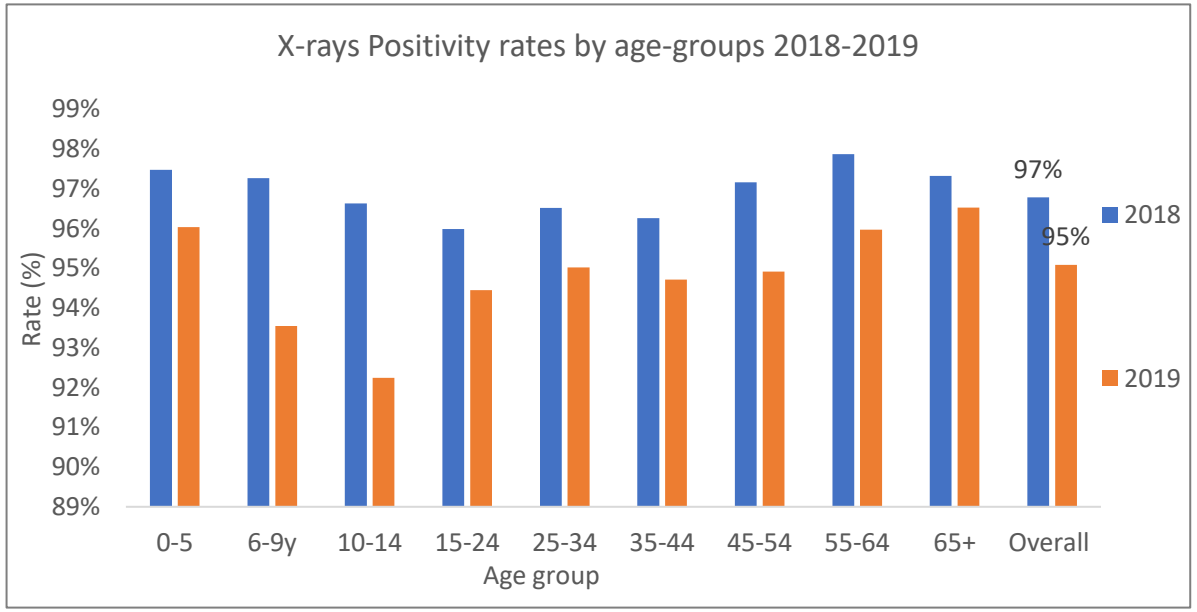
- ***Only 45% of children with TB are diagnosed.***
  (incidence 2020: 16,600)

In Kenya, highest burden is in children <5yr and rises after age 10yr
55% of children <15y with TB are missed

REPUBLIC OF KENYA

MINISTRY OF HEALTH

What is the access to CXR for TB diagnosis in Children & Adolescents? Kenya 2019 CXR Data



Age group	Total Patients 2019	X-rays Done 2019	X-ray Uptake (%)	Positivity rate (%)
0-5	5118	3380	**66%**	**96%**
5-9	1141	589	**52%**	**94%**
10-14	2057	851	**41%**	**92%**
15-24	15056	4039	27%	94%
25-34	21945	6329	29%	95%
35-44	18479	6058	33%	95%
45-54	10842	3953	36%	95%
55-64	5645	2309	41%	96%
65+	5537	2735	49%	97%
Overall	**85820**	**30243**	**35%**	**95%**

What % of presumed TB cases got CXR?

<5 yrs: 66% 5 – 9 yrs: 52%

10 – 14 yrs: 41% 15 – 24 yrs: 27%

For all that got CXR >90% of the CXRs were suggestive of TB

What is the access to Xpert for TB diagnosis in Children & Adolescents?

