Post Tuberculosis Lung Disease: Clinical Aspects

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New Directions in TB
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Houston, Texas

Elizabeth S. Guy, MD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

Post tuberculosis lung disease – clinical aspects

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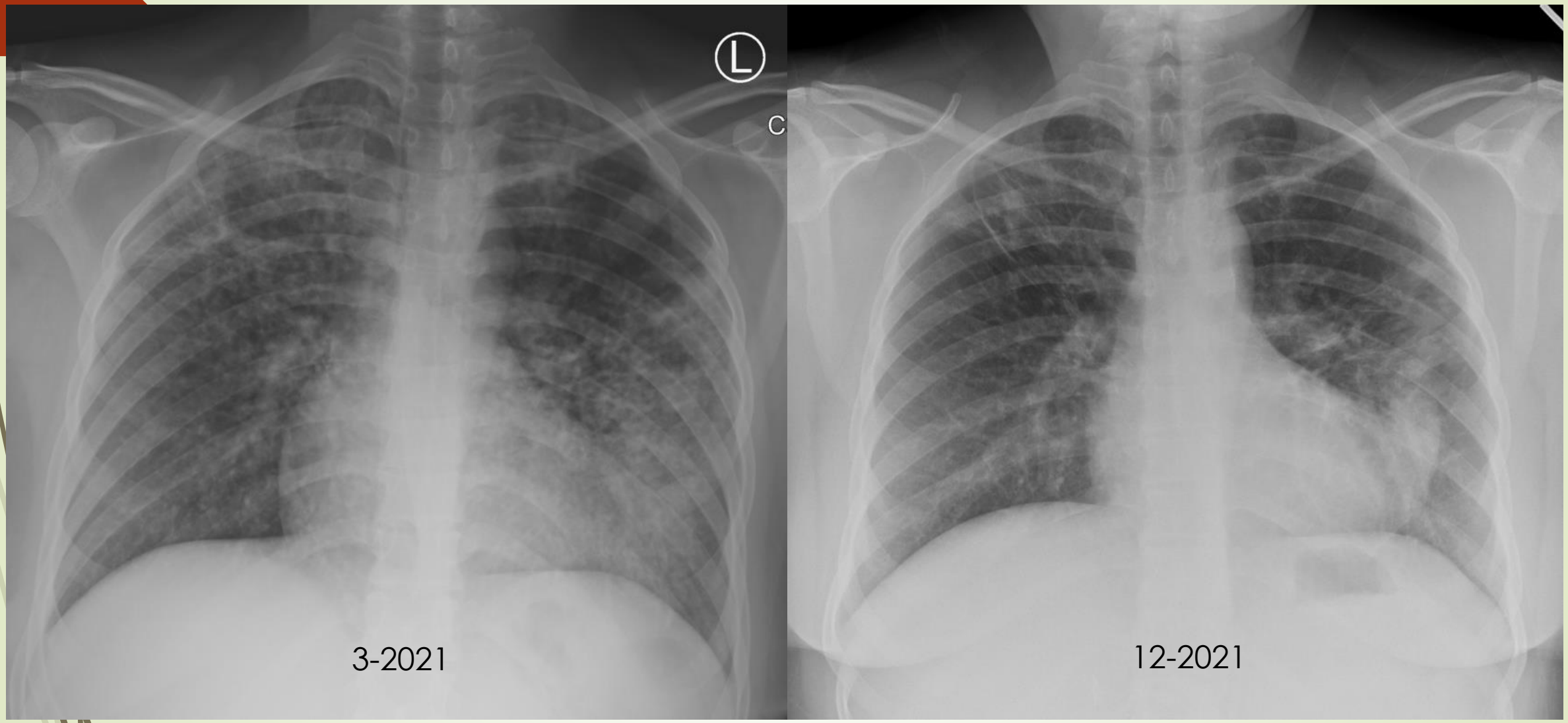
4-2-2024



3-2021

12-2021

- Estimated 155 m are living after treatment of tuberculosis in 2020
  - Substantial proportion report symptoms that affect quality of life
  - Estimated 50% have findings consistent with PTLD

Post Tuberculosis Lung Disease (PTLD)

- Chronic respiratory abnormality, with or without symptoms, attributable at least in part to previous pulmonary tuberculosis
  - Spectrum of disorders may affect large and small airways, lung tissue and vasculature and pleura
  - May be complicated by co-infection and hemoptysis
  - Increased risk of recurrent TB
- Results in significant disability with economic, social and psychological impact
- Stigmatization does not stop
- Shortened life expectancy
- No evidence-based recommendations for evaluation and management

