Thursday 26th September 2024

IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network | ANNUAL MEETING 2024

# Host blood transcriptomic signatures for paediatric tuberculosis treatment monitoring

Vanessa Mwebaza Muwanga
PhD candidate - Clinical Sciences & Immunology
South African Tuberculosis Vaccine Initiative (SATVI)
University of Cape Town (UCT)

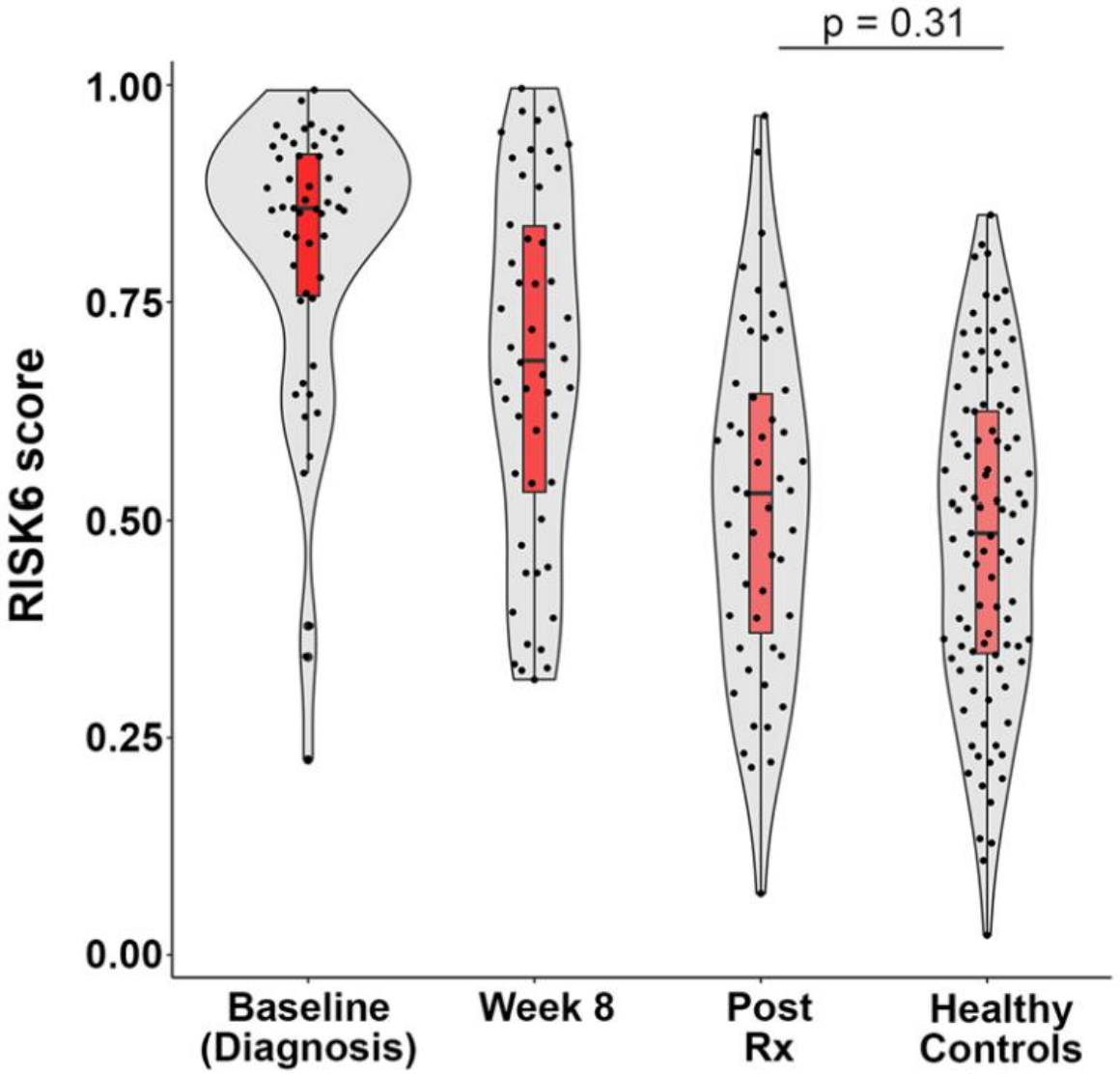
Supervisors: Prof. Thomas. J. Scriba and Dr. Simon. C. Mendelsohn
Collaborators: Prof. James Seddon, Dr. Myrsini Kaforou, Dr. Claire Dunican



