



What's new in TB and Malaria?

BY JUDY ROTHBERG
PAEDS ID CONSULTANT
RMMCH



TB – the last decade

- Diagnostics
 - What?
 - How?
 - Where?
- Treatment/prevention
 - Drugs
 - Duration
- Prevention

The World Health Organization's (WHO's) strategy for tuberculosis (TB) prevention, care and control for 2015–2035 (known as the End TB Strategy) prioritizes the early diagnosis of TB.

Diagnostics – specimens



Stool!!!

Children under 10
years of age,
suspecting
pulmonary TB

WHO guidelines
2021/2022

Nucleic acid
amplification
testing, not TB
culture

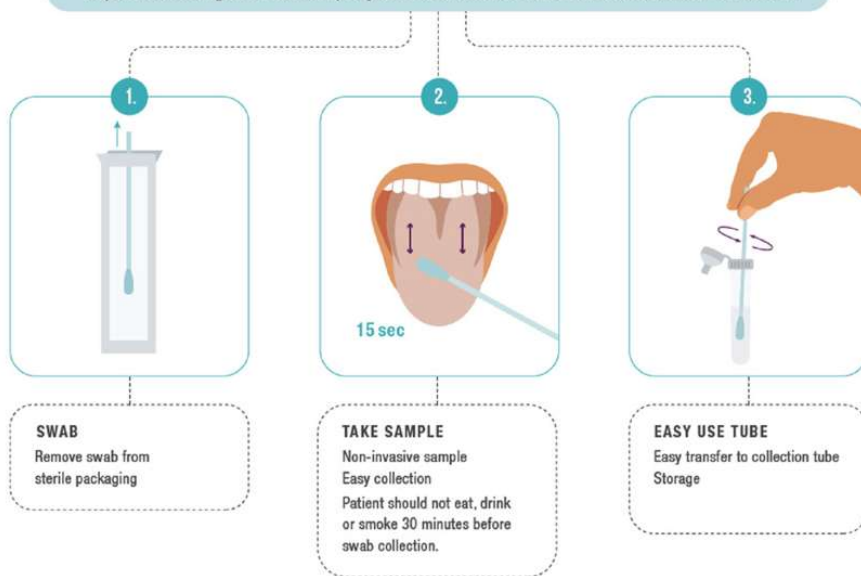
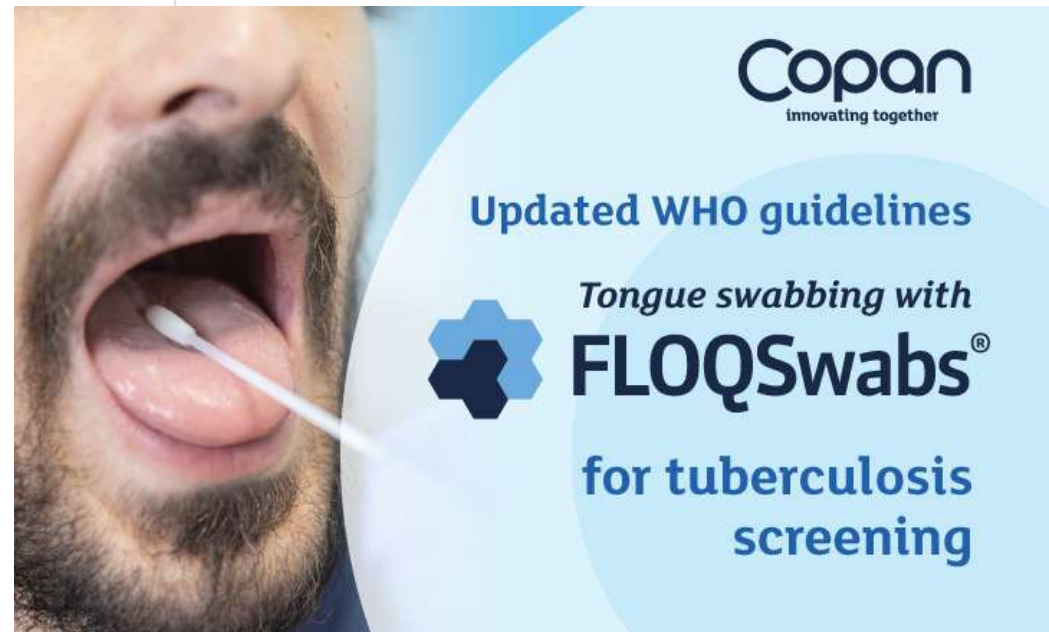
Yield equivalent
to gastric
aspirates, easier
to obtain

And at the other end...

Tongue swabs!

TONGUE SWAB COLLECTION

To provide a tongue swab sample you would need to follow the instructions as below:



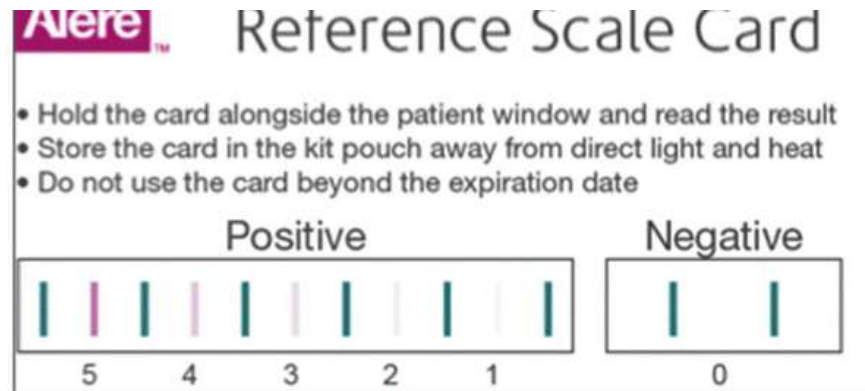


- **Introduction Date:** March 2026 (announced ahead of World TB Day).
- **Indication:** Recommended for initial detection of pulmonary TB using low-complexity automated NAATs or near-point-of-care molecular tests.
- **Target Group:** Specifically for adults and adolescents who cannot produce a sputum sample.
- **Recommendation Type:** Conditional recommendation (noting that conventional respiratory/sputum samples remain preferred when obtainable).



