Individual treatment in drug resistant: meet the challenges

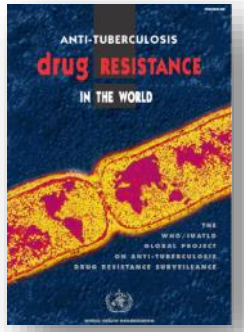
Harsini

FK UNS/ RSUD Dr. Moewardi

The Global Project on Anti-TB Drug Resistance Surveillance, 1994-2018

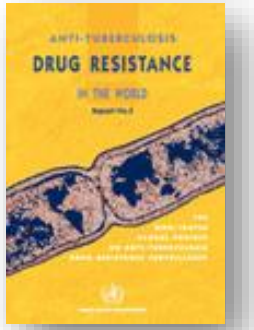
Global Project launched

SRL network launched

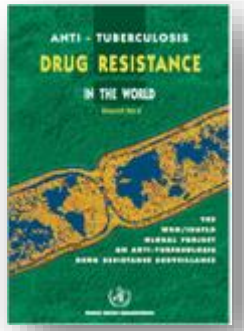


1st global DRS report

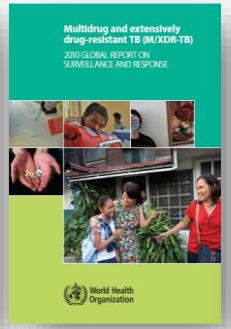
2nd global DRS report



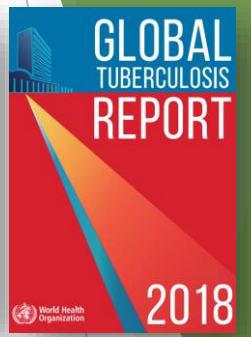
3rd global DRS report



4th global DRS report



M/XDR-TB report

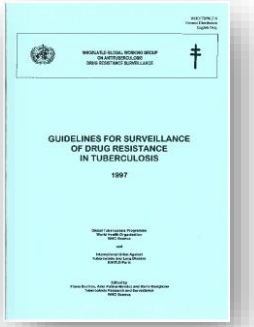


Global TB reports

1994 1997 2000 2003 2004 2008 2009 2010 2018

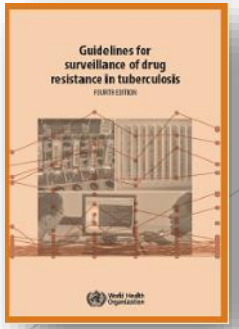
1st ed. DRS guidelines

2nd ed. DRS guidelines



3rd ed. DRS guidelines

4th ed. DRS guidelines



5th ed. DRS guidelines

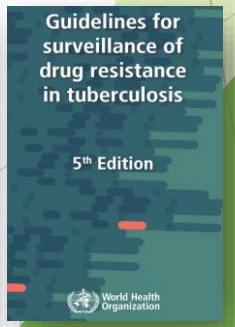


Table 6. Medicines recommended for the treatment of RR-TB and MDR-TB[a]

Group A. Fluoroquinolones[b]		Levofloxacin	Lfx
		Moxifloxacin	Mfx
		Gatifloxacin	Gfx
Group B. Second-line injectable agents		Amikacin	Am
		Capreomycin	Cm
		Kanamycin	Km
		(Streptomycin)[c]	(S)
Group C. Other core second-line agents[b]		Ethionamide / prothionamide	Eto / Pto
		Cycloserine / terizidone	Cs / Trd
		Linezolid	Lzd
		Clofazimine	Cfz
Group D. Add-on agents (not part of the core MDR-TB regimen)	**D1**	Pyrazinamide	Z
		Ethambutol	E
		High-dose isoniazid	H[h]
	D2	Bedaquiline	Bdq
		Delamanid	Dlm
	D3	*p*-aminosalicylic acid	PAS
		Imipenem–cilastatin[d]	Ipm
		Meropenem[d]	Mpm
		Amoxicillin-clavulanate[d]	Amx-Clv
		(Thioacetazone)[e]	(T)

