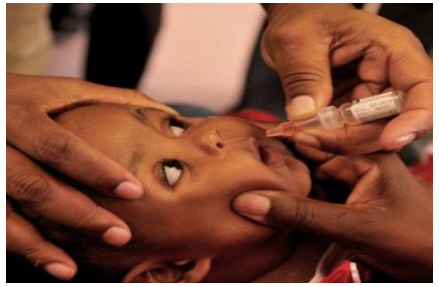

NEW TREATMENT REGIMEN FOR DR-TB PATIENTS: BPaL-L

30th August 2023

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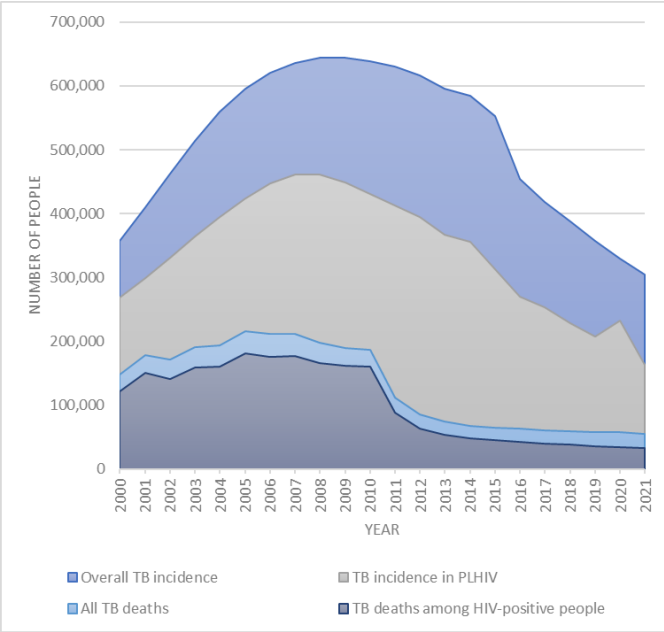
Outline

- The TB situation in SA
- TB Priorities for 2023/24
- Process of revision
- Major guideline changes
- Next steps