Kenya 2019 Data

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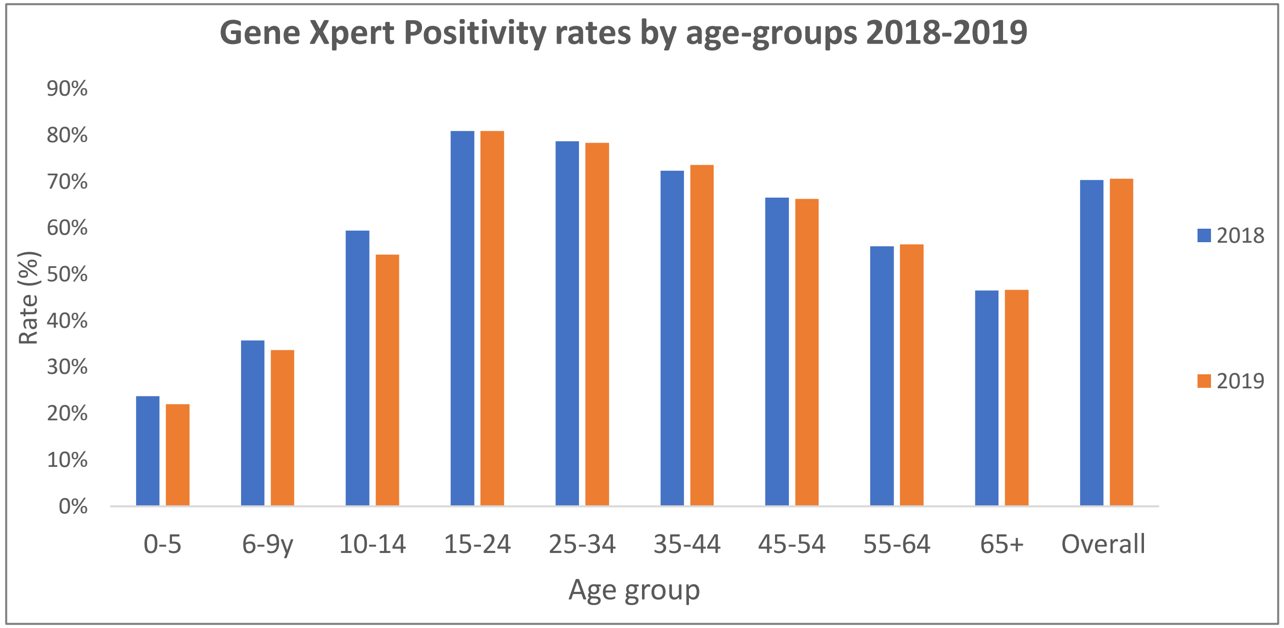


Age group	Total Patients 2019	Xperts Done 2019	Xpert Uptake (%)	Positivity rate (%)
0-5	5118	1103	22%	22%
5-9	1141	481	42%	34%
10-14	2057	1126	55%	54%
15-24	15056	9770	65%	81%
25-34	21945	14658	67%	78%
35-44	18479	12380	67%	74%
45-54	10842	7007	65%	66%
55-64	5645	3529	63%	56%
65+	5537	3389	61%	47%
Total	**85820**	**53443**	**62%**	**71%**

What % of presumed TB cases got Xpert tests?