Allwood et al 2021

Post TB lung disease

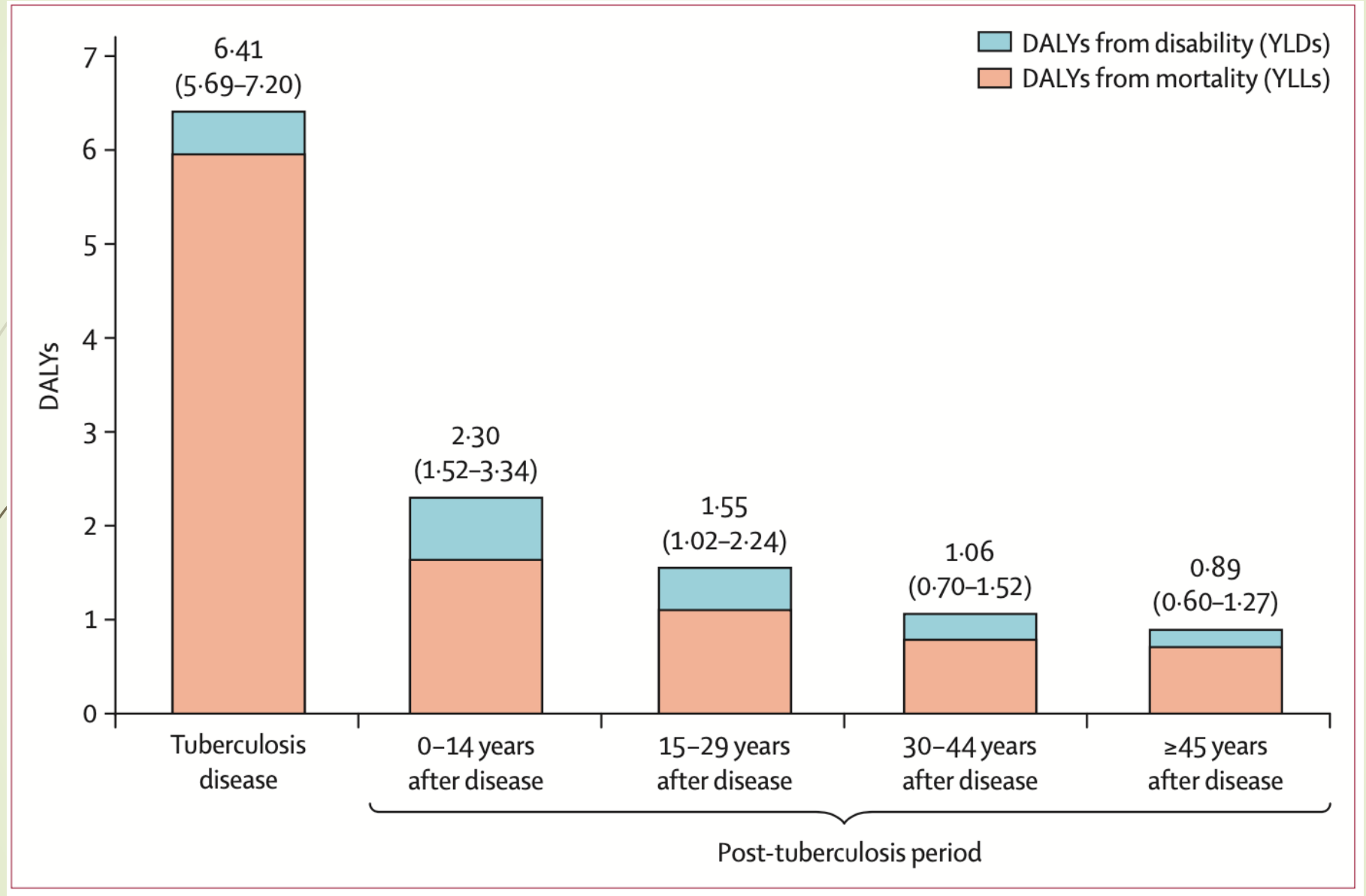
- Persisting respiratory symptoms
  - Pooled prevalence of 41% (sig heterogeneity)
- Radiography
  - High incidence of abnormalities (8 – 86%) with high variability
  - Bronchiectasis, cavitation, fibrosis. CT may show nodules and emphysema
- Lung function testing
  - Reduced DLCO was seen in 79%
  - Restriction and obstruction were seen
  - Increase in lung volumes after treatment completion associated with gas trapping (increased RV) – independent of emphysema and small airways obstruction
  - Disease not static, obstruction gets worse
- Quality of life: psychological, social and economic impact
  - Persistent symptoms, economic losses, impaired social life are associated with HRQoL
  - Depression and anxiety are 2x higher in TB compared to non-TB infected population

