Webinar

BPAL-L Implementation in South Africa:

Progress, Challenges, and Next Steps

Date: 12 March 2025

Time: 13h00 – 15h00

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

30 YEARS OF FREEDOM
South Africa 1994 - 2024

Thank you for your interest in this webinar

- The chat has been disabled for the attendees.
- **Please use the Q&A box to post questions for our panel of experts.**
- The session is recorded and will be shared with all the presentations on the Knowledge Hub – www.knowledgehub.health.gov.za/lms

Prof N Ndjeka

Prof Ndjeka serves as the Chief Director TB Control and Management, under the National Department of Health in South Africa.

Under his leadership, there has been a decline in the number of cases of DR - TB in South Africa and a remarkable improvement in proportion of patients successfully treated for DR- TB.

Programme Director: Prof N Ndjeka

Time	Duration	Topic	Presented by
13:00 - 13:05	5min	Opening and Welcome	Prof. Norbert Ndjeka
13:05 - 13:15	10min	Aims and objectives of webinar	Prof. Norbert Ndjeka
13:15 - 13:35	20min	BPaL – L implementation: programmatic progress	Ms Yulene Kock
13:35 – 13:55	20min	Refreshing Clinical Aspects of BPaL-L regimen implementation	Dr Francesca Conradie
13:55 - 14:15	20min	BPaL-L extension from 6 to 9 months: Case studies	Dr Pauline Howell
14:15 – 14:55	40min	Discussion (Q&A)	Prof. Norbert Ndjeka
14:55 – 15:00	5min	Vote of thanks	Prof. Norbert Ndjeka

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Ms Yulene Kock

Yulene Kock is a public health nurse with knowledge of infectious diseases of TB & HIV.

She is actively involved in support and clinical management of the DR-TB programme in the nine provinces; monitoring, reporting, and conducting Impact Assessment; providing training; supervision of & support to provinces and sub-directorate supervision

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Dr Francesca Conradie

Dr Conradie has been a Principal Investigator of over 20 clinical trials; the last 12 being TB clinical trials**.** She is a Co-chair of the National DR-TB Clinical Advisory Committee (NCAC) since 2012.

She had served on the Wits Ethics committee for over a decade and has extensive knowledge and understanding of ethical and regulatory requirements and procedures applicable to clinical research.

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Dr Pauline Howell

Dr Pauline Howell is a Clinical Research Site (CRS) Leader at the Sizwe CRS located at Sizwe Tropical Diseases Hospital in Johannesburg.

She is also the Chair of Safety Committee for Bring BPaL2Me trial and a Member of the SA DR-TB National Clinical Advisory Committee (NCAC).

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Thank you for attending this webinar

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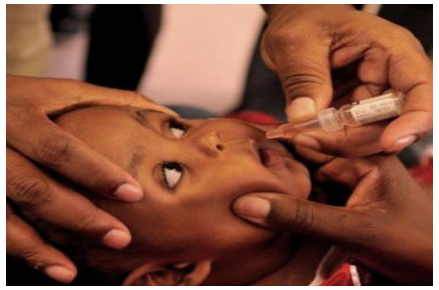
THANK YOU

BPaL-L Implementation: Programmatic Progress



Deputy Director: Drug Resistant TB
Ms Y Kock

12th March 2025

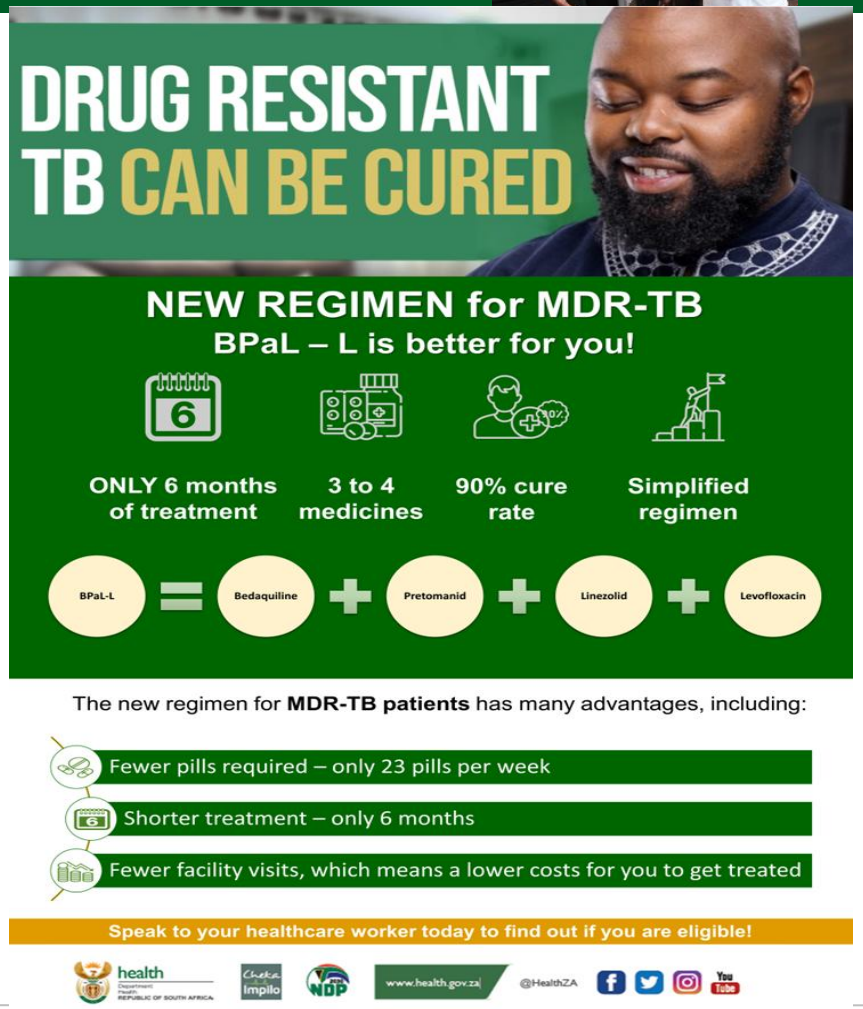
OUTLINE

1. Background/ Introduction

2. Data:
   - Historical
   - To date

3. Challenges

4. Conclusion



RR/MDR-TB treatment in South Africa - Evolution

Period	RR/MDR-TB Shorter Regimen	RR/MDR-TB Longer Regimen	XDR-TB Longer Regimen
2011 – 2016	• Not applicable	• 24 months (at least) • 5 drugs • **180 injections + 7 200 pills**	• 24 months (at least) • 7 drugs • **180 injections + 7 200 pills**
2017 – 2018 (Aug)	• 9 – 11 months • 7 drugs • **Up to 180 injections + at least 2 880 pills**	• 18 – 20 months • 5 drugs • **Up to 180 injections + at least 5 400 pills**	• 18 – 20 months • 5 drugs • All-oral: **at least 3 968 pills**
2018 (Aug) – 2023	• 9 – 11 months • 7 drugs • All-oral: **at least 3 038 pills**	• 18 – 20 months • 5 drugs • All-oral: **at least 5 048 pills**	• 18 – 20 months • 5 drugs • All-oralL: **at least 3 968 pills**

