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9th SA
TB
Conference
8 – 11 June 2026

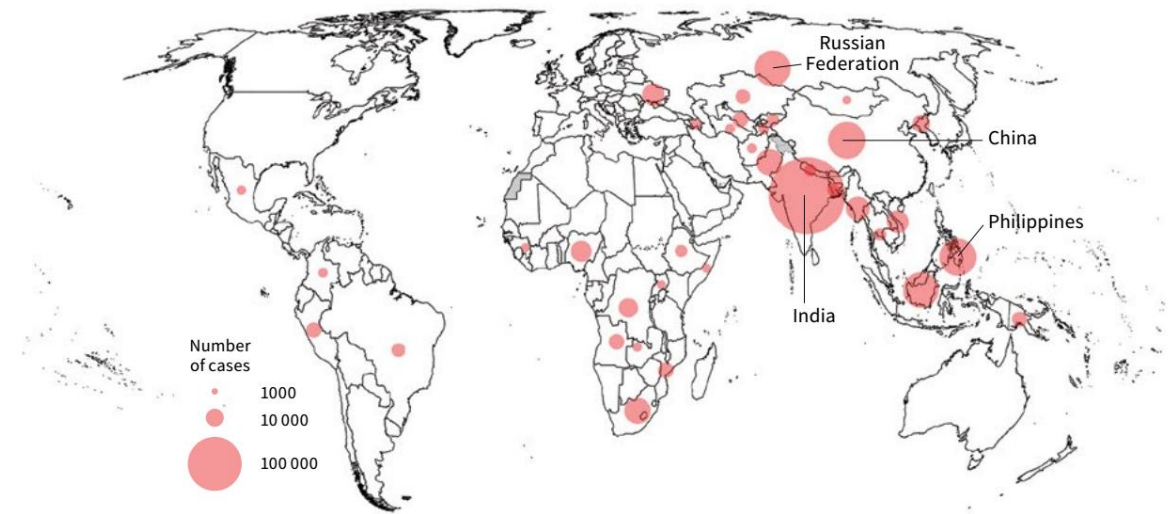


Effects of Pyrazinamide and/or Ethambutol Resistance on Tuberculosis treatment outcomes by Whole Genome Sequencing, South Africa 2020 – 2022

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INTRODUCTION

- An estimated 390,000 people globally developed **multidrug-resistant tuberculosis (MDR-TB)** in 2024.
 - MDR-TB caused an estimated 150,000 deaths worldwide in 2024
 - South Africa is one of the high-burden countries for **MDR-TB**
 - Accounting for 87 - 90% of the global incidence.
- Resistant Strains on MDR Isolates
 - Pyrazinamide (PZA) **59.1%**
 - Ethambutol (EMB) **44.1%**
- MDR-TB Outcome in South Africa
 - Only 68% of MDR-TB patients achieve successful treatment outcomes (cured, treatment completed).
 - Unsuccessful treatment outcomes (died, treatment failure and loss to follow-up).



^a The labels show the four countries that accounted for more than half of the global number of people estimated to have developed MDR/RR-TB in 2024.