1. Maleche-Obimbo, et al. PLOS Global Public Health 2022
2. Meghji, et al. PLOS One 2016
3. Allwood BW et al. Int J Chronic Obstr Pulm Dis 2020
4. Nightingale et al. IJTLD 2023

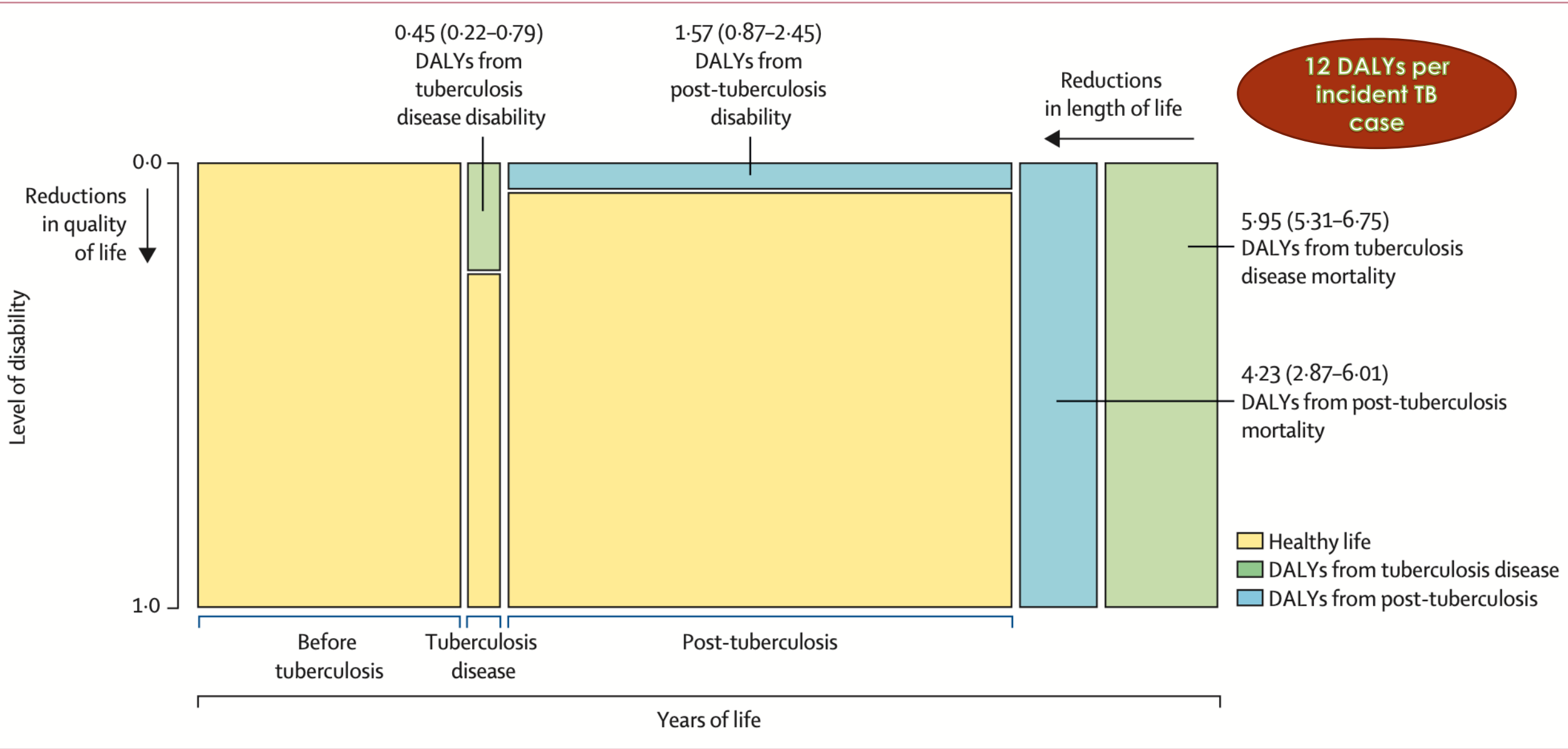
Predictors of poorer outcome

- From a cohort data in Malawi, modeling of variables that predict outcomes such as:
  - Chronic respiratory symptoms or functional limitation
  - Ongoing need for healthcare
  - Spirometry decline
  - Self reported financial impact of TB disease
  - Death
- Results:
  - Presence of respiratory symptoms at EOT - strongest predictor of functional limitation, spirometry decline and health seeking
  - Spirometry or imaging did not significantly improve the predictive models

Meghji et al. PLOS Global public Health Jan 2024



Menzies NA et al. Lancet 2021



Menzies NA et al. Lancet 2021

Clinical standards for assessment, management and rehabilitation of PTLD 2021

- Widely accepted level of diagnosis and care for all healthcare providers and clinicians to achieve optimal standards
- Universal principles that need to be adapted to specific settings and situations for implementation
- Used evidence available in other lung diseases
- 62 international experts were asked to comment on initial draft of 7 standards
  - 100% agreement on 6 standards