RR/MDR-TB treatment in South Africa - BPaL-L

Old 9-month regimen: ~3,038 pills

BDQ LZD LFX CFZ INH HD PZA EMB

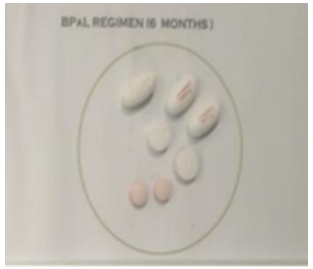
~~CFZ INH HD PZA EMB~~

\+ Pa

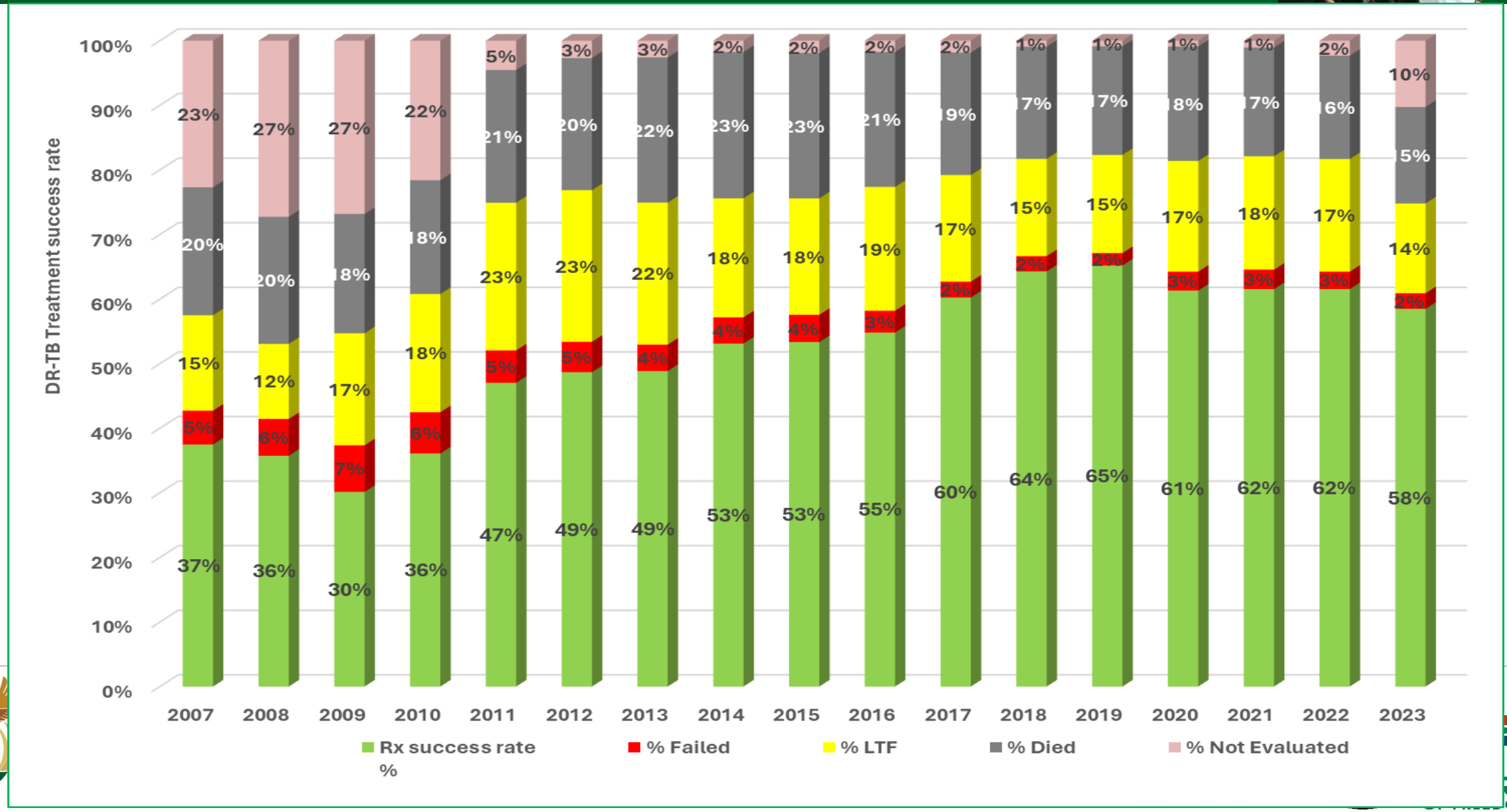
=

BDQ Pa LZD LFX

New 6-month BPaL-L regimen: ~860 pills

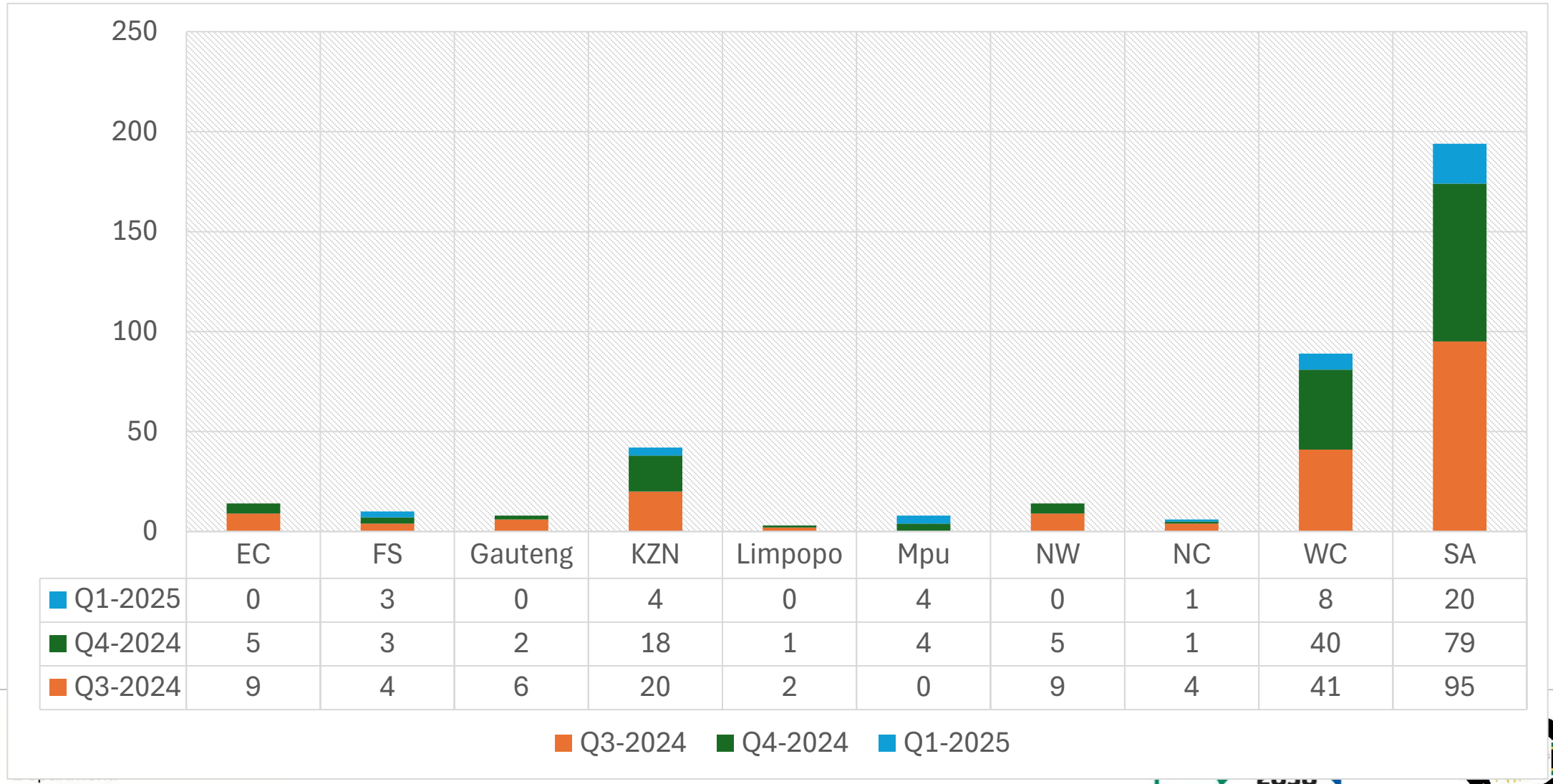


Factors affecting better DR-TB treatment outcomes - % only



DR-TB treatment success rate – Short Regimen 9-11 Months (%)