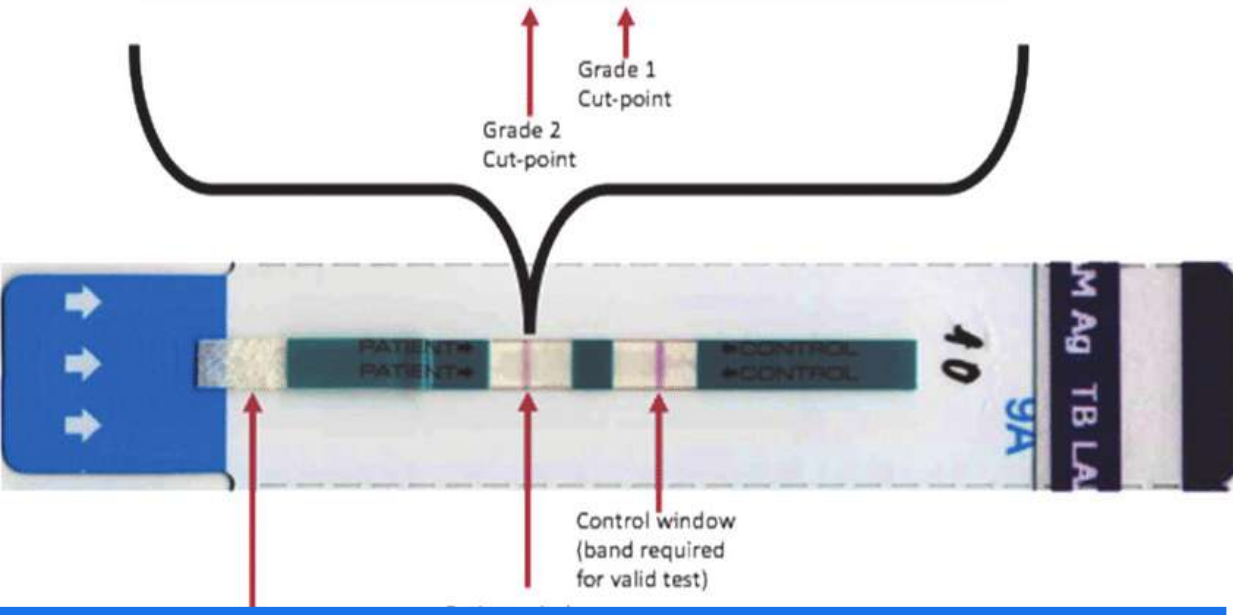
And UR-IN(e) luck – there's more you can send!

- Urine LAM – lipoarabinomannan – present in PTB and EPTB
- 2015, refined guidelines 2019
- Lateral flow assay – easy, safer, 25 minutes, 60ul urine
- BUT – diagnostic stewardship
 - In-patients – suspecting TB, advanced HIV, CD4 < 200/25%
 - Out-patients – NOT a screening test; TB suspected and low CD4 count, or seriously ill with HIV
- Sensitivity best in advanced HIV, specificity good (96%)



Some things to remember...

- Not from a urine bag specimen, can have false positives in bacterial, fungal, NTM infections and environmental contamination
- Wait 25 minutes
- Correct amount urine
- Range of possible positives
- Can not tell resistance – not a substitute for TB-NAAT/ culture





TESTS

- Gold standard, classic method – culture
 - Multitude of specimens – sputum, blood, tissue, fluids
 - Liquid (MGIT) and solid media
- Smear microscopy – acid fast (Ziehl-Neelsen) or auramine stain
 - Better if high bacillary load (not children) – 50-60% sensitivity
- NEWER – PCR – Nucleic Acid Amplification Tests (NAAT) – 85-90% sensitivity
 - Genexpert (Xpert MTB/RIF) – endorsed by WHO in 2011
 - Faster, much more sensitive, point of care, safer, resistance testing

- 2018 – Xpert MTB/Rif Ultra

Changed terminology to TB NAAT

Other assays used –
Roche Cobas, BD Max –
less sensitive but test
for Rif *and* INH
resistance

TB-NAAT: GeneXpert MTB/Rif Ultra

PCR result

Mycobacterium tuberculosis complex NOT detected

The negative TB-NAAT does not conclusively rule out TB. Please manage according to current national TB guidelines. If the patient is HIV infected, please submit another sample for TB culture and drug susceptibility testing, if this has not been done already.

TB Culture:

Mycobacterial Culture Liquid Medium:

Growth result

Negative

Incubation time

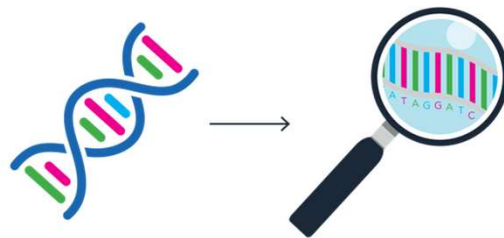
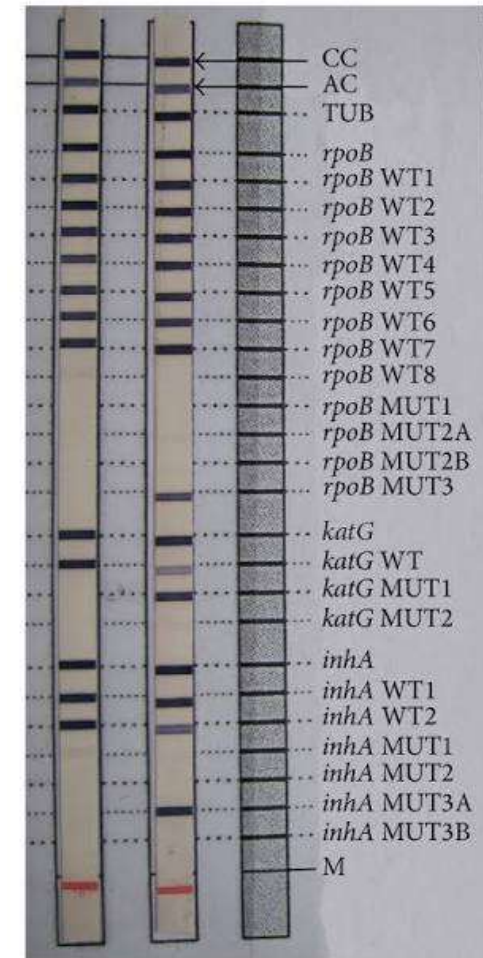
42 days

