

# TB ASSOCIATED MORBIDITY IN CHILDREN AND ADOLESCENTS - FEEDBACK FROM THE 2<sup>ND</sup> INTERNATIONAL POST TB SYMPOSIUM

*WHO child and adolescent TB working group meeting*

*Tuesday 14-11-2023 Paris*

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Paediatrician and associate professor

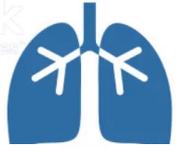
Desmond Tutu TB centre,

Stellenbosch University, South Africa



# TB associated morbidity in children and adolescents

- Brief overview literature & feedback from 2<sup>nd</sup> post TB symposium



- Post TB lung disease



- Post TBM disease



- Socio-economic and HRQoL



**Child  
& Adolescent  
TB Working Group**

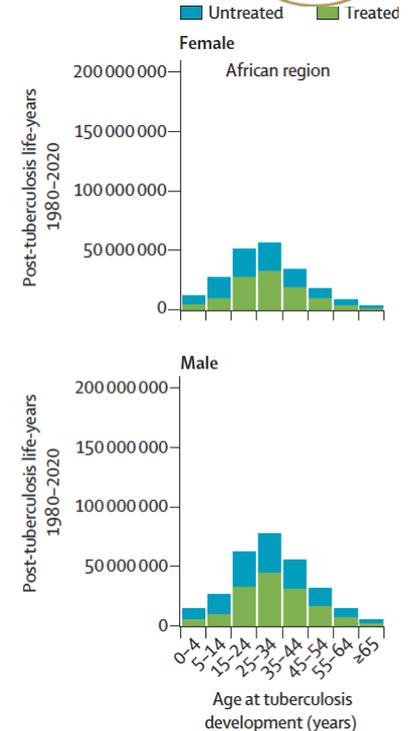


# The numbers

# Quantifying the global number of tuberculosis survivors: a modelling study

Peter J Dodd, Courtney M Yuen, Shamanthi M Jayasooriya, Marieke M van der Zalm, James A Seddon

- 155 million TB survivors (1980- 2019) were alive in 2020
  - ~ 6-18 million were <15 years
  - ~ 15.5 million were adolescents
- A total of 3480 million life-years were lived “after TB”
  - Children <15 years contribute 12% to these life-years

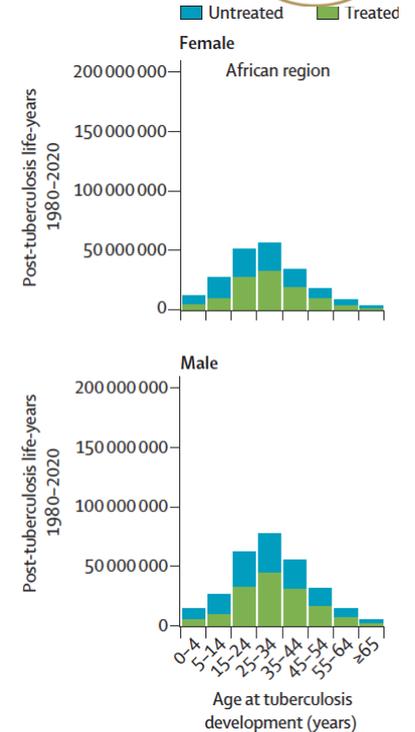


# Quantifying the global number of tuberculosis survivors: a modelling study

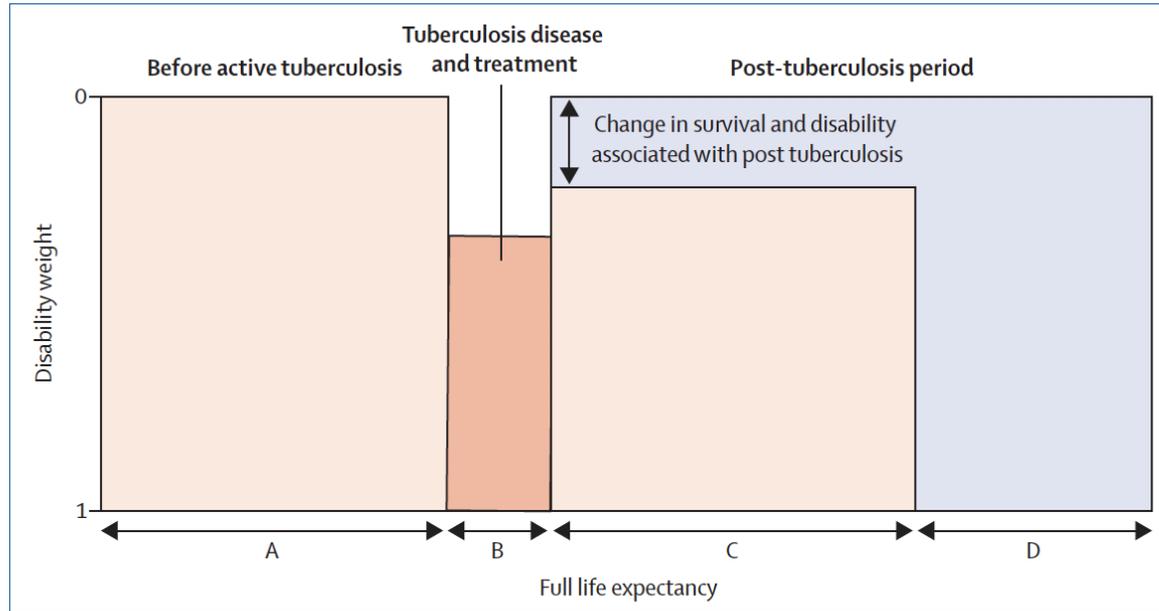
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→ These children and adolescents are potentially at risk for TB-associated morbidity