DR-TB treatment initiation – Short Regimen 9-11 Months

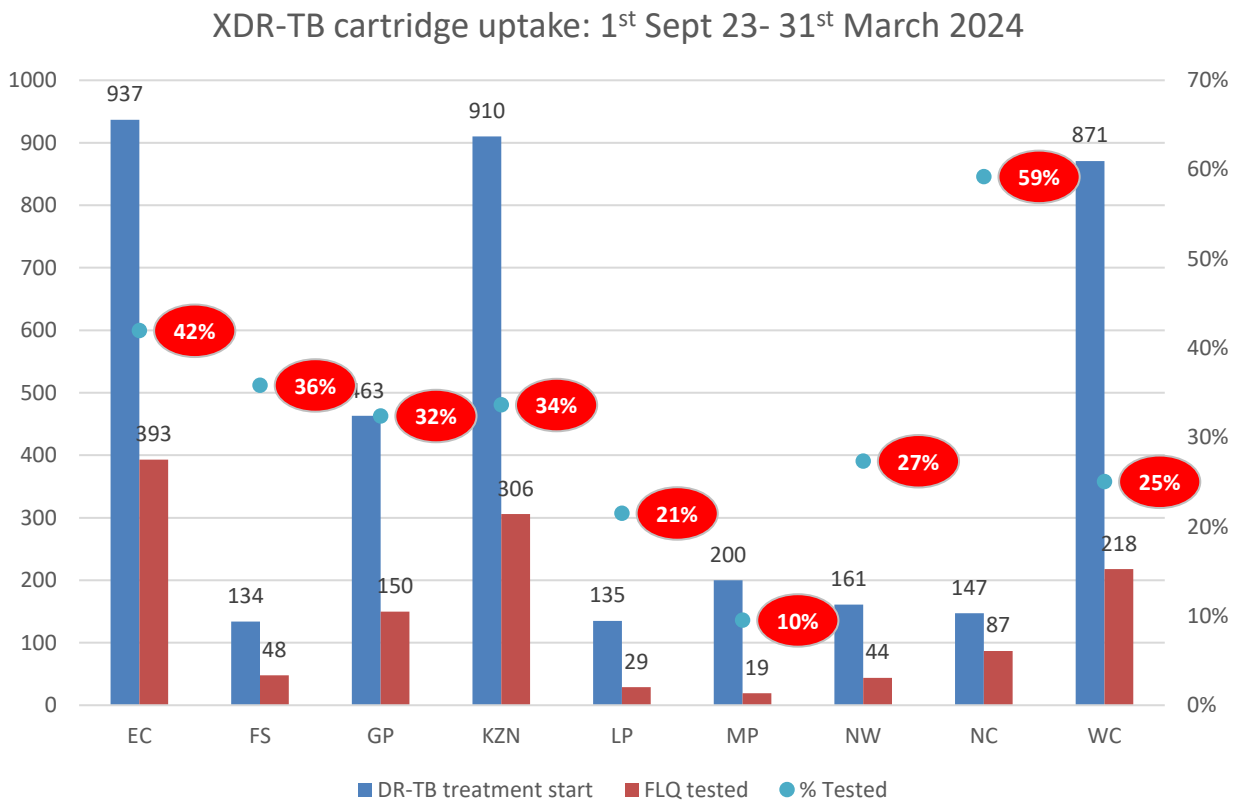


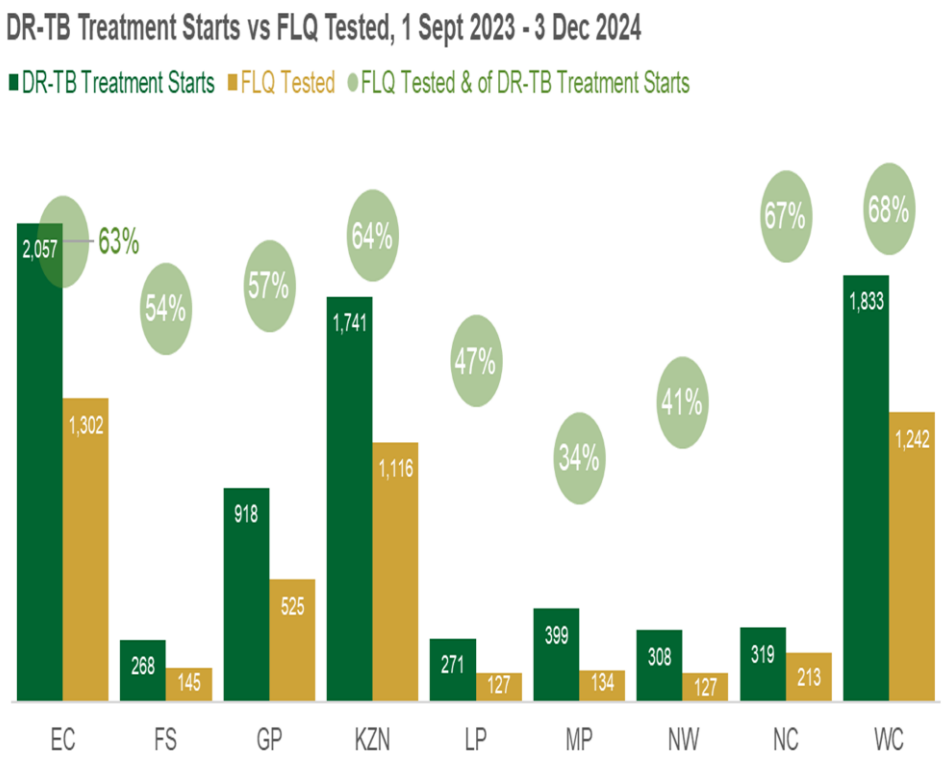
	EC	FS	Gauteng	KZN	Limpopo	Mpu	NW	NC	WC	SA
Q1-2025	0	3	0	4	0	4	0	1	8	20
Q4-2024	5	3	2	18	1	4	5	1	40	79
Q3-2024	9	4	6	20	2	0	9	4	41	95

DR-TB treatment success rate – BPaL-L

Provinces	Period	Cohort	Success	Success rate % *(Target – 72%)*	Failed	% Failed	LTF	% LTF	Died	% Died	Not Evaluated	% Not Evaluated
EC	Q4 2023	224	177	79%	13	6%	11	5%	22	10%	-	0%
	Q1 2024	347	270	78%	11	3%	19	5%	46	13%	-	0%
FS	Q4 2023	15	12	80%	-	0%	3	20%	-	0%	-	0%
	Q1 2024	46	36	78%	-	0%	2	4%	1	2%	5	11%
GP	Q4 2023	146	114	78%	1	1%	21	14%	10	7%	-	0%
	Q1 2024	145	121	83%	3	2%	14	10%	7	5%	-	0%
KZN	Q4 2023	267	207	78%	3	1%	21	8%	27	10%	9	3%
	Q1 2024	316	253	80%	4	1%	24	8%	14	4%	17	5%
LP	Q4 2023	53	43	81%	3	6%	1	2%	3	6%	1	2%
	Q1 2024	51	37	73%	2	4%	1	2%	6	12%	5	10%
MP	Q4 2023	48	35	73%	1	2%	6	13%	6	13%	-	0%
	Q1 2024	86	66	77%	1	1%	5	6%	9	10%	5	6%
NW	Q4 2023	55	49	89%	-	0%	1	2%	4	7%	-	0%
	Q1 2024	63	51	81%	-	0%	2	3%	6	10%	3	5%
NC	Q4 2023	53	40	75%	1	2%	7	13%	5	9%	-	0%
	Q1 2024	53	41	77%	-	0%	4	8%	7	13%	-	0%
WC	Q4 2023	103	57	55%	-	0%	24	23%	9	9%	13	13%
	Q1 2024	267	162	61%	5	2%	39	15%	15	6%	44	16%
SA	**Q4 2023**	**964**	**734**	**76%**	**22**	**2%**	**92**	**10%**	**89**	**9%**	**23**	**2%**
	Q1 2024	**1 374**	**1 037**	**75%**	**26**	**2%**	**110**	**8%**	**111**	**8%**	**79**	**6%**

DATA INCOMPLETENESS





CHALLENGES

- Patients being initiated on 9-month regimen

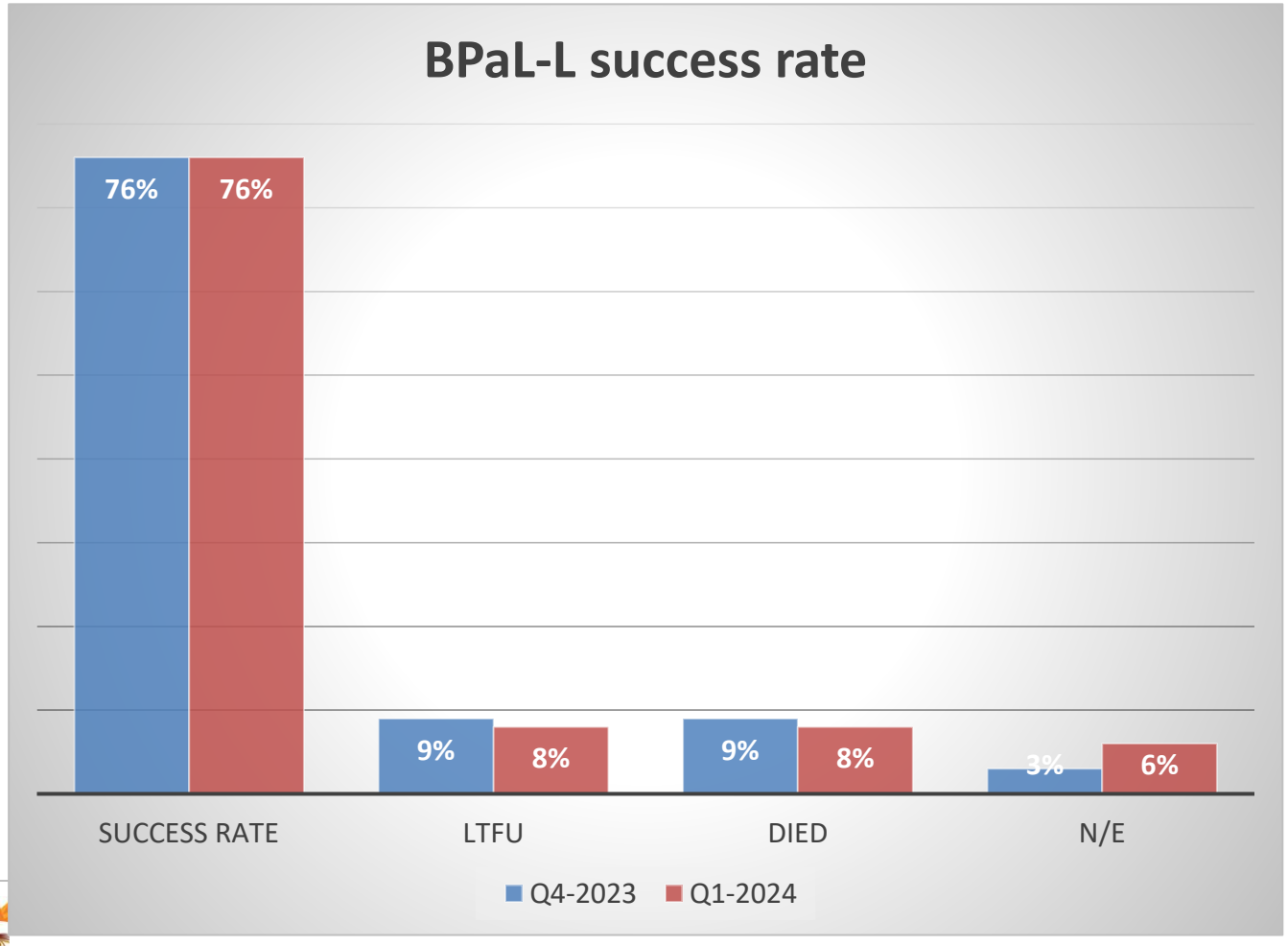
🤔 Reason patients still being initiated on this regimen - why