Migliori, et al. IJTLD 2021. 25(10): 797-813

Standard 1

- Every patient completing TB treatment should be evaluated for PTLD as soon as possible to identify patients at risk of deterioration and those who might benefit from pulmonary rehabilitation (PR)
  - Clinical assessment
  - CXR
  - PFT
  - 6 MWT
  - QoL questionnaire

Standard 2

- Evaluation for pulmonary rehabilitation
  - Core component of management of patients with chronic lung disease
  - Improves health status, exercise capacity, fatigue and social functioning
- Patients who should be assessed for PR
  - Impaired exercise capacity
  - Persistent respiratory symptoms
  - Hospitalization or exacerbations in last 12 months
  - PFT showing obstruction, restriction, mixed or impaired DLCO
  - Abnormal ABG
  - Ineffective cough or difficulty clearing secretions

Standard 3

- PR program should be organized according to feasibility, effectiveness and cost-effectiveness based on local availability and tailored to individual patient
  - Comprehensive baseline and post-PR outcome measures
  - Structured and supervised exercise program
  - Educational/behavioral component to foster long term health enhancing behavior
  - Generally effective in settings with adequate resources
  - Possible to adapt to local context and available resources

Standard 4

- Evaluate effectiveness of PR for former TB patients
  - Assess variables at the start and end of the program
  - Functional capacity, dyspnea and health status
  - St George's respiratory questionnaire
  - Short form health survey 36
  - Clinical COPD questionnaire

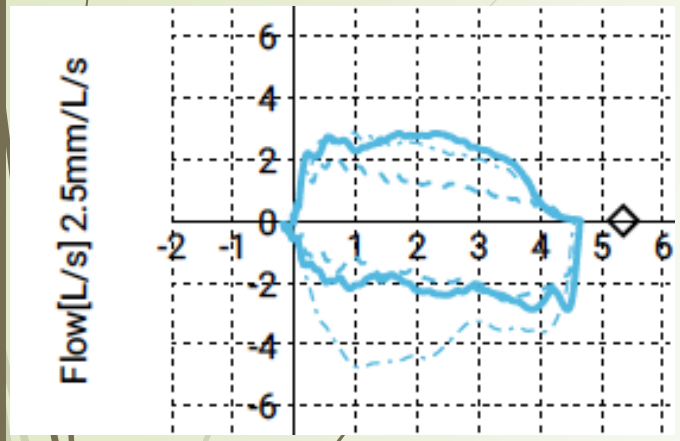
Standard 5

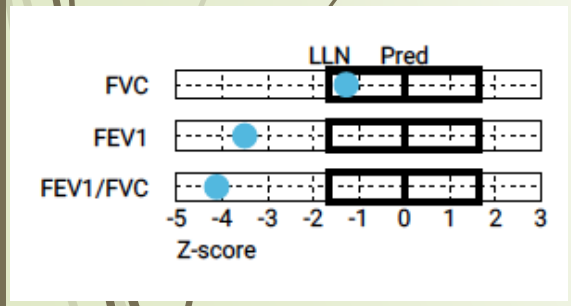
- Health education and counseling with follow up to maintain or improve the results achieved, based on local health organization

Standard 6

- Notify and include in the TB register a change in outcome of a patient during or after PR
  - WHO has revised outcomes definition that includes follow up of patients 6-12 months after treatment completion
- Support and social protection for patients with permanent sequela and disability

32 yo M Hispanic
Extensive pulmonary and disseminated tuberculosis, HIV
1.77m 83 kg