Research Question and Objectives

RESEARCH QUESTION

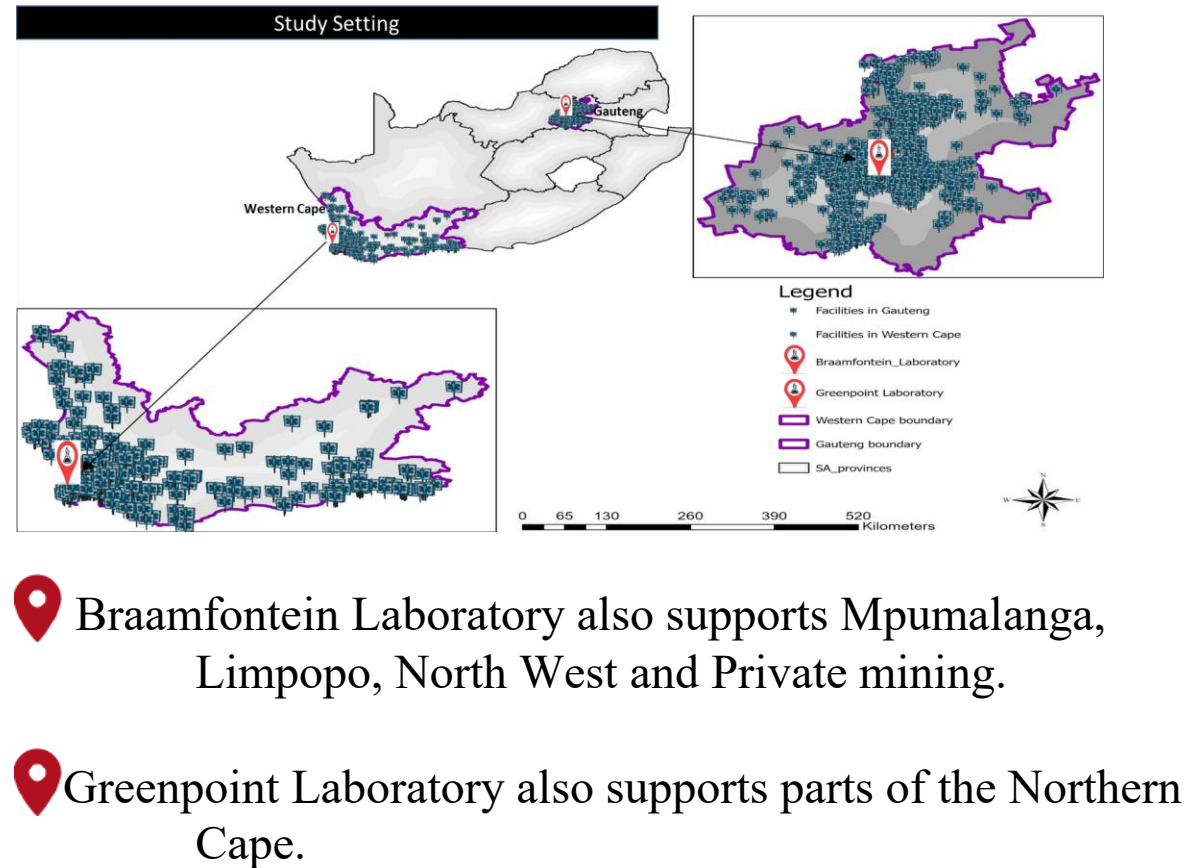
Does PZA and/or EMB resistance have an effect on TB treatment outcome amongst people with MDR-TB treated with the oral short-course regimen in South Africa?