- Low uptake of XDR-TB cartridge: 55%
- Post treatment discharge not done/recorded
- Incomplete data:
  - Outcomes not recorded
  - Treatment regimen not recorded or incorrectly recorded

CONCLUSION

- BPaL-L regimen has been fully implemented √
  - Goal is to initiate 90% of all eligible individuals on BPaL-L: phase-out 9 month regimen
- Patient adherence counselling of utmost importance
- Monitoring of patients on regimen
  - Completion of treatment journey
  - BDQ resistance
  - Adverse events
- Recording and reporting
  - Outcomes
  - Post treatment discharge
- Clinical governance utmost importance: clinical audits, data monitoring

SUCCESSES


BPaL-L success rate
76%
76%
9%
8%
9%
8%
3%
6%
SUCCESS RATE
LTFU
DIED
N/E
Q4-2023
Q1-2024


76 %

ACKNOWLEDGEMENTS

- Provincial managers & teams
- Supporting partners:
  - Global fund & the supporting partners
  - AURUM
  - USAID
  - TSU
  - CHAI
- NICD/ NHLS
- NDoH TB Management and Control cluster

YES WE CAN END TB

Thank you!

Clinical Aspects of BPaL L

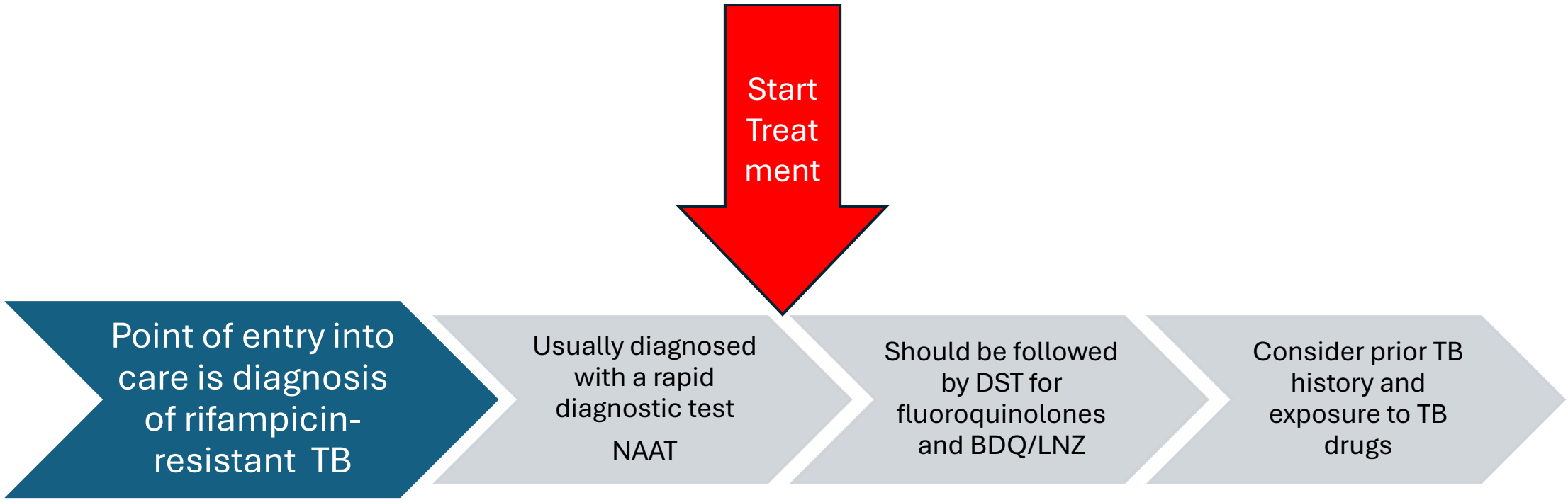
Francesca Conradie

Co-Chair of the NCAC

Topics to be covered

- When to start
- Eligibility for BPaL L
- Monitoring for BPaL L
- Exceptions

When to start



Treatment options in South Africa for RR-TB

- **First option**
- 6-month duration
- Maybe modified if FQ-R (pre-XDR TB) to BPaL

BPaL L (occasionally BDLLC)

- **Second option**
- 18-month duration
- Consider the grouping of drugs (A, B or C)

Longer individualised regimen

Who is eligible for BPaL L?

Individuals with RR-TB aged 14 years and above

- Except for complicated extrapulmonary TB, e.g. TBM, bone or joint, miliary
- Except for pregnant and breastfeeding women
- XDR TB or BDQ-R

Irrespective of HIV status and immunological status

- If HIV infected
  - Check VL if on therapy, support adherence if detectable
  - If not on ART, start TLD within 2-8 weeks

Irrespective of the severity of the disease

- Can be used in bilateral disease
- Can be used in the presence of cavities
- Can be used irrespective of smear grading

What about prior exposure to components of the regimen?

Linezolid and bedaquiline have been part of our shorter (9-11month regimen) regimen since 2018

Prior exposure could have been in individuals who were successfully treated or those who were lost to the program

This group has an increased risk of BDQ resistance.

However, pending the results of further susceptibility testing, BPaL L should be started.

Be vigilant for the BDQ resistance test, at this stage, by phenotype

Diagnosis of RR TB

WHO-recommended rapid diagnostic (mWRD)

- There are several options, depending on where the diagnosis was made

Followed by TB reflex test

- Genotypic: GeneXpert XDR TAT up to one week
- Phenotypic: BDQ and LNZ resistance testing: TAT up to 6 weeks

But do not delay the start of BPaLL

Monitoring BPaL L

Safety

Hematological	• Baseline Hb/ FBC with two weekly for the first month and then every month
Liver	• Baseline ALT and monthly
Cardiac	• Baseline ECG and monthly
Neurological	• Peripheral neuropathy assessment • Visual acuity

Efficacy

Smear	• Baseline and monthly
Culture	• Baseline and monthly

Results of addition resistance testing

FQ- R

Stop the levofloxacin

Continue BPaL

Treatment duration is 6 months from treatment initiation unless there is a microbiological or clinical indication to extend.

BDQ-R or LNZ-R

Stop BPaL L

Start individualised regimen

Contact NCAC

Response to treatment

- Culture conversion usually occurs within 60 days of treatment start
- Some resolution of symptoms by 60 days
- Delayed culture conversion
  - If still culture-positive at 3 months, consider
    - Imperfect adherence to treatment
    - Extensive disease
    - Undiagnosed resistance to components of the regimen either at baseline or acquired, do eDST, contact the lab for the baseline test

Response to treatment

- Culture conversion usually occurs within 60 days of treatment start
- Some resolution of symptoms by 60 days
- Delayed culture conversion
  - If still culture-positive at 3 months, consider
    - Impe
    - Exter
    - Undia ither at baseline or acqu

Treatment extension may be needed

6-month BDLLfxC regimen

MDR/RR-TB or pre-XDR-TB

PTB, children, adolescents, pregnant, breastfeeding women

EPTB, except CNS TB, osteoarticular, disseminated TB with multiorgan involvement

Children and adolescents without bacteriological confirmation of TB but with a high likelihood of MDR/RR-TB (based on TB symptoms, history of MDR/RR-TB contact and etc)

What is the composition of the BDLLfxC regimen?

- If DST for FQ is unknown or cannot be carried out at baseline.

BDLLfxC

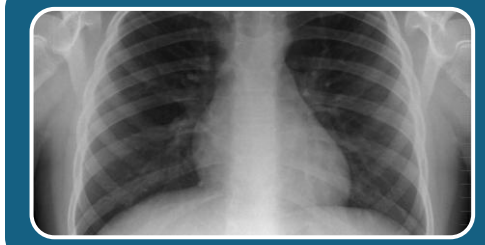
- If DST is susceptible to FQ.

BDLLfx

- If DST is resistant to FQ.