20 YEARS OF TB RESEARCH | satvi TOWARDS A WORLD WITHOUT TB

# Non-sputum tests for TB treatment monitoring in children are needed

1. Children typically present with paucibacillary tuberculosis (TB) disease that often tests negative on sputum-based diagnostics.
2. Young children cannot expectorate sputum, leading to missed diagnosis
3. Studies in adults have shown that host-response blood transcriptomic signatures can track responses to anti-TB treatment (Cliff et al; *JID* 2013, Thompson et al; *Tuberculosis* 2017)




Penn-Nicholson; Scientific Reports (2020) 10:8629

# Non-sputum tests for TB treatment monitoring in children are needed

p = 0.31

1. Chi
   pau
   dise
   spu
2. You
   spu
   diag
3. Stu
   hos
   trar
   resp
   (Cli
   al; 

## Research question:

Are host blood transcriptomic signatures of TB risk able to track paediatric TB treatment responses?

Penn-Nicholson; Scientific Reports (2020) 10:8629

(Diagnosis) Rx Controls

# Study design

Chabala et al; *Trials* 2018,
Turkova et al; *NEJM*, 2022

Out of 315 study participants from South Africa, **198** children had whole blood samples at all 4 time points of interest

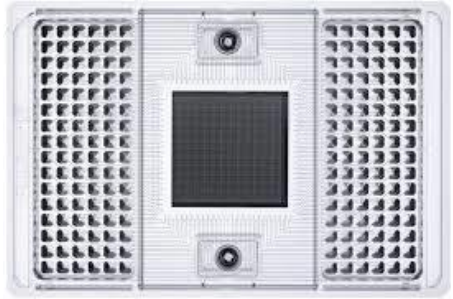
4 month-arm (n=91)

0 2 8 16 weeks

6 month-arm (n=107)