Situational analysis

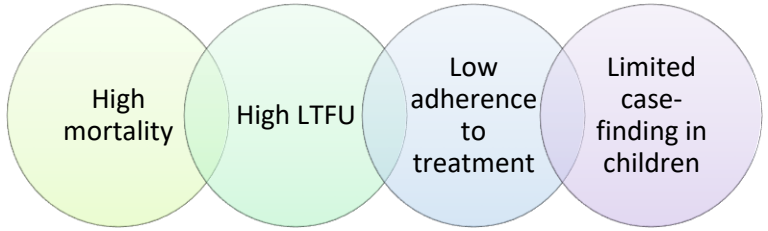
1 TB incidence & mortality



Incidence falling steadily – on track to meet global targets

Mortality falling much slower – did not reach WHO milestone

2 Critical issues across the programme

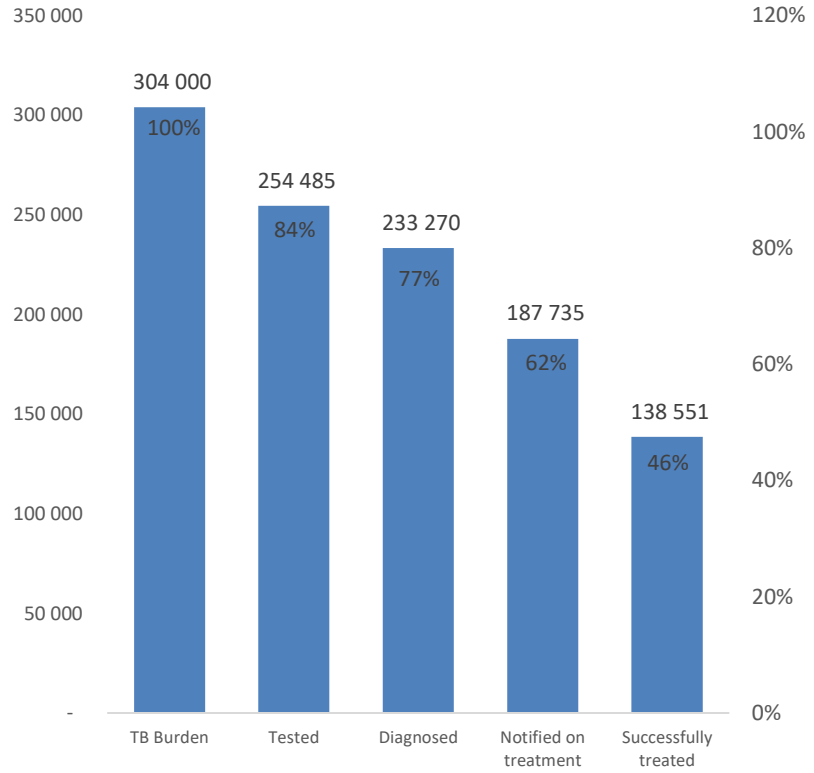


Important drivers

Patient factors: advanced HIV, late presentation, delayed diagnosis, use of alternative medicine, mobility, stigma, catastrophic costs, , misunderstanding of TB, conflicting health beliefs, alcohol and substance use, mental illness,

Health system factors: access barriers, gaps between levels of the health system, lack of system integration, limited ability of programme staff to track clients moving between facilities, lack of person-centred adherence approach, clinic congestion, health worker uncertainty, difficulty getting samples from young children.

3 TB Care Cascade, South Africa 2021



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TB Recovery Plan – Prioritizing impactful interventions

Pillar I: Communicate & Advocate	Pillar II: Find & Link	Pillar III: Treat & Retain	Pillar IV: Prevent & Prepare	Pillar V: Monitor & Assess
TB is a national priority across sectors	People with TB are linked to care within one week	People with TB have access to high quality treatment & support	TB prevention is valued as much as treatment	Provinces use high quality data to guide decisions
CREATE DEMAND FOR TB TESTING THROUGH ADVOCACY AND COMMUNICATION	**ACCELERATE IMPLEMENTATION OF TUTT**	**ESTABLISH RELIABLE LINKAGE PATHWAYS**	**IMPROVE RETENTION IN CARE**	**STRENGTHEN TB PREVENTION**	**STRENGHTEN TB PROGRAMME IN THE MINES**	**IMPROVE GOVERNANCE AND ACCOUNTABILITY**
Costed SBBC plan	3million GXP tests	TB result notification system	Shorter regimens (paeds and DR-TB)	Scale up treatment of latent TB infection	Situational analysis of TB in mines	Streamline and integrate TB data systems
Communication toolkit	Scale up DCXR	Initiate 224,776 patients on TB treatment	Strengthen adherence counselling	UVGI guidelines	Support examination and Compensation of ex-miners	100 Facilities Nerve Centre Approach Project
	Scale up ULAM					Partner coordination

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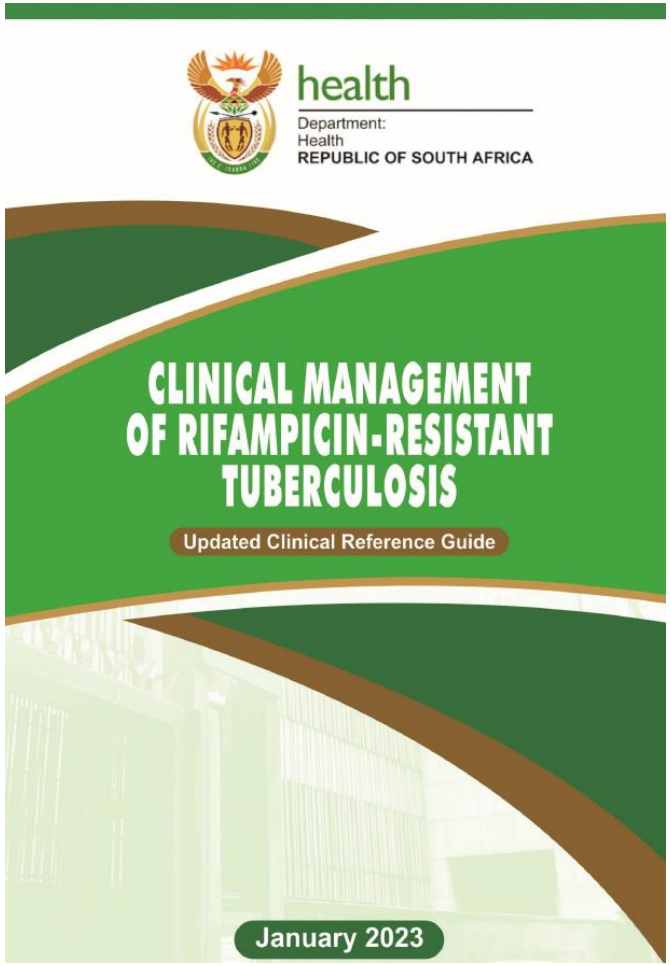
Revision process