BDLC

Conclusion



There are two options for the treatment of RR TB in South Africa

6

BPaL L

Longer individualised regimen

BPaL-L Extension from 6 to 9 months

Cases

Pauline Howell

WITS HEALTH CONSORTIUM

3 Cases

Case 1

- 24 year old lady presents
  - Coughing ~ > 1 month (unsure) but recently with blood in sputum
  - Some LOW and LOA, night sweats
  - No other symptoms
- No previous history of TB
- Unsure of her HIV status
- O/E: no features of meningitis nor bony involvement
- Pregnancy test negative
- NAAT shows Rifampicin resistance

- Q1: What do you do next?

slido

Please download and install the Slido app on all computers you use

Q1: 24 year old lady, not pregnant, diagnosed with RR-TB disease: What do you do next?

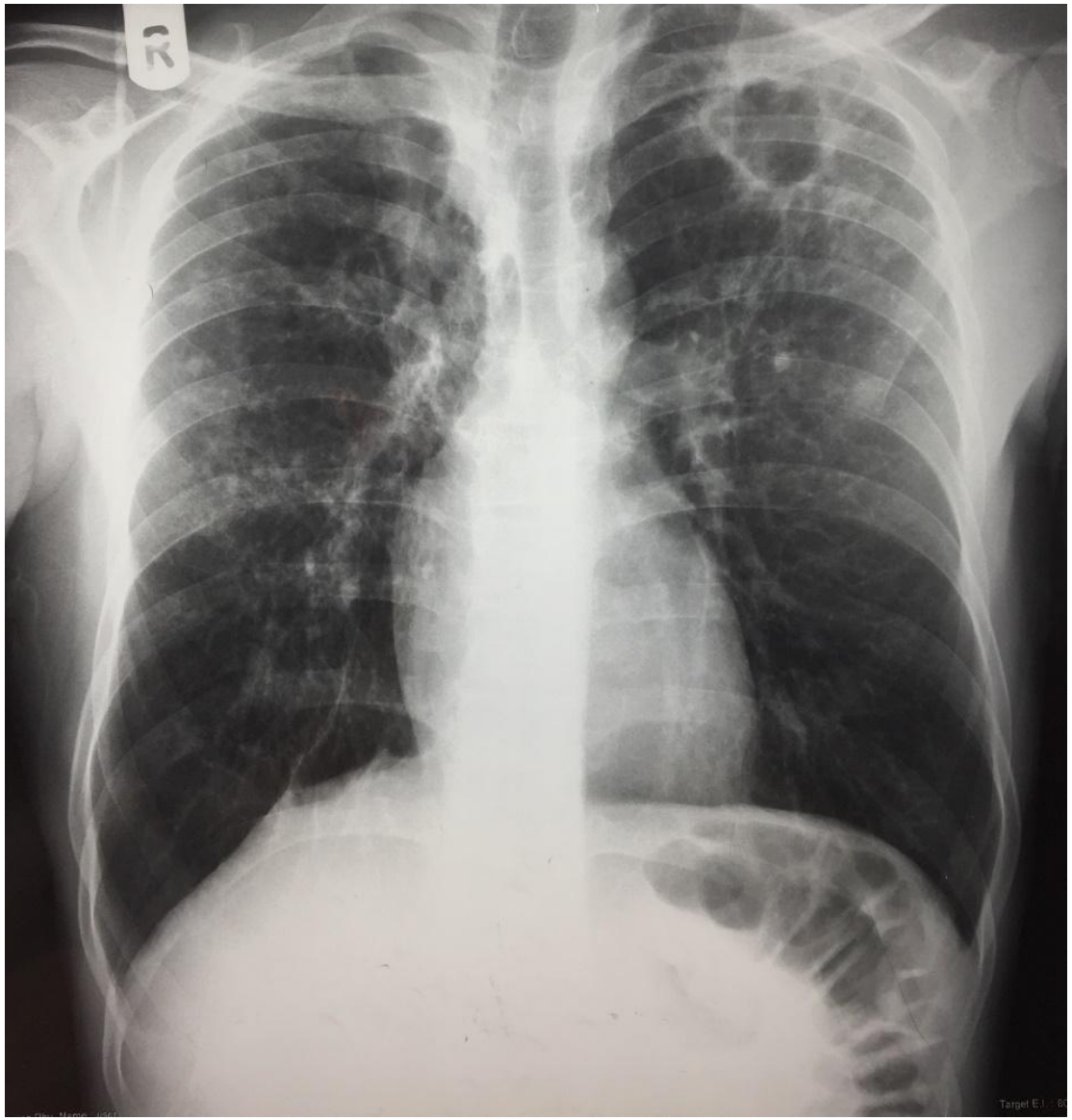
ⓘ Start presenting to display the poll results on this slide.

Case 1

- Start BPaL-L

- CXR
- GXP/XDR shows resistance to isoniazid and fluoroquinolones
- Person living with HIV

- Q2: Next steps?



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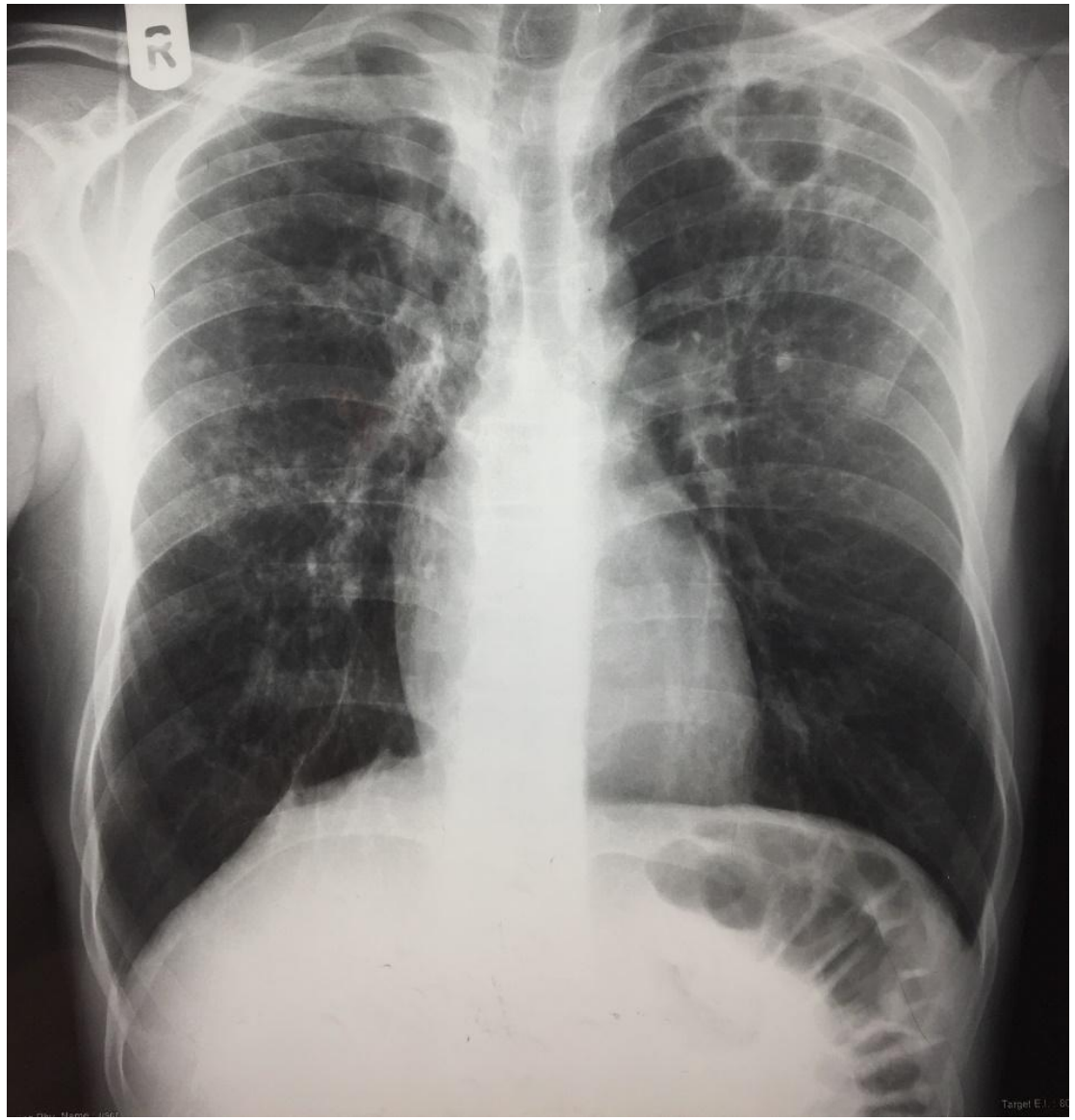
Q2: 24 year old lady, not pregnant, diagnosed with preXDR-TB (resistant to fluoroquinolones): Next step?

ⓘ Start presenting to display the poll results on this slide.