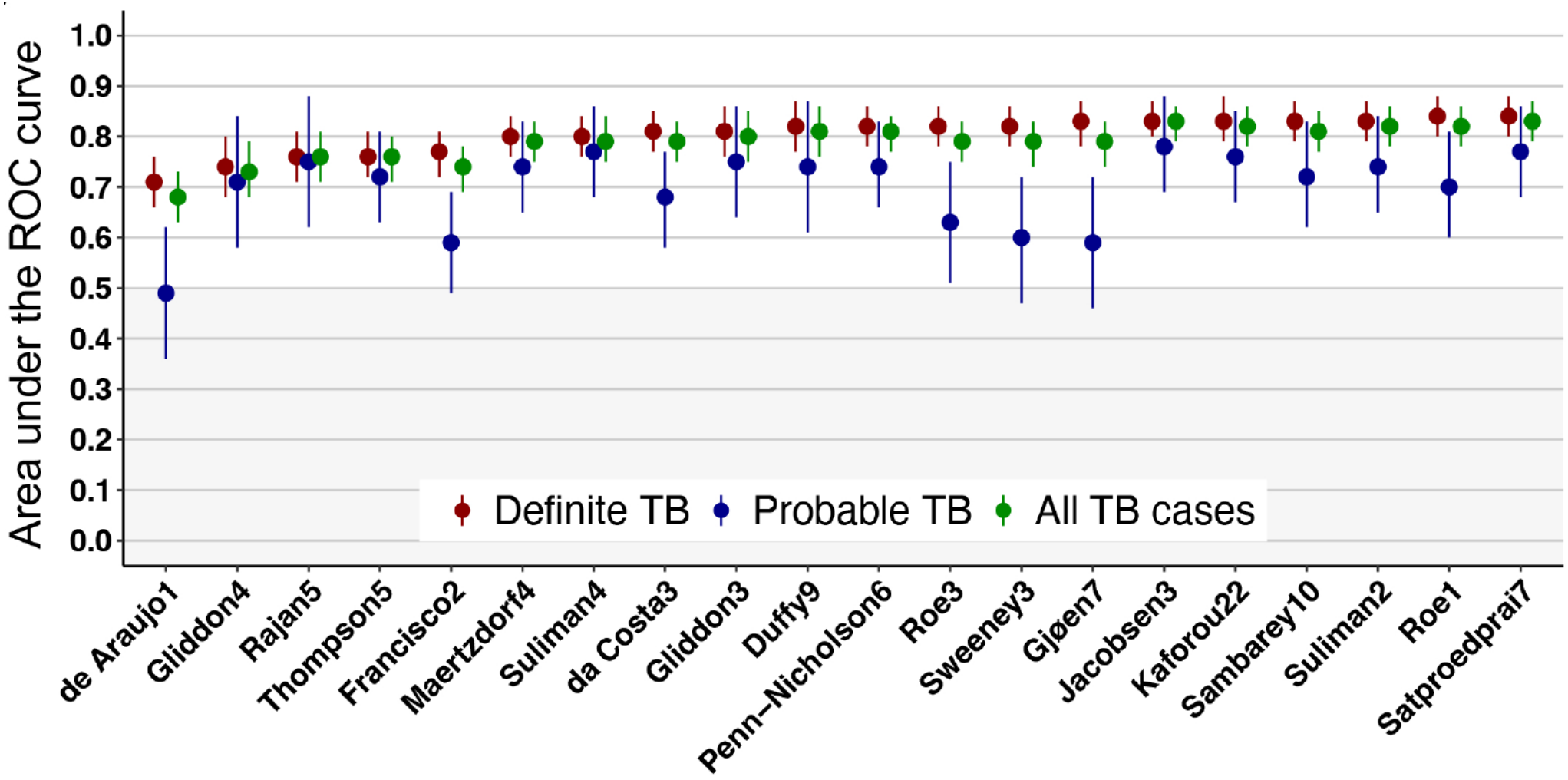
0 2 8 24 weeks

**20 host whole blood transcriptomic signatures of TB**



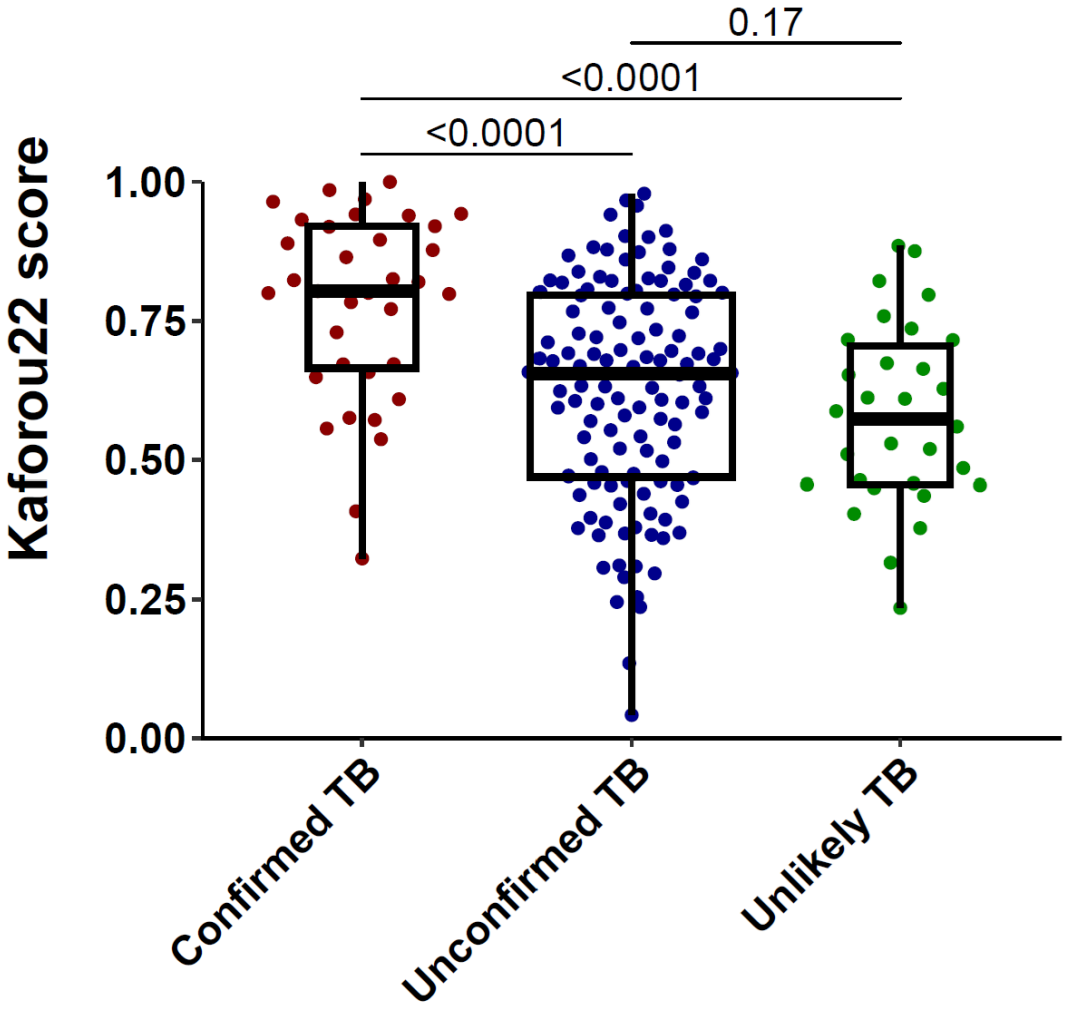
| | **Confirmed TB**, N = 37 | **Unconfirmed TB**, N = 129 | **Unlikely TB**, N = 32 |
|---|---|---|---|
| **Treatment arm**, n (%) | | | |
| 4-month arm | 14 (37.8) | 59 (45.7) | 18 (56.3) |
| 6-month arm | 23 (62.2) | 70 (54.3) | 14 (43.8) |