WHO. 2016

Longer/ individual treatment regimens for RR-TB

- In patients with RR-TB or MDR-TB, a regimen with at least five effective TB medicines during the intensive phase is recommended, including pyrazinamide and four core secondline TB medicines – one chosen from Group A, one from Group B, and at least two from Group C (conditional recommendation, very low certainty in the evidence). If the minimum number of effective TB medicines cannot be composed as given above, an agent from Group D2 and other agents from Group D3 may be added to bring the total to five.
- • In patients with RR-TB or MDR-TB, it is recommended that the regimen be further strengthened with high-dose isoniazid and/or ethambutol (conditional recommendation, very low certainty in the evidence).


WHO
consolidated
guidelines on
drug-resistant
tuberculosis
treatment
THE
END TB
STRATEGY
World Health
Organization

WHO 2019

Table 2.1. Grouping of medicines recommended for use in longer MDR-TB regimens[1]

Groups & steps	Medicine	
Group A: Include all three medicines	levofloxacin *OR* moxifloxacin	Lfx Mfx
	bedaquiline[2,3]	Bdq
	linezolid[4]	Lzd
Group B: Add one or both medicines	clofazimine	Cfz
	cycloserine *OR* terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	ethambutol	E
	delamanid[3,5]	Dlm
	pyrazinamide[6]	Z
	imipenem–cilastatin *OR* meropenem[7]	Ipm–Cln Mpm
	amikacin (*OR* streptomycin)[8]	Am (S)
	ethionamide *OR* prothionamide[9]	Eto Pto
	p-aminosalicylic acid[9]	PAS

- Group A: fluoroquinolones (levofloxacin and moxifloxacin), bedaquiline and linezolid were considered highly effective and strongly recommended for inclusion in all regimens unless contraindicated.

- Group B: clofazimine and cycloserine or terizidone were conditionally recommended as agents of second choice.

- Group C: included all other medicines that can be used when a regimen cannot be composed with Group A and B agents. The medicines in Group C are ranked by the relative balance of benefit to harm usually expected of each

The composition of longer MDR-TB regimens

- 1. (3 Group A + 1 Group B)

In MDR/RR-TB patients on longer regimens, all 3 Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of treatment after bedaquiline is stopped.

- 1-2 Group A +Group B + Group C
- If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it (conditional recommendation, very low certainty in the estimates of effect).

- 2.2. Kanamycin and capreomycin are not to be included in the treatment of MDR/RR-TB patients

- 2.3. Levofloxacin or moxifloxacin should be included in the treatment of MDR/RR-TB patients on longer regimens (strong recommendation, moderate certainty in the estimates of effect).

- 2.4. Bedaquiline should be included in longer MDR-TB regimens for patients aged 18 years or more (strong recommendation, moderate certainty in the estimates of effect). Bedaquiline may also be included in longer MDR-TB regimens for patients aged 6–17 years (conditional recommendation, very low certainty in the estimates of effect).

- 2.5. Linezolid should be included in the treatment of MDR/RR-TB patients on longer regimens (strong recommendation, moderate certainty in the estimates of effect).
- 2.6. Clofazimine and cycloserine or terizidone may be included in the treatment of MDR/RR-TB patients on longer regimens (conditional recommendation, very low certainty in the estimates of effect).
- 2.7. Ethambutol may be included in the treatment of MDR/RR-TB patients on longer regimens (conditional recommendation, very low certainty in the estimates of effect).