OBJECTIVES

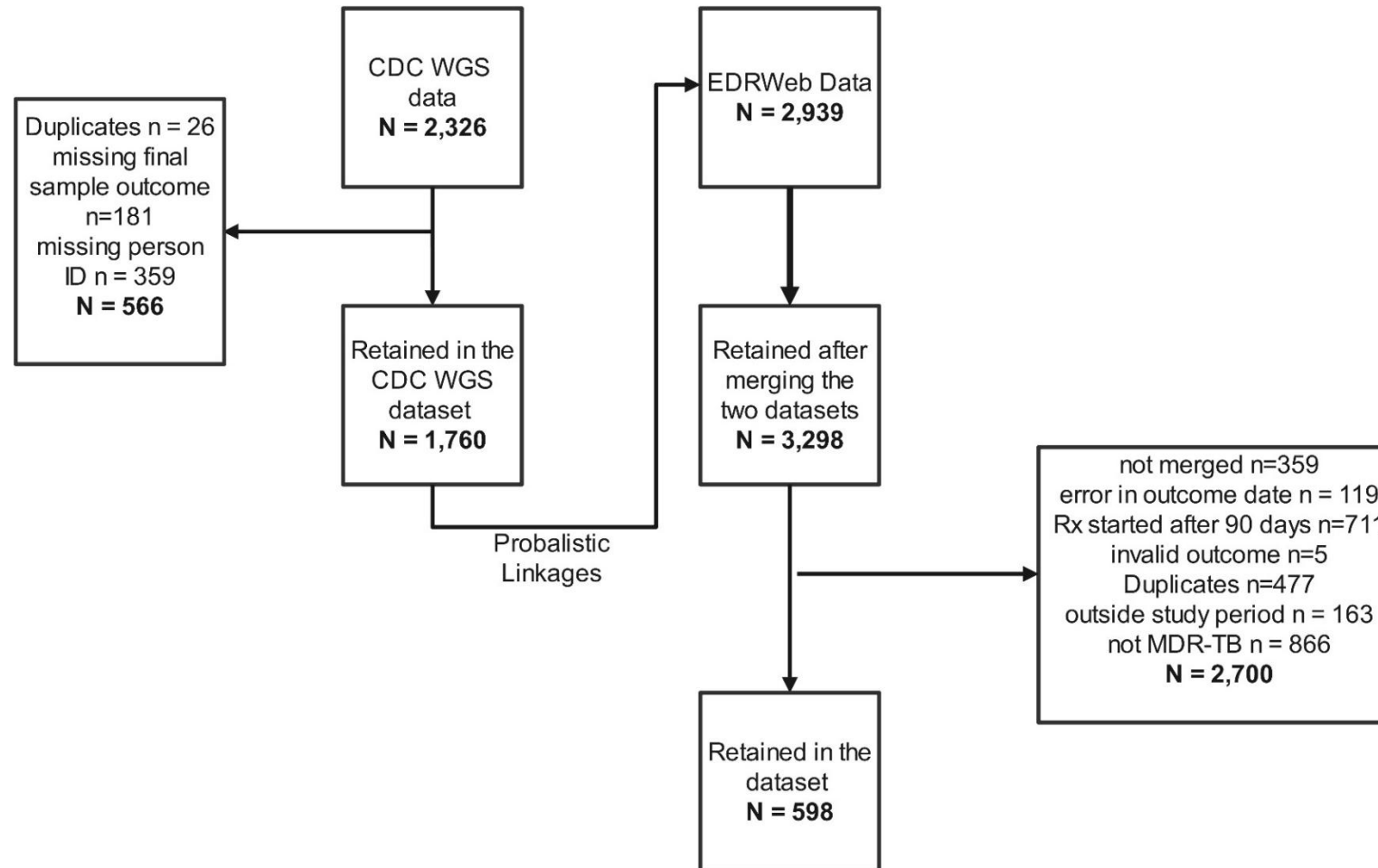
1. To describe the socio-demographic and clinical characteristics among MDR-TB patients with and without PZA and/or EMB resistance treated with the oral short-course regimen in South Africa, 2020 -2022.
2. To compare the treatment outcomes of PZA and/or EMB resistant patients to patients with susceptibility to both drugs among MDR-TB patients treated with oral short-course regimen in South Africa 2020 – 2022

Research Question and Objectives

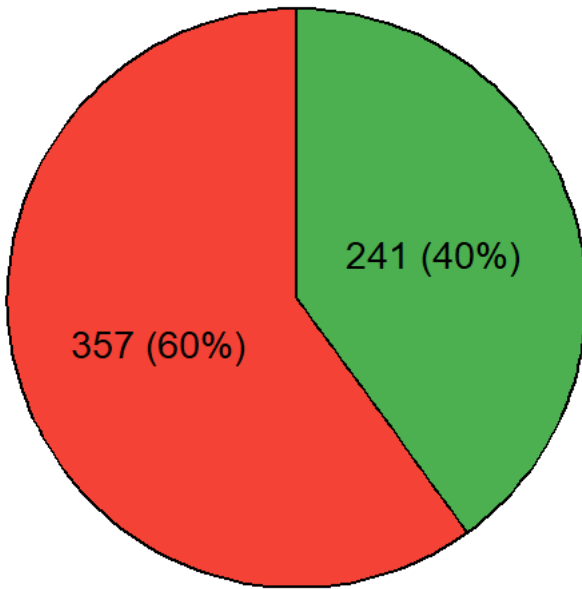
- **Study design:**
 - Retrospective Cohort study
- **Data sources:**
 - Centers for Diseases and Prevention Control (CDC), Whole Genome Sequencing (WGS) data
 - Electronic drug-resistant TB register (EDRWeb)
- **Study population:**
 - All MDR-TB people on the all oral short course regimen recorded from the Braamfontein and Greenpoint laboratory diagnosed with WGS from January 2020 – September 2022.



