TB/TB-HIV/MDR-TB Situation in Global/SEAR & Myanmar

Dr. Si Thu Aung

Director (TB/Leprosy/Trachoma)

Department of Public Health

26 November 2020

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- ✓DR-TB situation in Myanmar (2020 Global TB Report)
- ✓Milestones and service expansions
- ✓Program achievements (enrolled numbers and treatment outcomes)
- ✓Treatment regimens
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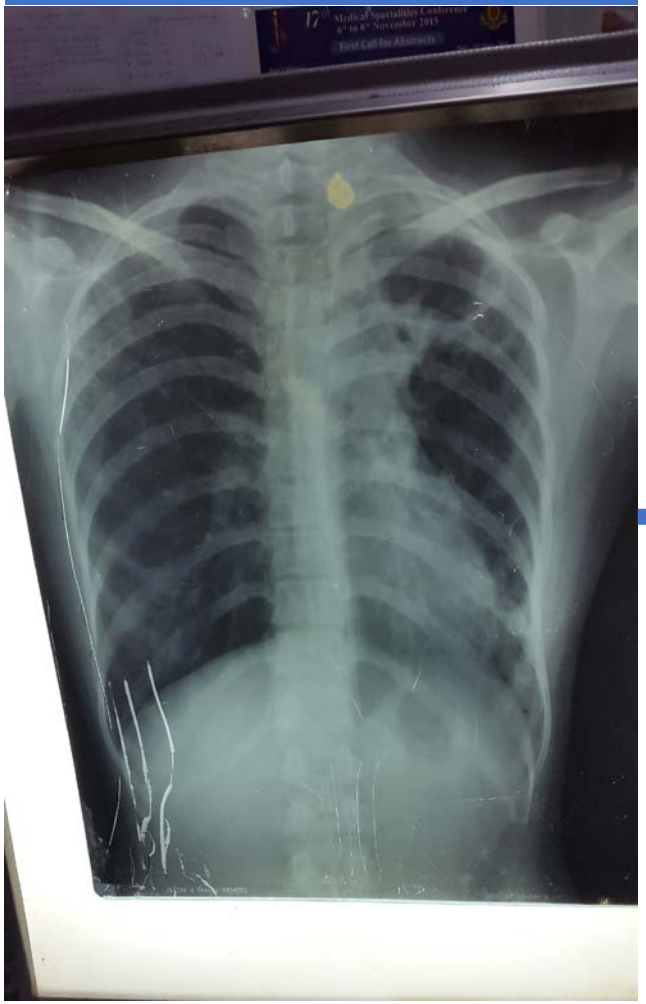
- ✓BPaL operational research
- ✓Challenges and way forward

Definitions of TB drug resistance

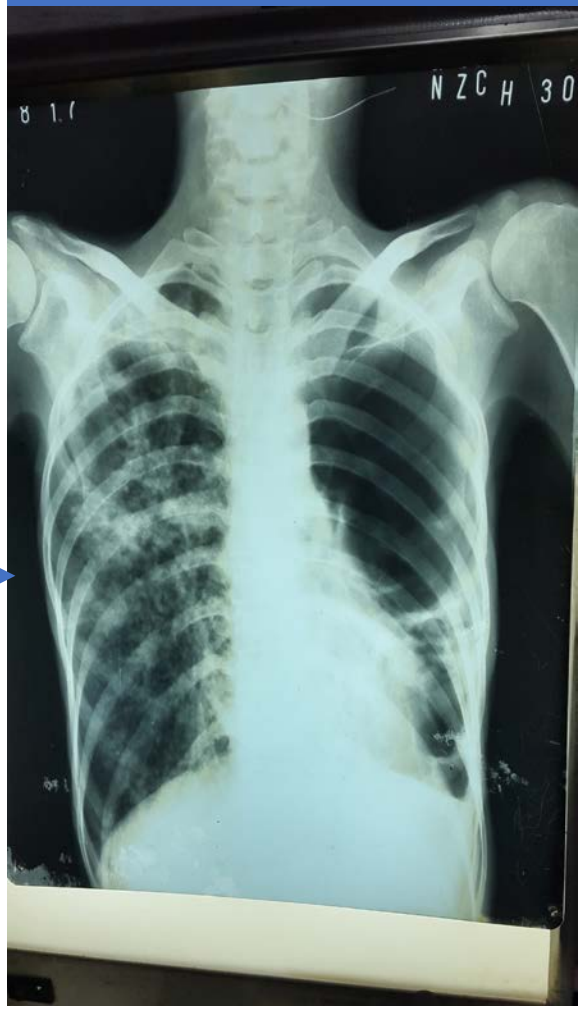
- **Mono-resistance:** Resistance to one anti-TB drug.
- **Poly-resistance:** Resistance to more than one anti-TB drug, other than isoniazid plus rifampicin.
- **Multidrug-resistant TB (MDR-TB):** Resistance to at least isoniazid plus rifampicin, the two most potent anti-TB agents.
- **Rifampicin-resistant TB (RR-TB):** Resistance to rifampicin detected using pheno-typic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, including mono-resistance, multi-drug resist- ance , poly-resistance (other than MDR-TB) and XDR-TB.
- **Extensively drug-resistant TB (XDR-TB):** MDR-TB, plus resistance to at least one of the fluoroquinolones, ***and*** at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin).

28 year old female, RR +ve in 2015



Refused for DR-TB treatment, disease progression after 2 years from initial diagnosis

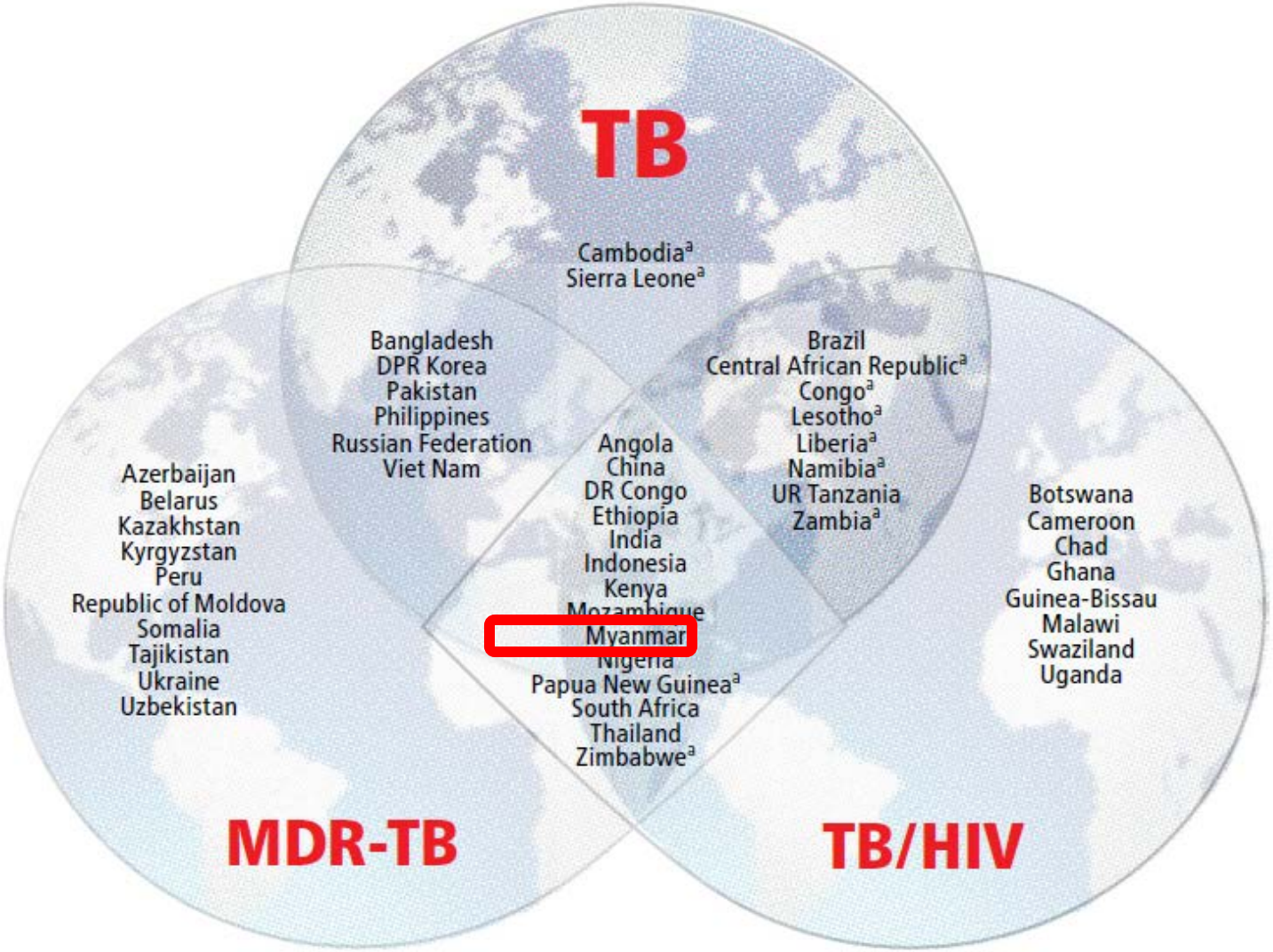
Same patient in 2017



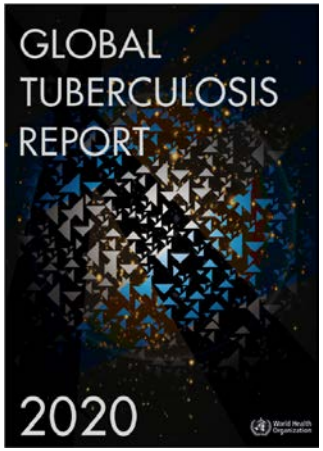
Issues around DR-TB control

Issues	Effort by NTP and partners	Appeal support from other sectors
Stigma Health literacy Loss of income	Encouraging counseling sessions	Infectious disease law Community support Job security
Access to diagnosis	Expansion of facilities equipped with rapid molecular tests	Sharing HR especially for sub-township level
Early initiation of treatment	Expansion of facilities to initiate treatment (MDR-TB centers)	Availability of hospital beds for DR-TB patients who need in-patient treatment Collaborative efforts from medical care side for aDSM
Access to quality care	Updating guidelines, trainings	
Management of side effects of second line medicines	Trainings, supply of required equipment (audiometers, ECGs, etc) and ancillary drugs	
Infection prevention and control	Trainings, supply of IPC materials such as masks.	Infectious disease law Work ethics (medical leave) Collaboration for contact tracing in the community and workplace

Countries in the three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020, and their areas of overlap