# TB associated morbidity- the concept



**Figure:** Illustration of post-tuberculosis DALY loss for a typical survivor of pulmonary tuberculosis treatment in India without HIV infection

# TB associated morbidity- the concept

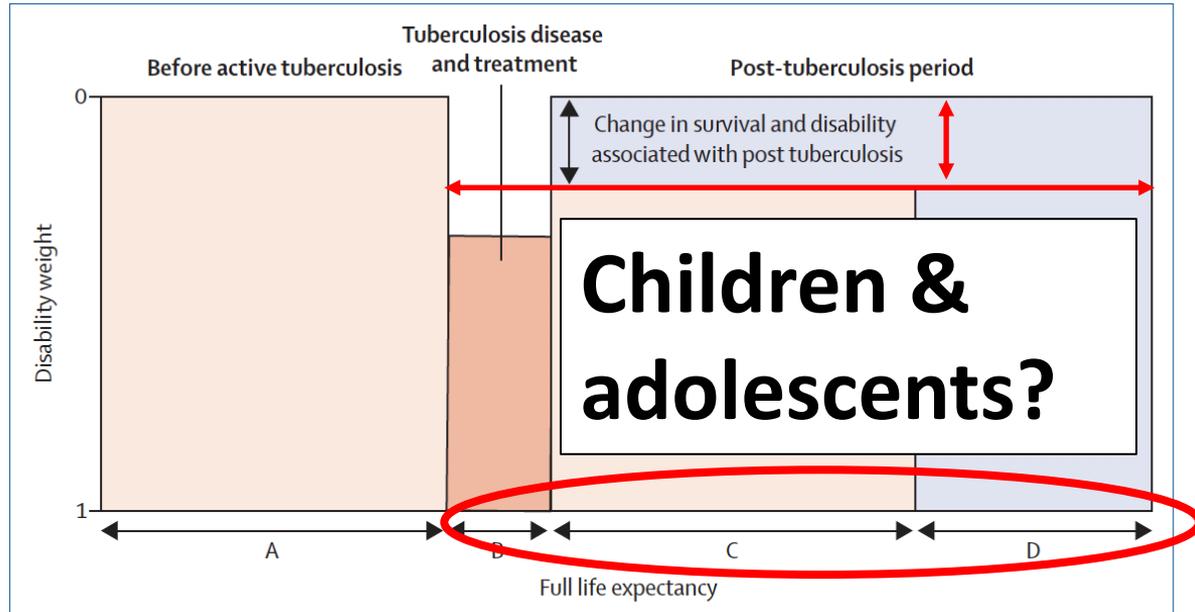
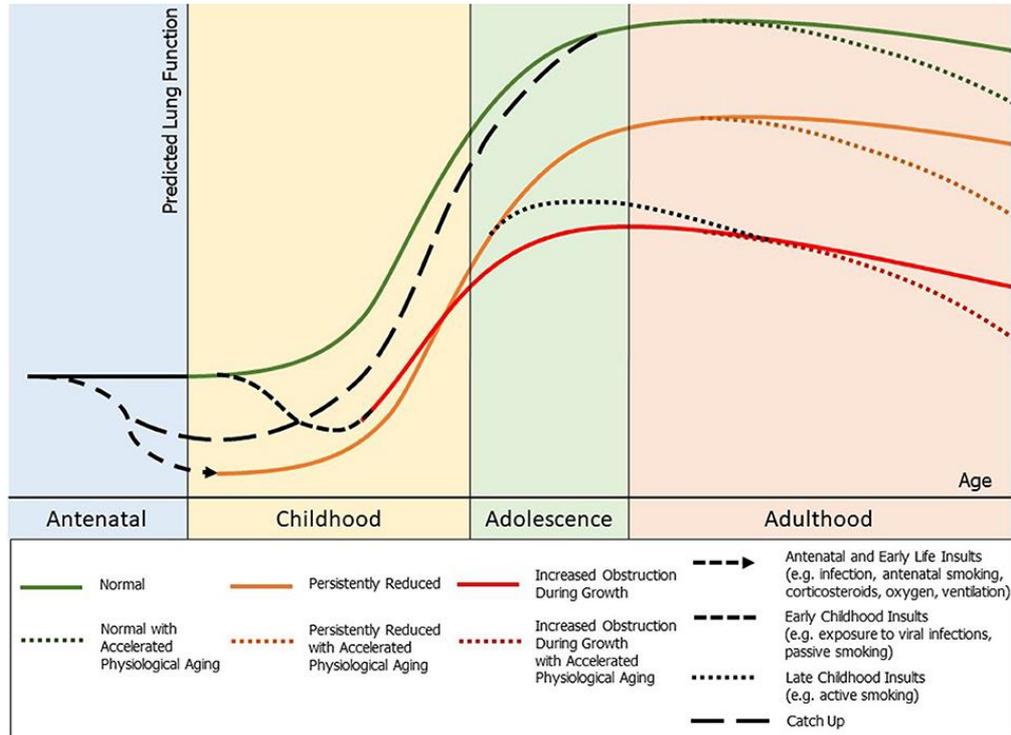