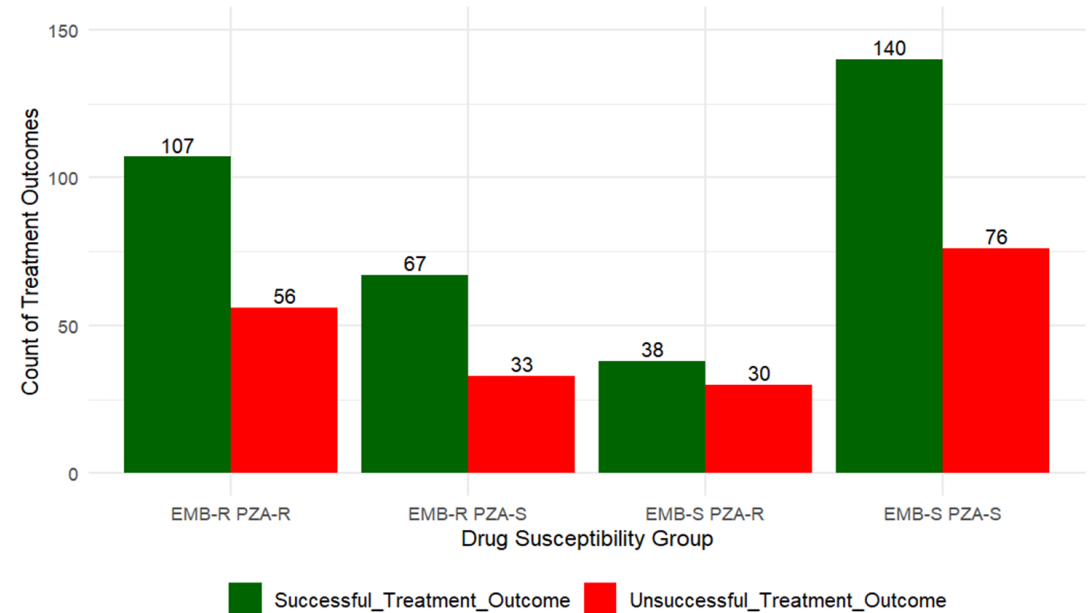
Inclusion & Exclusion Criteria for MDR-TB Individuals in South Africa 2020-2022



Distribution of MDR-TB Cases with PZA and/or EMB resistance, South Africa, 2020 - 2022



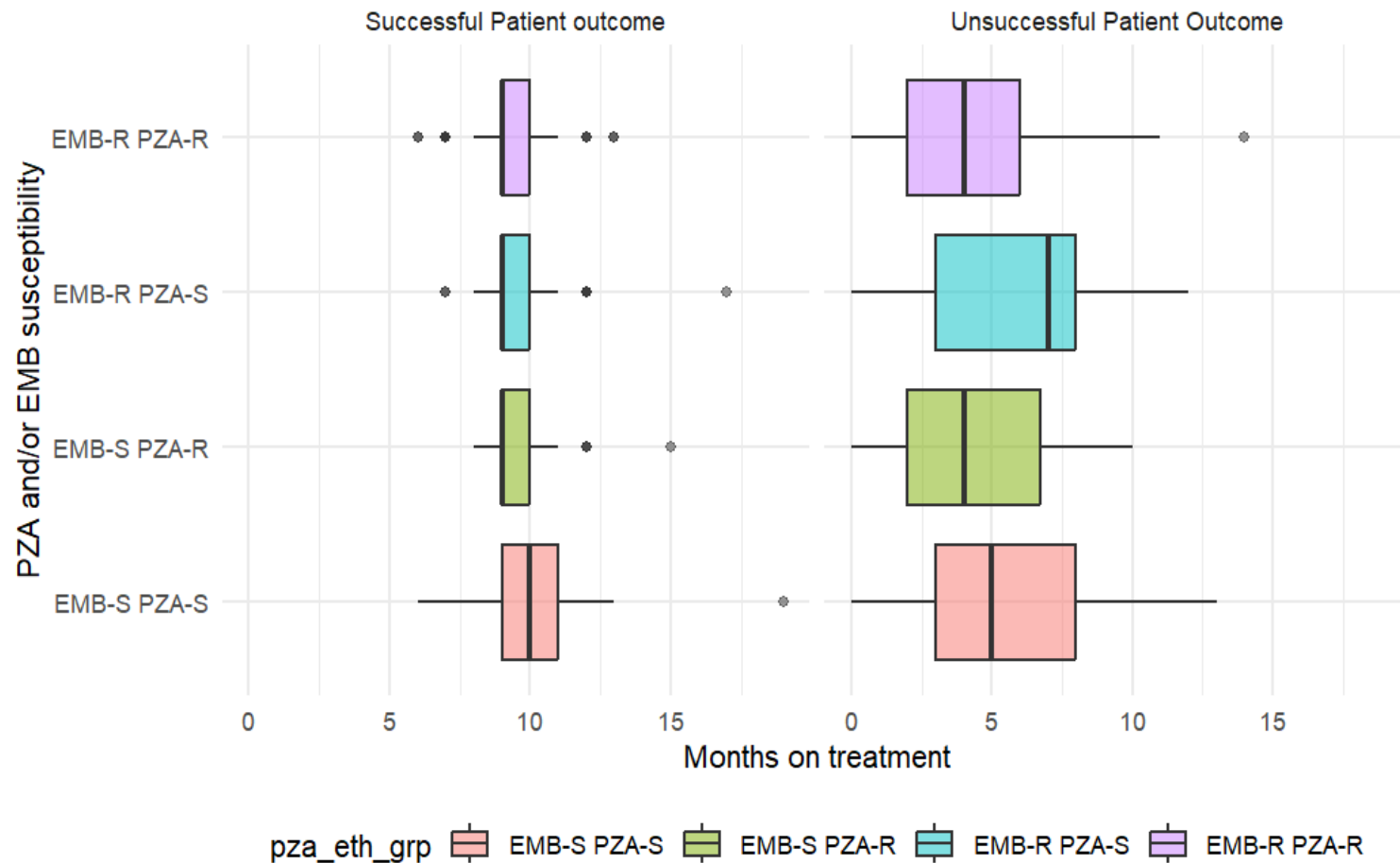
EMB-S & PZA-R, EMB-R & PZA-S, EMB-R & PZA-R EMB-S & PZA-S