DR-TB situation in Myanmar



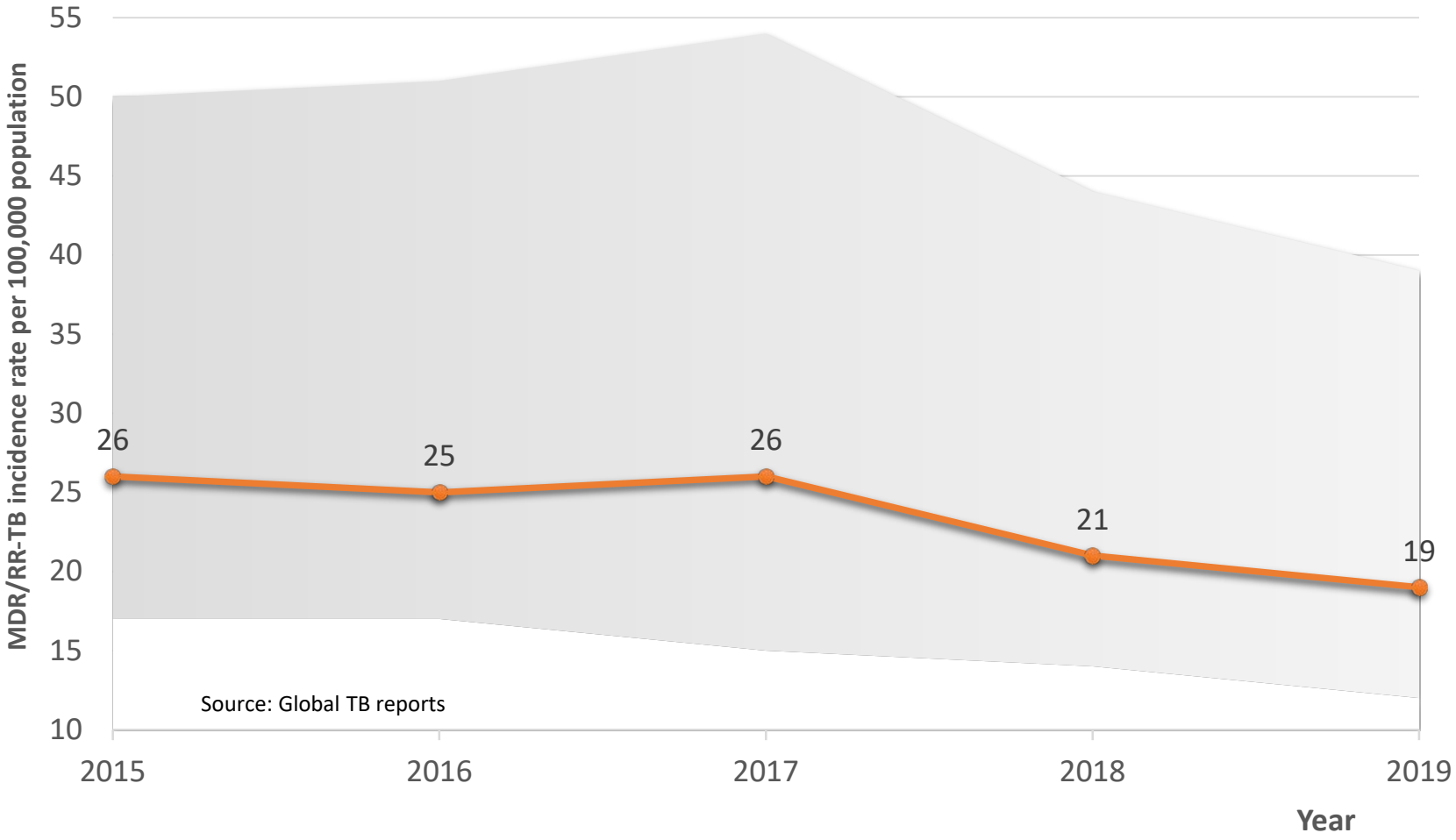
Myanmar

Population 2019 **54 million**

Estimates of TB burden[o], 2019	Number (thousands)	Rate (per 100 000 population)
Total TB incidence	174 (114–245)	322 (212–454)
HIV-positive TB incidence	14 (8.9–19)	25 (17–35)
MDR/RR-TB incidence[oo]	10 (6.8–15)	19 (12–27)
HIV-negative TB mortality	19 (12–29)	36 (21–54)
HIV-positive TB mortality	3.1 (2.1–4.4)	5.8 (3.8–8.1)

Estimated proportion of TB cases with MDR/RR-TB, 2019	
New cases	4.9% (4.7–5.1)
Previously treated cases	18% (17–19)

MDR /RR-TB incidence rate per 100,000 population, Myanmar (2011-2019)



Estimated TB Incidence per 100,000 population among 30 high TB burden countries (2019)

No.	Country	TB incidence per 100,000 population (2019)
1	Lesotho	654
2	South Africa	615
3	Philippines	554
4	Central African Republic	540
5	DPR Korea	513
6	Namibia	486
7	Papua New Guinea	432
8	Congo	373
9	Mozambique	361
10	Angola	351
11	Zambia	333
12	Myanmar	322
13	DR Congo	320
14	Indonesia	312
15	Liberia	308
16	Sierra Leone	295
17	Cambodia	287
18	Kenya	267
19	Pakistan	263
20	UR Tanzania	237
21	Bangladesh	221
22	Nigeria	219
23	Zimbabwe	199
24	India	193
25	Viet Nam	176
26	Thailand	150
27	Ethiopia	140
28	China	58
29	Russian Federation	50
30	Brazil	46

Source: Global TB report 2020

Estimated MDR/RR-TB Incidence per 100,000 population among 30 high TB burden countries (2019)

No.	Country	MDR/ RR-TB incidence per 100,000 population (2019)
1	Kyrgyzstan	43
2	Pepublic of Moldova	34
3	Russian Federation	27
4	Somalia	26
5	Tajikistan	26
6	Ukraine	25
7	South africa	23
8	Kazakhstan	22
9	Papua New Guinea	22
10	DPR Korea	20
11	Myanmar	19
12	Philippines	19
13	Mozambique	16
14	Angola	13
15	Belarus	13
16	Azerbaijan	12
17	Pakistan	12
18	Nigeria	11
19	Uzbekistan	9.7
20	Peru	9.6
21	India	9.1
22	Indonesia	8.8
23	Viet Nam	8.8
24	Zimbabwe	8.2
25	DR congo	7.5
26	China	4.5
27	Kenya	4.1
28	Thailand	3.6
29	Bangladesh	2
30	Ethiopia	1.3

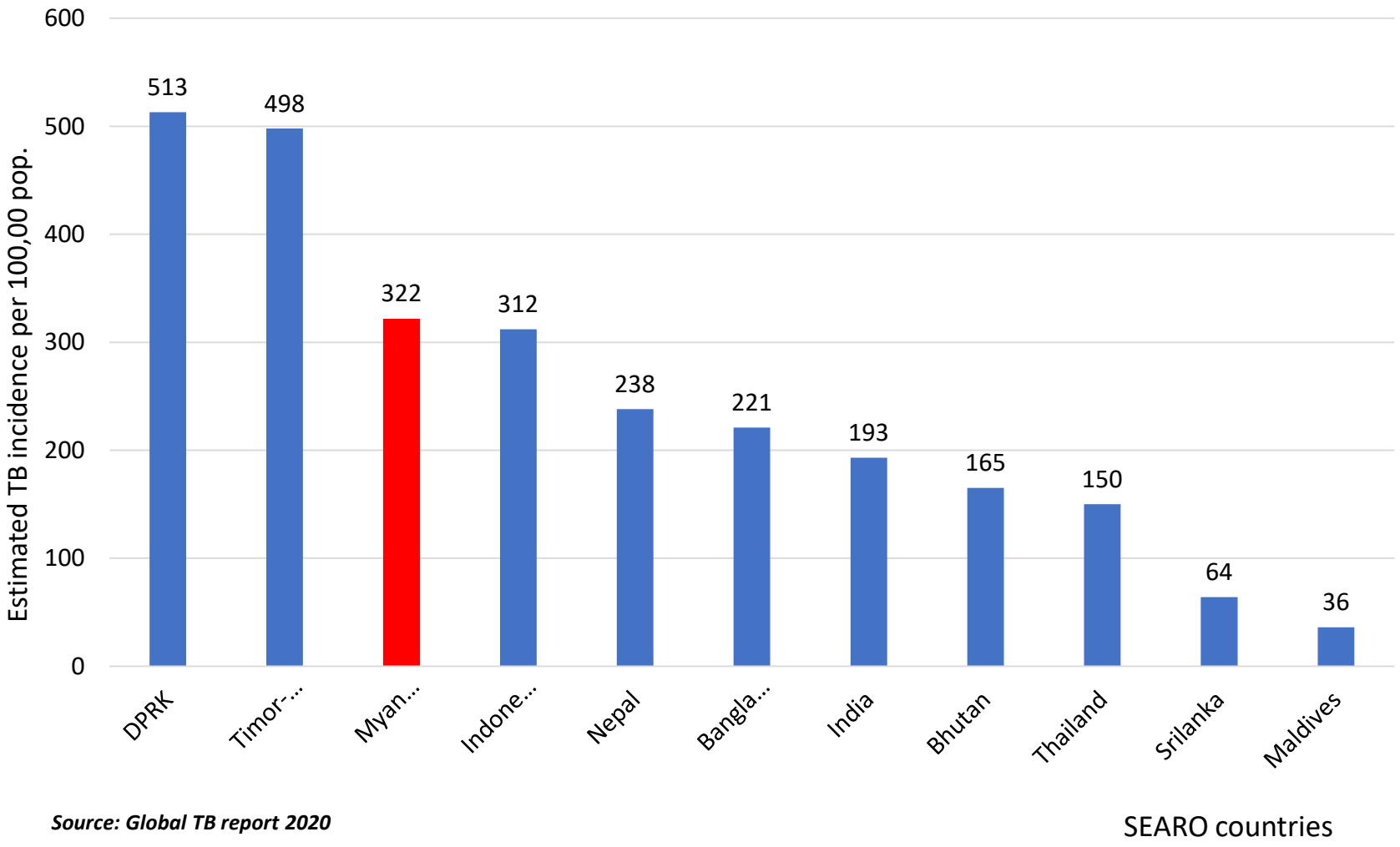
Source: Global TB report 2020

Estimated HIV Prevalence in incident TB (%) among 30 high TB burden countries (2019)

No.	Country	HIV PREVALENCE IN INCIDENT TB (%) (2019)
1	Lesotho	62
2	Zimbabwe	60
3	South Africa	58
4	Zambia	46
5	Mozambique	34
6	Namibia	32
7	Congo	29
8	Kenya	26
9	Central African Republic	25
10	UR Tanzania	24
11	Russian Federation	23
12	Liberia	14
13	Sierra Leone	13
14	Brazil	11
15	DR Congo	11
16	Nigeria	11
17	Thailand	10
18	Myanmar	7.8
19	Angola	7.6
20	Ethiopia	6.5
21	Papua New Guinea	3.8
22	Viet Nam	3.3
23	Cambodia	2.7
24	India	2.7
25	Indonesia	2.2
26	Philippines	1.9
27	China	1.6
28	Pakistan	0.9
29	Bangladesh	0.19
30	DPR Korea	