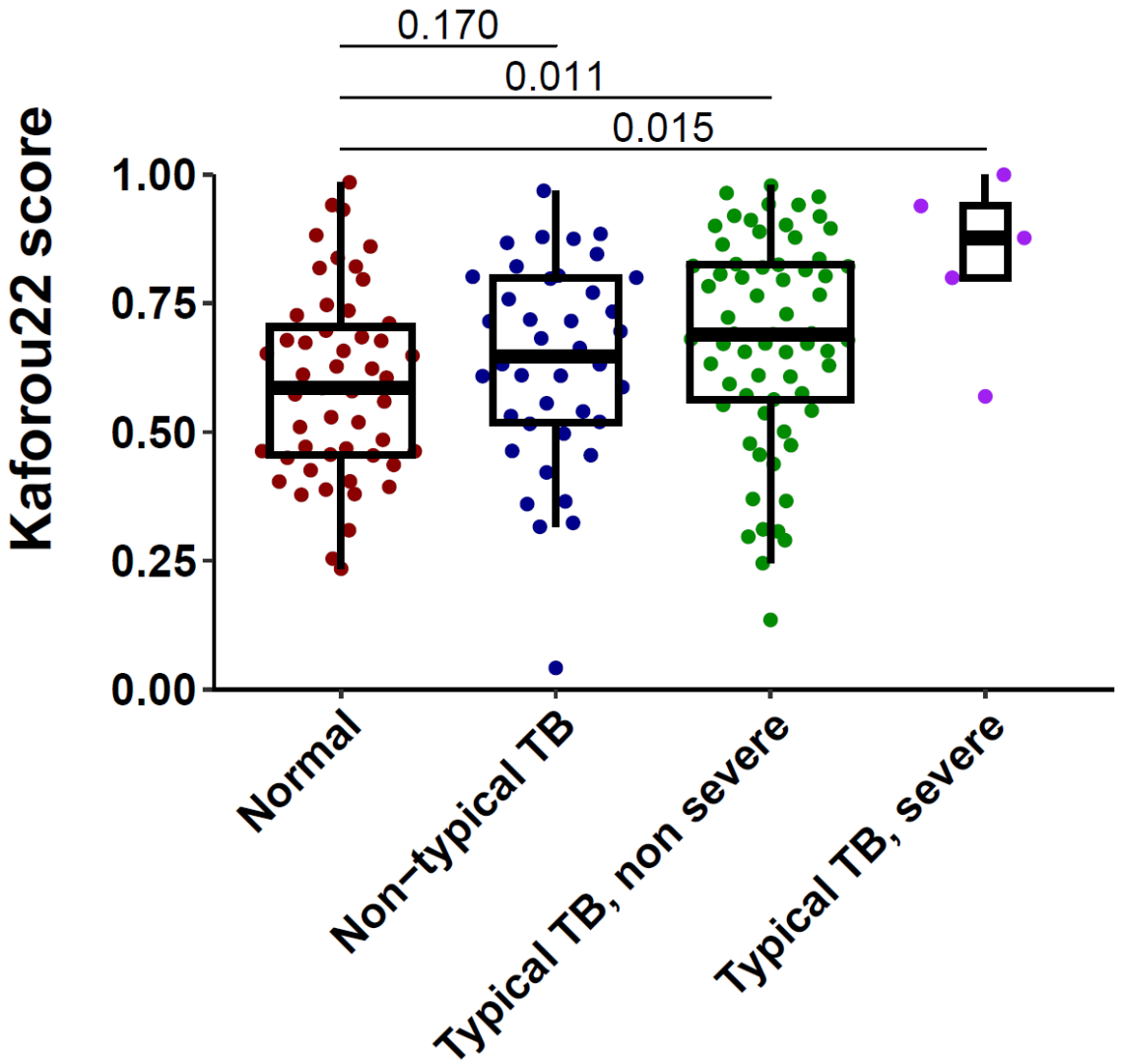
# Signature scores differentiated definite and probable TB from other respiratory diseases in adults