Socio-demographic Characteristics of MDR-TB Individuals with PZA and/or EMB resistance, South Africa, 2020 - 2022

	EMB-S PZA-S n (%)	EMB-S PZA-R n (%)	EMB-R PZA-S n (%)	EMB-R PZA-R n (%)	Total (%) 598 (100%)
*Treatment Outcome					
Successful Treatment Outcome	140 (65)	38 (56)	67 (67)	107 (66)	352 (64)
Unsuccessful Treatment Outcome	76 (35)	30 (44)	33 (33)	56 (34)	195 (36)
*Age category					
0 - 14 years	5 (2)	0 (0)	2 (2)	1 (1)	8 (1)
15 - 24 years	45 (19)	7 (10)	24 (23)	35 (19)	111 (19)
25 - 34 years	66 (28)	22 (30)	26 (25)	51 (28)	165 (28)
35 - 44 years	70 (29)	24 (33)	28 (27)	47 (26)	169 (28)
45 - 54 years	36 (15)	12 (16)	12 (12)	30 (17)	90 (15)
55 - 64 years	12 (5)	8 (11)	7 (7)	12 (8)	39 (7)
65 years & older	6 (3)	0 (0)	4 (4)	4 (2)	14 (2)
Gender					
Female	103 (43)	31 (43)	45 (43)	58 (32)	237 (40)
Male	138 (57)	42 (58)	59 (57)	122 (68)	361 (60)

Effects of adherence in MDR-TB Individuals with PZA and/or EMB Resistance, South Africa 2020–2022

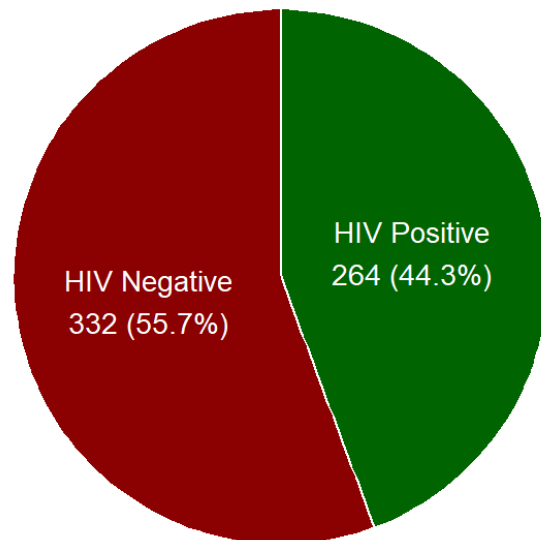


SPO = 9.5 months (IQR : 9 – 11)