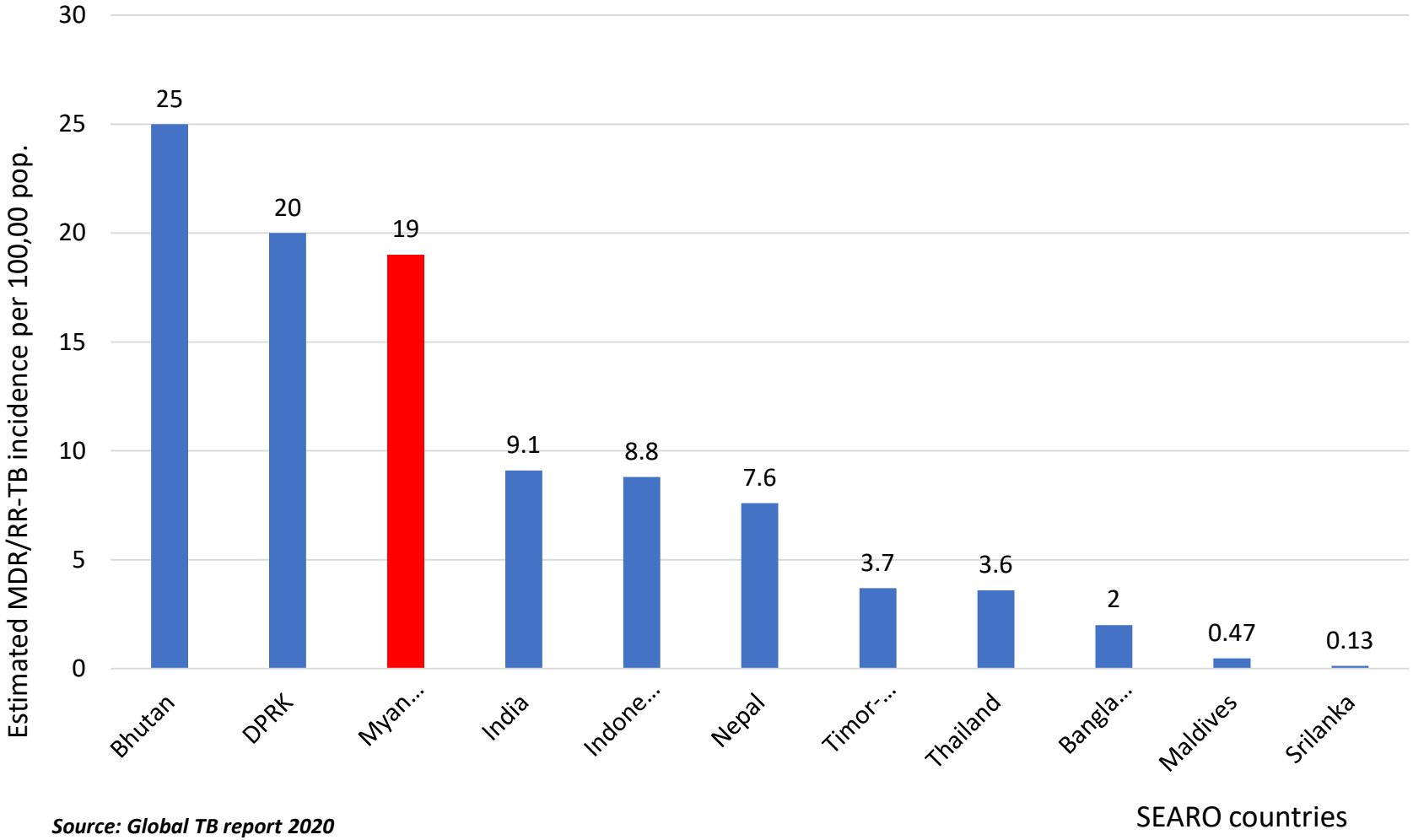
Source: Global TB report 2020

Estimated TB Incidence per 100,000 population among SEARO countries (2019)



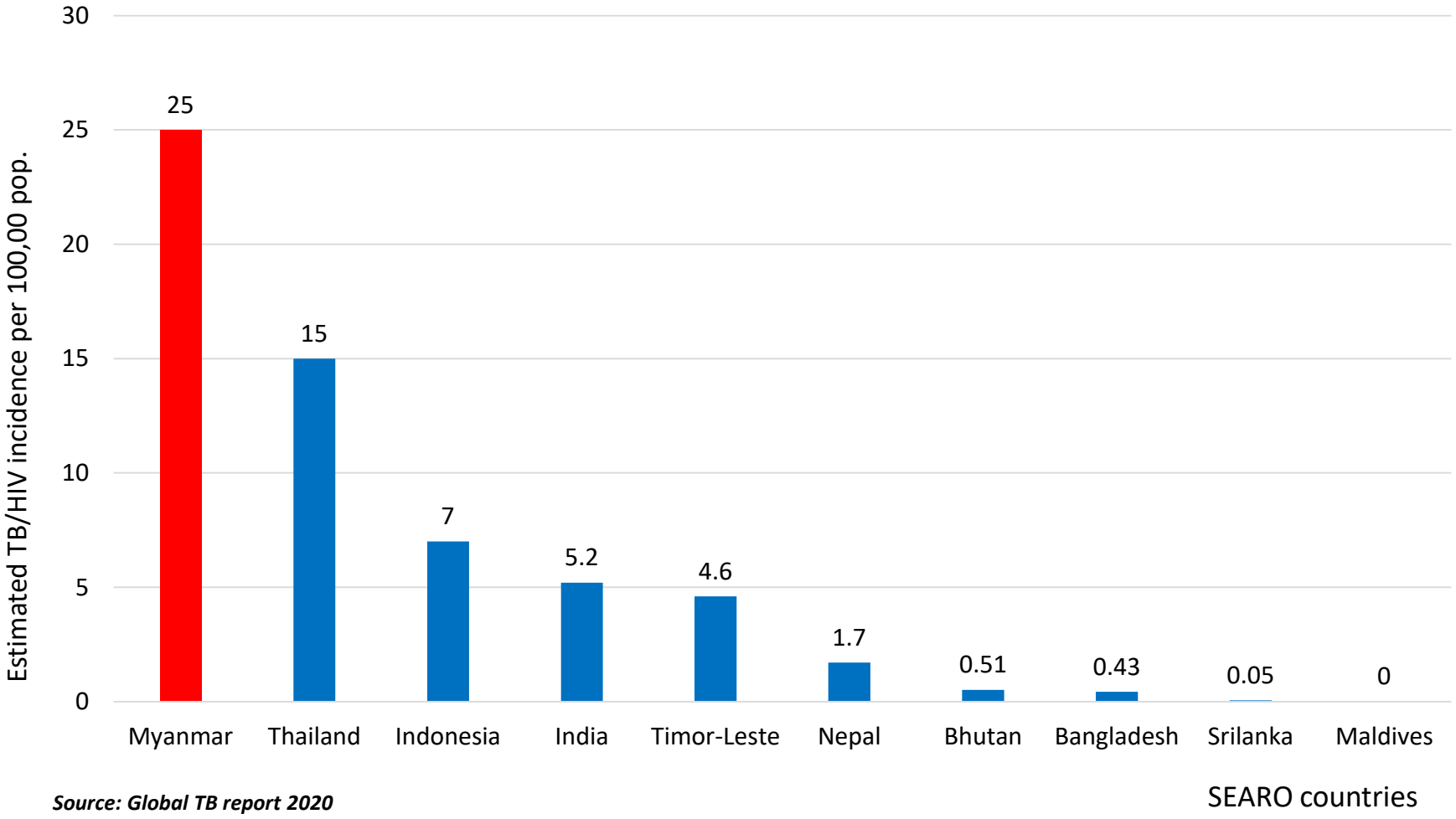
Source: Global TB report 2020

Estimated MDR/ RR-TB Incidence per 100,000 population among SEARO countries (2019)



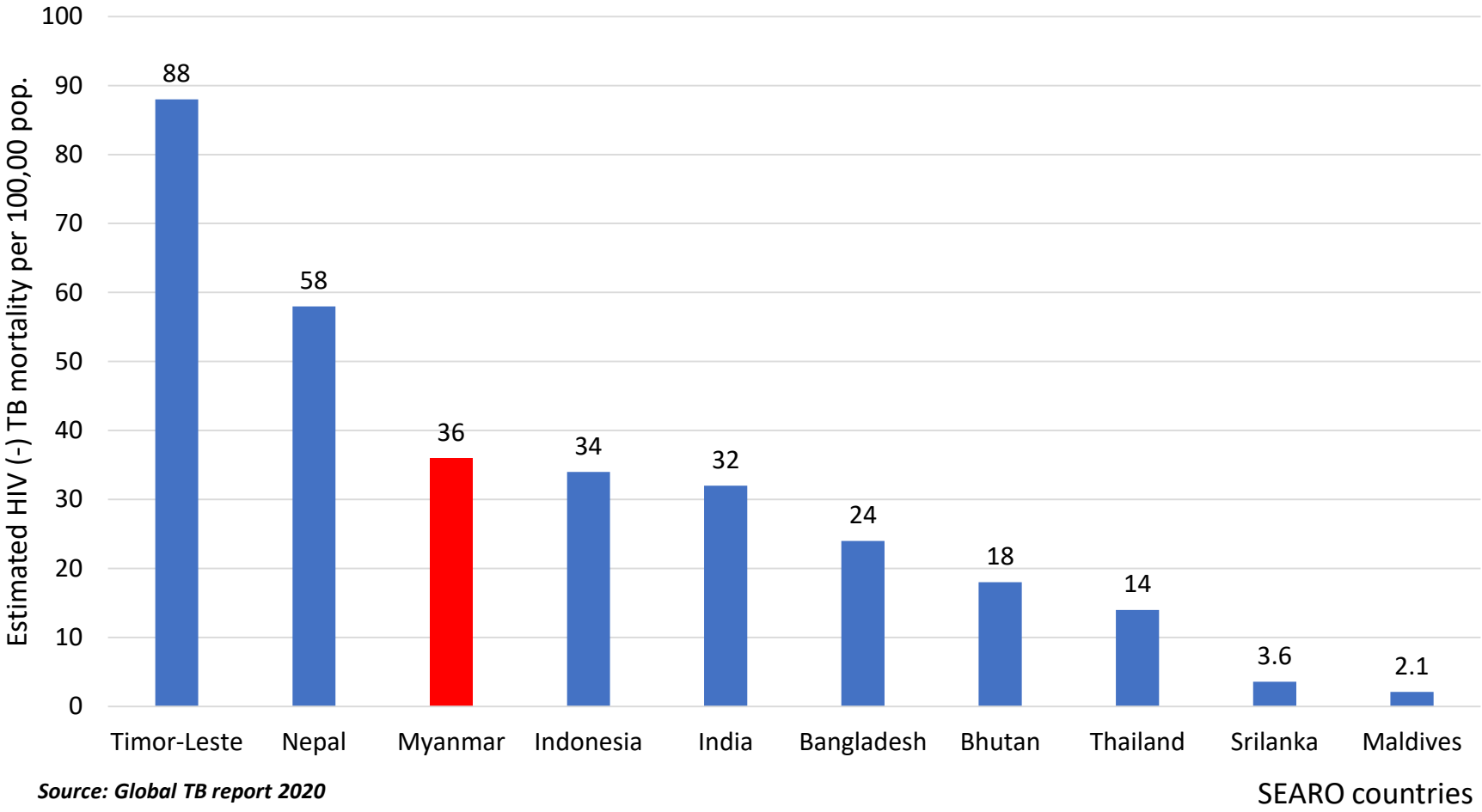
Source: Global TB report 2020

Estimated HIV Positive TB Incidence per 100,000 population among SEARO countries (2019)



Source: Global TB report 2020

Estimated HIV negative TB Mortality Rate per 100,000 population among SEARO countries (2019)



Source: Global TB report 2020

Mile Stones (DR-TB care in Myanmar)

Time lines	Accomplishment
2006 September,15	MOH established National DR TB Committee
2007 June, 28-29	Workshop on National Guidelines for the management of drug resistant TB
Q3 2009 to Q3 2011	DOT PLUS pilot project (Aung San Hospital and Patheingyi Hospital)
2012-2015	Stepwise geographic expansion of Programmatic Management of DR-TB along with expansion of Xpert installation and criteria
2016	All 330 townships became MDR-TB townships with borderless approach. Expansion of New drugs (EndTB program-NTP+Aung San+ MSF (H)) started in Aung San Hospital
2017, February 2017, July 2017, November	"National Guidelines for the Management of Drug Resistant TB (DR-TB) in Myanmar" was published aDSM (active TB drug safety monitoring and management) was introduced Pilot Shorter MDR-TB Treatment Regimen was launched in Yangon and Mandalay. New diagnostic tool "SL LPA" was used to rule out additional resistance to (FQ/ SLI).
2018, March 2018, July	Enrollment of pre XDR and XDR-TB as well as functional pre-XDR-TB patients with new and repurposed drugs (Aung San/ PTG hospital + NTP) Trainings for the improvement of quality MDR-TB care (ECG, audiometry)
2019, July	Pilot Shorter MDR-TB Treatment Regimen was expanded to Pathein, Ayeyarwaddy. Clinical trainings were organized to improve management of side effects. Transition plan to adopt new WHO recommendations (Injection free fully oral regimen) was prepared.
2020	Launched all oral regime (pilot) in Yangon and Mandalay Region. Expanded use of SL LPA.