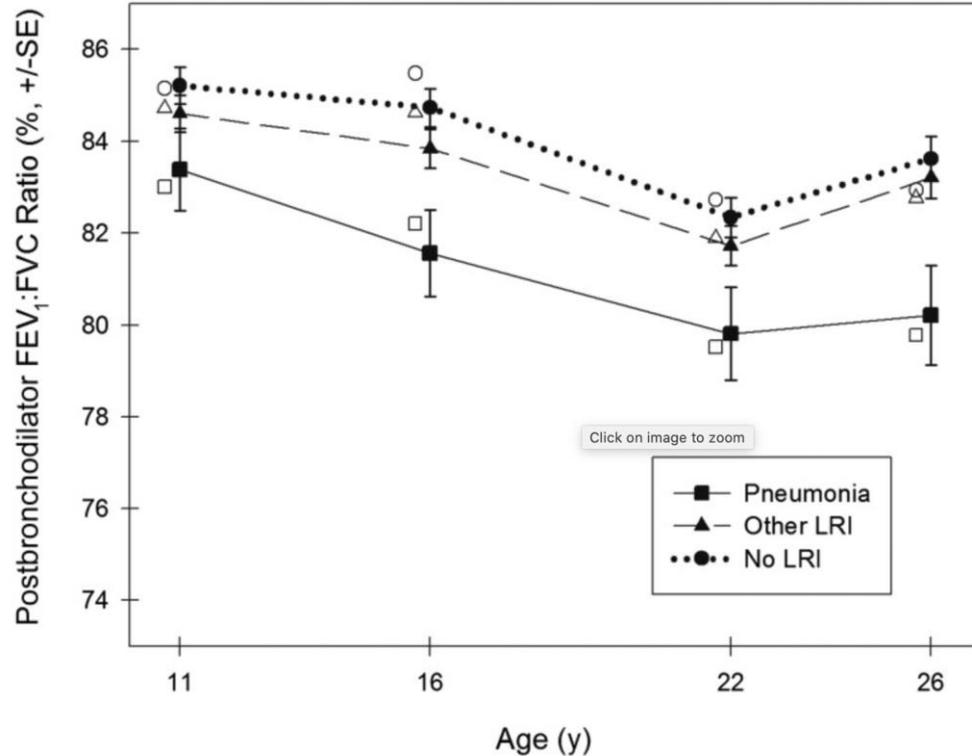
Figure: Illustration of post-tuberculosis DALY loss for a typical survivor of pulmonary tuberculosis treatment in India without HIV infection

# PRINCIPLES OF LUNG FUNCTION TRACKING



- Early life insults can affect trajectory of lung function
- Timing and severity of insult might impact on trajectory
- Catch up growth vs accelerated decline

# The impact of LRTIs on lung function



**Impact LRTI on tracking  
What happens after PTB?**

# Post TB lung disease in children and adolescents

Magnitude and factors associated with post-tuberculosis lung disease in low- and middle-income countries: A systematic review and meta-analysis

Elizabeth Maleche-Obimbo<sup>1\*</sup>, Mercy Atieno Odhiambo<sup>2</sup>, Lynette Njeri<sup>3</sup>, Moses Mburu<sup>4</sup>, Walter Jaoko<sup>5</sup>, Fredrick Were<sup>1</sup>, Stephen M. Graham<sup>6</sup>