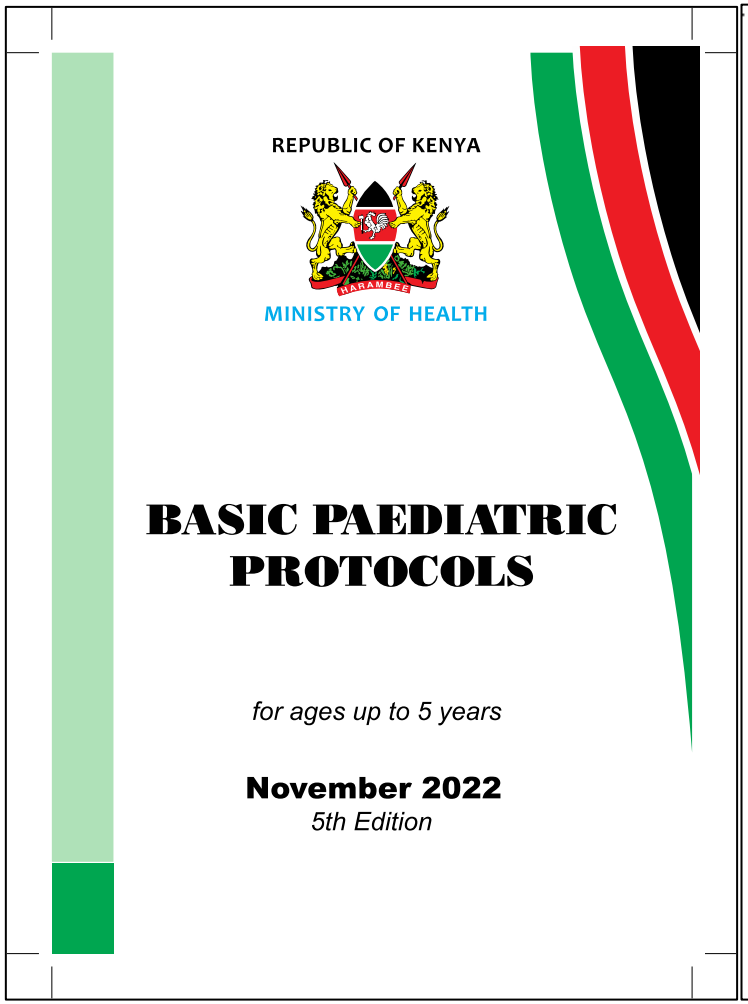
<5 yrs: 22% — 5 – 9 yrs: 42%

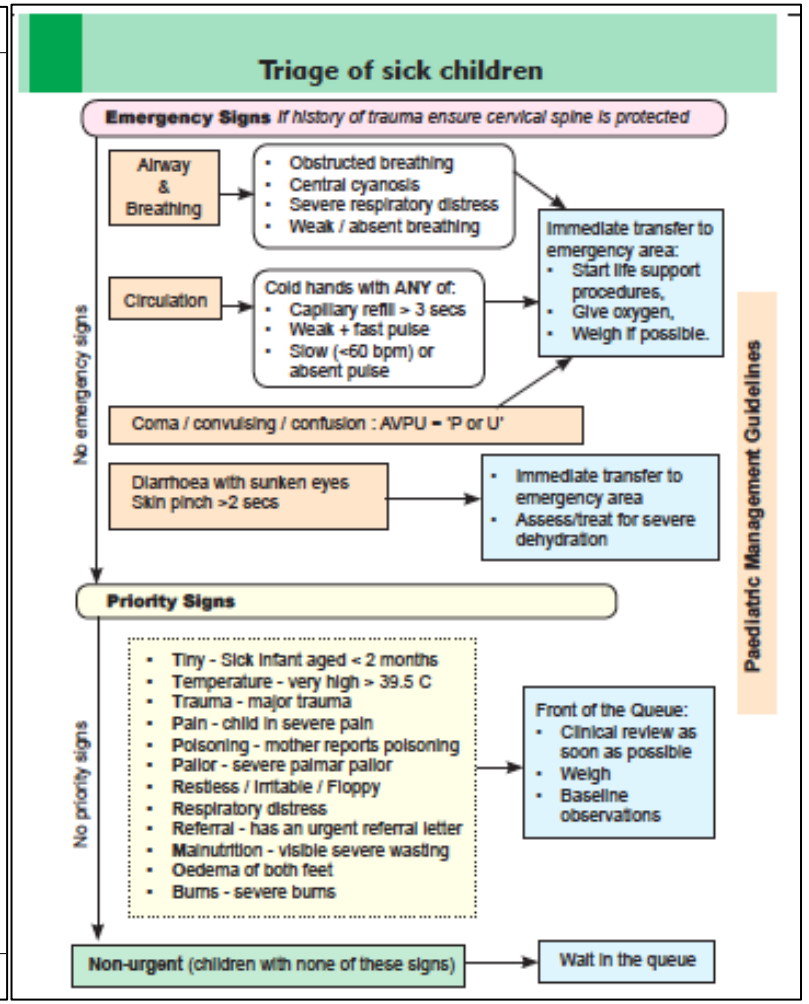
10 – 14 yrs: 55% — 15 – 24 yrs: 65%

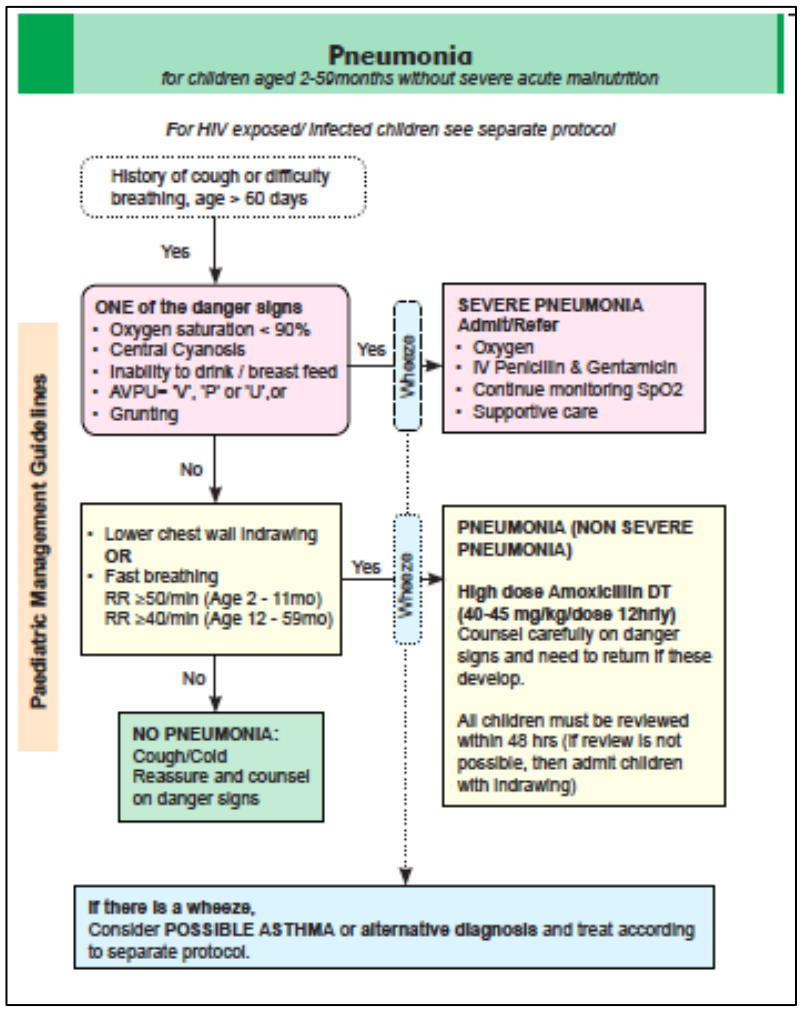
TB was detectable in Xpert for only 22% of U5s, and 34% of 5-9yr olds

Even in younger adolescents 10-14yr Xpert is + in only half (NTLP 2019)

Kenya Paediatric Protocols – Approach to define severity of disease *(evolved from IMCI / ETAT)*



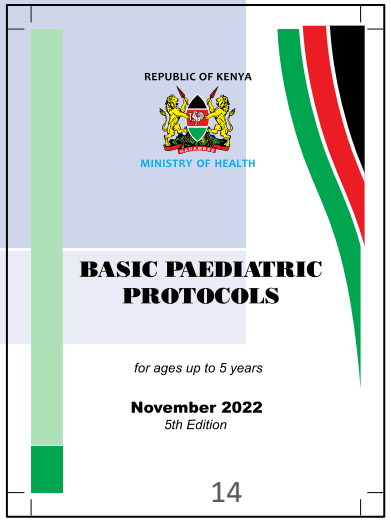




Kenya Paediatric Protocols – Approach to define severity of disease *(evolved from IMCI / ETAT)*

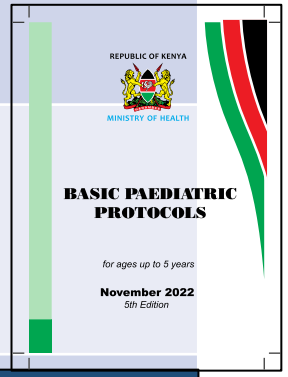
Category	Detail	Severe	Non-severe
Respiratory	Distress SPO2 Work of breathing	Resp distress Cyanosis, SPO2 <90% Increased work of breathing (alar flaring, chest indrawing, grunting)	Not in distress SPO2 NORMAL
Circulatory	Dehydration Shock	Capillary refill 2 sec+, weak pulse Cold extremities, temp gradiant	No dehydration
Neurologic	Level of consciousness	Drowsy Reduced level consciousness (AVPU <A) (Alert-Verbal-Pain-Unresponsive <A) Unable to feed or drink	Alert