Drug Resistant-TB Control Activities in Myanmar

Dr. Si Thu Aung

Director (TB/Leprosy/Trachoma)

Department of Public Health

26 November 2020

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- ✓Definitions of TB drug resistance
- ✓Geographical coverage of MDR-TB
- ✓Program achievements (enrolled numbers and treatment outcomes)

Definitions of TB drug resistance

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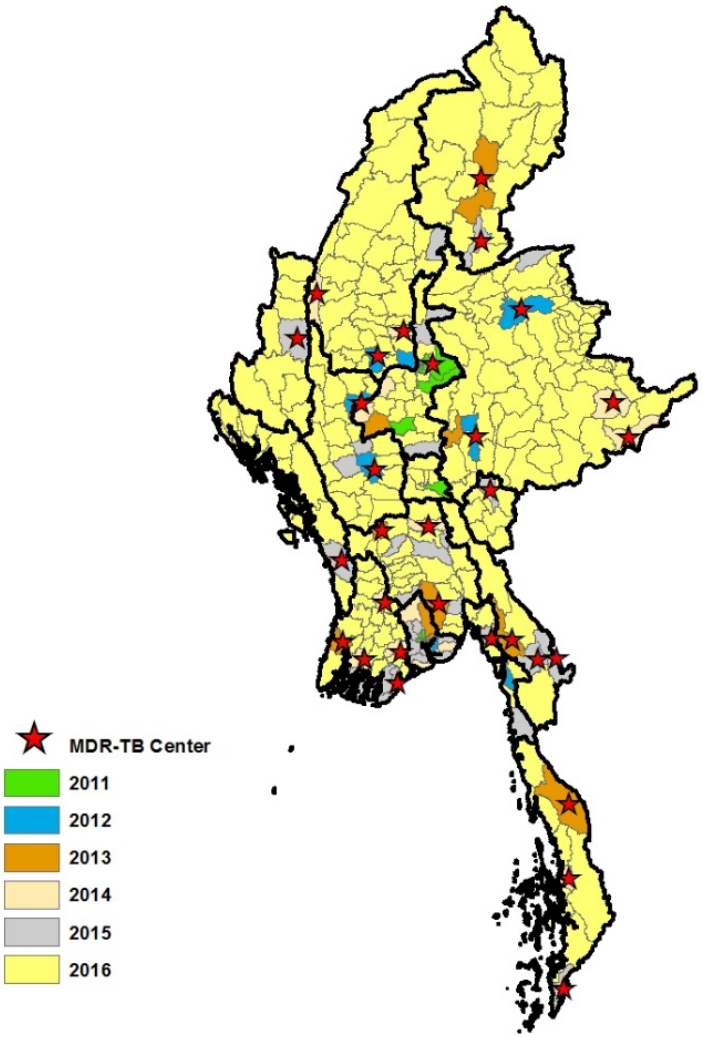
Geographical coverage for MDR-TB Management



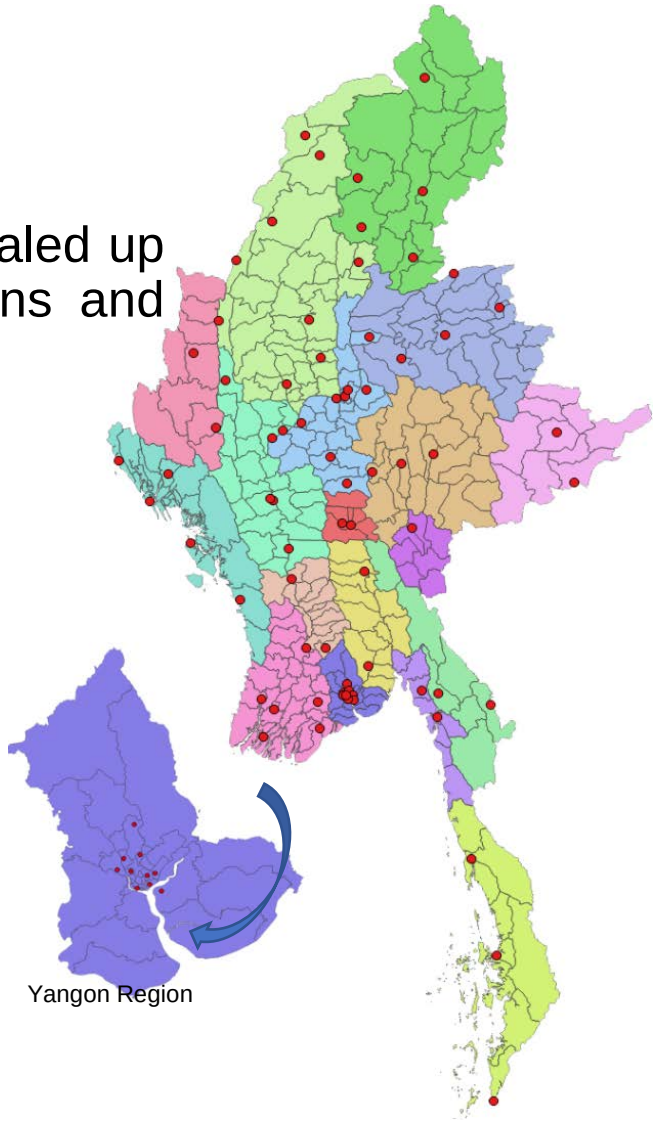
- 2009-2010 (10 townships)
- 2011 (10+additional 12 = 22 townships)
- 2012 (22+additional 16 = 38 townships)

2013 (38+additional 15 = 53 townships)
2014 (53+additional 15 = 68 townships)
2015 (68+additional 40 = 108 townships)

Entire Yangon Region is covered by MDR-TB management in 2015
All 330 townships became MDR-TB townships since Q1, 2016 with borderless approach.

Gene Xpert was introduced in 2011; has scaled up to 104 machines at 80 sites in 17 Regions and States by June 2020.

- One Gene Xpert Machine Available Township
- Two Gene Xpert Machines Available Township
- Three Gene Xpert Machines Available Township
- Four Gene Xpert Machines Available Township
- Five Gene Xpert Machines Available Township



GXP machine location and machines distribution by Region and State as of June 2020

Sr.	Region/States	No. of Site	No. of machine	GeneXpert Site
1	Ayeyarwaddy	6	7	2 machines at **Regional TB Center** (Pathein), **District TB Center** (Maupin/Myaungmya/Hinthada/Pyarpon/Labutta)
2	Bago	4	5	2 machines at **Regional TB Center** (Bago), **District TB Center** (Pyay / Taungoo / Tharyarwaddy)
3	Chin	2	2	**District TB Center** (Hakha / Mindat)
4	Kachin	5	6	2 machines at **State TB Center** (Myitkyina), **District TB Center** (Bamaw / Moenyin / Putao), **TB/HIV High Burden** Township (Phakant)
5	Kayah	1	1	**District TB Center** (Loikaw)
6	Kayin	2	3	2 machines at **State TB Center** (Hpa-an)**,** **District TB Center** (Myawaddy)**,**
7	Magway	5	5	**Regional TB Center** (Magway), **District TB Center** (Pakokku / Gangaw / Minbu / Thayet)
8	Mandalay	10	12	3 machines at **Upper Myanmar TB Center***, Patheingyi TB **Specialist Hospital,** MGH TB OPD, **District TB Center** (Myingyan / Meiktila / NyaungOo / POL / Yamethin), **HIV High Prevalence Township** (Mogoke), CPH_Mandalay,
9	Mon	2	3	2 machines at **State TB Center** (**Mawlamyine**), **District TB Center** (Thaton)
10	Naypyitaw	2	2	Naypyitaw Council TB Center (Pyinmana), (1000) bedded hospital,
11	Rakine	5	5	**Regional TB Center** (Sittwe), **Border township** (Maungtaw) **District TB Center** (Thandwe / Kyaukphyu / Mrauk U)

GXP machine location and machines distribution by Region and State as of June 2020

Sr.	Region/States	No. of Site	No. of machine	GeneXpert Site
12	Sagaing	10	11	2 machines at Regional TB Center (Monywa), District TB Center (Shwebo / Kalay / Katha / Tamu / Kanbalu / Sagaing / Khamti) TB High Burden Township (Homalin), Hard to reach Townsip (Lehe)
13	Shan (East)	2	2	State TB Center (Kengtun), District TB Center (Tachileik),
14	Shan (North)	4	5	2 machines at State TB Center (Lashio), District TB Center (Kyaukme, Kunlone), Border township (Muse),
15	Shan (South)	3	4	2 machines at State TB Center (Taungyi), District TB Center (Loilin), MDR-TB Decentralized site (Kalaw)
16	Tanintharyi	3	3	Regional TB Center (Dawei), District TB Center (Myeik/Kawthaung)
17	Yangon	14	23	5* machines at Lower Myanmar TB Dx Center (Aung San), 2* machines at Latha TB Dx Center, 4 machines at District TB Center (North Okkalapa / Thanlyin), MDR-TB decentralized Site (Thaketa/Thingankyun/Dagon (South), Hlaing,Hlaingtharya) 4 Specialist Hospital (Mingalardon / Waibargi / Thaketa / NOKA) 1 Central Prison (Insein)
18	NDRS		5	1 Gene Xpert machine at UMTBC and 4 GeneXpert Machines at NTRL are temporary assign for National Drug Resistance Survey.
Total (NTP Only)		**80**	**104**	
	PR 2	5	5	PSI - Yangon, MDM - Moegaung, AHRM - Phakant/Waingmaw, IOM – Mawlamyine,
	IPs	5	5	MSF – Myitkyina/Phakant/Lashio/Dawei, SMRU – Myawaddy,
Grand Total		**90**	**114**	

Report on Gene Xpert tests in Myanmar

	2012 (5) machine	2013 (11) machine	2014 (22) machine	2015 (48) machine	2016 (66) Machine	2017 (73) Machine	2018 (92**) Machine	2019 (96) Machine
Total Test done	3,136	14,246	26,240	41,957	66,237	93,062	126,328	140,920
MTB not detected	2,303 (73%)	8,895 (62%)	16,089 (61%)	24,265 (58%)	37,056 (56%)	47,225 (51%)	67,069 (53%)	76,918 (55%)
Total MTB detected	833 (27%)	5351 (38%)	10210 (39%)	17692 (42%)	29,172 (44%)	45,837 (49%)	59,259 (47%)	64,002 (45%)
TB with Rif-resistant	259 (9%)	1,689 (12%)	2,631 (10%)	2,719* (6%)	3,213* (5%)	3,175* (3.4%)	3,479* (2.8%)	3,205* (2.3%)
TB with No Rif-resistant	556	3435	6986	14215	25,252	41330	53,809	58,382
TB with Rif-resistant Indeterminate	18	227	534	425	353	457	585	1,028
Proportion "RR+ve" among patients with MTB diagnosed by GXP	31%	32%	26%	16%	11%	7%	6%	5%

*Including DST/LPA Positive MDR-TB Cases and excluding repeated/confirmation tested of RR+ Cases and overlapping cases between DST/LPA and RR+.