- Following the NEMLC's ADOLOPMENT (GRADE review), the National Clinical Advisory Committee revised the 2019 RR-TB Clinical Reference guidance
- **The 9-month RR-TB regimen has been replaced by a 6-month treatment regimen**
- The 6-month regimen is part of the TB Recovery Plan
- The TB Recovery Plan was approved last year by the National Health Council

DR-TB Patient Journey

Primary Health-Care Facilities/General Hospitals

- Identify people with signs and symptoms of TB disease
- Collect specimen for microbiological testing (refer to NHLS diagnostic algorithm)
- Advise patient that results will follow by SMS and he/she needs to act accordingly

On receipt of results confirming RR-TB:

- Recall patient and send second specimen for RR-TB reflex
- Counsel patient and explain RR-TB management plan
- Conduct contact evaluation and post-exposure management

Laboratory

- Diagnosis of RR-TB
- Report sent to requesting facility and SMS to patient within 24 hours of confirmation of diagnosis

Patients are either hospitalised or initiated on treatment as outpatients

Before initiating treatment:

- Patient to be registered in a RR-TB register at appropriate facility (usually at a centralised or decentralised unit); this includes children who are clinically diagnosed and do not have microbiological confirmation of RR-TB
- Counsel the patient and family; obtain consent for RR-TB management; use appropriate DR-TB stationery; conduct psychosocial assessment including history of substance use and mental health screen; refer for NSP if necessary; refer for further social assessment and support as required

Patients to start in ambulatory care	Main indications for hospitalisation of patients with RR-TB
• Patient is ambulant, in fair to good general condition (BMI ≥18.5) • Patient is willing and able to attend clinic regularly for clinical review and monitoring, and to receive treatment under directly observed therapy (DOT) at facility or in the family with the option of self-administered therapy later in the treatment journey according to locally accepted policies.	• Respiratory insufficiency • Haemoglobin <8.0 g/dL • Body Mass Index (BMI) <18 kg/m^2 • Central nervous system (CNS) RR-TB disease • Clinically unstable • Unstable social situations that require intensive multi-disciplinary management • Administration of intravenous therapy • Unable to attend primary care facility for treatment (e.g. too weak to ambulate) • Infection control challenges in the patient's home environment • Recurrent treatment interruption where previous outpatient treatment has been unsuccessful • Any condition that in the opinion of the treating clinician would be better managed in the inpatient setting • Patient preference for inpatient care

On discharge from hospital, ask patient about most convenient RR-TB unit or facility for referral for ongoing outpatient management; notify receiving clinic or hospital of the down-referral; arrange transport; complete appropriate documentation (follow up card and DR-TB stationery)

Centralised DR-TB Units	Decentralised DR-TB Units	Satellite MDR-TB Units	Mobile Team

- All RR-TB units are responsible for providing treatment according to local best practices and for monitoring progress of patients throughout their treatment journey
- RR-TB stationery should be maintained at the facility at which the patient is being managed

Diagnostic updates

The **Line Probe assay is phased out**

Introduction of **GeneXpert XDR (Xpert MTB/XDR) cartridge** is used to detect fluoroquinolone and INH resistance, ethionamide and second line injectables (amikacin, kanamycin and capreomycin)

If **RR-TB and FLQ resistance**

Phenotypic testing for linezolid, bedaquiline and clofazimine

Phenotypic testing for pretomanid at the National TB Reference Laboratory

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Treatment updates

Two treatment options:

> The Short, all-oral, 6-month regimen (BPaL-L)

> A long-individualized regimen

As the BPaL/L regimen is implemented, the 9–11-month regimen will be phased out gradually

The treatment regimen for children < 15 yrs has been updated to also include shorter regimens