Widely used across paediatric services nationally
Enables clinical decisions at first assessment



Kenya Paediatric Protocols – Approach to define children at high risk of poor outcome or death

Category	High risk of poor outcome	Low risk of poor outcome
Age	Below age one year	Above age one year
HIV Status	HIV Infected	HIV uninfected
Nutritional Status	Severe malnutrition Age <5yr: WHZ or WAZ < -3 Age >5yr: BMI < -3	Well nourished
Other immune-suppressive conditions	Renal disease On steroid therapy Diabetes, Cancer	No major co-morbidity



Widely used across paediatric services nationally

Enables clinical decisions by health practitionser at first assessment

SHORTER 6 MONTH REGIMENS FOR TB MENINGITIS (WHO 2022 update)

- Current recommendation: 2 months HRZE followed by 10 months HR
  - (Based on 2009 literature review, non-randomized, non-comparative studies, not entered into GRADE)

- Systematic review and meta-analysis to compare the effectiveness of a shorter intensive regimen (6HRZEto, with slightly higher H and R dosing) vs WHO recommended regimen
  - Shorter intensive regimen: lower death rates, and higher successful treatment rates….

    ……but a high proportion of survivors with neurological sequelae

- Key update: In children and adolescents with bacteriologically confirmed or clinically diagnosed **TB meningitis** (without suspicion or evidence of MDR/RR-TB), **a 6-month intensive regimen (6RHZ + Ethionamide) may be used**
  - ***[as an alternative option to the 12-month regimen (2HRZE/10HR).]***

Kenya retained 12 month regimen for TB meningitis & bone-joint TB.

Rationale: ethionamide expensive & high toxicity seen in MDR Rx program

Proposed treatment regimens for Kenya for children 10 years and below

**** All children 11 years and above will require the 6 month regimen***

Criteria	Eligibility for 4 month regimen	Eligibility for 6 month regimen	Eligibility for 12 month regimen
Type of TB	Non-severe Pulmonary TB Cervical LN TB	Severe Pulmonary TB Extra Pulmonary TB *(excluding TB meningitis, Osteoarticular and peripheral LN TB)*	TB Meningitis Osteo-articular TB
Indicators of severity	Stable enough to be managed as an outpatient	All hospitalised patients	Any setting
	No danger signs	A sick child at diagnosis with any danger sign Respiratory danger signs: In respiratory distress (oxygen saturation <90%, cyanosis, grunting, chest in-drawing)	All
Immune status	Is HIV negative, not severely malnourished, not immune suppressed	Infants < 1yr (immature immune system), HIV positive, severe malnutrition, any immunosuppressed child	All
Bacteriologic status *(where available)*	Bacteriologically negative / Clinically diagnosed TB	Bacteriologically confirmed drug-susceptible TB	All
Treatment regimen	**4 month regimen: 2HRZE/2HR**	**6 month regimen: 2HRZE/4HR**	**12 month regimen 2HRZE/10HR**

- ***If the child has known contact with a person with drug-resistant TB, this table does not apply….***
- ***Start the child on treatment as per the DR TB guidelines***

Steps taken in adoption & implementation of the new child & adolescent TB guidelines in Kenya

Presentation at the TB Interagency Coordinating Committee

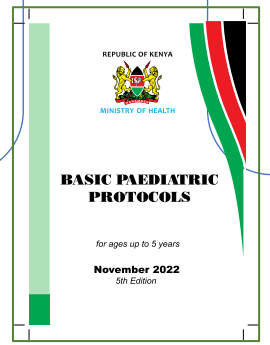
Endorsement & adoption

October 2022

Dissemination at Kenya Lung Conference

~250 participants from all over Kenya

Adopted in new updated Kenya Paediatric Protocols



November 2022

Roll out the algorithm in December 2022

Roll out of the shorter regimen 2023

(training, jobaids, commodity planning, transition period)

December 2022

Thank you! Asante! Merci!

Gracias! Orio! Obrigado!