Test1 27.12.2023 02:47 PM

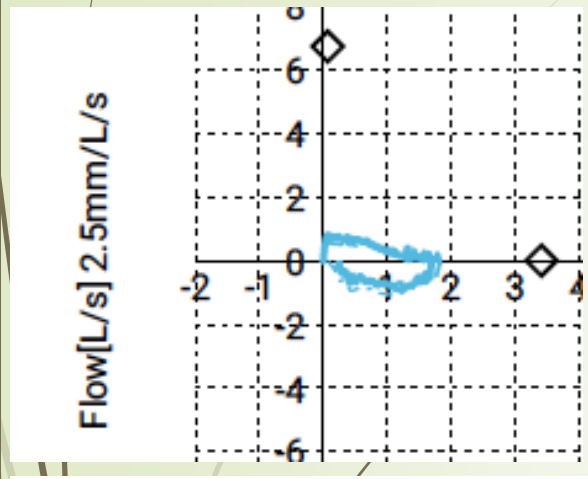
Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial4	Trial3	Trial2
FVC[L]	4.65	4.45	-1.27	87.0	5.35	4.65	4.65	4.55
FEV1[L]	LLN 2.80	3.66	-3.50	63.3	4.43	LLN 2.80	LLN 1.72	LLN 2.59
FEV1/FVC	LLN 0.60	0.74	-4.12		0.83	LLN 0.60	LLN 0.37	LLN 0.57
FEF2575[L/s]	LLN 2.53	2.97		54.1	4.68	LLN 2.53	LLN 1.13	LLN 2.24
PEF[L/s]	LLN 2.87	7.81		27.5	10.44	LLN 2.84	LLN 2.07	LLN 2.87
FET[s]	10.52					9.91	10.52	8.56
FIVC[L]	4.84	4.45		90.5	5.35	4.84	4.84	4.65
PIF[L/s]	2.88	–		–	–	2.88	2.59	4.76

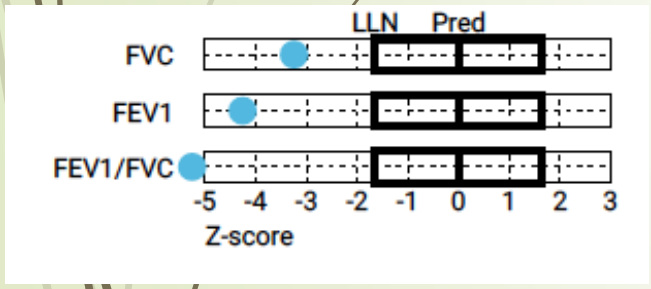
FEV1 Var = 211mL 7.5%, FVC Var = 2mL 0.0%
Test quality FEV1 - D, FVC - B
Moderate obstruction

Operator Notes: Acceptable effort

Clinical Notes:
12 months into ATT
Symptoms: no pulm; 2nd episode IRIS

75 M Vietnamese
H 165 cm 60 Kg



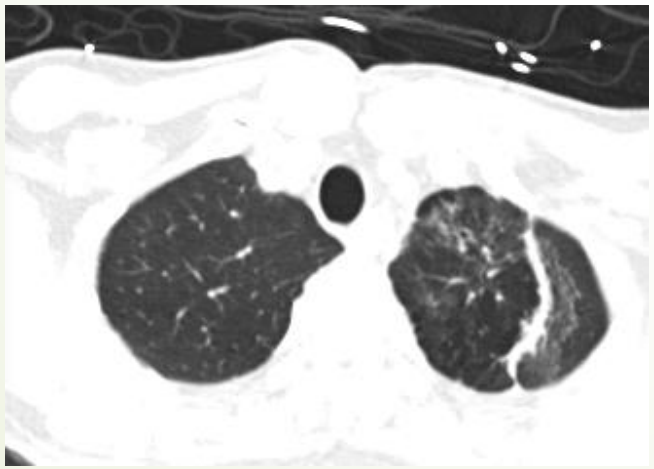


Test1 27.12.2023 03:10 PM

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial1	Trial3	Trial2
FVC[L]	▼1.84	2.61	-3.24	53.7	3.42	▼1.71	▼1.84	▼1.67
FEV1[L]	▼0.69	1.77	-4.26	28.3	2.45	▼0.69	▼0.54	▼0.61
FEV1/FVC	▼0.38	0.63	-5.90		0.73	▼0.41	▼0.30	▼0.37
FEF2575[L/s]	▼0.33	0.40		18.5	1.77	▼0.33	▼0.34	▼0.39
PEF[L/s]	▼0.81	4.74		12.0	6.73	▼0.81	▼0.68	▼0.63
FET[s]	8.82					8.63	8.82	8.30
FIVC[L]	▼1.58	2.61		46.1	3.42	▼1.45	▼1.55	▼1.58
PIF[L/s]	1.08	–		–	–	0.91	0.83	1.08

FEV1 Var = 83mL 12.0%, FVC Var = 129mL 7.1%
Test quality FEV1 - A, FVC - A
Very severe obstruction