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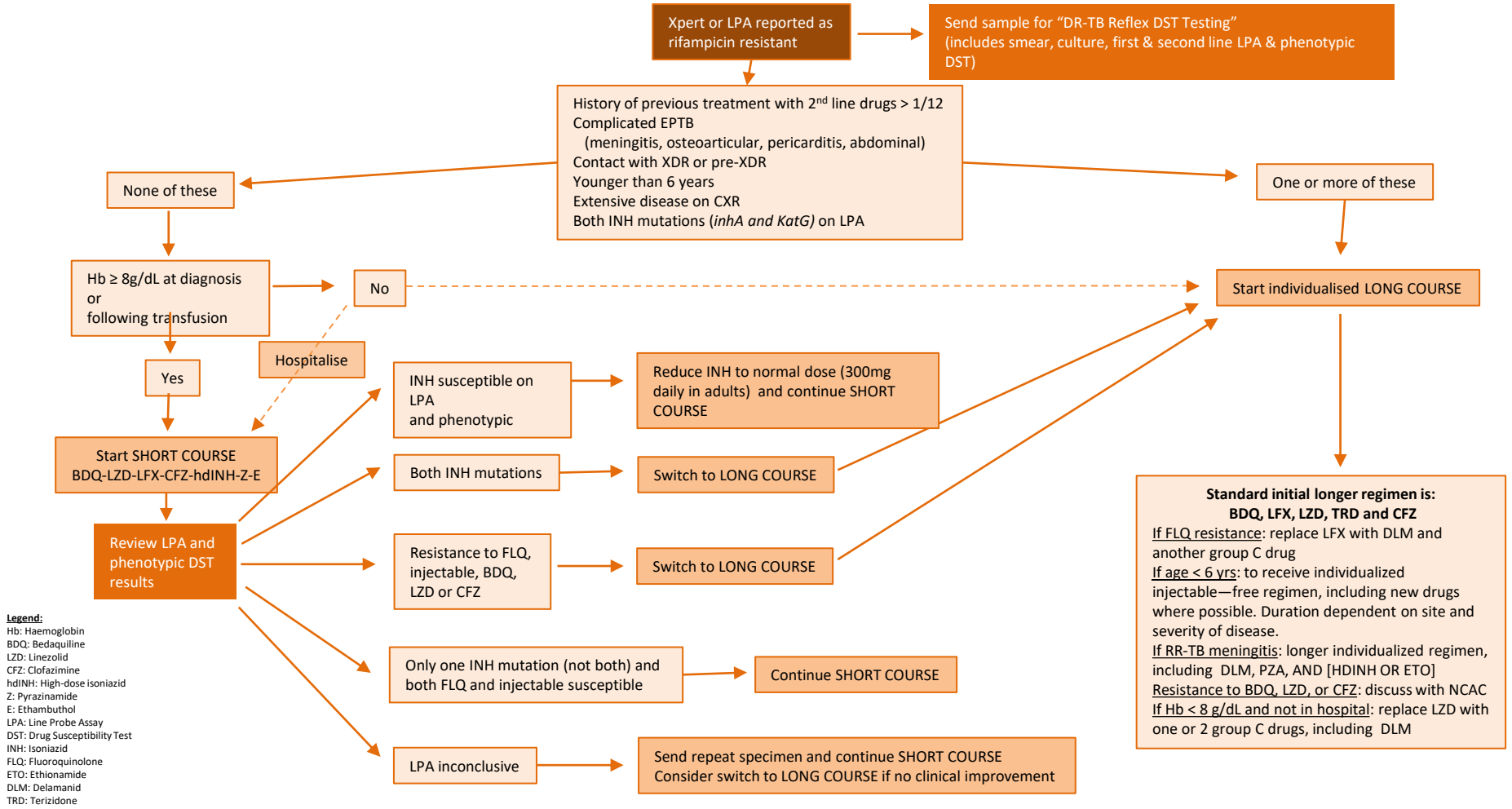
Current RR-TB Treatment Regimens & Eligibility



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DR-TB Monitoring

Monitoring parameters at baseline and beyond	Longer regimen: intensive phase					Longer regimen: continuation phase												
	Shorter regimen: intensive phase					Shorter regimen: continuation phase												
Month	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18-20
Counselling	X	Sessions 1-3			X	Additional counselling as required throughout treatment													
Substance use and mental health screen	X	WHO ASSIST and mental health screen			X	Review substance use and mental health status at every visit throughout treatment													
Evaluation by Clinician	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse event assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Assess for TB symptoms	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X	Monthly if aged <6 years																	
BMI, and NSP (if BMI <18.5)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review family planning	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Sample for smear, culture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LPA first line	X				X (if culture still positive)	X (if reconversion to positive culture after initial culture conversion)													
LPA second line	X				X (if culture still positive)	X (if reconversion to positive culture after initial culture conversion)													
Phenotypic INH susceptibility	In-lab reflex if first-line LPA shows INH susceptible																		
Phenotypic FLQ susceptibility	In-lab reflex if second-line LPA shows FLQ susceptible				X (if culture positive at month 4 or reconversion to positive after initial conversion)														
Phenotypic extended DST	In-lab reflex if second- line LPA shows FLQ resistant				X (if culture positive at month 4 or reconversion to positive after initial conversion)														