** Results including 10 Gene Xpert machines from Partners Organization.

NSP (2021-2025) and DR-TB

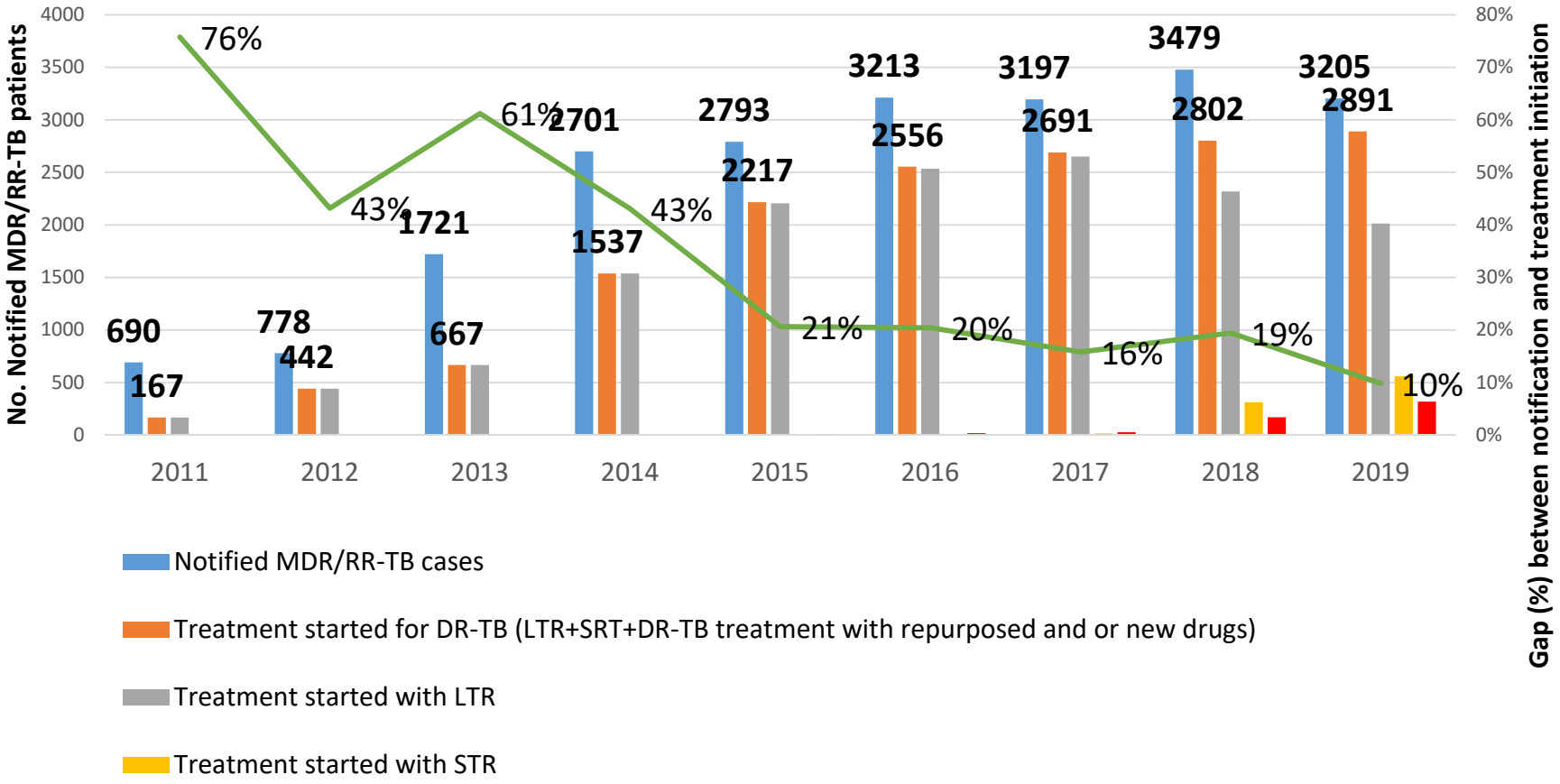
Indicators and Targets

Standard Indicators	Benchmark 2015	Baseline 2019	Targets 2021	2022	2023	2024	2025
Percentage of TB patients with DST results for at least Rifampicin among the total number of notified (new and retreatment) cases in the same year	NA (New) 67% (Retreatment)	49% (Among bact. Confirmed 92%-New and 84%-Retreatment	80%	85%	90%	90%	90%
Number of bacteriologically confirmed drug resistant TB cases (notified)	2,793	3,205	5,121	5,437	5,598	4,864	4,638
Number of cases with drug resistance TB that began second-line treatment	2,217	2,581	4,763	5,110	5,318	4,621	4,406
Percentage of cases with drug resistance TB that began second-line treatment	79%	90%	93%	94%	95%	95%	95%
Percentage of confirmed drug resistance TB cases tested for resistance to second-line drugs	NA	66%	60%	70%	>70%	>70%	>70%
Number of XDR-TB cases diagnosed	19	58	136	146	152	132	126
Number of XDR-TB cases initiated on treatment	10	23	95	102	106	92	88
Percantage of cases with RR-TB and/or MDR-TB started on	3% (2013)	2.6%	<3%	<3%	<3%	<3%	<3%

Enhanced case finding and Criteria for Xpert MTB/RIF testing

1. All PTB cases (New and Retreatment)
2. Sputum smear positive at the end of intensive phase (non-converter and positive converter)
3. TB patients with diabetes mellitus
4. Presumptive TB cases (PLHIV, contact of MDR-TB)
5. Other cases to be considered individually by MDR-TB committee

Comparison of Notified MDR/RR-TB cases and Treatment initiation 2011 - 2019

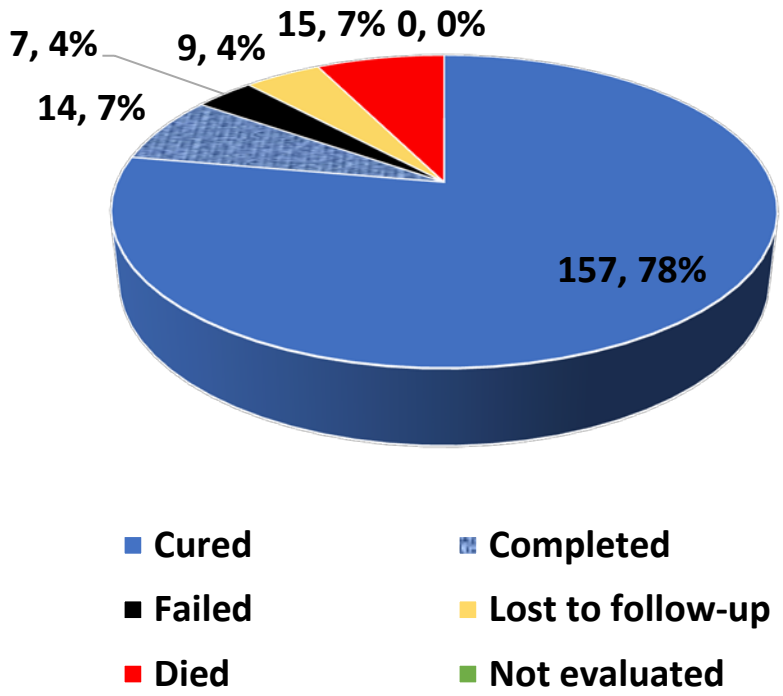


Historical PMDT treatment outcomes: patients treatment started in (2012 – 2017)

Year	Number evaluated	Cured	Completed	TSR	Failed	Lost to follow-up	Died	Not evaluated	Moved to XDR
2013	667	60%	23%	**83%**	1%	3%	13%	0%	0%
2014	1,495	68%	13%	**80%**	1%	5%	13%	0%	0%
2015	2,174	72%	8%	**80%**	1%	4%	14%	0%	1%
2016	2,529	70%	9%	**79%**	1%	4%	**16%**	0%	1%
2017	2,647	70%	10%	**80%**	1%	4%	14%	0%	1%

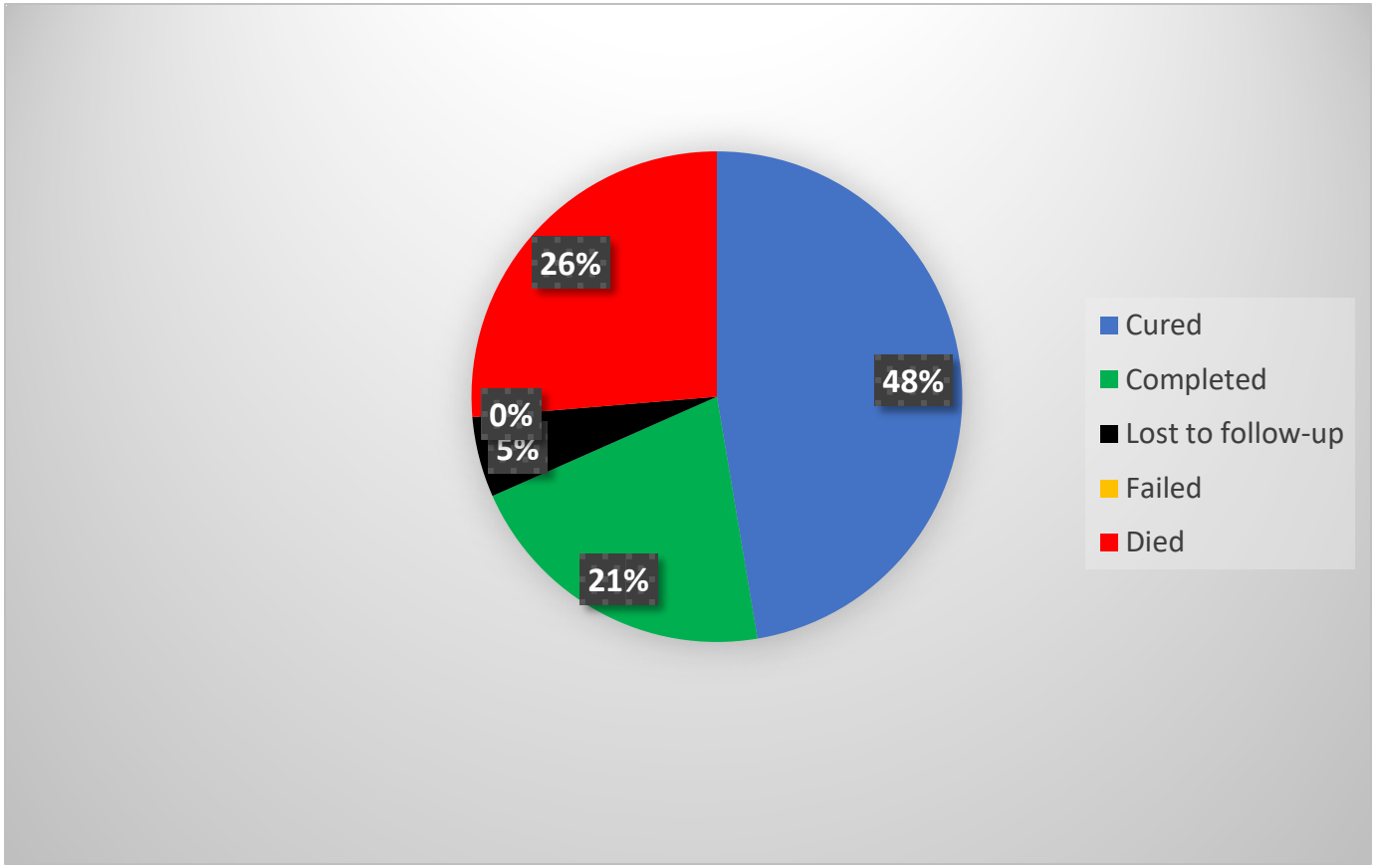
Treatment outcomes of MDR-TB patients on Shorter Treatment Regimen (n=202, TSR=85%)

THE OUTCOMES OF PATIENTS ON STR REGISTERED
NOV 2017 – SEP 2019
(N=202; TSR=85%)



Excluded moved to LTR cases due to
1) patient's preference;
2) doctor's preference;
3) intolerance to drugs in STR and not due to failure.