Culture result

No growth after 42 days

Other molecular tests in use

- Lamp – loop-mediated isothermal amplification (also used for Malaria diagnosis)
- Whole genome sequencing (identify complex drug-resistance patterns)
- Line probe assays (resistance to first line drugs)



Where?

- Increasing move away from large central laboratories
- To point of care or near POC testing
- Easily-obtained samples
- Same-day results, treatment initiation
- Endorsed by WHO



How has treatment changed in the past decade?

- 3 drugs *or* 4 drugs
- 6-12 months
- Different FDC's
- Fear of ethambutol
- Drug resistant TB – long course of treatment, included injectable agents
- 4 drugs for standard DSTB
- 4-6 months (may need 12 months)
- Newer formulations
- Ethambutol regarded as safe – 1st line agent
- Shorter, all oral courses of treatment for DRTB

- HRZ (50/75/150) and HR (50/75)
- July 2021 – available in public sector

You may remember...

- Rimcure (H/R/Z 75/150/400) and Rimactazid



TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

A Clinical Guideline
for the Diagnosis and Treatment
of Drug-susceptible TB in
Children and Adolescents
in South Africa

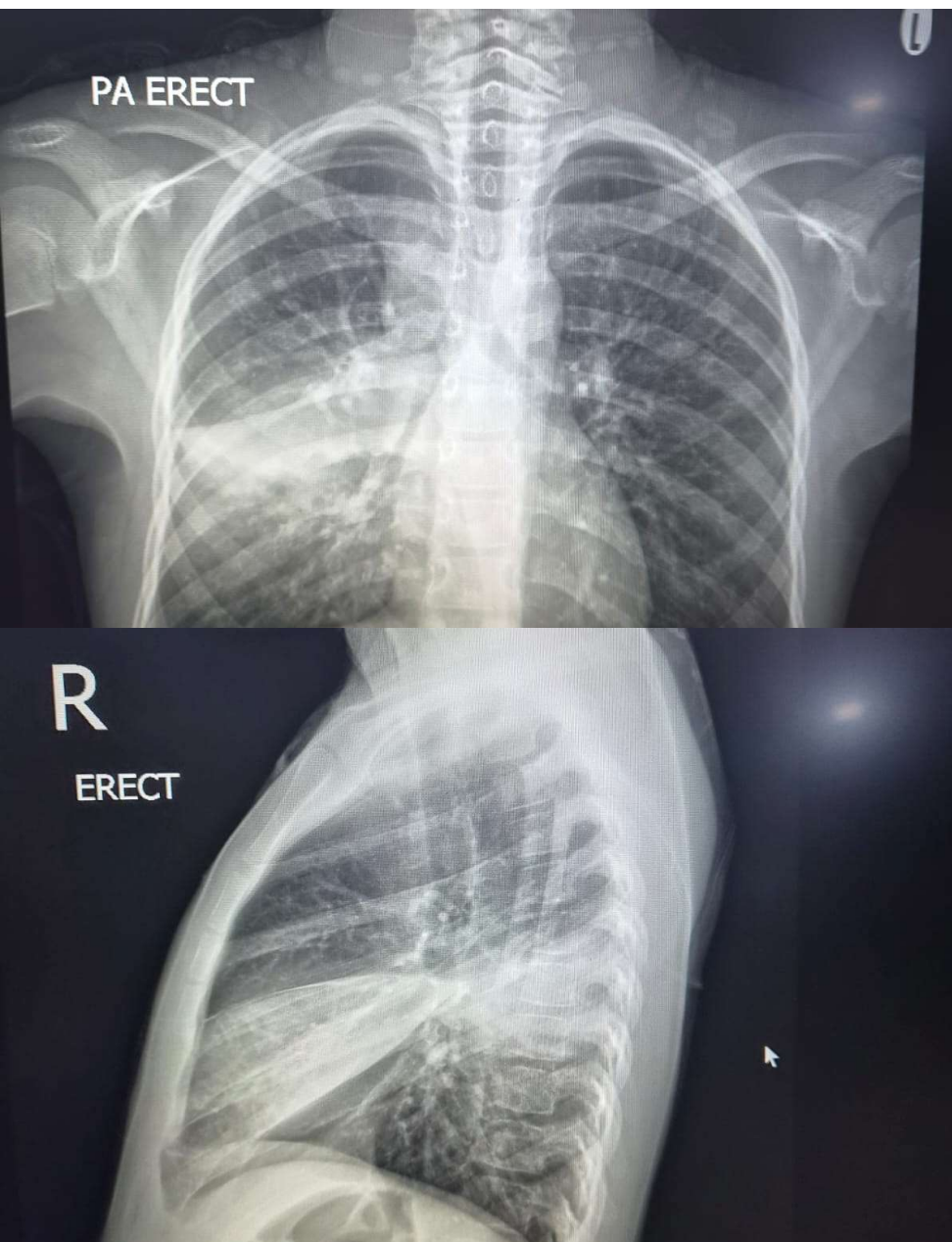
September 2024

Most current
South African
TB guidelines

The Shine trial: “Shorter is better”, or at least just as good... for a good number of cases



- Non- severe TB
 - Pulmonary, less than 1 lobe, lymph nodes WITHOUT compression, simple pleural effusion
 - Extrapulmonary – if lymphadenitis only
 - Children > 3/12, < 16 years
 - < 8 years if no CXR
 - CALHIV – if stable on treatment, viral suppression
 - Drug sensitive, can be TB-NAAT positive (trace, very low), TB culture positive
- NOT in SAM, extrapulmonary, previous treatment, severely ill at presentation, smear positive



10 year old girl with weight loss, cough, night sweats and this CXR 6 weeks apart:
For 4 month course?