- 2.8. Delamanid may be included in the treatment of MDR/RR-TB patients aged 3 years or more on longer regimens (conditional recommendation, moderate certainty in the estimates of effect).
- 2.9. Pyrazinamide may be included in the treatment of MDR/RR-TB patients on longer regimens (conditional recommendation, very low certainty in the estimates of effect).
- 2.10. Imipenem–cilastatin or meropenem may be included in the treatment of MDR/RR-TB patients on longer regimens (conditional recommendation, very low certainty in the estimates of effect).2

- 2.11. Amikacin may be included in the treatment of MDR/RR-TB patients aged 18 years or more on longer regimens when susceptibility has been demonstrated and adequate measures to monitor for adverse reactions can be ensured. If amikacin is not available, streptomycin may replace amikacin under the same conditions (conditional recommendation, very low certainty in the estimates of effect).

- 2.12. Ethionamide or prothionamide may be included in the treatment of MDR/RR-TB patients on longer regimens only if bedaquiline, linezolid, clofazimine or delamanid are not used or if better options to compose a regimen are not possible (conditional recommendation against use, very low certainty in the estimates of effect).

- 2.13. p-aminosalicylic acid may be included in the treatment of MDR/RR-TB patients on longer regimens only if bedaquiline, linezolid, clofazimine or delamanid are not used or if better options to compose a regimen are not possible (conditional recommendation against use, very low certainty in the estimates of effect).

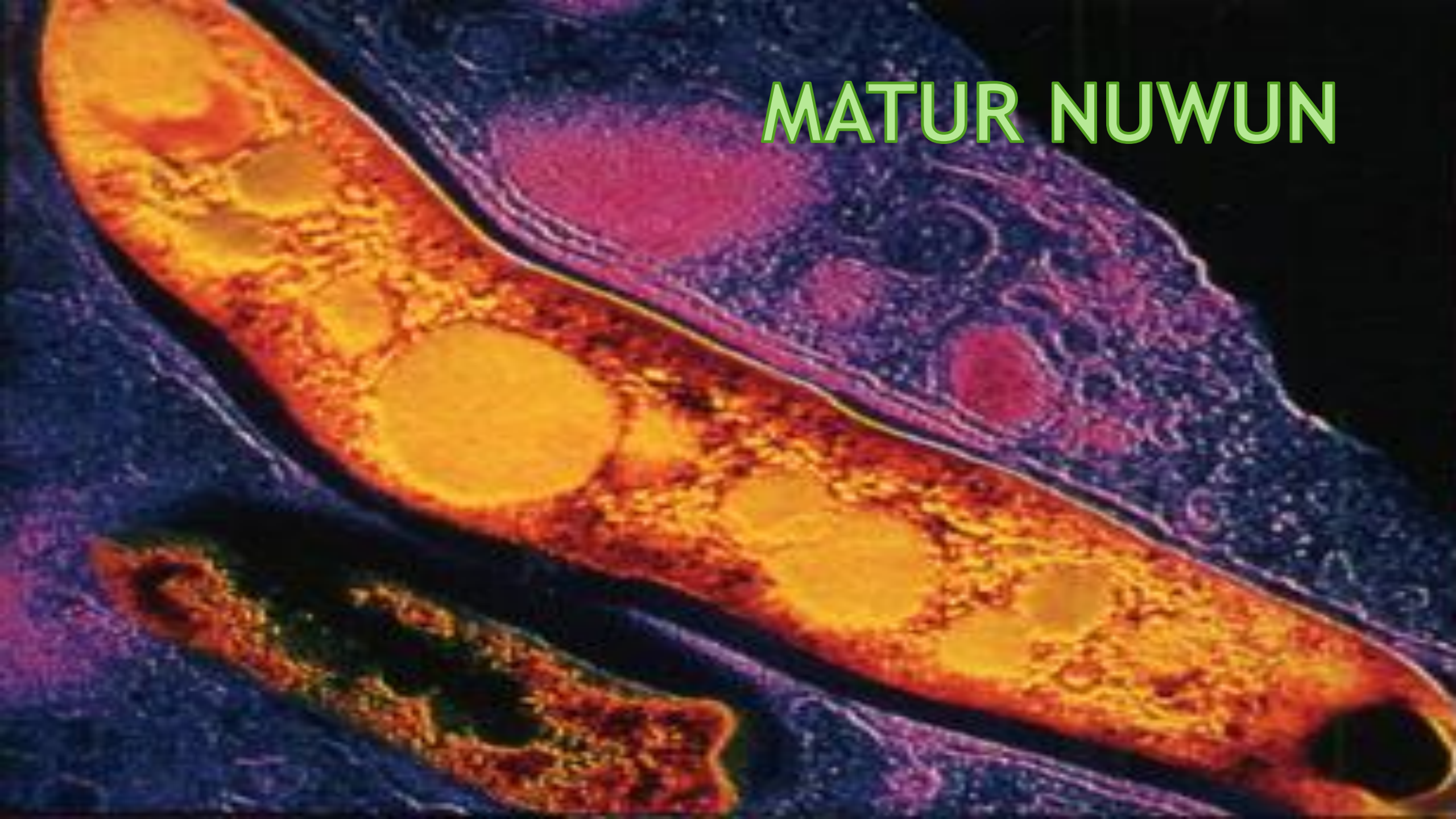
- 2.14. ~~Clavulanic acid should not be included in the treatment of MDR/RR-TB patients on longer regimens~~ (strong recommendation against use, low certainty in the estimates of effect).