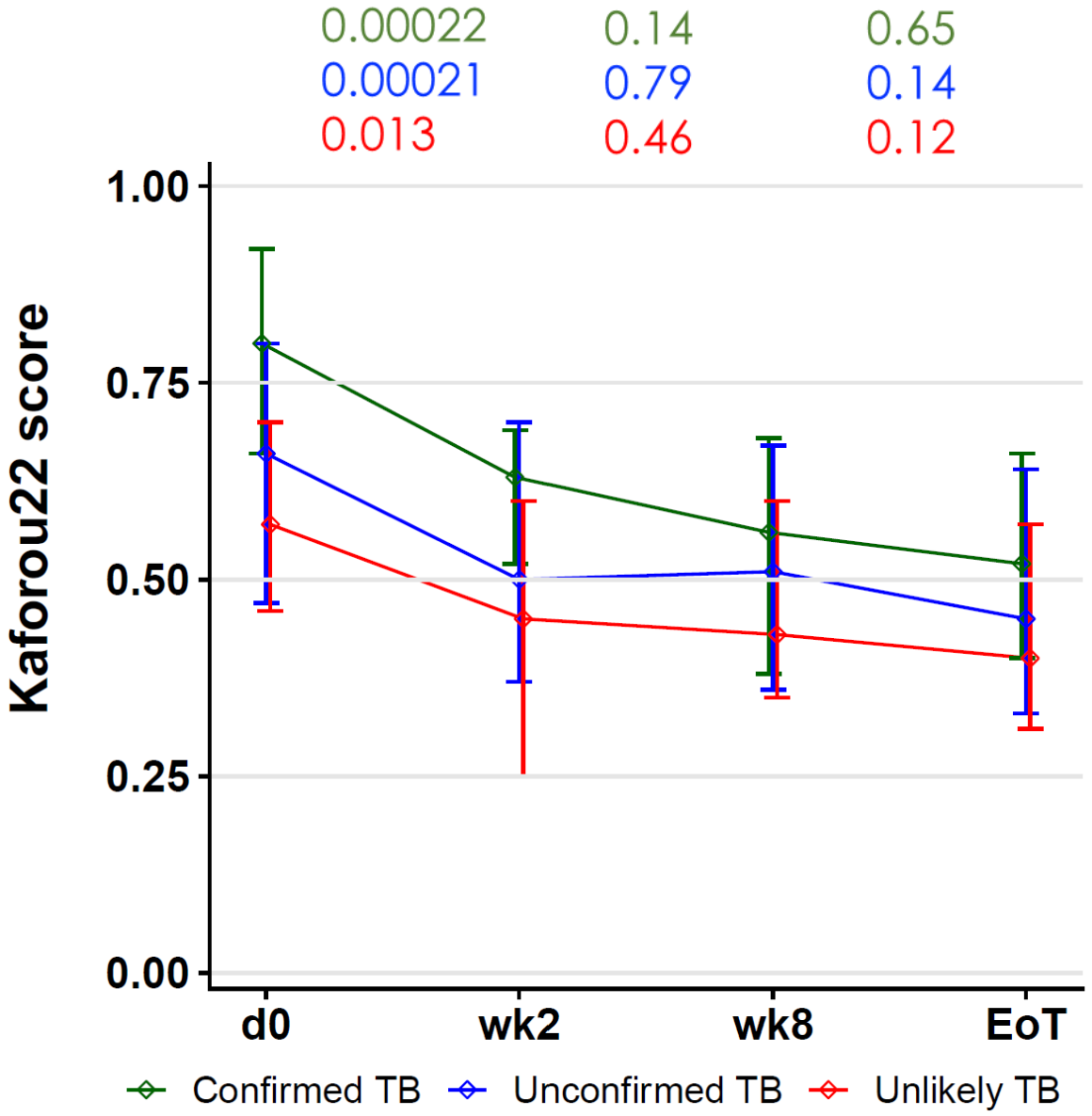

Muwanga et al, *ERJ* 2024

# At baseline, scores were higher in confirmed TB cases and children with more radiologically severe TB disease

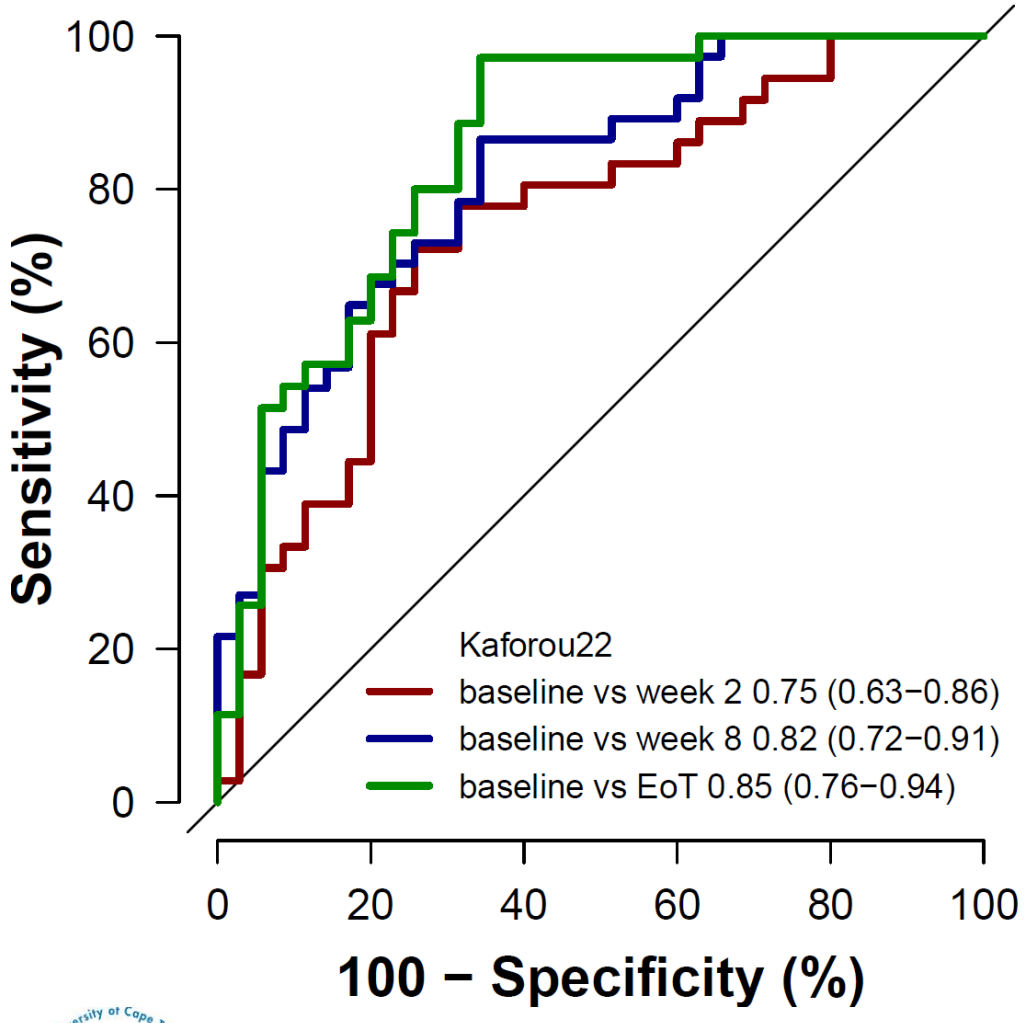


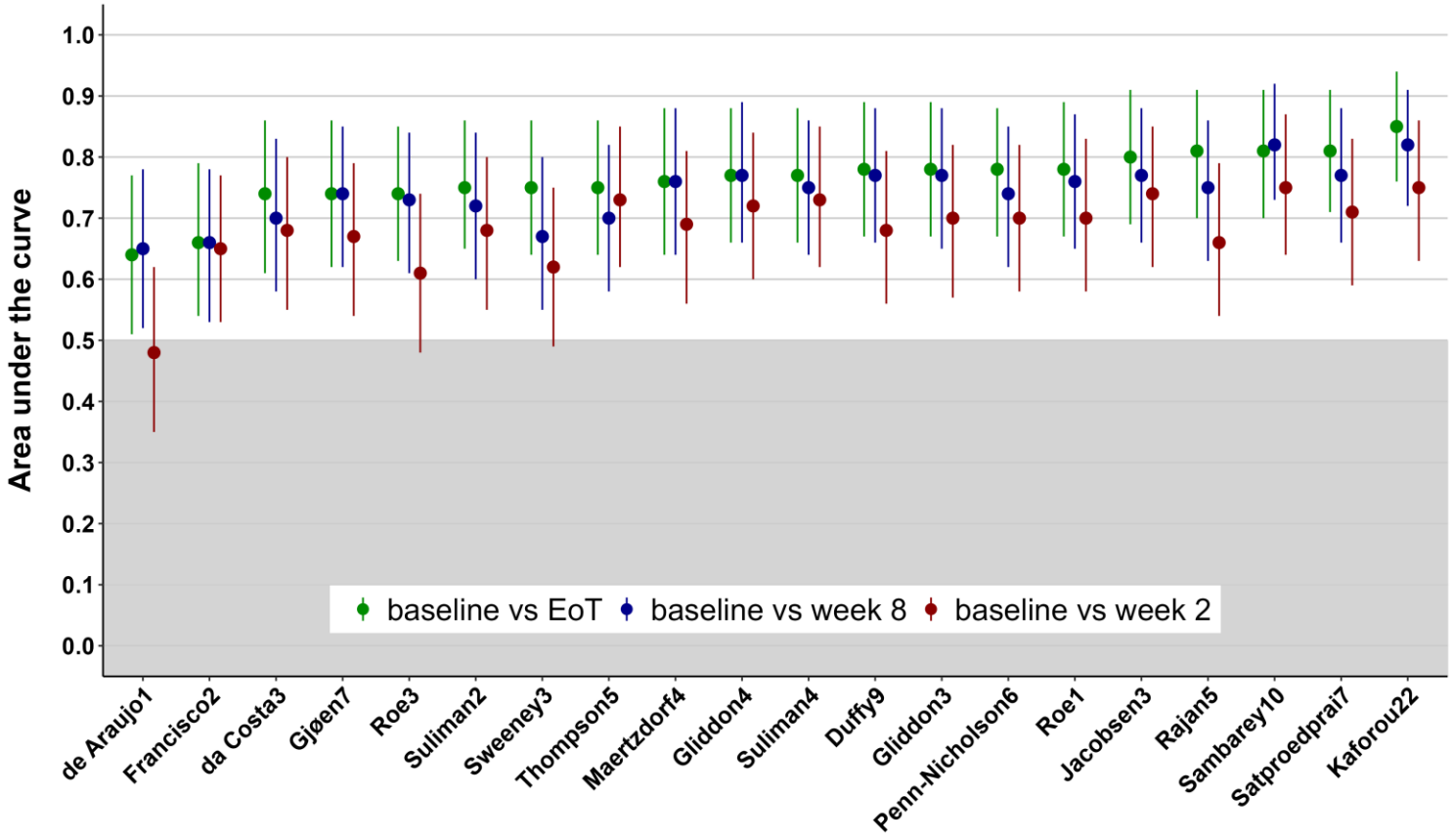



# Signature scores decrease in the first two weeks of treatment; no significant changes between subsequent timepoints thereafter



# Transcriptomic signatures distinguish baseline from all other treatment time points (confirmed TB cases shown)



# Main messages

1. Children with confirmed TB, who tended to have more