- N=1 with radiological outcomes in children
- N= 8 studies with adolescents included, but no disaggregated data

REVIEW | VOLUME 23, ISSUE 4, E138-E150, APRIL 2023

Post-tuberculosis sequelae in children and adolescents: a systematic review

Vanessa Igbokwe • Lisa C Ruby • Ayten Sultanli, MSc • Prof Sabine Bélard, PhD  

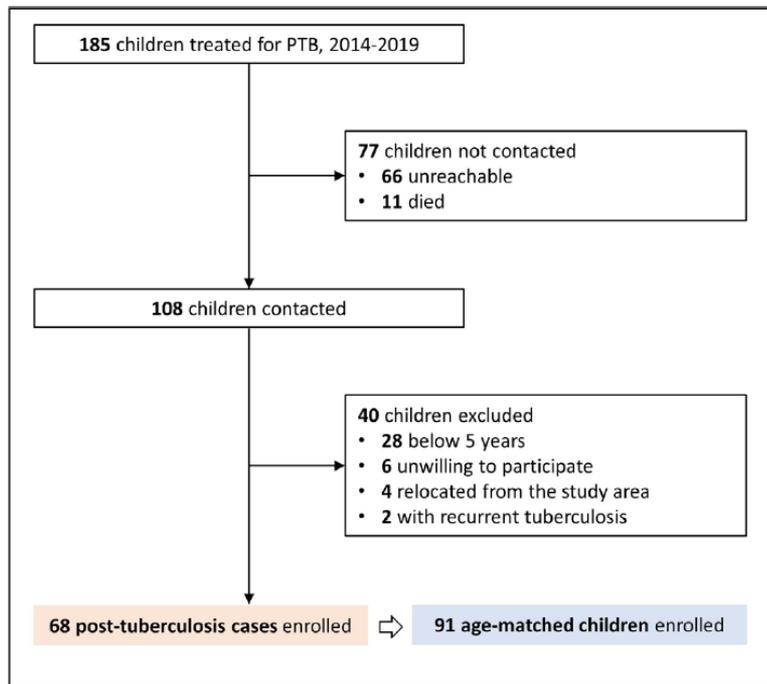
Published: April, 2023 • DOI: [https://doi.org/10.1016/S1473-3099\(23\)00004-X](https://doi.org/10.1016/S1473-3099(23)00004-X) •



- N=6 with symptoms & radiological outcomes
- 7-49% abnormal radiology

# Reduced lung function and health-related quality of life after treatment for pulmonary tuberculosis in Gambian children: a cross-sectional comparative study

 Esin Nkereuwem<sup>1, 2</sup>, Schadrac Agbla<sup>3, 4</sup>, Azeezat Sallahdeen<sup>1</sup>, Olumuyiwa Owolabi<sup>1</sup>, Abdou K Sillah<sup>1</sup>, Monica Genekah<sup>1</sup>, Abdoulie Tunkara<sup>1</sup>, Sheriff Kandeh<sup>1</sup>, Maryama Jawara<sup>1</sup>, Lamin Saidy<sup>5</sup>,  Andrew Bush<sup>6, 7</sup>,  Toyin Togun<sup>1, 2, 8</sup>,  Beate Kampmann<sup>1, 2, 9</sup>