Monitoring parameters at baseline and beyond	Longer regimen: intensive phase						Longer regimen: continuation phase												
	Shorter regimen: intensive phase				Shorter regimen: continuation phase														
Month	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18-20
Chest X-ray	X						X												
HIV testing	X			X (repeat test after 3 months if previously negative)									X (repeat test if previously negative)						
CD4 count	X						X						X						
Viral load	X	If not suppressed, repeat earlier per national guidance					X						X						X
FBC and neutrophil count on LZD	X	Wks 2 and 4		X	Repeat monthly, or more often as required, while on linezolid														
Finger prick blood glucose	X	As required throughout treatment																	
Creatinine	X	Repeat monthly if on injectable agent, otherwise repeat as required if baseline creatinine was abnormal, or if person is clinically unwell through treatment																	
K+ and Mg2+	X	Repeat monthly if on injectable agent, otherwise repeat as required if vomiting or diarrhoea or if QTcF prolonged, or if person is clinically unwell through treatment																	
TSH – only if on PAS or ETO	X			X	Repeat every 3 months while on PAS or ETO, or as required if QTcF is prolonged														
ALT	X	Repeat if vomiting, right upper quadrant pain, jaundice, or if person is unwell or any evidence of liver injury																	
Audiometry	X			X	Only mandatory at selected facilities, but service is available for any patient in need														
ECG	X	X	X	X	X	X	X			X			X			X			X
Visual acuity and PNP while on LZD	X	X	X	Assess VA using Snellen chart; repeat monthly, or more often as required, while on linezolid															

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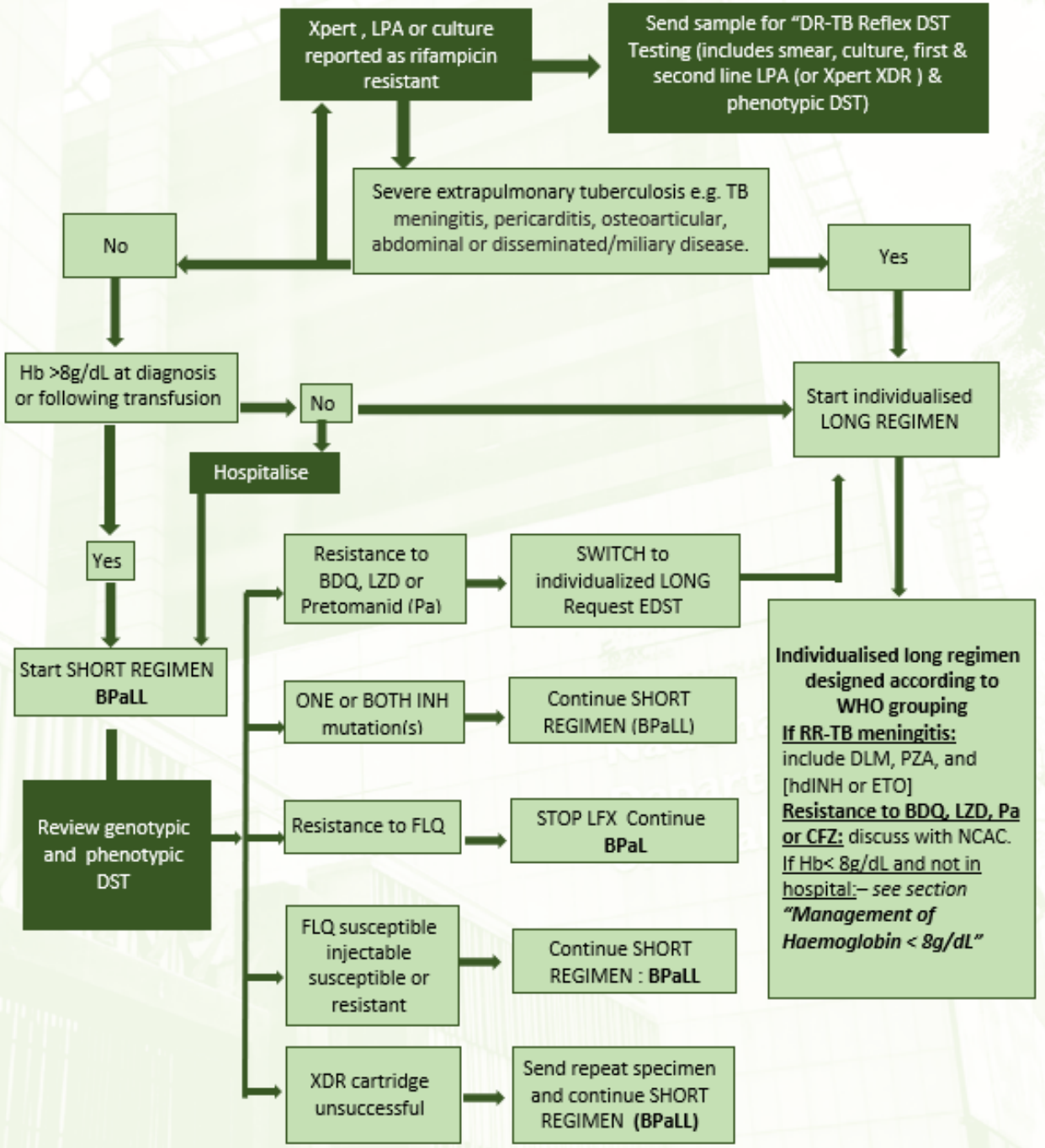
1.7. Overall Flow Diagram for people ≥ 15 years of age