Treatment outcomes of XDR-TB and preXDR-TB, 2016 Cohort (n=19, TSR=69%)



Treatment outcomes of patients on New and repurposed drugs

XDR-TB Treatment outcomes (2016 cohort)							TSR
	Cured	TC	Failed	Died	LFU	Total	
Country	5	0	0	3	0	8	63%
MDR/RR-TB with New and Rp drugs (2016 cohort)							
Country	8	0	0	2	1	11	73%
XDR-TB Treatment outcomes (2017 cohort)							**TSR**
	Cured	TC	Failed	Died	LFU	Total	
Country	7	0	0	2	0	9	78%
MDR/RR-TB with New and Rp drugs (2017 cohort)							
Country	9	2	1	3	1	16	69%
XDR-TB Treatment outcomes (Jan Jun 2018 cohort)							**TSR**
	Cured	TC	Failed	Died	LFU	Total	
Country	5	2	1	5	1	14	50%
MDR/RR-TB with New and Rp drugs (Jan Jun 2018 cohort)							
Country	28	0	0	6	5	39	72%

Drug Resistant-TB in special situations & treatment regimens including BPaL (OR)

Dr. Si Thu Aung

Director (TB/Leprosy/Trachoma)

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- ✓Transition to oral regimens
- ✓BPaL Operational Research
- ✓Challenges and way forward

The most prevalent co-morbidities Jan-Sep 2018

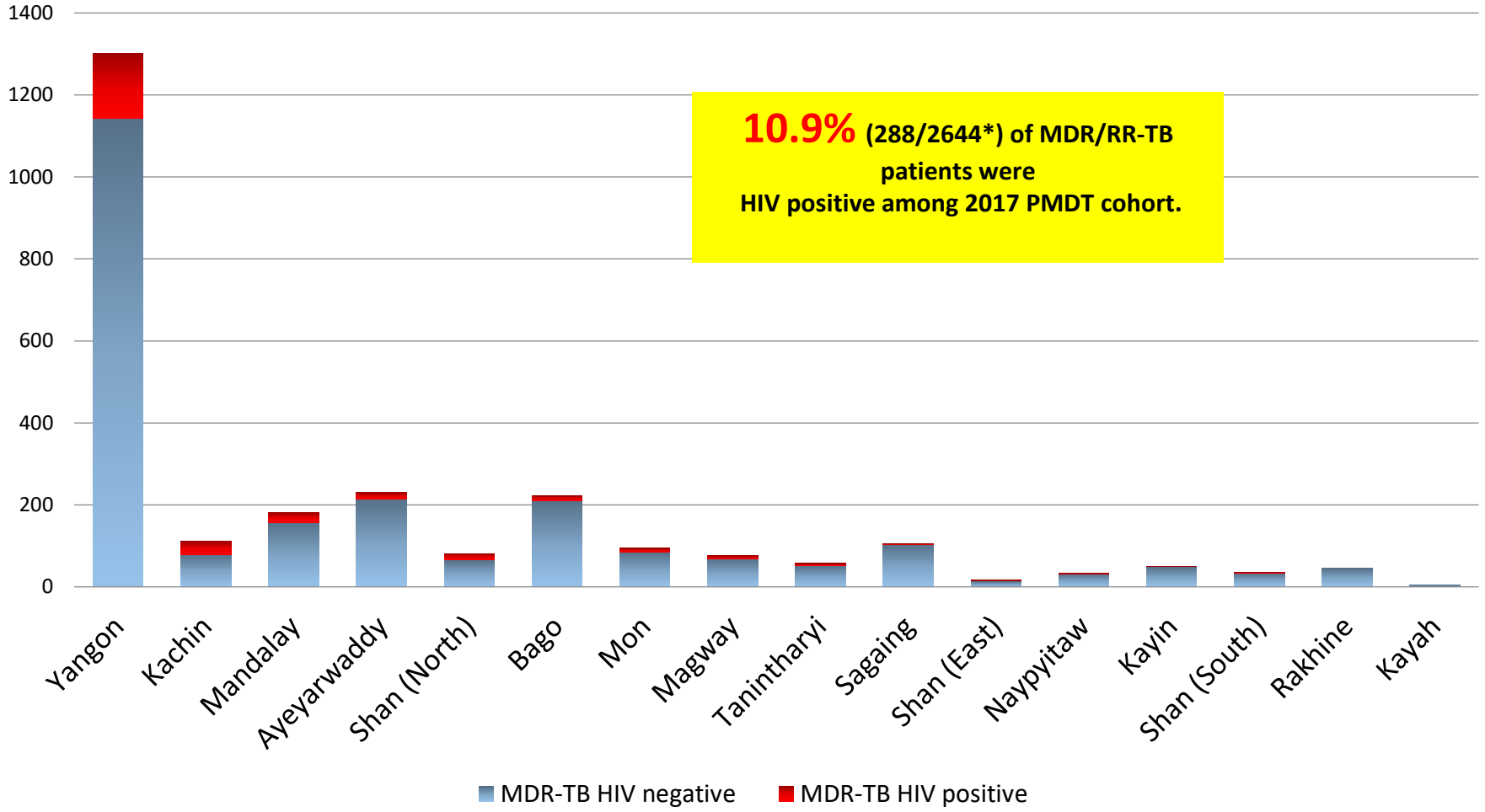
(only R&S who contributed "both DM and HIV data" are included in below table for description)

Regions and States	M	F	Grand Total	Number		%	
				DM	HIV	DM	HIV
Ayeyarwaddy	146	84	230	12	16	5%	7%
Bago	150	78	222	17	11	8%	5%
Magway	49	27	76	4	8	5%	11%
Mandalay	114	67	181	14	24	8%	13%
Mon	67	27	94	17	9	18%	10%
Shan (North)	55	26	81	5	15	6%	19%
Shan (South)	25	10	35	2	1	6%	3%
Yangon	829	472	1301	169	159	13%	12%
Kachin	77	34	111	7	32	6%	29%
Total (9 R&S)	1512	825	2331	247	275	**11%**	**12%**

Challenges

- MDR-TB/DM: to have optimal glycemic control (NTP supports OHA while insulin is the better option)
- MDR-TB/DM: Complication with renal insufficiency and intolerance to injection Amikacin
- MDR-TB/HIV: drug-drug interactions
- MDR-TB/HIV: optimal infection control in HIV clinics

Number of MDR-TB patients treatment started – segregated by HIV status in Regions and States (2017)



*Bago and Kayin revised DR-TB 07 data on 23 Nov 2018.

Drug-resistant TB in children

Global Situation

An estimated
25 000
children <15 years
fell ill with MDR-TB
in 2014

Less than 10%
of them were diagnosed and had access to treatment

Myanmar

- ✓ **0.7% (18/2666), 0.65% (17/2633) and 1.4% (35/2574) of total enrolled patients in PMDT were children in 2017, 2018 and 2019 respectively.**
- ✓ **Need to strengthen case finding of MDR-TB cases in children**

Child formulation TB medicines available in NTP

Treatment regimens

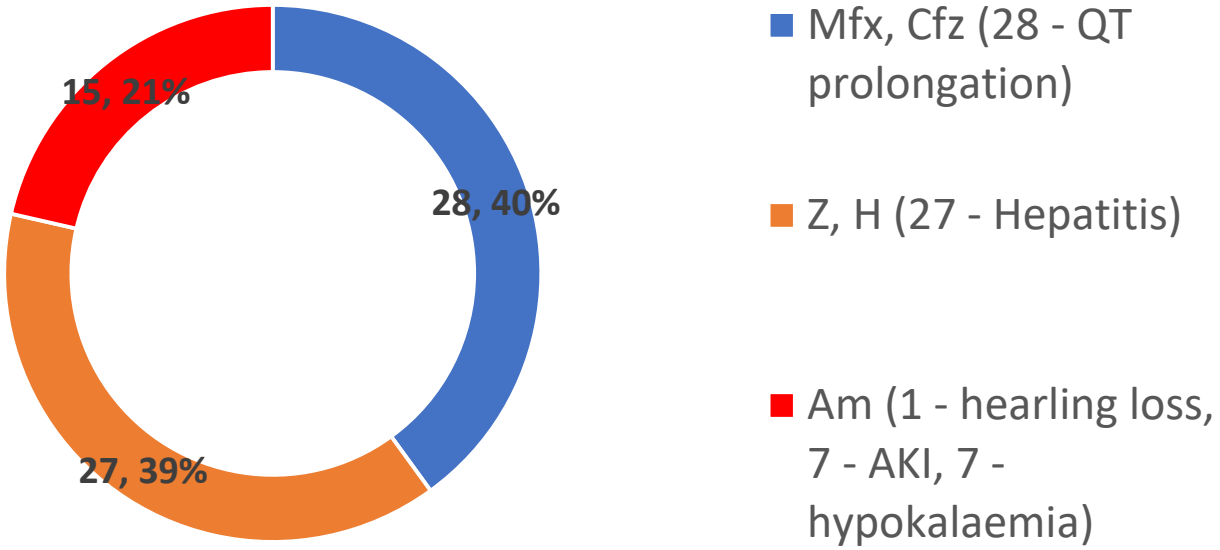
Transition to all oral regimens

MDR-TB treatment regimen in Myanmar

The regimens	Period used	Total number of patients (cumulative number) who received regimen up to June 2020	Remark
Conventional Longer Regimen (18-20 months) 6-8 (**Am**,Lfx,Cs,Eto.Z)/12-14 (Lfx,Cs,Eto,Z)	Mid 2009 to June 2020	15,668	Will be phased out by Q1 2021
Shorter treatment regimen with Am (9-11 months) 4-6 (**Am** Mfxh*,Cfz,E,Z,Hh*,Eto)/ 5 (Mfxh,Cfz,Etb,Z)	Nov 2017 to June 2020	1,129	Will be phased out by Q1 2021