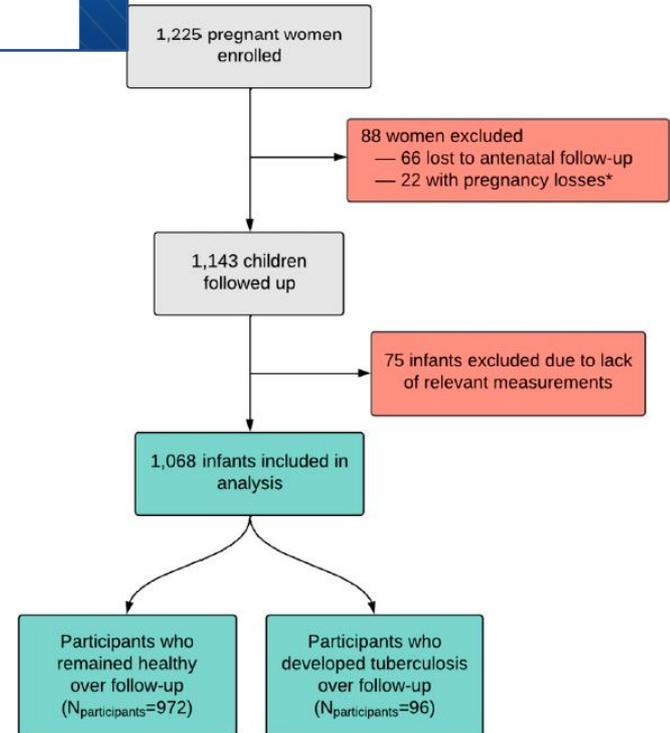


	Post-tuberculosis cases	Comparison group	P value
<b>Spirometry</b>	<b>n=52</b>	<b>n=86</b>	
FEV <sub>1</sub> z-score, mean (SD)	-1.52 (-0.99)	-0.83 (-0.84)	<0.001‡
FVC z-score, mean (SD)	-1.32 (1.02)	-0.87 (0.89)	0.014‡
FEV <sub>1</sub> /FVC ratio z-score, mean (SD)	-0.54 (0.91)	-0.03 (0.81)	0.001‡
Abnormal spirometry, n (%)	20 (38.5)	15 (17.4)	0.009†
<b>Pattern of spirometry</b>			
Normal, n (%)	32 (61.5)	71 (82.6)	0.029§
Obstructive, n (%)	1 (1.9)	2 (2.3)	
Restrictive, n (%)	19 (36.4)	13 (15.1)	

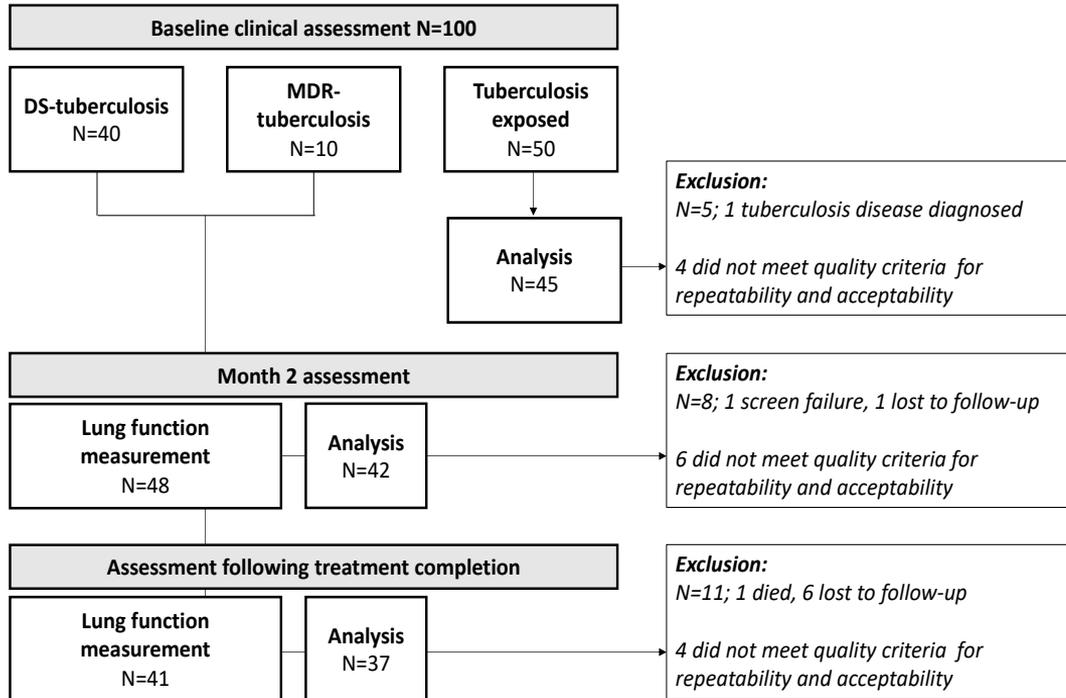
## The Long-Term Impact of Early-Life Tuberculosis Disease on Child Health: A Prospective Birth Cohort Study

Leonardo Martinez ; Diane M Gray , Maresa Botha , Michael Nel , Shaakira Chaya , Carvern Jacobs , Lesley Workman ; Mark Nicol , and Heather J Zar ;