severe disease on X-ray, had higher scores at baseline than unconfirmed and unlikely TB cases.

2. Signature scores decreased rapidly during the first two weeks of treatment and were stable thereafter.

3. There were not enough children from the SHINE trial with poor treatment outcomes, in this sub-study, for us to assess biomarker performance for treatment failure.

# A BIG THANK YOU TO…..

**SATVI Cape Town**

Thomas Scriba
Simon Mendelsohn
Stanley Mbandi
Denis Awany
Miguel Rodo
Michelle Fisher
Nicole Bilek
Asma Toefy
Mzwandile Erasmus
Rodney Raphela
Lungisa Jaxa
Onke Nombida
Kate Hadley
Kelvin Addicott
Ashley Veldsman
Faheemah Meyer

**Desmond Tutu TB Centre, Stellenbosch**

James Seddon
Anne-Marie Demers
Anneke Hesseling
Megan Palmer
Marieke M. van der Zalm
Jessica Workman
Simon Schaaf
Robert Gie
Elisabetta Walters
Warren Zimri
Graeme Hoddinott
Anneen van Deventer
Pierre Goussard
Julie Morrison

**Imperial College London**

Myrsini Kaforou
Ortensia Vito
Louise Choo

**Medical Research Council (MRC) Clinical Trials Unit (CTU), University College London (UCL)**

Anna Turkova
Kristen Lebeau
Angela Crook
Diana Gibb

**SHINE clinical trial team**

Every breath counts