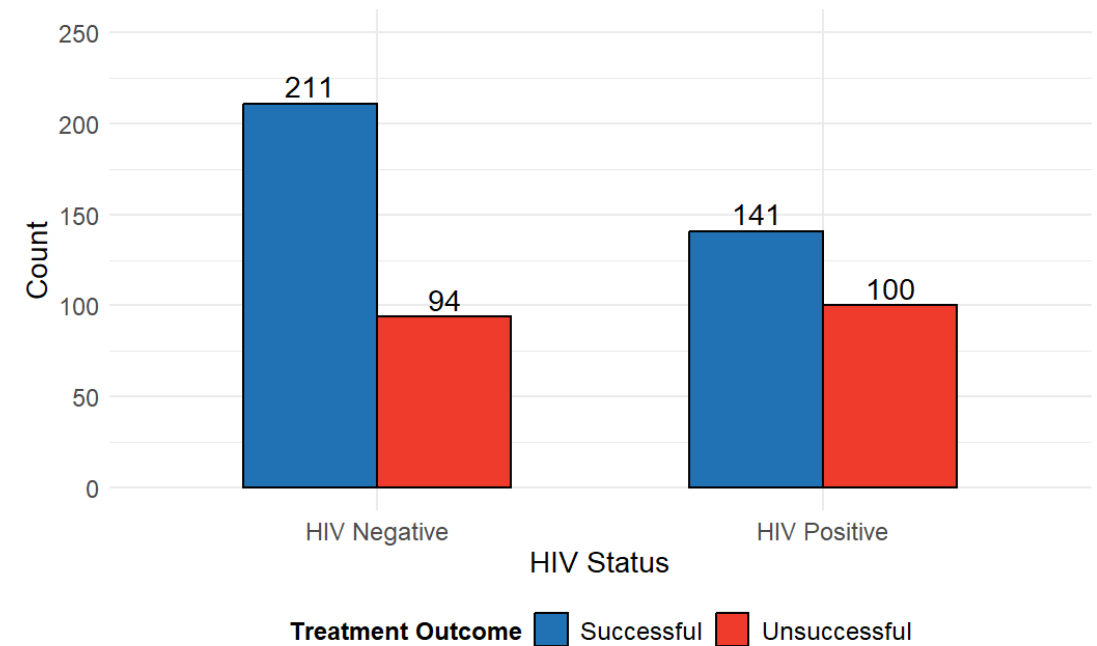
USPO = 5 months (IQR : 2 – 8)

HIV Status Distribution in MDR-TB Cases with PZA and/or EMB Resistance, South Africa 2020–2022