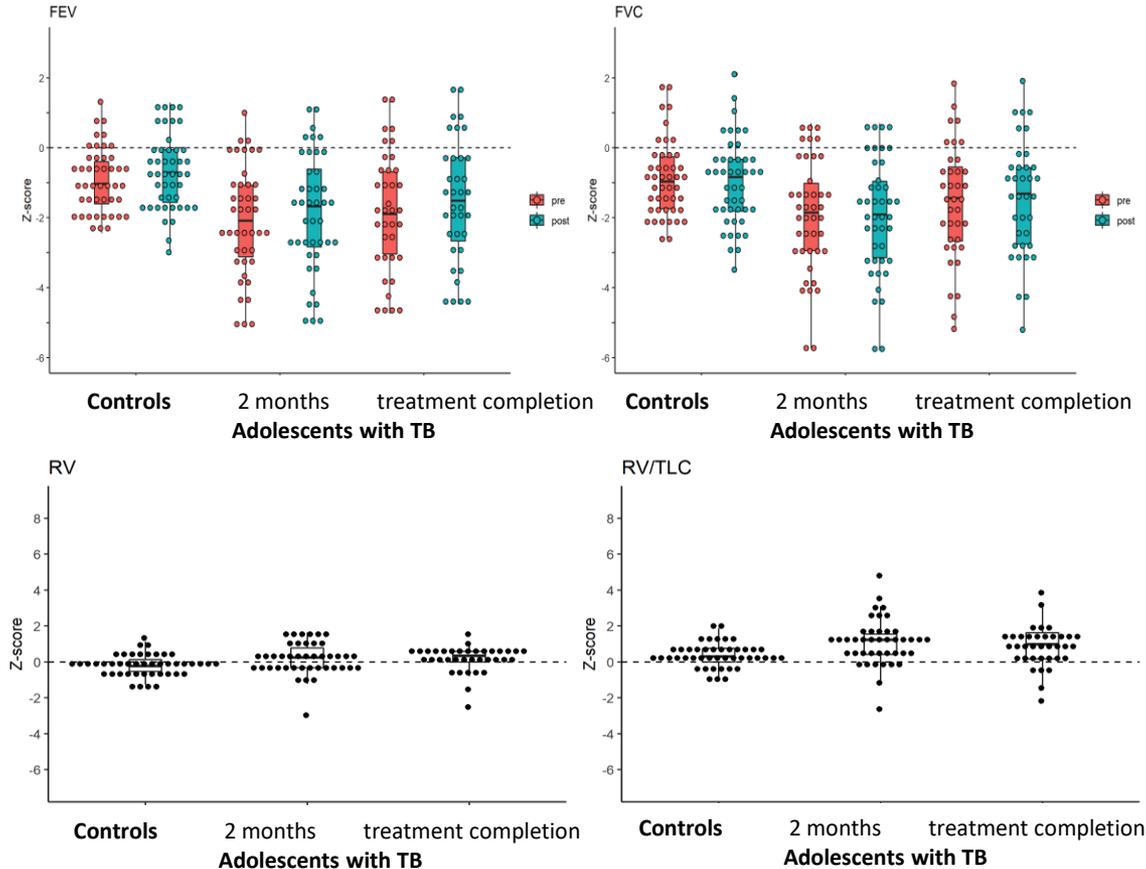
- Children with PTB (0-5y)→
  - ↓Anthropometry at age of 5 years
  - Greater risk of subsequent wheezing
  - Lower lung function at age of 5 years
- Premorbid lung function was not associated with PTB



# Teen TB study, Cape Town South Africa



# Teen TB study, Cape Town South Africa



- Adolescents with TB had
  - Restrictive disease was most common
  - Lower spirometry and plethysmography indices even after treatment completion
- Overall lung health was poor in both groups

# PTLD: More data is needed

The data says  
we need  
more data.