*h=high dose

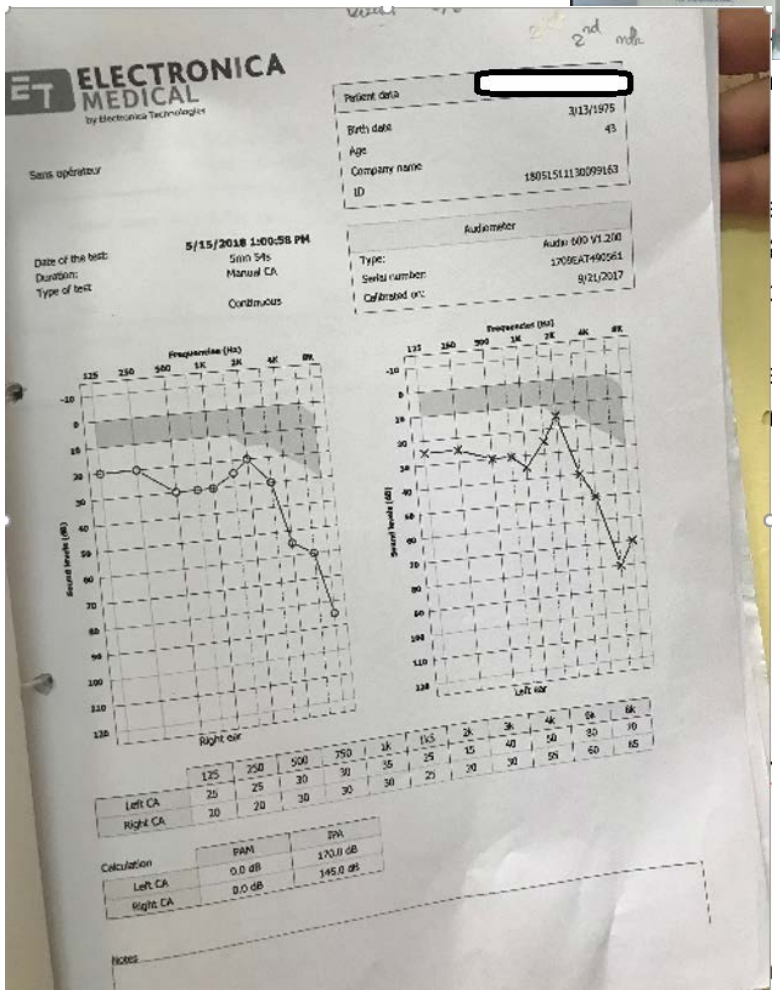
Numbers and percentages of SAEs (Severe Adverse Effects) determined to be causality relationship with “Amikacin-based Standard Shorter Treatment Regimen component drugs” (n=70) in 2019



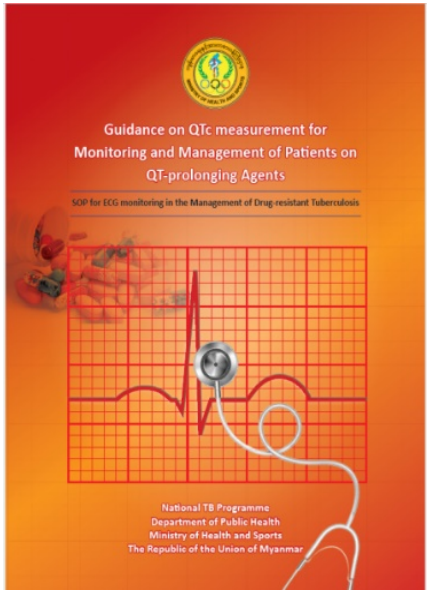
Side Effect Occurrence (n=309) 2017 Dec -1st Q 2019, Yangon NTP

Nausea and vomiting	231 (75%)
Tinnitus	117 (37%)
Joint pain	106(34%)
Dizziness	95 (31%)
Sleep disturbance	56(18%)
Hearing loss	40(13%)
Loss of appetite	41(13%)
Skin discoloration	25(8%)
Abdominal pain	13(4%)

- In Myanmar, about 2,800 MDR-TB patients are started treatment each year and treatment success rate is 80% among MDR-TB. Although recovered from MDR-TB, there are about **13%** of patients who had **total deafness**. Therefore, **Amikacin containing regimens will be phasing out by end of 2020 along with global transition.**



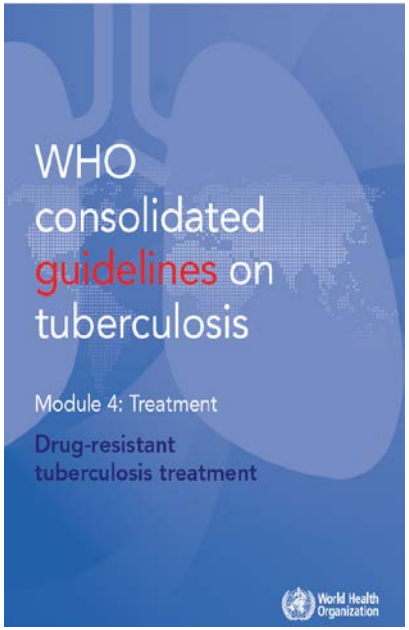
- The fact that other second line anti TB drugs also have side effects **active TB drug safety, monitoring and management (aDSM) must be applied for patients' safety.**
- **Eg;**
- **QTc prolongation (BDQ, Mfx/Lfx, Cfz, Dlm)**
- **Bone marrow suppression (Lzd)**



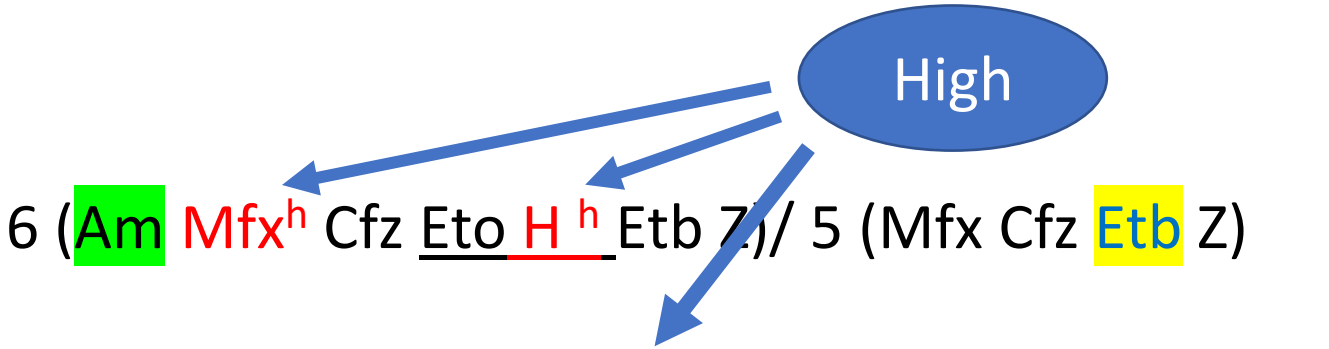
Treatment of DR-TB

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

GROUP	MEDICINE	Abbreviation
Group A: Include all three medicines (unless they cannot be used)	Levofloxacin OR Moxifloxacin	Lfx Mfx
	Bedaquiline[1,4]	Bdq
	Linezolid[2]	Lzd
Group B: Add both medicines (unless they cannot be used)	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[3,4]	Dlm
	Pyrazinamide[5]	Z
	Imipenem-cilastatin OR Meropenem[6]	Ipm-Cln Mpm
	Amikacin (OR Streptomycin)[7]	Am (S)
	Ethionamide OR Prothionamide	Eto Pto
	p-aminosalicylic acid	PAS



The shorter MDR-TB regimen and its phases

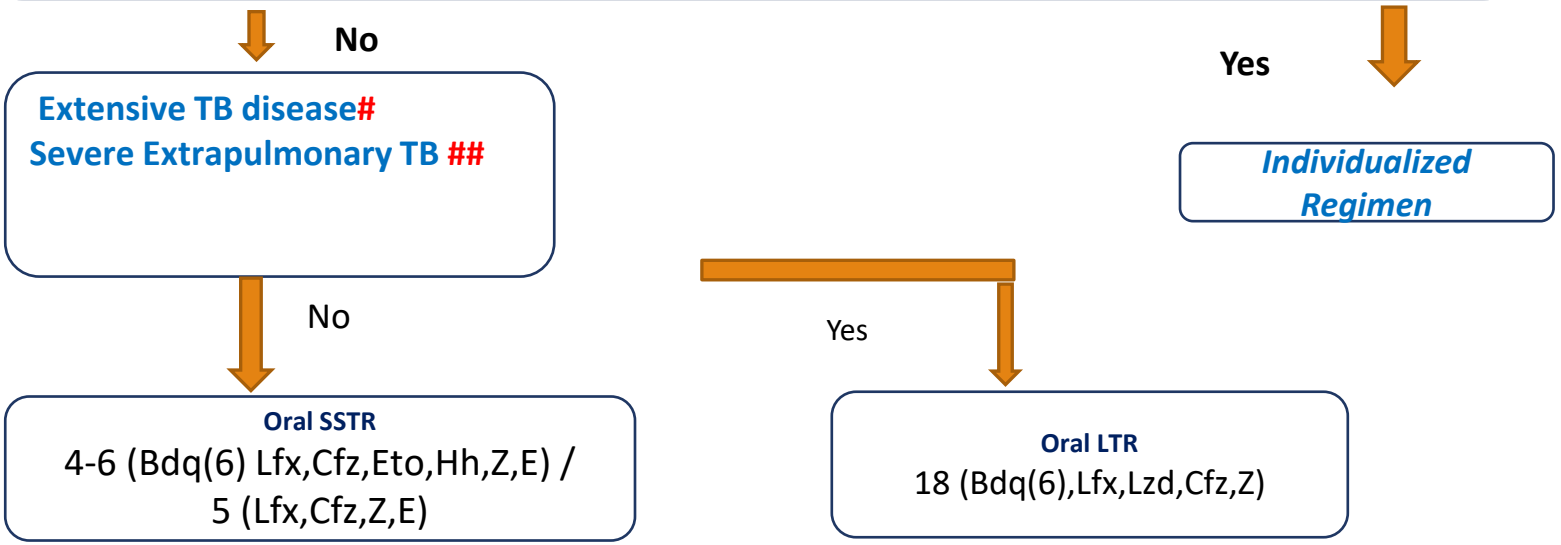


Drugs/Regimens used to treat MDR-TB and XDR-TB patients in Myanmar

	Regimen and drug composition (total duration of treatment)	remark
1.	Conventional Longer Regimen (20 months) 6-8 (Amk,Lfx,Cs,Eto.Z)/12-14 (Lfx,Cs,Eto,Z)	Will be phased out by Q1 2021
2.	Shorter treatment regimen with Amk (9-11 months) 4-6 (Amk,Moxih,Cfz,Etb,Z,Hh,Eto)/ 5 (Moxih,Cfz,Etb,Z)	Will be phased out by Q1 2021
3.	Oral longer regimen (18 months) 18 (BDQ(6), Lfx,Lzd, Cfz, Z)	Has started as pilot since Aug 2020
4.	Oral Standardized Shorter Treatment Regimen (9-11 months) 4-6 (BDQ(6),Lfx,Cfz,Etb,Z,Hh,Eto)/ 5 (Lfx,Cfz,Etb,Z)	Has started as pilot since Aug 2020
5.	Individualized regimen following WHO principle of regimen construction (20-24 months) for XDR-TB, MDR-TB with additional resistance, MDR/RR-TB with intolerance.	Started in 2016 as END TB Program, and as NTP's enrollment since 2017 onward.