- Narrowing of bronchi, involvement of whole middle lobe
- NOT for short course

Table 8 Drug dosing chart for children and adolescents with drug-susceptible TB

2023 TB Drug Dosing Chart for Children / Adolescents <16 years					
With Confirmed or Clinically Diagnosed Drug-Susceptible Non-severe TB, Severe Pulmonary TB and Extrapulmonary TB excluding TB meningitis / central nervous system (CNS) TB / miliary TB (refer to chart on next page)					
	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	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 *		Formulation
Body weight (kg)					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) *	1.5 ml	¾ tab (3 ml) *		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					
• 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.					
• 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)					

Table 9 Drug dosing chart for treatment of DS-TBM, CNS TB and miliary TB

2023 TB Drug Dosing Chart for Children / Adolescents <16 years				
With Confirmed/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	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 (not scored) OR 250 mg/8 ml suspension *	Formulation
Body weight (kg)				Body weight (kg)
<2	Obtain expert advice			<2
2 – 2.9	¼ tab (3 ml) *	1 ml	1.5 ml	2 – 2.9
3 – 3.9	1 ½ tabs	2 ml	2 ml	3 – 3.9
4 – 4.9	<3 months: 1 ½ tabs ≥3 months: 2 tabs	2.5 ml	2.5 ml	4 – 4.9
5 – 5.9	2 ½ tabs	3 ml	3 ml	5 – 5.9
6 - 7.9	3 tabs	½ tab or 4 ml	½ tab or 4 ml	6 – 7.9
8 - 8.9	3 ½ tabs			8 – 8.9
9 – 9.9		¾ tab or 6 ml	¾ tab or 6 ml	9 – 9.9
10 – 11.9	4 tabs			1 tab or 8 ml
12 – 12.9	4 ½ tabs	1 tab or 8 ml	12 – 12.9	
13 – 14.9			5 tabs	1 ¼ tabs or 10 ml
15 – 15.9	6 tabs	1 ¼ tabs or 10 ml	15 – 15.9	
16 - 16.9			7 tabs	1 ½ tabs or 12 ml
17 – 17.9	1 ½ tabs	1 ½ tabs or 12 ml		
18 – 19.9			2 tabs	2 tabs or 16 ml
20 – 24.9	2 ½ tabs	2 ½ tabs or 20 ml	20 – 24.9	
25 – 29.9	HR 150/300 mg tablet: 3 tabs		3 tabs	3 tabs or 24 ml
30 – 34.9		3 ½ tabs		
35 – 39.9			4 tabs	4 tabs or 32 ml
40 – 49.9				
≥50				≥50
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 if possible				
• To make an oral suspension for weight band 2 - 2.9 kg, for each dose, disperse 1 x HR 50/75 mg tablet 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.				
• To make an oral suspension, crush 1 x 500 mg Pyrazinamide tablet to a fine powder, disperse in 8 ml water to prepare a concentration of 500 mg/8 ml (62.5 mg/ml), administer required dose as indicated in above chart, discard unused suspension.				
• To make an oral suspension, crush 1 x 250 mg Ethionamide tablet to a fine powder, disperse in 8 ml of water to prepare a concentration of 250 mg/8 ml (31.3 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)				

Body weight (kg)	Single phase of treatment, 6 months. Once daily; 7 days a week		
	Rifampicin/Isoniazid (RH)*	Pyrazinamide (Z)	Levofloxacin
	75/50 mg dispersible tablet (scored)	500 mg tablet (scored) OR 500 mg/8 mL suspension**	250 mg tablet OR 500 mg tablet OR 25 mg/ml suspension***
< 2	Obtain Expert Advice		
2–2.9	¾ tablet or 3 mL	1 mL	2 mL
3–3.9	1 ½ tablet or 6 mL	2 mL	3 mL
4–4.9	< 3 months: 1 ½ tablets or 6 mL ≥ 3 months: 2 tablets or 8 mL	2.5 mL	4 mL
5–5.9	2 ½ tablets or 10 mL	3 mL	5 mL or ½ x 250 mg tablet
6–7.9	3 tablets or 12 mL	½ tablet or 4 mL	6 mL
8–8.9	3 ½ tablets or 14 mL		7 mL
9–9.9		¾ tablet or 6 mL	10 mL or 1 x 250 mg tablet
10–11.9	4 tablets or 16 mL	1 tablet or 8 mL	
12–12.9	4 ½ tablets or 18 mL		
13–14.9	5 tablets or 20 mL		
15–15.9	6 tablets or 24 mL	1 ¼ tablets or 10 mL	1 x 500 mg tablet or 2 x 250 mg tablet or 20 mL
16–16.9		1 ½ tablets or 12 mL	
17–17.9			
18–19.9		2 tablets or 16 mL	
20–24.9	7 tablets or 28 mL	1 ½ tablets or 12 mL	1 ½ x 500mg or 3 x 250mg tablets daily
25–29.9	Choose one option	2 tablets or 16 mL	
30–34.9	RH 150/75 mg	RH 300/150 mg	2 ½ tablets or 20 mL
35–39.9	6 tablets	3 tablets	
40–49.9			3.5 tablets or 28 mL
≥ 50			4 tablets or 32 mL

*If oral suspension required, for each dose, disperse 1 x RH 75/50 mg tablet in 4 mL of water, administer dose as indicated in above chart, discard unused suspension.