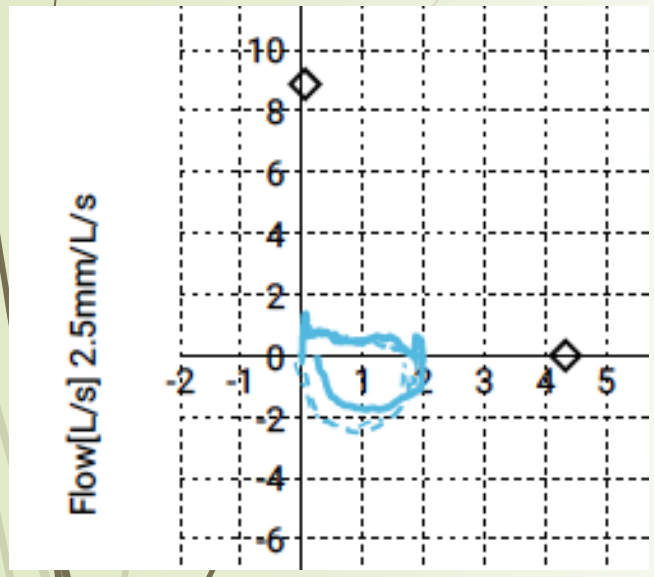
Operator Notes: Good effort



Nov 2023

Clinical Notes:
ATT started August 2023
Walking very slow. Denies cough.

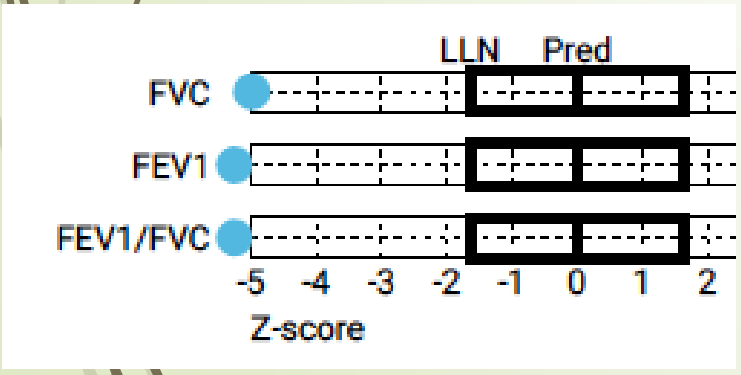
43 M Hispanic
1.64 m 51.7 kg



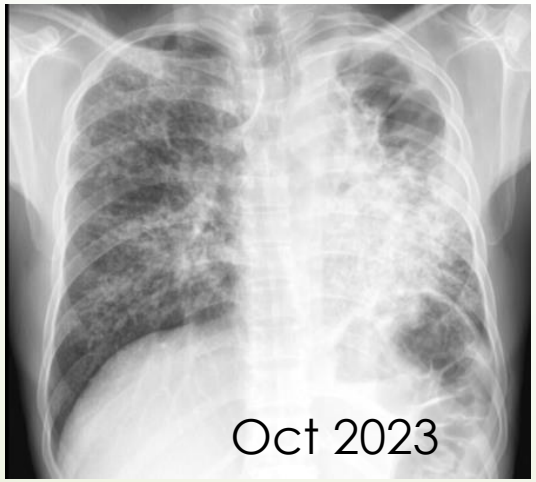
Test1 03.01.2024 04:24 PM

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial3	Trial2	Trial1
FVC[L]	LLN 1.99	3.56	-4.99	45.9	4.34	LLN 1.99	LLN 1.88	LLN 1.91
FEV1[L]	LLN 0.78	2.81	-6.74	22.5	3.46	LLN 0.67	LLN 0.78	LLN 0.70
FEV1/FVC	LLN 0.39	0.72	-7.54		0.81	LLN 0.34	LLN 0.41	LLN 0.37
FEF2575[L/s]	LLN 0.51	2.07		14.5	3.54	LLN 0.51	LLN 0.43	LLN 0.48
PEF[L/s]	LLN 1.42	6.61		16.0	8.88	LLN 1.35	LLN 1.42	LLN 1.05
FET[s]	7.90					7.13	7.90	8.35
FIVC[L]	LLN 2.02	3.56		46.5	4.34	LLN 1.74	LLN 1.91	LLN 2.02
PIF[L/s]	2.51	--		--	--	1.76	2.51	2.42

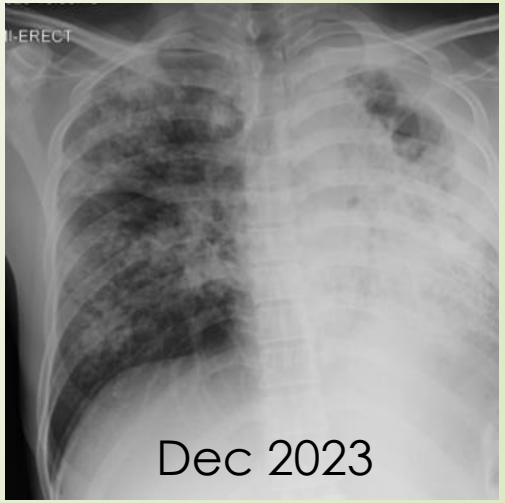
FEV1 Var = 106mL 13.6%, FVC Var = 111mL 5.6%
Test quality FEV1 - B, FVC - B
Very severe obstruction