Case 1

- CD4 = 98
- HAART started at week 2
- Culture converted at wk 4
- Culture conversion with good clinical response
- Developed peripheral neuropathy at week 18
- Linezolid stopped at week 20
- Completed BPa to 6months
- Cured, relapse-free for 24 months

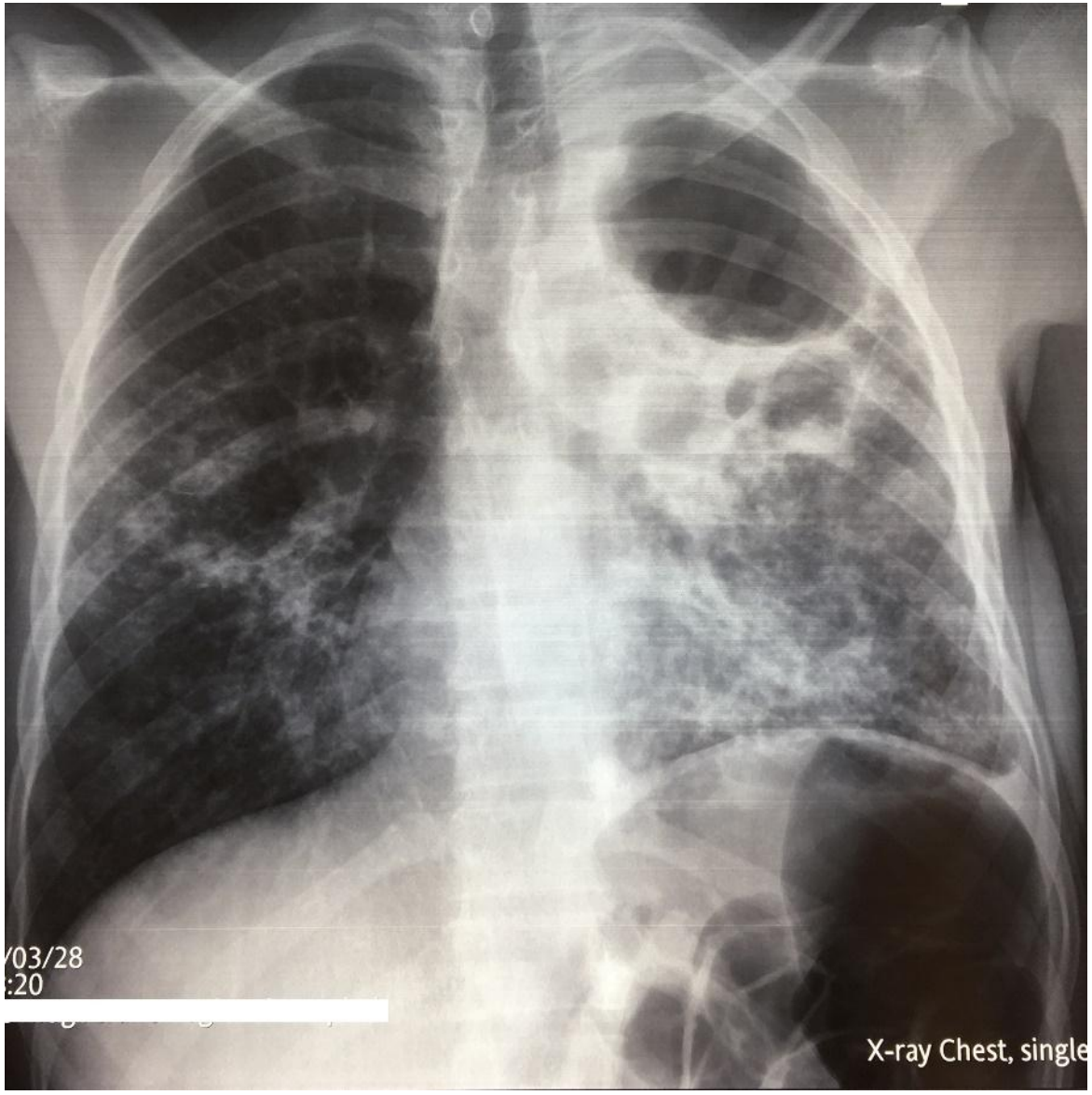


Case 2

- Mr N, 37 years old presents:
  - Difficulty playing soccer w/ his son
  - HIV negative
  - Haemoptysis “for a long time”
  - Clothes looser but denies LOA

- No features of meningitis nor bony involvement
- NAAT shows rifampicin resistance; Smear 3+

- Q3: Next steps?



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Q3: 37 year old man with extensive lung disease, smear 3+ and haemoptysis, next steps?