**If oral suspension is required, crush 1 x 500 mg pyrazinamide tablet to a fine powder, disperse in 8 mL prepare a concentration of 500 mg/8 mL (62.5 mg/mL), administer required dose as indicated in above chart, discard unused suspension.

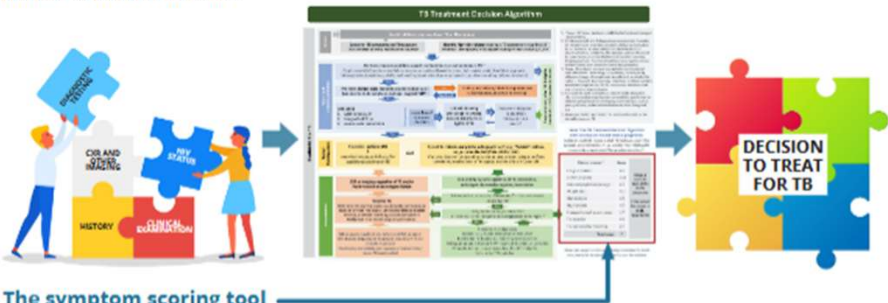
***For Levofloxacin 25mg/ml suspension: Crush and disperse 1 x 250mg tablet in 10 mL water.

An all-too-common problem – stock-outs

– in absence of ethionamide for CNS TB/ miliary TB, use Levofloxacin or Ethambutol
– however Ethambutol shortage continues => use **Levofloxacin**

6.5 TB Treatment Decision Algorithm

Now that we have looked at the specific details of each puzzle piece in the preceding text, the TB Treatment Decision Algorithm in Figure 6 on page 29 will help us interpret all the puzzle pieces together to decide whether to treat for TB or not.



The symptom scoring tool

The symptom scoring tool in the TB Treatment Decision Algorithm in Figure 6 on page 29 aims to facilitate TB diagnosis, particularly at the PHC level, where CXR and bacteriological testing may not be readily available. It features only the signs and symptoms section based on the child's clinical history and physical examination. When a clinical feature is present, the corresponding score is noted, and the scores are added. A decision to start treatment is made based on a score equal to or more than 11.

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

For example:

- If a child has a cough for more than 2 weeks (+5 points), fever for 5 days (0 points as it is less than 2 weeks) and tachypnoea (+2 points), the child is assigned 7 points and should not start TB treatment. The child should be treated for the most likely alternative diagnosis and reassessed in 1–2 weeks.
- If a child has a cough for more than 2 weeks (+5 points), weight loss (+5 points) and swollen lymph nodes (+7 points), the child is assigned 17 points and should start TB treatment.

Remember:

- If necessary, obtain telephonic advice to facilitate decision-making.
- The TB Treatment Decision Algorithm guides decision-making but does not replace clinical judgment.
 - A clinician could still choose to start TB treatment, even if the symptom score is less than 11.
 - Many TB symptoms are non-specific: a clinician could still consider other common childhood illnesses, even if the symptom score is 11 or more.

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. If sufficient clinical or radiological evidence suggests TB, treatment may be started without bacteriological confirmation.

Treatment decision algorithm (TDA)

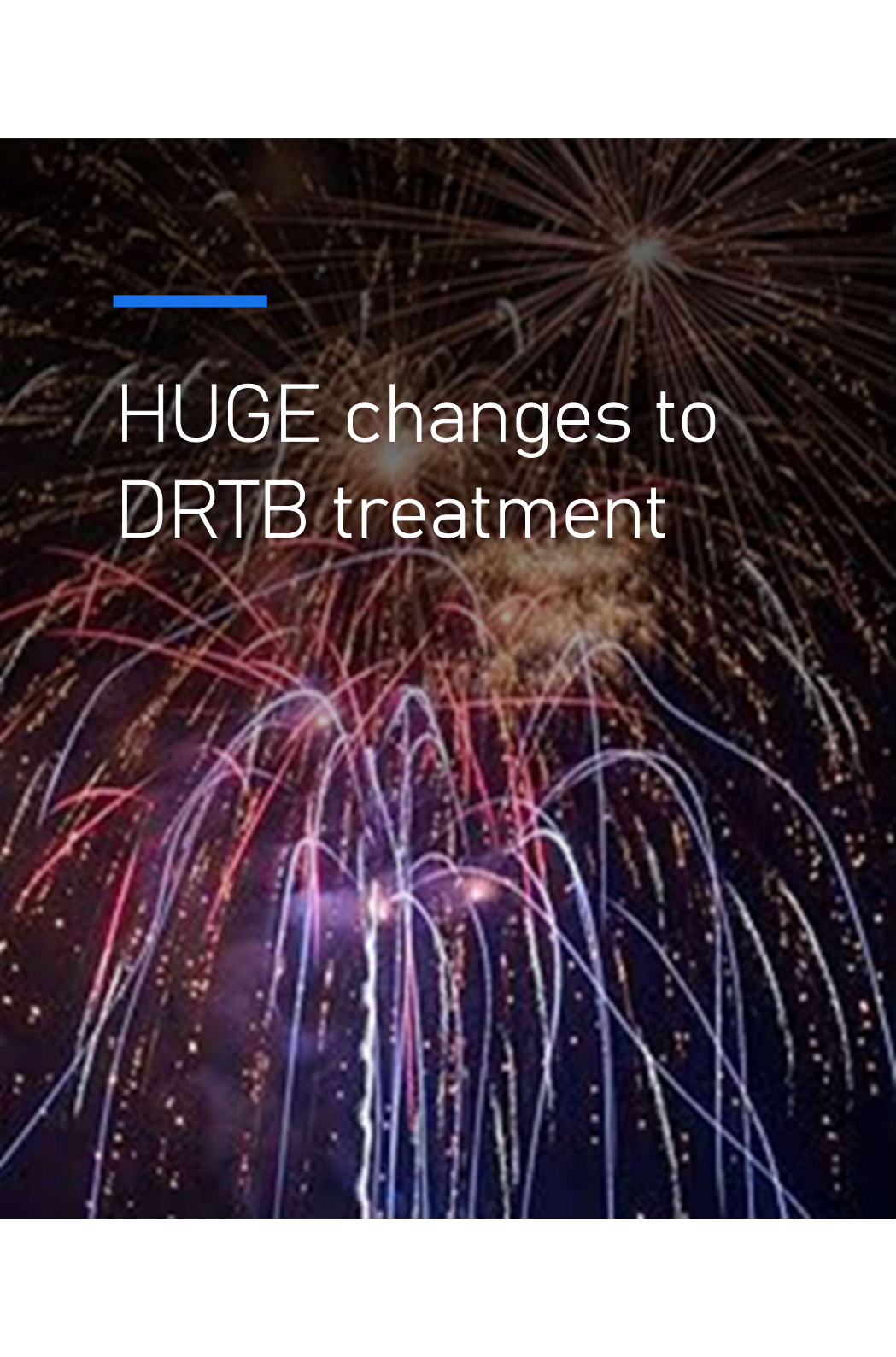
- introduced in 2022
- studies shown 86–90% sensitivity, 31–51% specificity