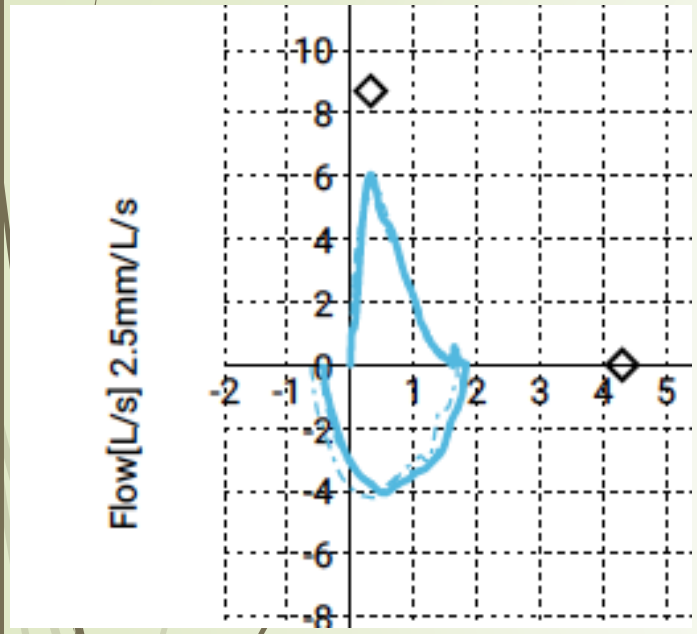
genotypic testing: +Asp435Tyr, +Gln429His RIF resistance; +Ser315Thr katG INH resistance; +met306Ile embB resistance, +Gly108Glu resistance; +A140G rrs AMB resistance; on BPaLM

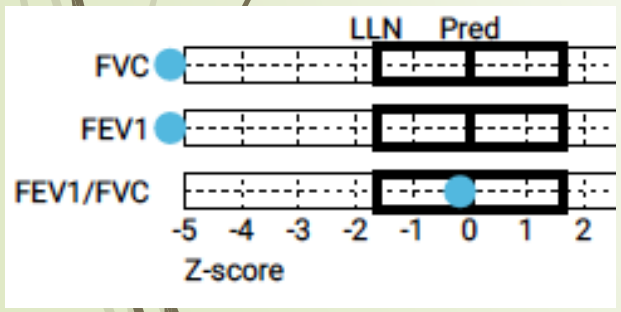

Oct 2023


Nov 2023


Dec 2023

33 M Hispanic
1.60 m 70.4 kg



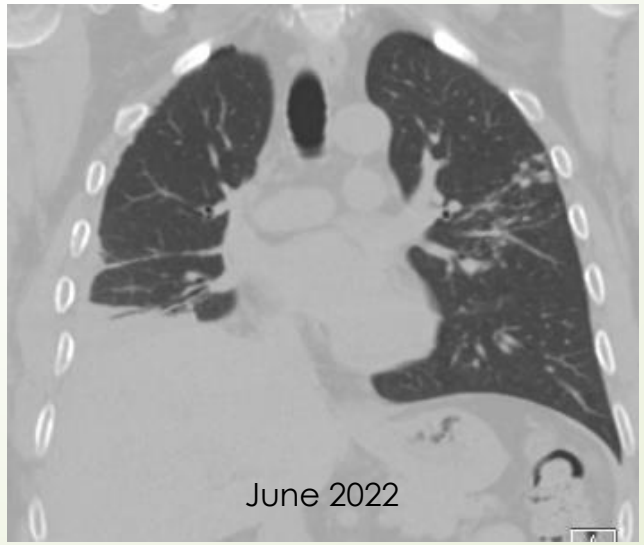


Test1 01.01.2007 01:16

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial5	Trial4	Trial3
FVC[L]	LLN 1.84	3.57	-5.52	42.6	4.31	LLN 1.84	LLN 1.78	LLN 1.69
FEV1[L]	LLN 1.50	2.91	-5.35	42.6	3.53	LLN 1.48	LLN 1.50	LLN 1.48
FEV1/FVC	0.82	0.74	-0.17		0.83	0.81	0.84	0.87
FEF2575[L/s]	LLN 1.58	2.40		41.5	3.80	LLN 1.58	LLN 1.92	LLN 2.12
PEF[L/s]	LLN 6.05	6.55		69.6	8.70	LLN 6.05	LLN 5.39	LLN 5.75
FET[s]	6.40					5.29	6.40	4.82
FIVC[L]	LLN 2.31	3.57		53.7	4.31	LLN 2.26	LLN 2.24	LLN 2.31
PIF[L/s]	4.22	–		–	–	4.07	3.88	4.22