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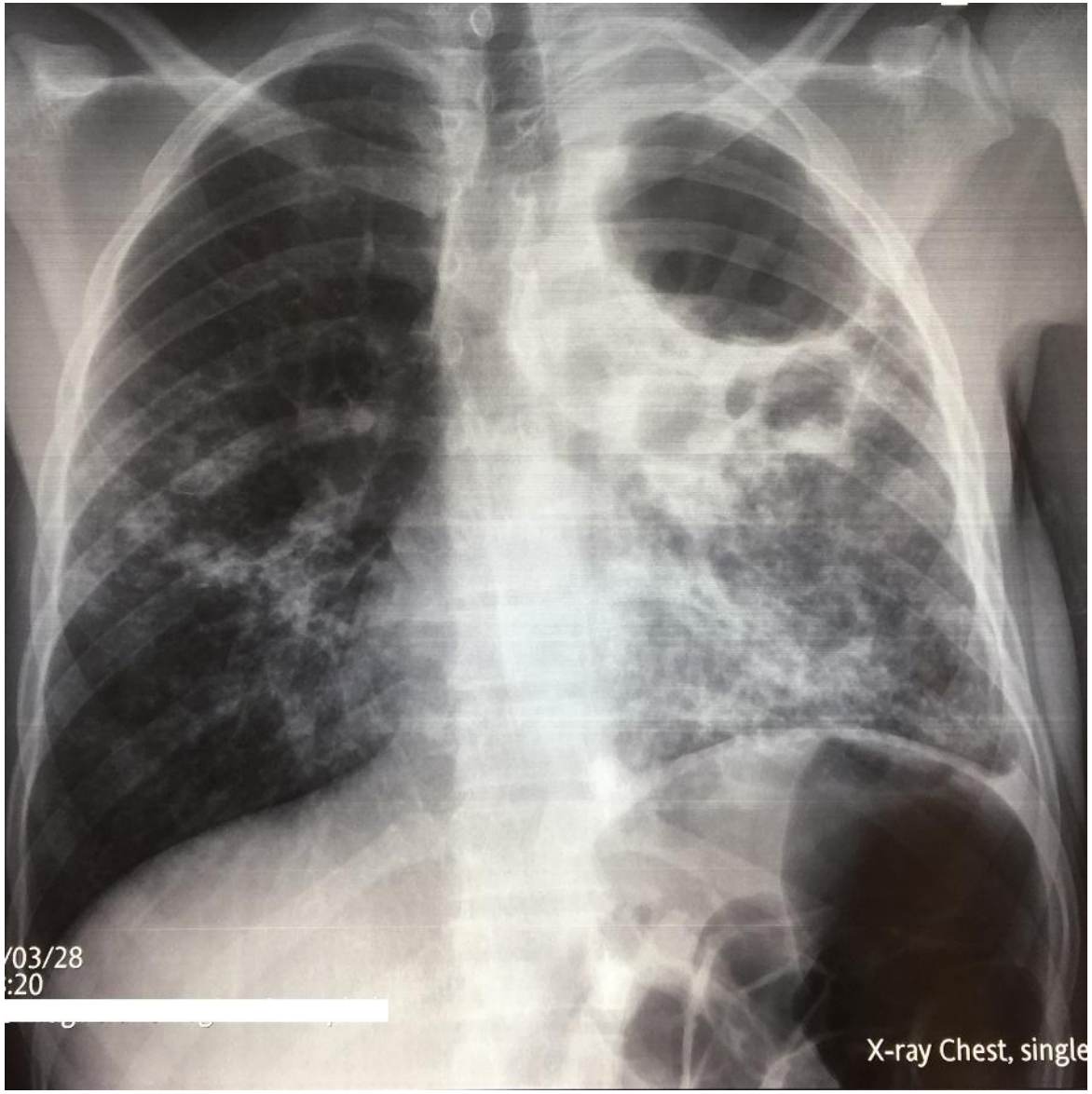
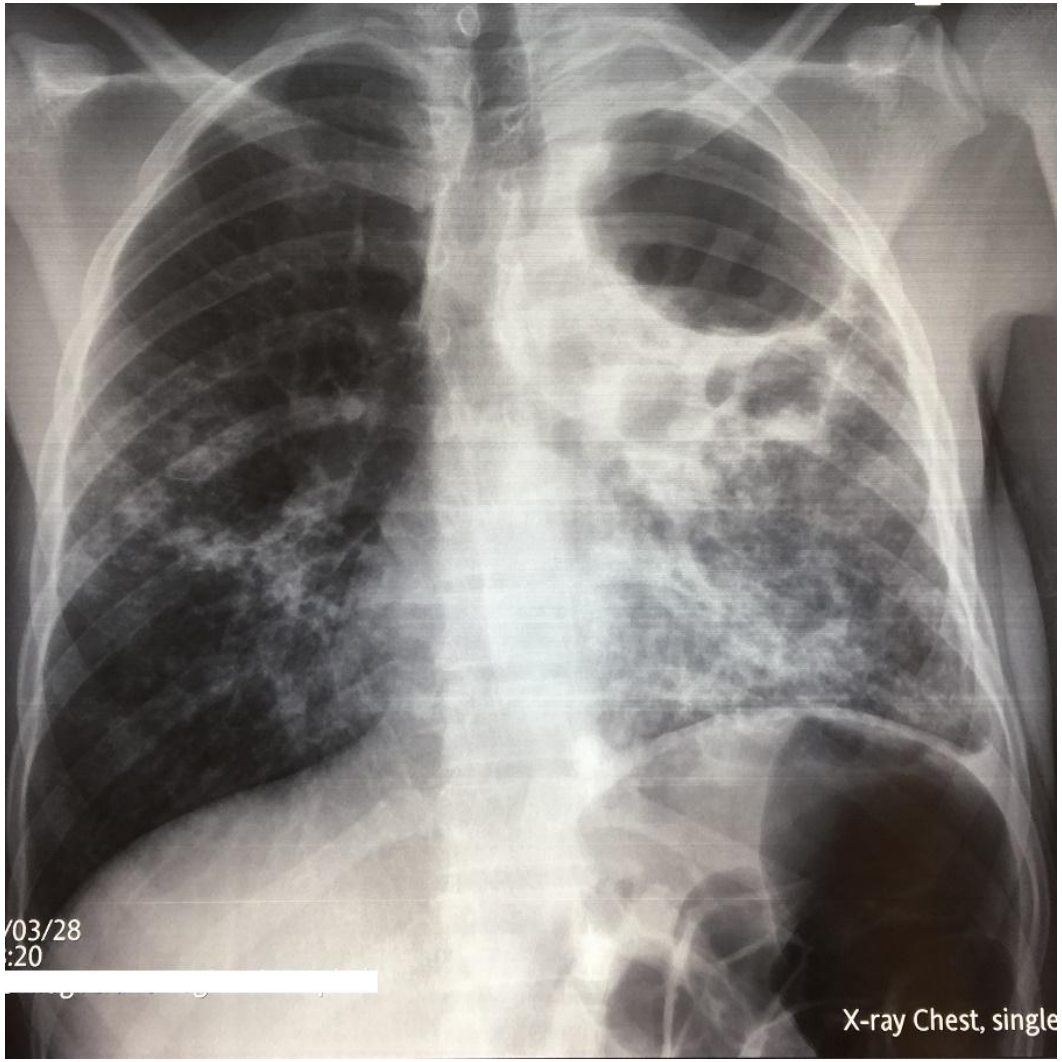
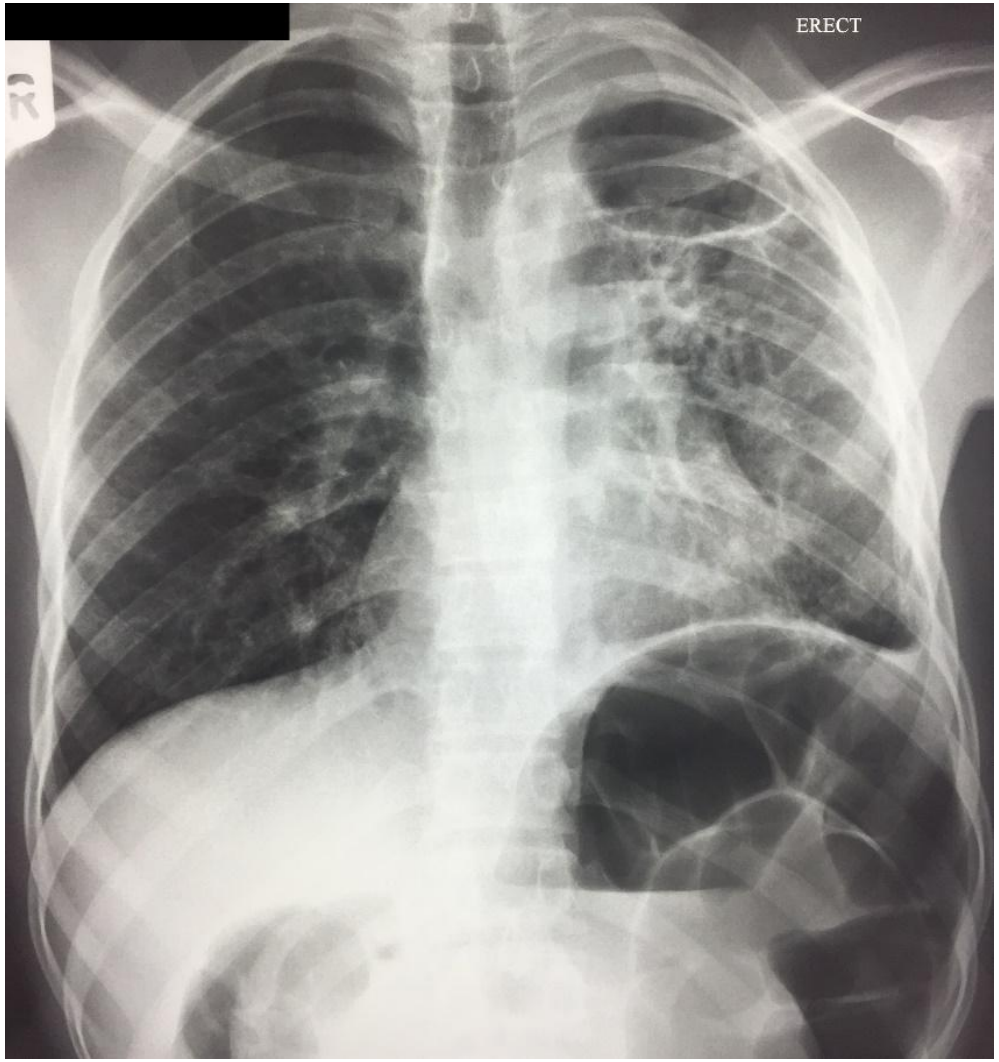
Case 2

- Start BPaL-L and monitor
- Further DST showed resistance to isoniazid, and susceptibility to FQ/SLID/BDQ/LZD.
- Culture converted at wk 6 with sustained negative cultures and symptomatic resolution.
- Stopped LZD for hyperlactataemia at week 8. Rechallenged week 9.
- Completed 6 months of treatment and despite poor resolution of CXR he was followed up for 24 months relapse-free.