HELPFUL IN THE ABSENCE OF INVESTIGATIONS



Drug resistant TB

- Much more likely diagnosed in adults
- Children – trace contact's TB sensitivity results whenever possible
- TB-NAAT tests detect Rifampicin resistance – triggers further testing for multi-drug resistance
- Some TB-NAAT tests also look for INH resistance – commonly found with RR, but also exists as monoresistance
 - Therefore often missed
 - Reported as low or high level resistance
 - Looking at ways to detect this



HUGE changes to DRTB treatment

- 2018/2019 – WHO recommended changing from injectable agents to all oral agents
 - Some new (Pretomanid, Bedaquiline, Delamanid), some repurposed (Linezolid, fluoroquinolones, Clofazimine)
- South Africa – September 2023 – BPaL-L/M regimen – 6 month regimen!!!
 - Rifampicin resistant or Pre XDR TB, 15 years of age and older
 - For pulmonary and non-severe EPTB
 - HIV

Some other options – for children, pregnant and lactating women, PLHIV with DR TB

- BEAT TB trial (2023)
 - Bedaquiline, Delamanid, Linezolid, Levofloxacin, and Clofazimine for 6 months
 - All clinical TB *except* CNS, osteoarticular, disseminated TB (need drugs that will penetrate CNS, and/or longer duration)
- END TB trial (2023)
 - Similar eligibility criteria
 - 4-5 drugs for 9 months
 - Not for pre XDR TB

2022 – Delamanid and Bedaquiline
age limit dropped to zero years

Still not happy to use Pretomanid in
under 14 though



TPT updates

- For contacts of RRTB cases: 6 months of Levofloxacin
- For contacts of DSTB – new, shorter regimens available (where in stock)
 - 3HP – 3 months WEEKLY Rifapentine and INH
 - 1HP – 1 month DAILY Rifapentine and INH
 - 3HR – 3 months daily INH and Rifampicin
- PREVIOUSLY children < 5 years and PLHIV were prescribed TPT
- 2024 guidelines – suggest offering ALL contacts of any age, TPT

TB vaccines: a few in the pipeline



- **MTBVAC** – live attenuated, derived from human MTB strain – broader, more natural response
- **M72/AS01E** – an investigational subunit vaccine candidate combining M72 fusion protein and the AS01E adjuvant system
 - Prevent pulmonary TB in infected adolescents and adults

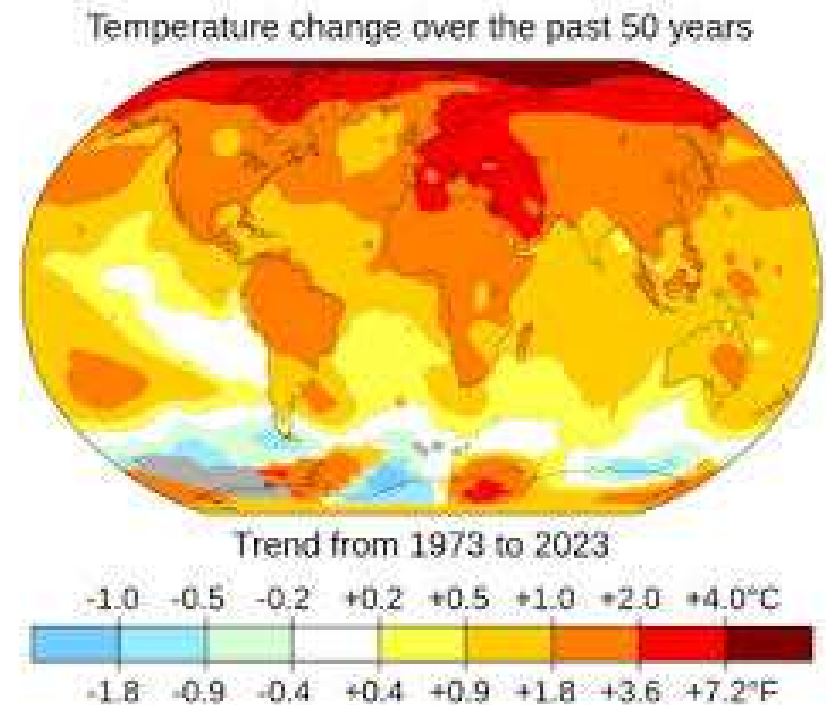


Malaria – what's been happening?