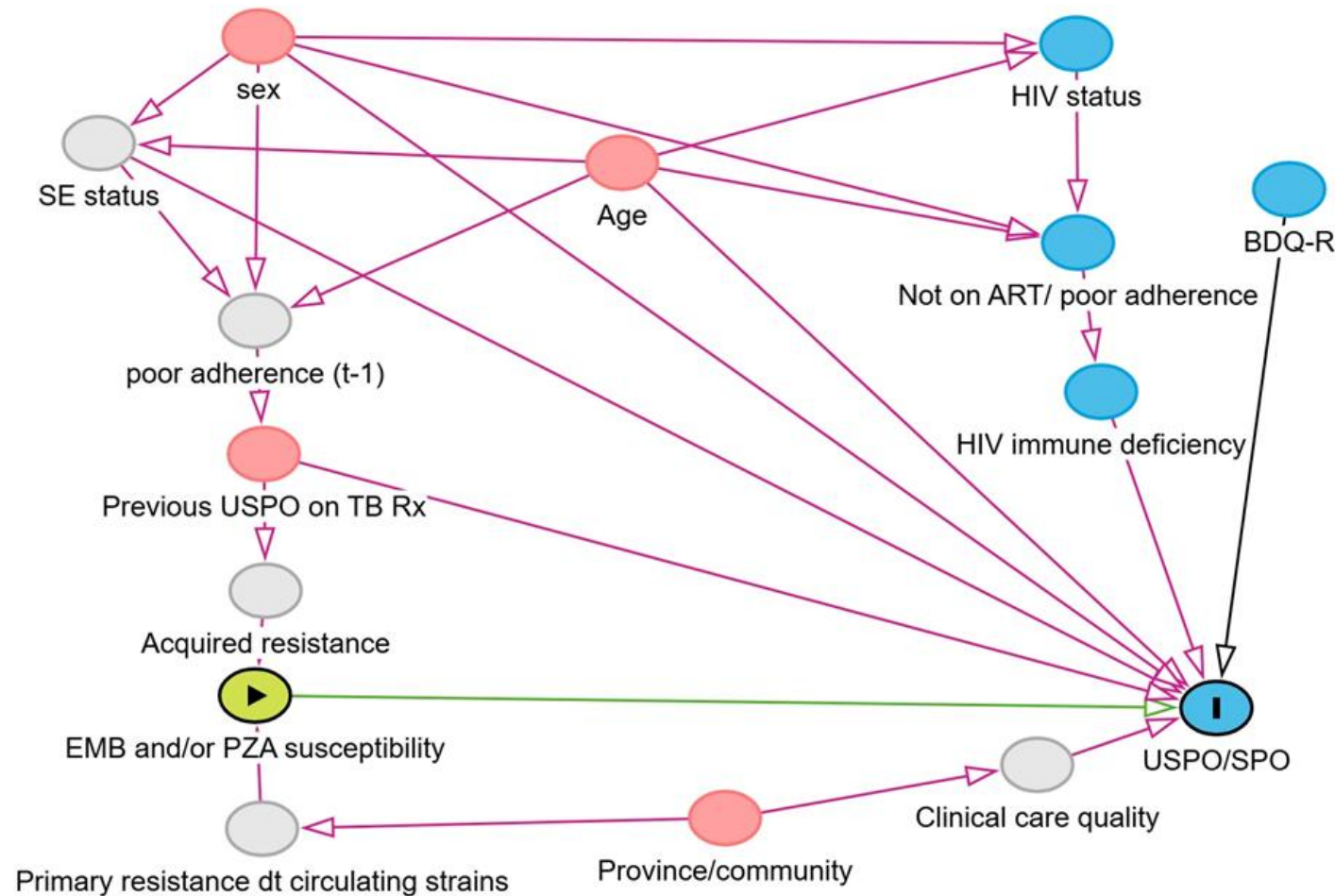
HIV Status for MDR-TB Cases



Treatment outcomes in MDR-TB Cases



DAG for MDR-TB Individuals with PZA and/or EMB Resistance, South Africa 2020–2022