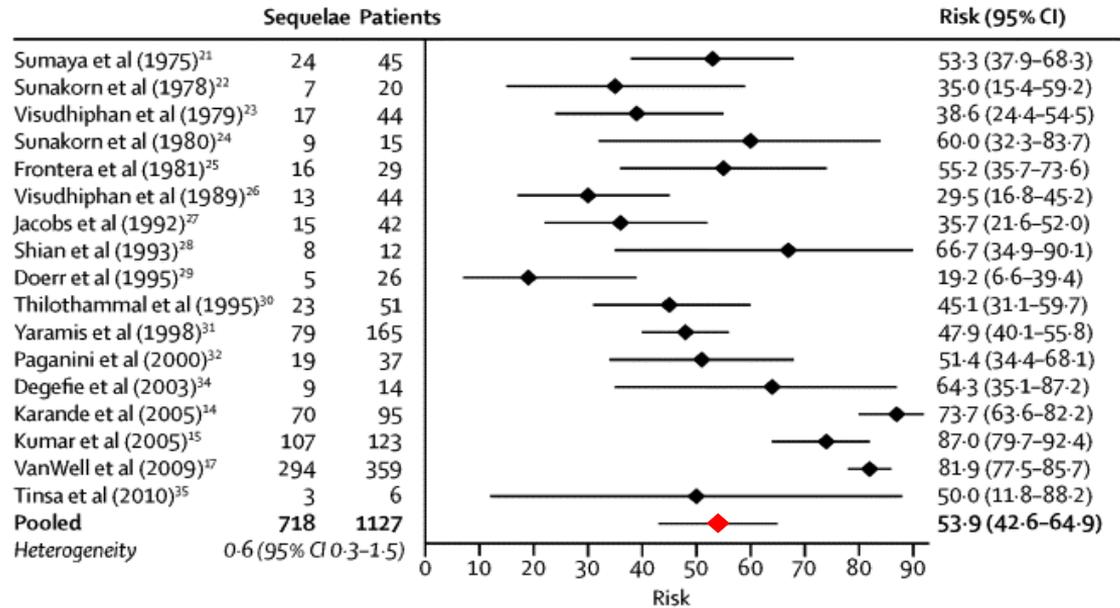


# TB meningitis in children and adolescents

- Most severe form of extrapulmonary TB, especially among young children
- Deadliest, most debilitating form of TB
  - Deaths: 19.3% (14.0 – 26.1)
  - Neurological sequelae among survivors: 53.9% (42.6 – 64.9)
  - Probability of survival without sequelae: 36.7% (27.9 – 46.4)
- TBM modelling study by Du Preez/ Dodd/ Seddon. in progress → **Presentation @ Union tomorrow**
  - Estimated burden: ~24,000 children each year
  - Estimated mortality: ~16,100 children each year
  - Estimated morbidity: 70% of all TBM survivors each year



# Substantial between-study heterogeneity in assessment of neurological sequelae measures



# Evaluation and Management of TBM Sequelae

- Lack of uniform approach to evaluate sequelae
  - Functional
  - Neurodevelopmental
  - Neurocognitive
  - Neurobehavioural
- Paucity of appropriate rehabilitation and other therapies
- No standard measure of impact on quality of life or socio-economic burden



# Economic and psycho-social consequences following TB

- For children – mostly spinal TB and TBM are described
- Rapid review of post-TB literature to gain an understanding of the available evidence on the economic, psychological, and social impacts of TB (Nightingale et al, 2023)
  - **lack of studies on children and adolescents**
- Scoping review on the long-term socio-economic effect of TB among children and adolescents (Atkins et al, 2022)
  - **lack of studies on children and adolescents**
- Scoping review of interventions to address TB-associated respiratory disability
  - **lack of studies on children and adolescents**

# Scoping review to identify HRQoL measures

No disease-specific measure for children and adolescents affected by TB available

The PedsQL™  
Measurement Model for the  
Pediatric Quality of Life Inventory<sup>1</sup>



TANDI  
(Toddler and Infant Questionnaire)

WHOQOL-BREF  
INTRODUCTION, ADMINISTRATION, SCORING  
AND GENERIC VERSION OF THE ASSESSMENT

- No disease specific measure available
- Lacks a holistic understanding of HRQoL
  - Impact on family
  - Impact on development of child
- Most measures developed in high-income countries
  - Lack of socio-economic context



# Consensus research definition

## Definition 2019 Post TB symposium PTLT paediatrics:

“Evidence of chronic respiratory **impairment** in an individual previously ~~adequately~~ treated for pulmonary tuberculosis in whom active tuberculosis is excluded, and in whom no other cause of chronic lung disease is the predominant cause.”

With the consideration of toolbox to add layers to further define

## New post TBM?

“Evidence of chronic neurological, **cognitive, behavioural and developmental** impairment in an individual previously ~~adequately~~ treated for tuberculosis meningitis in whom active tuberculosis is excluded, and in whom no other cause of ~~neurological~~ impairment is the predominant cause.”

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# Toolbox development and standardization