- Epidemiology
- Diagnostics
- Resistance – vector and parasite
- Treatment
- Prevention

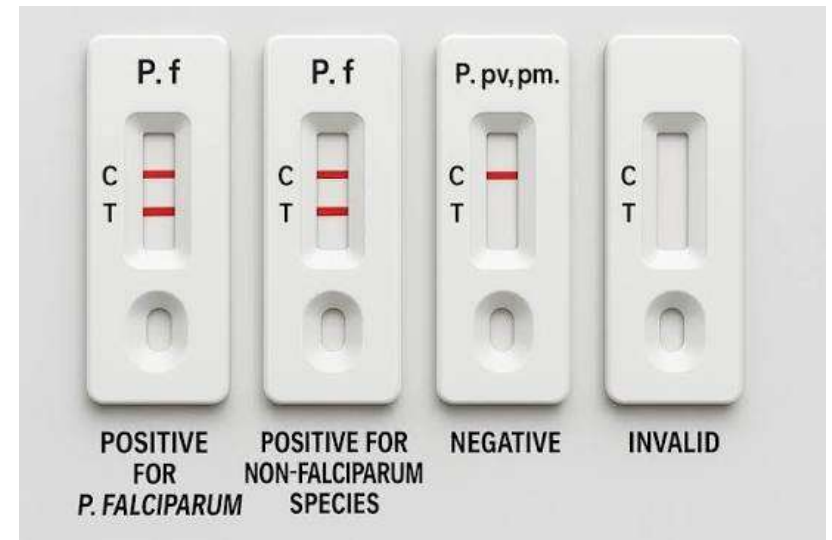
Malaria's changing epidemiology

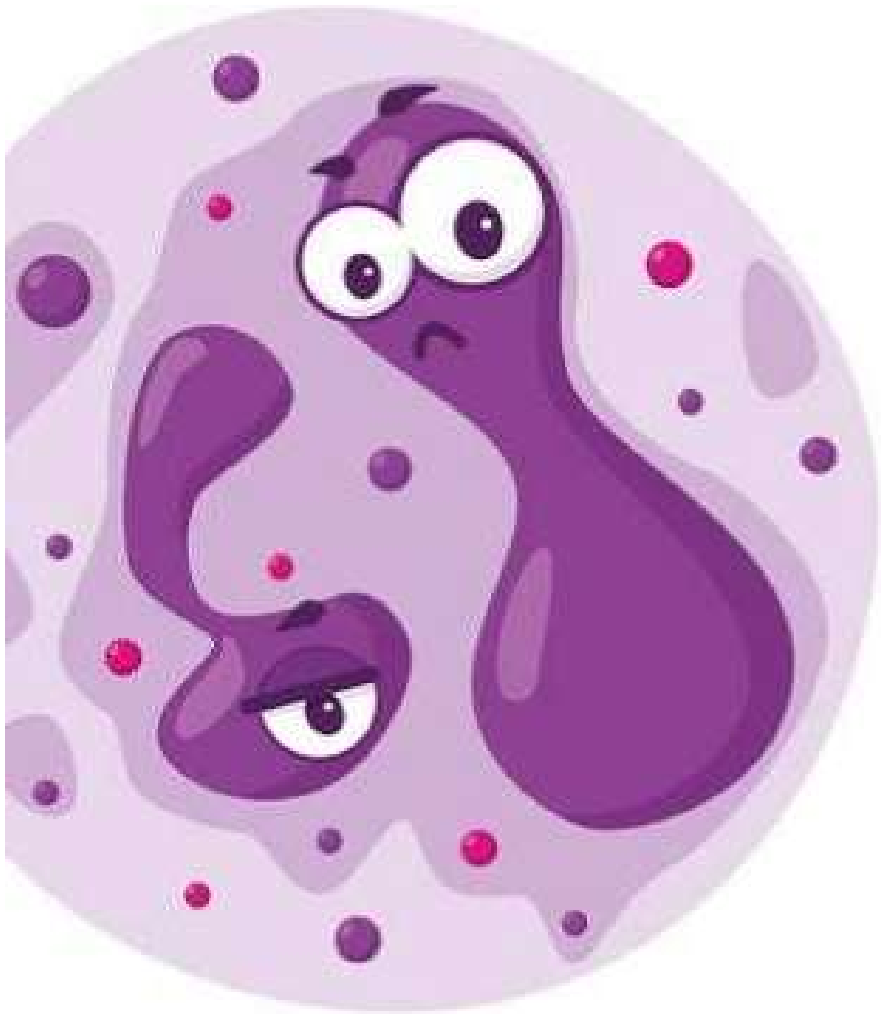
- Climate change
 - Higher temperatures = finding malaria in higher-altitude areas (E Africa)
 - Floods, cyclones – more breeding of vectors, also human migration from natural disasters
 - Surveillance and control efforts disrupted by unpredictable weather events
 - Increased heat may actually decrease vector survival and decrease malaria in some areas (W Africa)
 - Longer seasons of heat and rain



Diagnostics

- Gold standard still experienced microscopy
- Rapid tests cheap, quick, require minimal training
- PCR and LAMP are useful for:
 - low-density infection;
 - species confirmation;
 - elimination programmes;
 - epidemiological surveillance;
 - unresolved microscopy/RDT discrepancies





- Diagnostic escape: *pfhrp2/3* deletion
- Some *P. falciparum* parasites **lack** the HRP2 or HRP3 antigen targeted by many rapid diagnostic tests
- Can produce a **false-negative** HRP2 RDT
- This is not antimalarial resistance, but it selects diagnostically “invisible” parasites and **can coexist with K13**

Resistance

- Mosquitoes developing resistance to insecticides
- Plasmodium parasite developing resistance to artemisinin-based treatments
 - partial resistance
 - delayed parasite clearance
 - problem when existing partner drug resistance or if develops
- Main molecular markers occur in *Pfkelch13* gene
- Partial resistance established/ suspected in several parts of East Africa and the Horn of Africa



Uncomplicated malaria: medication and duration

- Uncomplicated *P. falciparum* (and in all trimesters of pregnancy)
- Treat with a locally effective artemisinin-based combination therapy, commonly:
 - artemether–lumefantrine; or
 - another nationally recommended ACT.
- 3 days – 6 doses, with fatty meals
- Do not use:
 - oral artemisinin monotherapy;
 - chloroquine for uncomplicated *P. falciparum* acquired in most of Africa;
 - an incomplete ACT course merely because fever resolves



Severe malaria: treat first, refine later

- First-line treatment
- Intravenous or intramuscular artesunate (rectal also an option)
- Quinine ONLY when no artesunate or artemether available
- After parenteral therapy, complete a full 3-day ACT. The parenteral doses do not replace the definitive oral combination course.