RENCANA REJIMEN DI INDONESIA

1.	TB RR/MDR eligible STR dengan injeksi Km	4-6 Km-Mfx-Cfz-Eto-H^{DT}-Z-E/5 Mfx-Cfz-Z-E
2.	TB RR/MDR tidak eligible STR and Pre-XDR SLI (*all oral longer regimen*).	6 Bdq-Lfx-Lzd-Cfz-Cs / 12 - 14 Lfx-Lzd-Cfz-Cs 6 Bdq-Lfx-Cfz-Cs-E / 14 Lfx-Cfz-Cs-E 6 Bdq-Lfx-Lzd-Cfz-E / 14 Lfx-Lzd-Cfz-E 6 Bdq-Mfx-Lzd-Cfz-E / 14 Mfx-Lzd-Cfz-E
3.	TB pre-XDR Resisten Flourokuinolon dan TB XDR	6 Bdq-Lzd-Cfz-Cs-E / 14 Lzd-Cfz-Cs-E 6 Bdq-Lzd-Cfz-Cs-Eto / 14 Lzd-Cfz-Cs-Eto
4.	Intoleran atau ada efek samping Bdq atau pasien usia di bawah 18 tahun, di mana Bedaquilin tidak bisa digunakan, HIV, DM,	6 Dlm-Lfx-Lzd-Clz-Cs / 14 Lfx-Lzd-Clz-Cs 6 Dlm-Lzd-Clz-Cs-E / 14 Lzd-Clz-Cs-E 20 Lfx-Lzd-Cfz-Cs-Eto 20 Mfx-Lzd-Cfz-Cs-E 20 Mfx-Lzd-Cfz-Cs-Z 6 Lfx-Lzd-Cfz-Cs-Amk / 14 Lfx-Lzd-Cfz-Cs 6 Lfx-Lzd-Cfz-Cs-S / 14 Lfx-Lzd-Cfz-Cs 6 Lfx-Lzd-Clz-Eto-PAS / 14 Lfx-Lzd-Clz-Eto

DURATION OF LONGER MDR-TB REGIMENS

- 1. A total treatment duration of 18–20 months is suggested for most patients; the duration may be modified according to the patient's response to therapy
- 2. A treatment duration of 15–17 months after culture conversion is suggested for most patients; the duration may be modified according to the patient's response to therapy
- 3. In MDR/RR-TB patients on longer regimens containing amikacin or streptomycin, an intensive phase of 6–7 months is suggested for most patients; the duration may be modified according to the patient's response to therapy


MATUR NUWUN