Flow chart for enrolment

- Resistance or suspected ineffectiveness of medicine in the oral treatment regimens (except isoniazid resistance*)
- Resistance to fluoroquinolone with second line LPA or phenotypic DST
- History of hypersensitivity or contraindication to medicine in the oral treatment regimens
  Eg .QTc >500ms ,ALT & AST >4 times
- Taking any medicine contraindicated with medicines in Oral regimens
- Exposure to previous treatment with second line medicine in the oral regimens for more than one month (unless
  susceptibility is confirmed)
- Pregnancy
- Children under 6 yrs of age



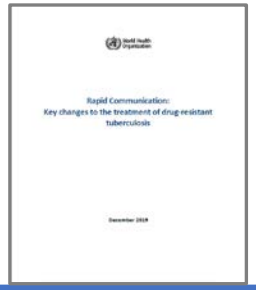
Extensive (or advanced) tuberculosis (TB) disease: presence of bilateral cavitary disease or extensive parenchymal damage on chest radiography. In children aged under 15 years, advanced disease is usually defined by the presence of cavities or bilateral disease on chest radiography.

Severe extrapulmonary TB: presence of miliary TB or TB meningitis. In children aged under 15 years, extrapulmonary forms of disease other than lymphadenopathy (peripheral nodes or isolated mediastinal mass without compression) are considered as severe.

WHO Guidelines

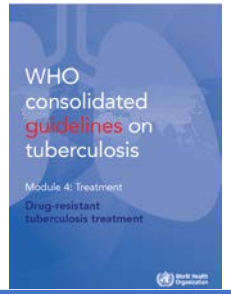
Mar 2019

1. Regimen for Hr TB
2. Composition in longer regime (3 gp A + 1 gp B)
3. **Shorter regimen with SLI** (same as 2016 recommendation + role of MTBDRplus rapid assay and to exclude if there is resistant to both KatG and InhA mutation.



Dec 2019

1. Shorter, all-oral, bedaquiline-containing regimen for eligible MDR/RR-TB patients
2. **Novel treatment regimen – BPaL under OR**



Jun 2020

1. Oral Shorter regimen with BDQ
2. **BPaL (6-9 month) under OR**
3. Extended BDQ use beyond 6 month , Concurrent use of BDQ and DLM, use of BDQ during pregnancy in longer regimen for MDR TB

Shorter, Simpler Treatment for Highly Drug-Resistant Forms of TB

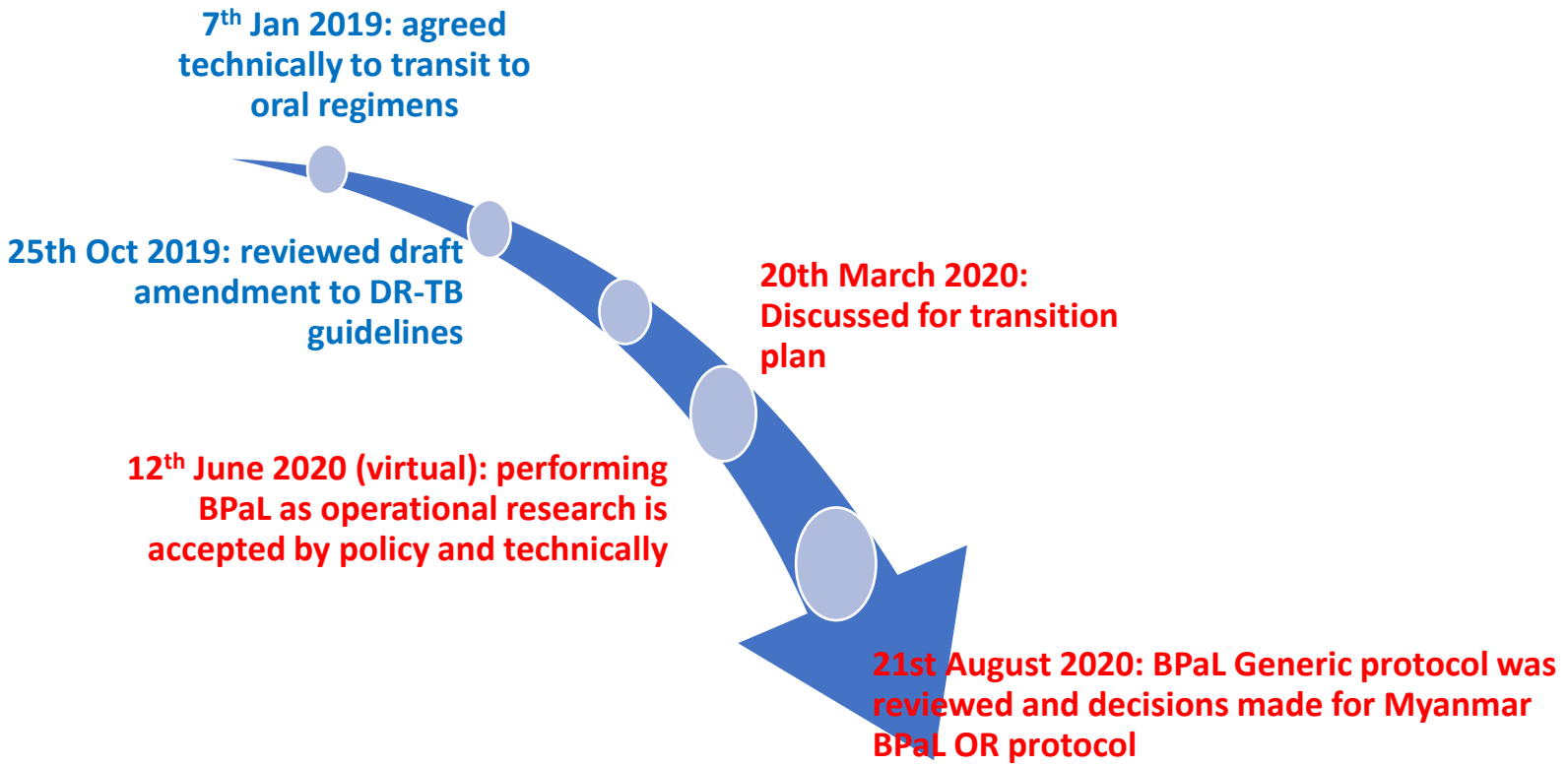
NixTB

Please see Full Prescribing Information at:
www.accessdata.fda.gov

Costs for DR-TB regimens (US$)

	Second line medicines	Conventional Regimen (LTR)	STR with Amk (9-11) M	STR with BDQ (9-11) M	All oral longer (18-20) month	Bpal (6-9) months	XDR-TB with 2 new drugs 2 repurposed drugs +Imp+PAS
	Levofloxacin 250 mg	72		40	72		-
	Moxifloxacin 400 mg		144				-
	Bedaquiline			340	340	362	340
A	Linezolid 600 mg				405	270	405
	Clofazimine 100 mg		297	297	486		486
B	Cycloserine 250 mg	322					-
	Ethambutol 400 mg		37	37			-
	Isoniazid 300 mg		5	5			-
	Delamanid 50 mg (1,700 $ for 6 month)						1,700
	Pyrazinamide 500 mg	38	21	21	38		34
	Imp/Cls						3,756
	Amikacin 500 mg/2ml inj	261	261				-
	Ethionamide 250 mg	191	57	57			-
C	PAS						1,488
	Pretomanid 200 mg tab					360	-
X	**Cost for SL medicine**	**883**	**822**	**797**	**1,341**	**992**	**8,209**
	investigation cost per one MDR-TB pat	93	120	120	200	120	200
	Xpert cartridages	9	9	9	9	9	9
	Ancillary drugs	10	6	6	10	50	10
	BHS	460	253	253	460	138	460
	Pt support	460	253	253	460	138	460
Y	**Cost other than SL medicine**	**1,032**	**641**	**641**	**1,139**	**455**	**1,139**
(X + Y)	**Total estimated cost (drugs+others)**	**1,915**	**1,463**	**1,438**	**2,480**	**1,447**	**9,348**

National Expert DR-TB Committee Meetings



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Treatment of Highly Drug-Resistant Pulmonary Tuberculosis

Francesca Conradie, M.B., B.Ch., Andreas H. Diacon, M.D., Nosipho Ngubane, M.B., B.Ch., Pauline Howell, M.B., B.Ch., Daniel Everitt, M.D., Angela M. Crook, Ph.D., Carl M. Mendel, M.D., Erica Egizi, M.P.H., Joanna Moreira, B.Sc., Juliano Timm, Ph.D., Timothy D. McHugh, Ph.D., Genevieve H. Wills, M.Sc., Anna Bateson, Ph.D., Robert Hunt, B.Sc., Christo Van Niekerk, M.D., Mengchun Li, M.D., Morounfolu Olugbosi, M.D., and Melvin Spigelman, M.D., for the Nix-TB Trial Team*

A total of **109** patients were enrolled in the study and were included in the evaluation of efficacy and safety end points. At 6 months after the end of treatment in the intention-to-treat analysis, **11 patients (10%) had an unfavorable outcome** and **98 patients (90%; 95% confidence interval, 83 to 95) had a favorable outcome**. The 11 unfavorable outcomes were 7 deaths (6 during treatment and 1 from an unknown cause during follow-up), 1 withdrawal of consent during treatment, 2 relapses during follow-up, and 1 loss to follow-up. The expected linezolid toxic effects of peripheral neuropathy (occurring in 81% of patients) and myelosuppression (48%), although common, were manageable, often leading to dose reductions or interruptions in treatment with linezolid.

Nix-TB Trial: Results

Ref: New England Journal of Medicine, March 2020, Vol 382, No.10

- 109 people enrolled on treatment(XDR=65%, MDR failures and non responders= 34%)
  - 76% were black, and 23% were of mixed race
  - Ages ranged from 17 years to 60 years (mean 36 years)
  - Fifty-six (51%) patients were HIV-positive
- Results among 107 assessed
  - Success reported for 95 (89%) patients
  - Failure for 12 (11%) patients (7 death; 2 relapse; withdrawal, loss to follow-up, or culture contamination – 3)
  - The outcomes were similar in both HIV negative and HIV positive patients and regardless of Lzd dosing scheme

Particulars of drugs in BPaL

	Bedaquiline	Linezolid	Pretomanid(New Drug)
Chemical Class	diarylquinoline	oxazolidinone	nitroimidazooxazine
Mode of Action	inhibits mycobacterial ATP synthase	inhibits bacterial protein synthesis	• Inhibits mycolic acid biosynthesis and thereby blocks mycobacterial cell-wall production • also acts as a respiratory poison against nonreplicating bacteria after nitric oxide release under anaerobic conditions
Daily dosage	400 mg once daily for 2 weeks followed by 200 mg three times a week for 24 weeks	1200 mg OD	200 mg OD
Duration of tm	24 wk	26 wk	26 wk

Pretomanid and common side effects

- nerve damage
- acne, vomiting
- Headache
- low blood sugar
- Diarrhea
- liver inflammation.

Challenges

- HR and capacity limitation for clinical management for pre & XDR-TB, complicated MDR-TB patients
- case base E- Recording & Reporting (Open MRS)
- Mandatory reporting from private sectors for both Drug sensitive and Drug resistant TB
- Further narrowing the gap between notified and enrollment of MDR-TB patients
- Lab Capacity & additional infrastructure/maintenance
- Regular supervision & monitoring at all levels
- Sputum transportation to GeneXpert sites & Culture facilities

Future Plan

- Universal Access to MDR-TB diagnosis and treatment (Reaching to Un-reach)
- Promote case finding including childhood MDR-TB by awareness raising, contact tracing, linkage with other programs
- DST will be further expanded. (Xpert MTB/RIF and second-line DST)
- Strengthening infection control measures & facilities
- MDR-TB patients case-based E- Recording & Reporting

THANK YOU