FEV1 Var = 21mL 1.4%, FVC Var = 56mL 3.1%
Test quality FEV1 - U, FVC - U
Poor quality, no interpretation possible

Operator note: Good effort


June 2022


Feb 2024

18 M Hispanic
170 cm, 59.6 Kg
Study 2

Test1 25.10.2023 03:53 PM

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial1	Trial2	Trial3
FVC[L]	4.15	3.99	-1.33	86.0	4.82	4.05	4.10	4.15
FEV1[L]	▼2.56	3.46	-3.77	61.3	4.17	▼2.56	▼2.13	▼1.99
FEV1/FVC	▼0.62	0.77	-4.41		0.86	▼0.63	▼0.52	▼0.48
FEF2575[L/s]	▼1.70	3.14		35.9	4.72	▼1.70	▼1.46	▼1.23
PEF[L/s]	▼3.93	6.52		43.8	8.95	▼3.93	▼2.68	▼2.78
FET[s]	7.83					5.65	7.83	6.24
FIVC[L]	4.14	3.99		85.8	4.82	4.06	4.06	4.14
PIF[L/s]	4.78	–		–	–	4.13	4.78	3.71

FEV1 Var = 431mL 16.9%, FVC Var = 48mL 1.1%
Test quality FEV1 - E, FVC - A
Moderate obstruction

Test1 27.12.2023 04:25 PM

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial1	Trial5	Trial4
FVC[L]	4.47	3.99	-0.70	92.6	4.82	4.47	4.12	4.29
FEV1[L]	3.79	3.46	-0.90	90.8	4.17	3.79	▼3.31	▼2.96
FEV1/FVC	0.85	0.77	-0.24		0.86	0.85	0.80	▼0.69
FEF2575[L/s]	3.93	3.14		83.2	4.72	3.93	3.24	▼2.78
PEF[L/s]	▼4.50	6.52		50.2	8.95	▼4.50	▼3.68	▼3.38
FET[s]	4.37					3.57	2.45	4.37
FIVC[L]	4.20	3.99		87.1	4.82	▼3.61	4.19	4.20
PIF[L/s]	4.86	–		–	–	4.47	4.60	4.86

FEV1 Var = 479mL 12.6%, FVC Var = 178mL 4.0%
Test quality FEV1 - E, FVC - C
Normal spirometry

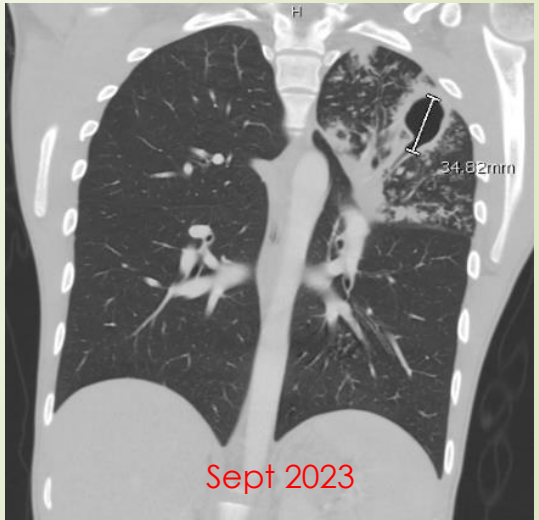
Pre 06.03.2024 02:59 PM

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial2	Trial3	Trial1
FVC[L]	4.43	3.99	-0.77	91.9	4.82	4.43	4.27	4.37
FEV1[L]	3.94	3.46	-0.52	94.6	4.17	3.94	3.94	3.67
FEV1/FVC	0.89	0.77	0.54		0.86	0.89	0.92	0.84
FEF2575[L/s]	4.26	3.14		90.4	4.72	4.26	4.41	3.77
PEF[L/s]	▼5.58	6.52		62.4	8.95	▼5.35	▼5.58	▼4.22
FET[s]	7.71					4.15	4.46	7.71
FIVC[L]	4.54	3.99		94.1	4.82	4.41	4.19	4.54
PIF[L/s]	6.32	–		–	–	6.26	6.32	4.03

FEV1 Var = 0mL 0.0%, FVC Var = 64mL 1.5%
Test quality FEV1 - A, FVC - A
Normal spirometry

Clinical Notes:
Started ATT Sept 2023
Cough less but still present

Clinical Notes:
Started ATT Sept 2023
Cough resolved
DOE 5 min walking (better)
Architecture student complaining of "brain slowness" during studying



Sept 2023

Tall Order for the TB Community

- After TB cure or completion of treatment, have our patients recovered their health?
- If not, what can we do to help them maximize the benefits after being rid of TB
- Can we do more to remove the stigma of TB?