Adjustment (total effect) ▾

Exposure: EMB and/or PZA susceptibility

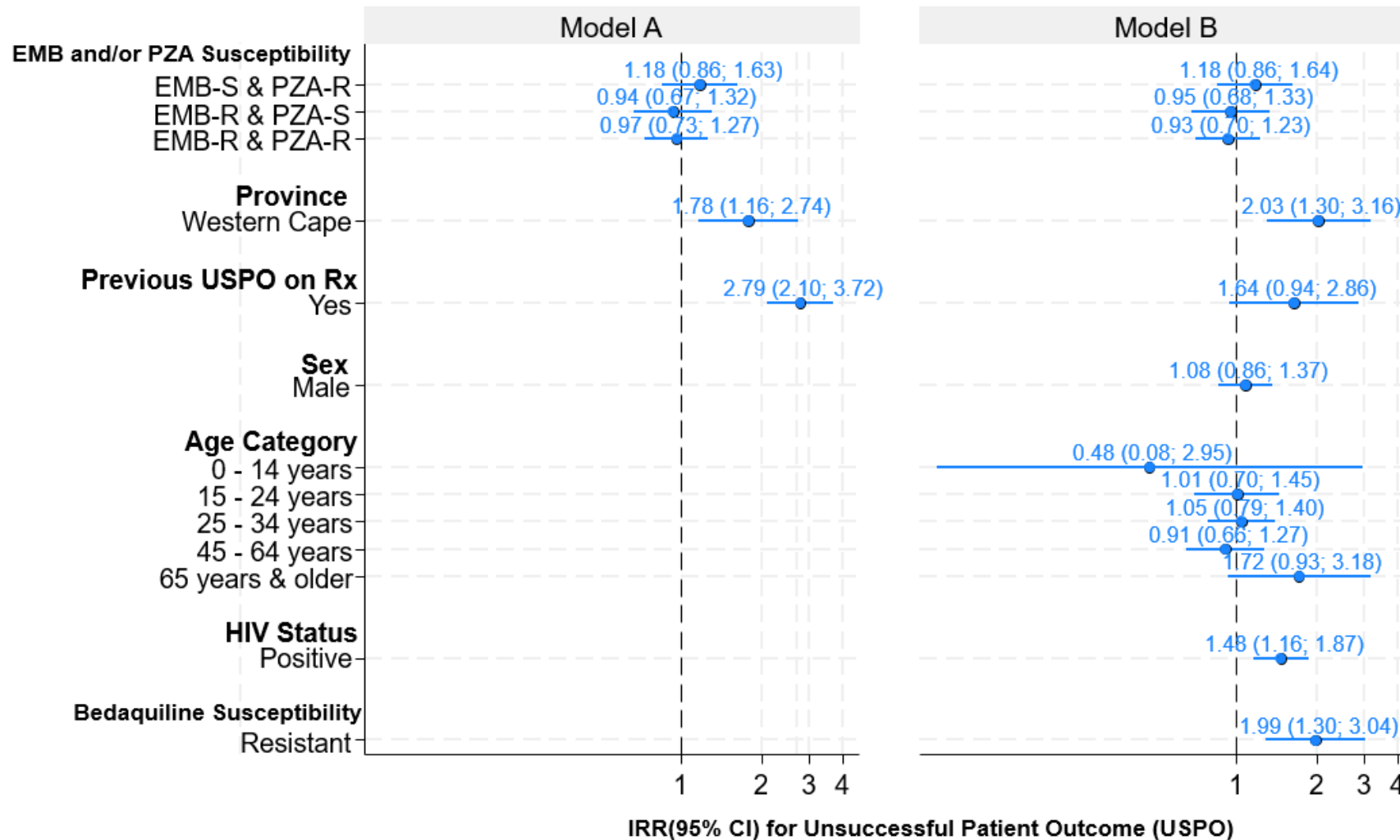
Outcome: USPO/SPO

Biasing paths are open.

Minimal sufficient adjustment sets for estimating the total effect of EMB and/or PZA susceptibility on USPO/SPO:

- Previous USPO on TB Rx, Province/community

Risk factors associated with USPO among MDR-TB individuals, South Africa 2020-2022



Discussion

- This study did not find that PZA and/or EMB susceptibility had an effects of TB treatment outcome
 - Literature have reported that expanding WGS surveillance to include PZA and EMB provides insights into resistance patterns and help guide treatment regimen
- People living with HIV are at a higher risk of USPO
 - A higher proportion of individuals without HIV had MDR-TB.
 - Moyo et al. (2018): Focus on HIV-positive patients has led to under-prioritization of MDR-TB in HIV-negative populations despite high disease risk.
- Bedaquiline is the cornerstone of the BPAL-L regimen for treating drug-resistant TB.
 - Emerging resistance threatens treatment success and global TB control efforts.

Conclusion

- Strengthen the integration of WGS into routine drug-resistant TB surveillance and patient management.
- Expand access to comprehensive drug susceptibility testing to support individualized treatment decisions.
- Enhance surveillance for emerging resistance to key anti-TB drugs, particularly bedaquiline, to preserve the effectiveness of current DR-TB regimens.
- Maintain integrated TB and HIV services to improve early diagnosis, treatment monitoring, and patient outcomes.
- Strengthen treatment monitoring and retention in care to reduce unfavorable treatment outcomes.
- Conduct larger prospective studies to further evaluate the impact of pyrazinamide and ethambutol resistance on treatment outcomes in the era of all-oral DR-TB regimens.
- Continued investment in genomic surveillance and evidence-based TB programmes is essential to support South Africa's progress towards TB elimination.

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Organisation

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- SAFETP