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Introduction of the short regimen: BPaL-L

- Most people with a diagnosis of RR-TB will be eligible to receive the short regimen BPaL-L
- This contains:

Bedaquiline + **Pretomanid** + **Linezolid** +/- **Levofloxacin**

- If fluoroquinolone resistance is detected, BPaL can be used without levofloxacin for 6 months
- Prior use of bedaquiline and linezolid (>1 month) is not a contraindication for BPaL-L
- **BPaL-L must not be used if there is resistance to bedaquiline or linezolid or pretomanid**

Summary of changes: Medicines

Old 9-month regimen: BDQ, LZD, LFX, CFZ, INH HD, PZA, EMB

−: ~~CFZ~~, ~~INH HD~~, ~~PZA~~, ~~EMB~~

+: Pretomanid (Pa)

=: BDQ, LZD, LFX, Pretomanid (Pa) → New 6-month regimen = BPaL-L

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Inclusion and exclusion criteria for BPaL-L

INCLUSION Criteria
Individuals with RR-TB Resistance based on initial GXP result, while further awaiting further susceptibility results
Non-severe extra-pulmonary RR-TB, including lymphadenopathy or pleural effusion
Persons with extensive pulmonary disease (i.e. bilateral, cavitary disease with significant fibrosis, scarring or cavities in 3 or more lung zones) should have their treatment extended to 9 months

EXCLUSION Criteria
Persons with **severe extra-pulmonary RR-TB;** meningitis, pericarditis, osteoarticular, abdominal or disseminated/miliary disease
RR-TB with **additional resistance to BDQ or LZD, or pretomanid or delamanid**
Children under the age of 15 years (pretomanid safety is not yet confirmed in this population)
Pregnant women (pretomanid safety is not yet confirmed in this population)

Significant impact delivered through these interventions

GOAL: Accelerate reductions in TB incidence and mortality

Pillar I: Communicate & Advocate	Pillar II: Find & Link	Pillar III: Treat & Retain	Pillar IV: Prevent & Prepare	Pillar V: Monitor & Assess
TB is a national priority across sectors	People with TB are linked to care within one week	People with TB have access to high-quality treatment & support	TB prevention is valued as much as treatment	High quality data is used to guide decisions
	Improved DR-TB Diagnostics	**Shorter regimen** -increased efficacy - Improved retention in care		
	MOST IMPACT ON TB INCIDENCE AND MORTALITY (Thembisa model)			

BPaL-L Way forward

- Guideline dissemination and training in place including a webinar for all provinces on August 30th, 2023.
- Meeting held with Affordable Medicines Cluster and Provincial Pharmacy Directors to prepare.
- Provincial HODs and TB Managers informed.
- The existing 4 BPaL CAP sites will start as soon as possible, not later than 30th September 2023; starting with Jose Pearson Hospital in Gqebera (previously known as Port Elizabeth).
- Scale up will be closely monitored from NDOH and Provincial Offices starting from 1st September to 30th November 2023 subject to availability of pretomanid and training roll-out..

Thank you