New on treatment of Childhood DR-TB

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CHILDHOOD TB

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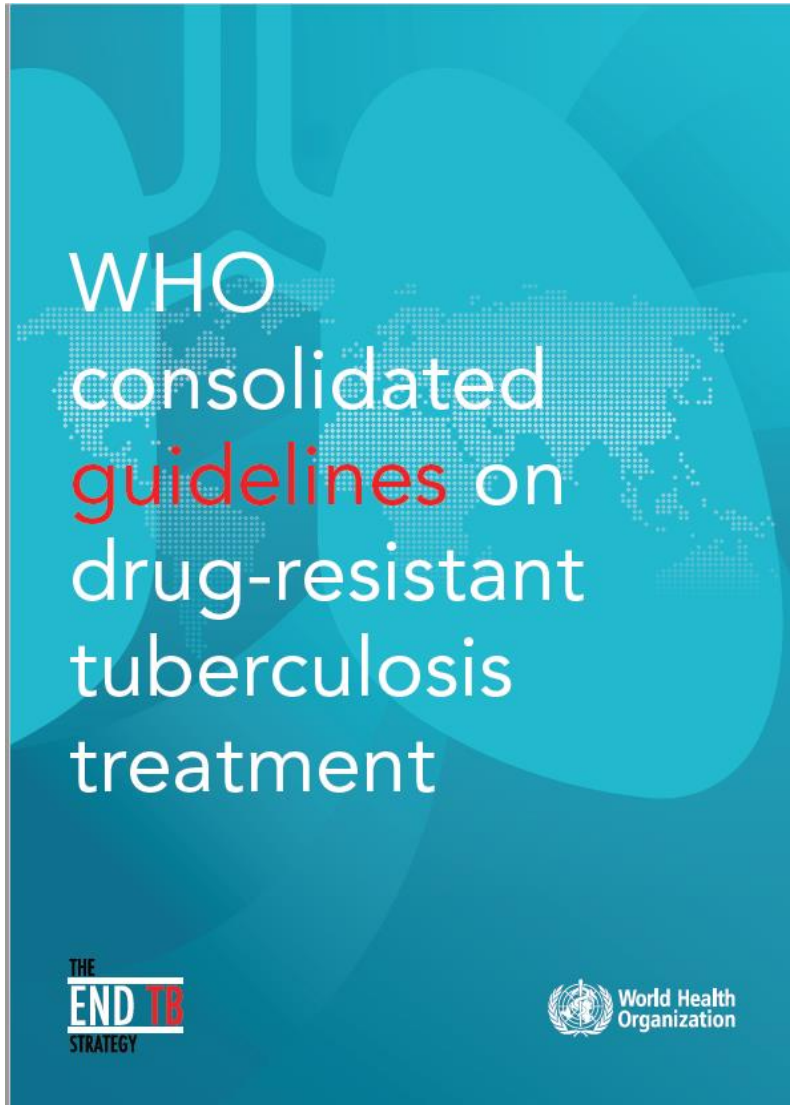
WHO CONSOLIDATED DR-TB guidelines 2019 update

Highlights on children and adolescents



CHILDHOOD TB

https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf?ua=1

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Recommendations on longer MDR-TB regimen composition applicable for children

- **Avoidance of injectable-containing regimen** particularly desirable
- **Bedaquiline** recommended for children **>6 years**
- **Delamanid*** recommended for children **>3 years**

**dispersible tablet used in trial not yet available*

Photo: Maxime Fossat

Dosage of medicines for children 1

Medicine	Weight-based daily dose[b]	Formulation	Weight bands among patients not yet 15 years old[a]						
			5–6 kg	7–9 kg	10–15 kg	16–23 kg	24–30 kg	31–34 kg	>34 kg
Fluoroquinolones									
Levofloxacin	15–20 mg/kg	100 mg dt	1	1.5	2 or 3	3 or 4	(>14 y)	(>14 y)	(>14 y)
		250 mg tab	0.5	0.5	1 or 1.5	1.5 or 2	2	3	(>14 y)
Moxifloxacin	10–15 mg/kg	100 mg dt	0.8	1.5	2	3	4	(>14 y)	(>14 y)
		400 mg tab[c]	2 ml[c]	3 ml[c]	5 ml[c]	0.5 or 0.75	1	(>14 y)	(>14 y)
Bedaquiline	-	100 mg tab	-	-	-	2 tabs od for two weeks; then 1 tab od M/W/F for 22 weeks		4 tabs od for 2 weeks; then 2 tabs od M/W/F for 22	
Linezolid	15 mg/kg od in <16 kg 10–12 mg/kg od in >15 kg	20 mg /ml susp	4 ml	6 ml	8 ml	11 ml	14 ml	15 ml	20 ml[d]
		600 mg tab[c]	0.25	0.25	0.25	0.5	0.5	0.5	0.75[d]
Clofazimine	2–5 mg/kg	50 mg cap	1 alt days	1 alt days	1 alt days	1	2	2	(>14 y)
		100 mg cap	M/W/F	M/W/F	1 alt days	1 alt days	1	(>14 y)	(>14 y)
Cycloserine or terizidone	15–20 mg/kg	125 mg mini capsule (cycloserine)	1	1	2	3	4	(>14 y)	(>14 y)
		250 mg cap[c]	4–5 ml[c]	5–6 ml[c]	7–10 ml[c]	2	2	2	(>14 y)