Case 2

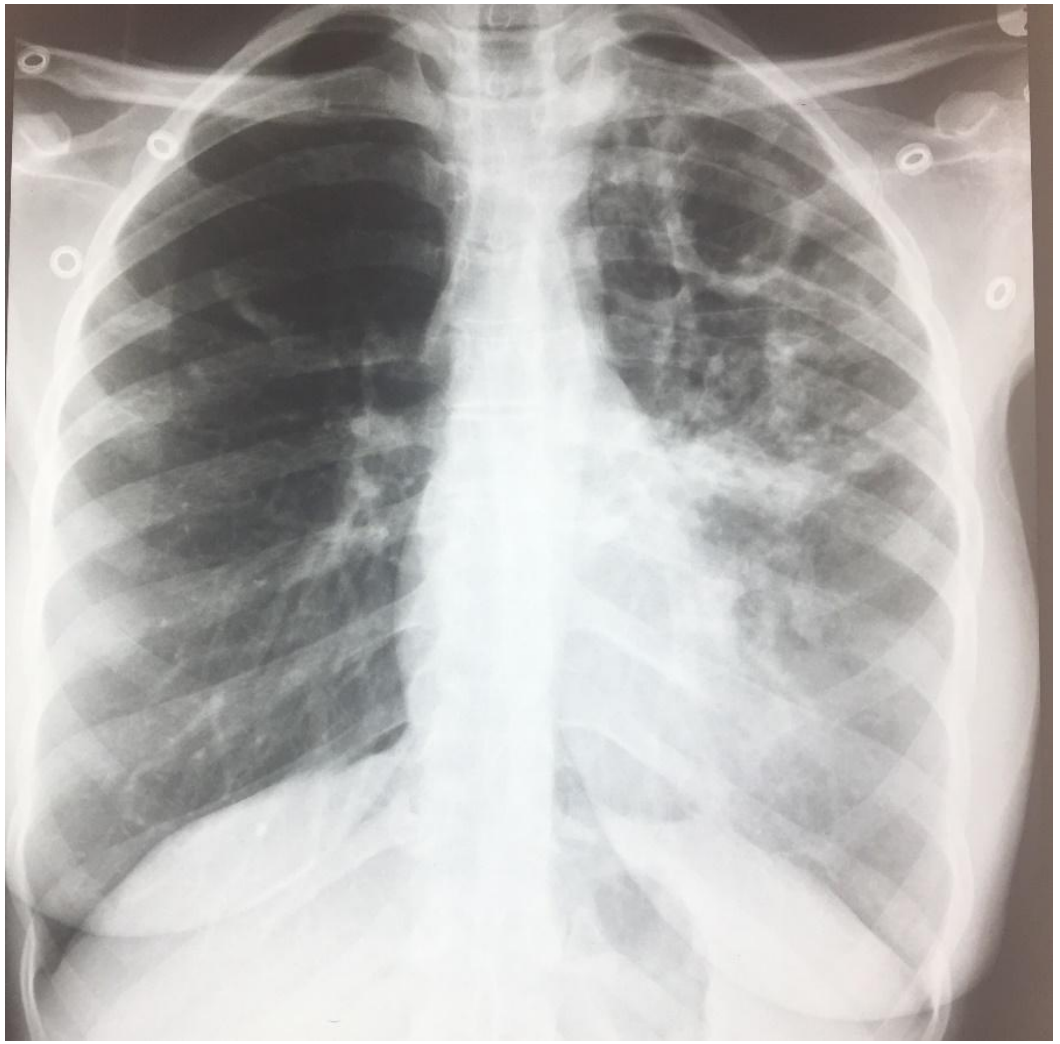




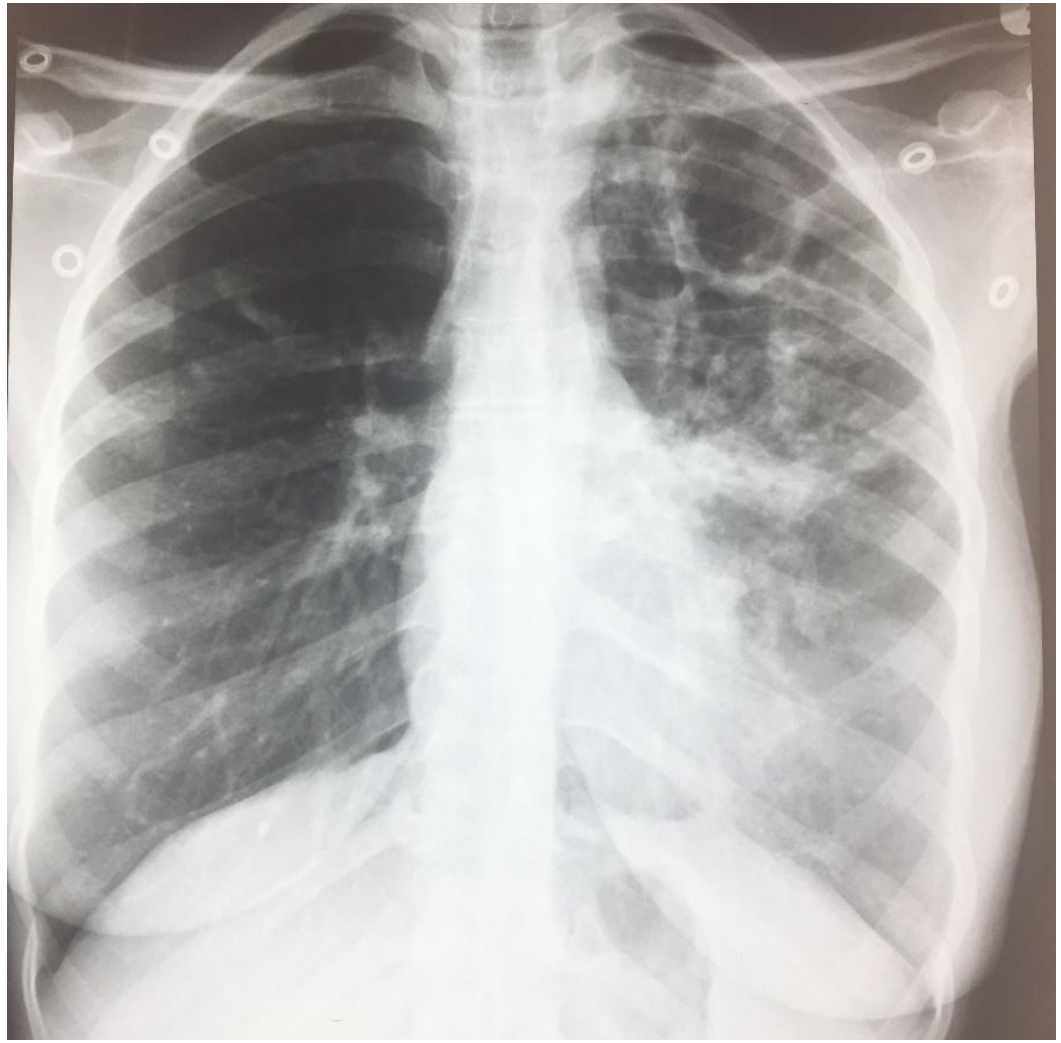
Case 3

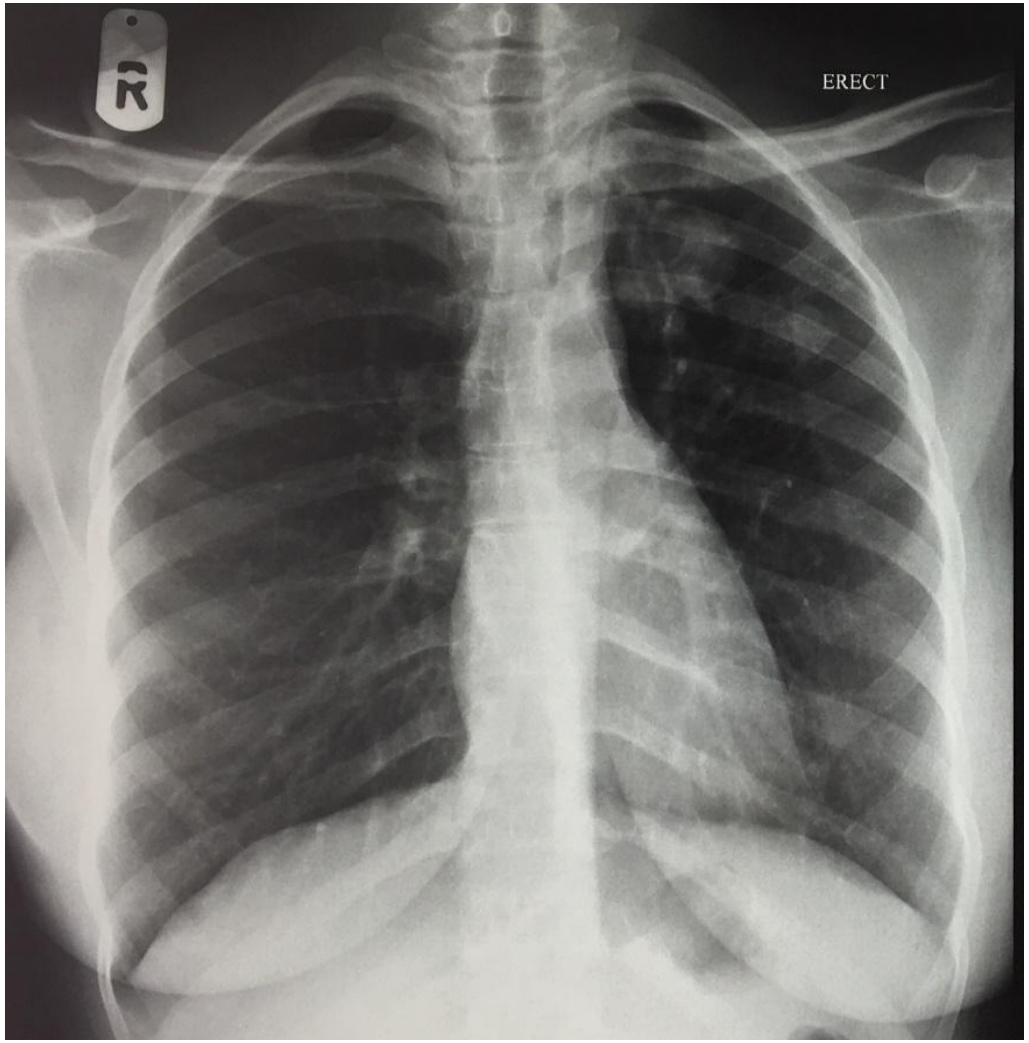
- Ms Z, 29 year old.
  - DS-TB in 2021 treated 9/12 pleural effusion.
  - RR-TB on NAAT, HIV neg.
  - Culture pos after 3 days
  - Pregnant ~9/40
  - No further DSTs available

- Started BDLLfxC
- Culture converted wk 4
- Completed treatment 6 months
- Mild PN, resolved by end of F/U
- Well baby, term delivery, no signs and symptoms of active TB, mom encouraged to BF with active infection control



Case 3





Remember:

- Adherence is key
- If patients complete the 6 month regimen they are highly likely to culture convert and do well
- Efficacy is largely driven by linezolid
- Extension is the exception and based on poor clinical response or delayed culture conversion, NOT for BDQ/LZD resistance
- If culture positive at week 12, be aggressively curious:
  - CXR, clinical review (weight gain? resolution of symptoms? Adherence? Consider further DST testing)

Questions?

Thank you