**Self-reported symptoms**



**Clinical measures**



**Functional testing**

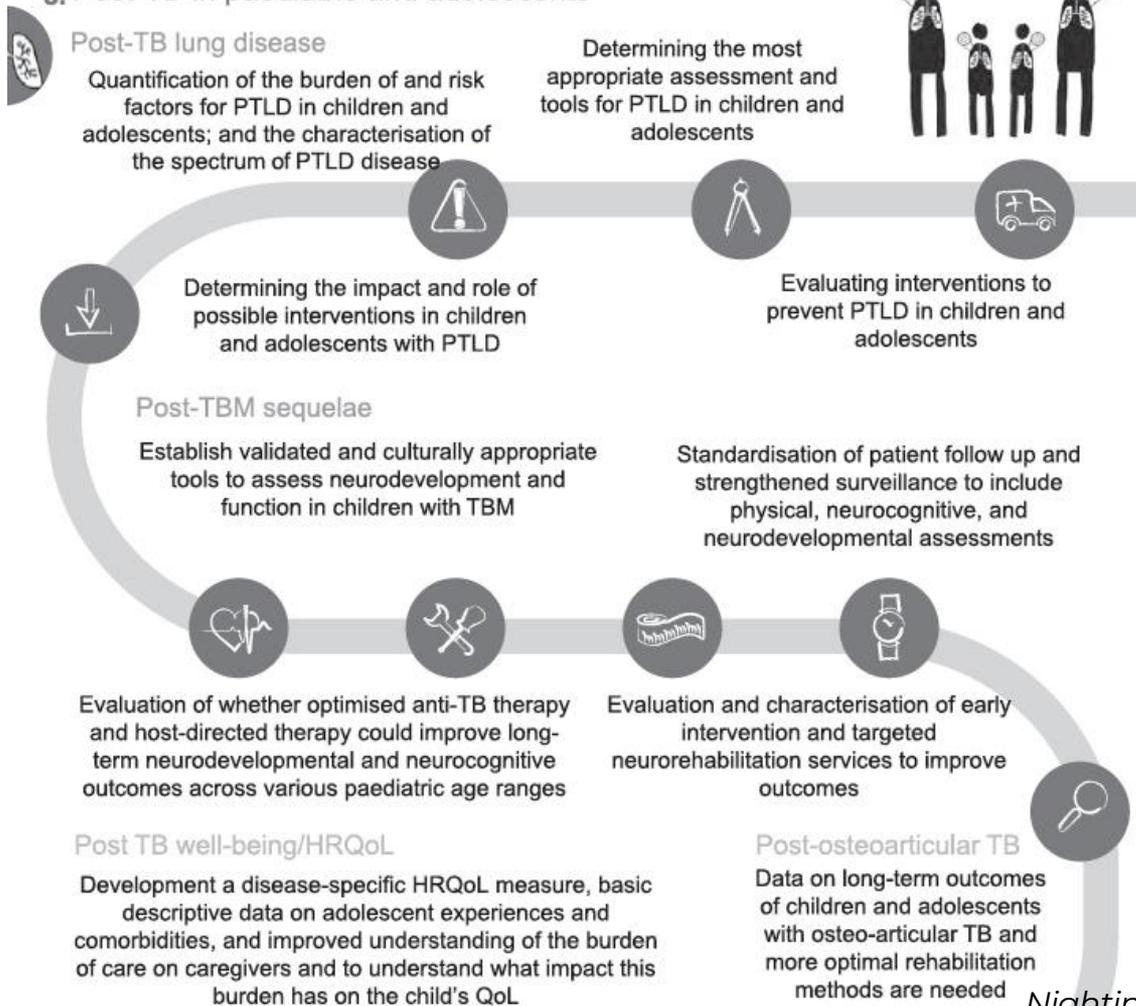


**Imaging**



**Other tests incl HRQoL**

## 5. Post-TB in paediatric and adolescents

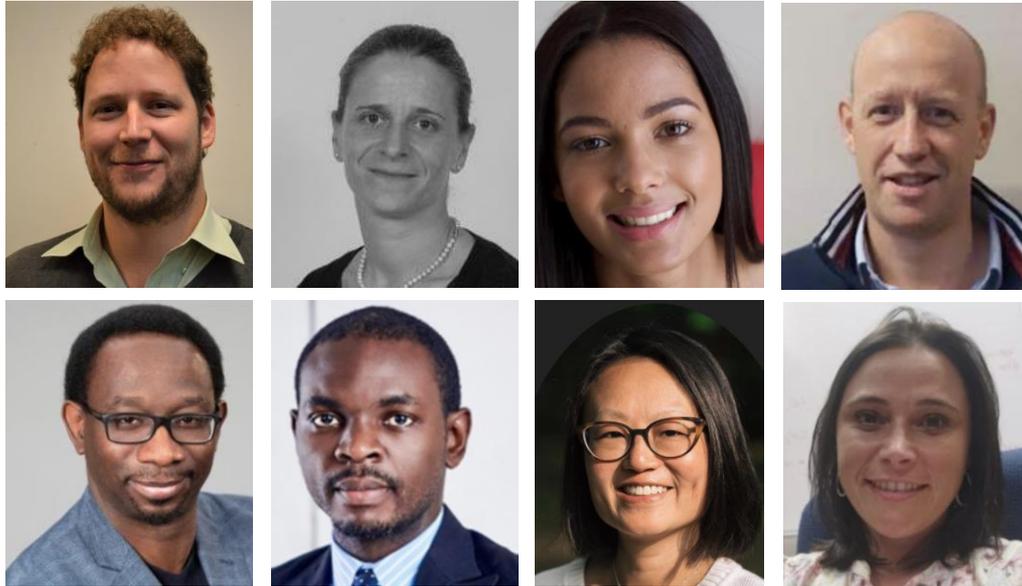




## “Post tuberculosis”: the urgent need for inclusion of lung health outcomes in tuberculosis treatment trials

- Prevention is key!
- TB-associated morbidity measures need to be included in treatment studies
- Consensus on standardization of measurements/ tools and outcomes is needed

# Acknowledgments



Workshop participants and academic working group

This project is part of the EDCTP2 programme supported by the European Union



EDCTP