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Dosage of medicines for children 2

Medicine	Weight-based daily dose[b]	Formulation	Weight bands among patients not yet 15 years old[a]						
			5–6 kg	7–9 kg	10–15 kg	16–23 kg	24–30 kg	31–34 kg	>34 kg
Ethambutol	15–25 mg/kg	100 mg dt	1	2	3	4	-	-	(>14 y)
		400 mg tab[c]	3 ml[c]	4 ml[c]	6 ml[c]	1	1 or 1.5	2	(>14 y)
Delamanid	-	50 mg tab	-	-[e]	-[e]	-[e]	1 bd	1 bd	2 bd
Pyrazinamide	30–40 mg/kg	150 mg dt	1	2	3	4 or 5	-	-	(>14 y)
		400 mg tab	0.5	0.75	1	1.5 or 2	2.5	3	(>14 y)
		500 mg tab	0.5	0.5	0.75 or 1	1.5	2	2.5	(>14 y)
Imipenem-cilastatin	-	0.5 g + 0.5 g vial	-	-	-	-	-	-	-
Meropenem	20–40 mg/kg iv every 8 hours	1 g vial (20 ml)	2 ml	4 ml	6 ml	8-9 ml	11 ml	(>14 y)	(>14 y)
Amikacin	15–20 mg/kg	500 mg/2 ml vial[f]	0.4 ml	0.6 ml	0.8 - 1.0 ml	1.2 - 1.5 ml	2.0 ml	(>14 y)	(>14 y)
Streptomycin	20–40 mg/kg	1 g vial[f]	Calculate according to the dilution used					(>14 y)	(>14 y)
Ethionamide or prothionamide	15–20 mg/kg	125 mg dt (ethionamide)	1	1	2	3	4	4	(>14 y)
		250 mg tab	0.5	0.5	1	2	2	2	(>14 y)
p-aminosalicylic acid	200–300 mg/kg in 2 divided doses	PAS acid (4 g) sachet	0.5–0.75 g bd	0.75–1 g bd	1–2 g bd	2–3 g bd	3–3.5 g bd	(>14 y)	(>14 y)

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DR-TB treatment duration in children

- Largely guided by achieving 18-20 months as many may only be clinically diagnosed or have extrapulmonary disease
- **Shortening to less than 18 months may be considered** in the case of children without severe disease
  - *No presence of cavities or bilateral disease on chest radiography*
  - *No extrapulmonary forms of disease other than lymphadenopathy (peripheral nodes or isolated mediastinal mass without compression)*

Sentinel guide – linking theory with practice

Management of Multidrug-Resistant Tuberculosis in Children:

A FIELD GUIDE

Fourth Edition: February 2019

Cover photo courtesy of Marcela Tommasi

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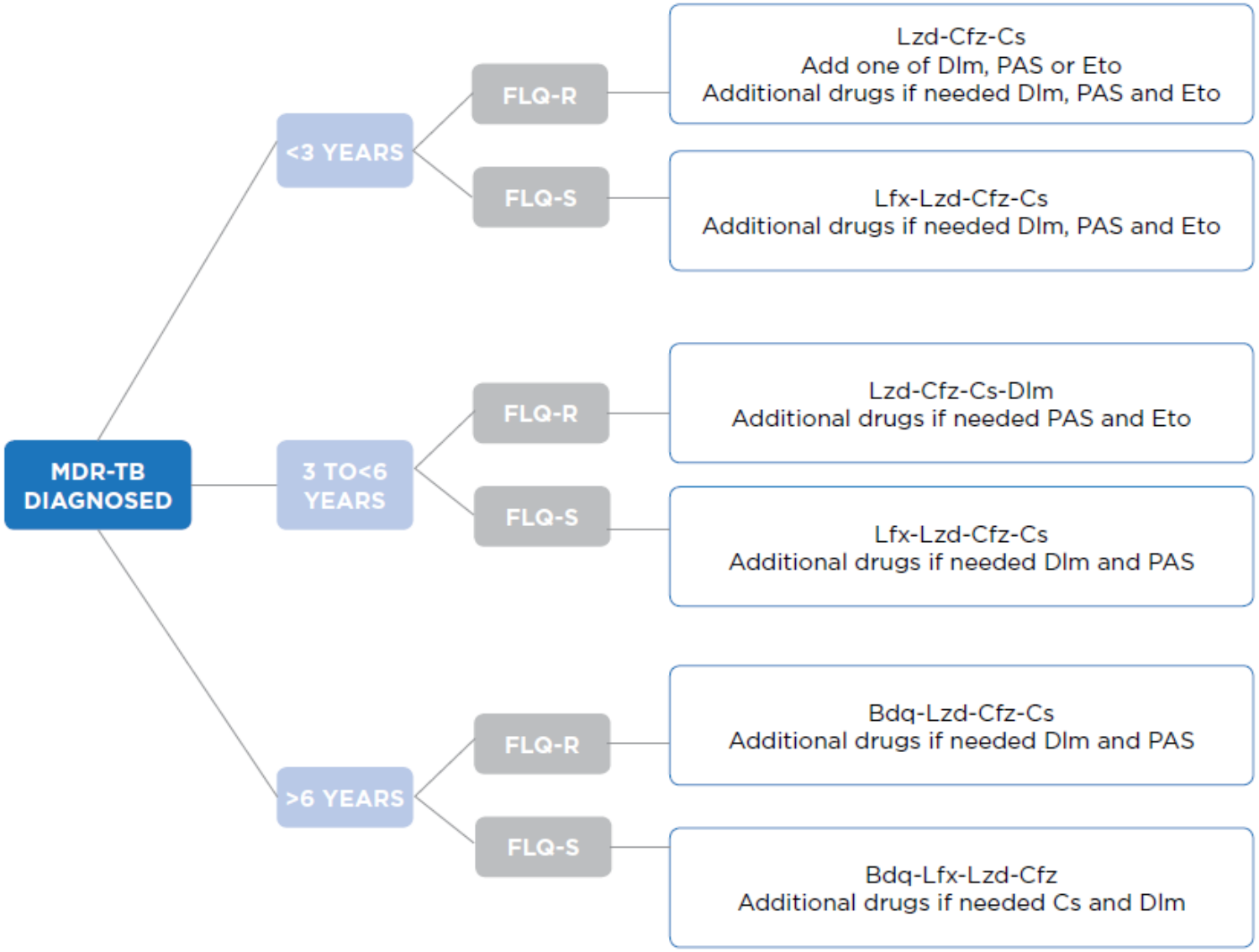
Suggested regimens for children of different ages and with different resistant profiles to the fluoroquinolones



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Key points 1

- Treatment based on the DST pattern of any known close contacts if the child does not have a DST of his or her own
- The duration of therapy should depend upon the extent of disease: children with **non-severe disease** can be treated **for 9 to 12 m** while **children with severe disease** will require **12-18 m** of therapy

Key points 2

- Regimens consist of **4 to 5 presumed effective drugs**: using more drugs adds to the toxicity of the regimen and does not likely improve efficacy if **Group A and B drugs and/or delamanid** are used
- Linezolid should be given to all children with TB meningitis
- **Child-friendly formulations** of the medications should be used whenever possible

Adult formulations for children – incorrect dosage and bad taste

Photo: Maxime Fossat

Formulations available from the Global Drug Facility

Drug	Formulation	Approval	Supplier
Ethambutol	100mg scored, dispersible tablet	WHO Pre-Qualified (PQ)	Via Global Drug Facility (GDF)
Isoniazid	100mg scored, dispersible tablet	Submitted	Via GDF
Pyrazinamide	150mg scored, dispersible tablet	WHO PQ	Via GDF
Levofloxacin	100mg scored, dispersible tablet	WHOPQ	Via GDF
Moxifloxacin	100mg scored, dispersible tablet	Expert Review Panel (ERP)	Via GDF
Linezolid	150mg scored, dispersible tablet	ERP	Not yet available
Ethionamide	125mg scored, dispersible tablet	WHOPQ	Via GDF
Cycloserine	125mg minicapsule	WHOPQ	Via GDF

SOPs available in English and Russian
For TA, please, contact Dr. Jennifer Furin jenniferfurin@gmail.com and GDF focal point

Next steps

- Facilitate, advocate, negotiate
  - *Update national policy, SOPs*
  - *Overcome regulatory barriers*
  - *Address acceptance issues*
- Collect/share data on children (disaggregated by **weight** and age) to estimate the real needs and to contribute to the global evidence

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