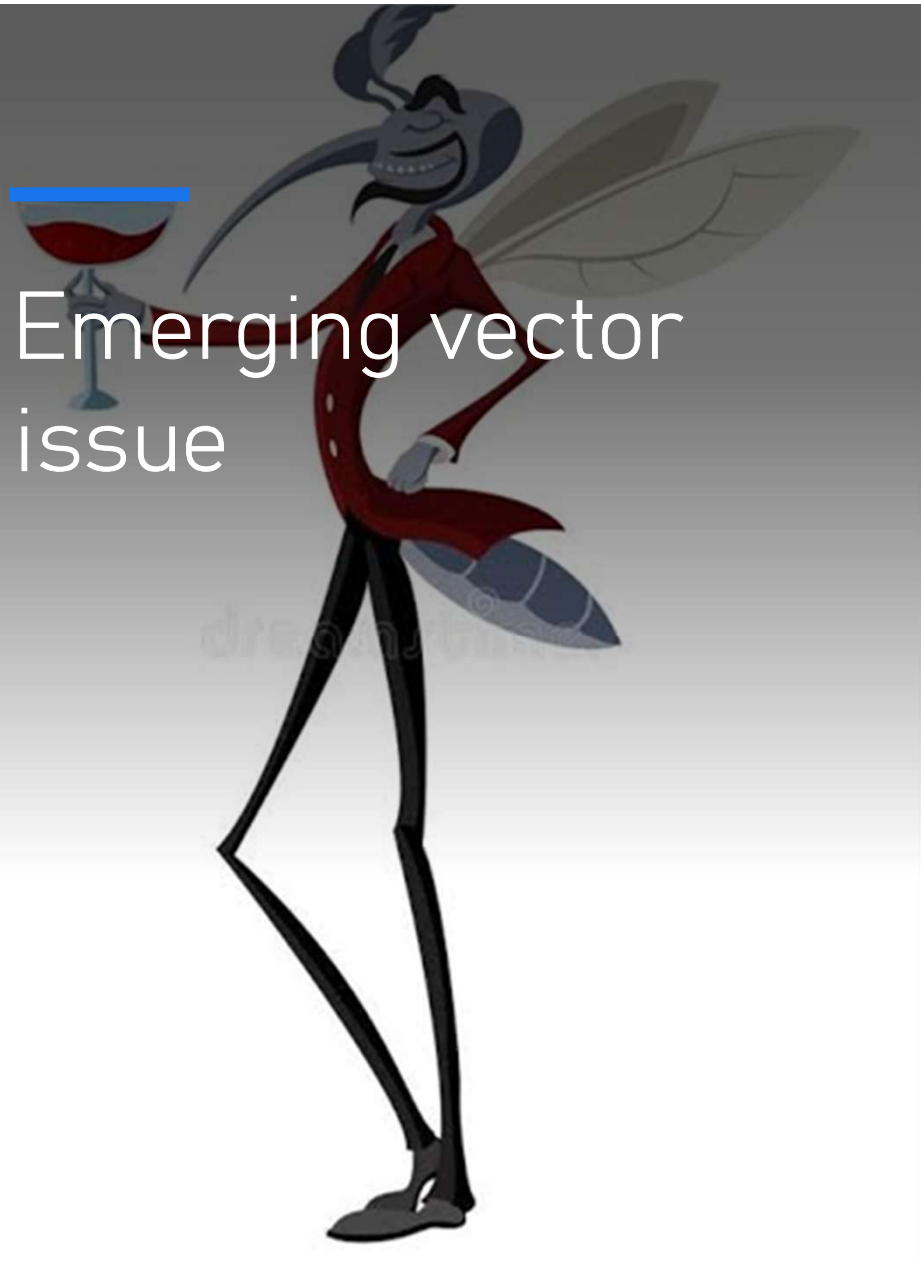
Vaccines, vector control and the future

- Malaria vaccines
- WHO recommends two vaccines for prevention of *P. falciparum* malaria in children living in endemic areas:
- RTS,S/AS01 (2019)
- R21/Matrix-M (2023)
- four-dose schedules
 - from 5 months of age according to local programme design
 - population programmes in endemic settings, particularly moderate- to high-transmission areas
 - not as traveller vaccines or replacements for nets, prophylaxis and treatment.

Vector control/avoidance

- **Dual-Active Bed Nets:** Next-generation nets (such as those combining pyrethroids with chlorfenapyr)
- **Spatial Repellents:** Devices releasing safe airborne compounds create zones that deter mosquitoes from biting people indoors.
- **Larval Source Management:** Treating small standing water pools with safe microbial or chemical agents to stop young mosquitoes from growing.
- **Sterile mosquito technology** – releasing sterile male mosquitoes to reduce population





Emerging vector issue

- *Anopheles stephensi* is an invasive, urban-adapted vector spreading in parts of Africa. It breeds effectively in artificial water containers and could make malaria increasingly urban in affected regions
- (Main vectors are *A. gambiae*, *A. funestus*, and *A. arabiensis*)

Travelling with small kids?

- Prophylaxis: Atovaquone proguanil ideal choice
 - paed's formulation > 5kg not available
 - Adult formulation cannot be divided
- Mefloquine not available in SA
- Doxycycline not an option < 8 years
- Solution – other preventive measures
 - Avoidance if possible



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