Cost-Effectiveness of Levofloxacin for Tuberculosis Prevention in MDR/RR-TB Contacts in South Africa

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Introduction

- Multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) remains a major global health threat, especially in high-burden countries like South Africa [1,2].
- Contacts of MDR/RR-TB patients have a high risk of TB infection (TBI) and progression to disease [3,4].
- Preventive treatment (TPT) is essential to reduce transmission and disease burden [3,5].
- Recent trials (V-QUIN and TB-CHAMP) show that 6-month levofloxacin preventive therapy (LPT) reduces TB incidence [6-8].
- Economic evaluations in resource-limited settings are needed to guide implementation [9,10].

Objectives

- To evaluate the cost-effectiveness of LPT for contacts of MDR/RR-TB patients in South Africa, from the healthcare provider's perspective.

Methods

- **Decision-analytical model:** Short-term decision tree + 10-year Markov cohort with annual cycles
- **Population: :** Hypothetical cohort of MDR/RR-TB contacts with confirmed TBI
- **Comparators :** LPT vs. No Preventive Therapy (NPT)
- **Outcomes:** TB incidence, TB-related mortality, QALYs, direct medical costs, ICER
- **Model parameters:** Clinical, utility and cost parameters retrieved from WHO reports, South African TB program data, published literature (Table 1).
- **Sensitivity analyses**: To evaluate uncertainty and model robustness
  - One-way (to identify influential factors)
  - Probabilistic (using 10,000 Monte Carlo simulations)

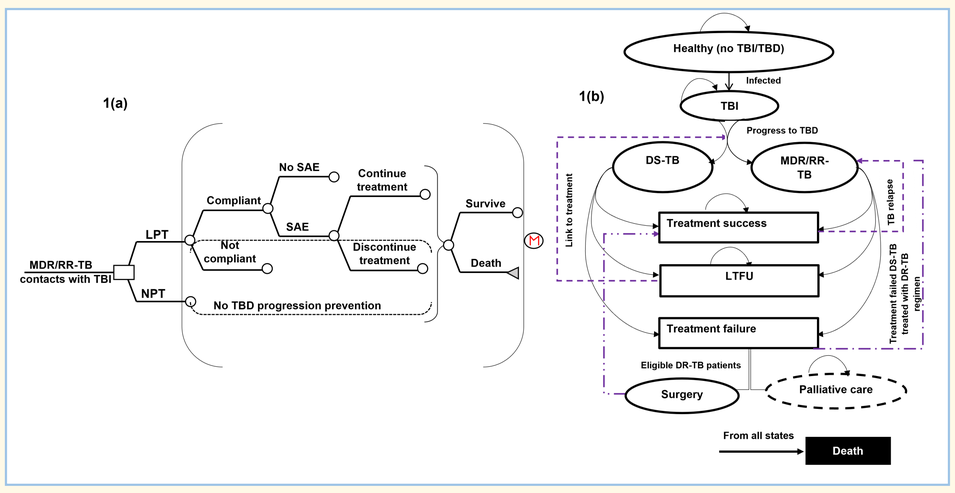


Fig 1. Simplified decision analytical model for TB prevention in MDR/RR-TB contacts (a) decision tree (b) Markov Model

DS-TB: drug-susceptible tuberculosis; LFTU: lost to follow-up; LPT: levofloxacin preventive therapy; MDR/RR-TB: multidrug-resistant or rifampicin-resistant tuberculosis; NPT: no preventive treatment; SAE: severe adverse event; TBI: tuberculosis infection; TBD: tuberculosis disease; TB: tuberculosis.

Table 1.Model input parameters

Parameters	Baseline and ranges	Distribution
Clinical inputs		
Compliance rate with LPT (≥80% of doses)	74.00% (61.20–91.75)	β
Severe adverse event (SAE) rate with LTP	1.00% (0.30–2.40)	β
Discontinuation rate of LPT due to adverse events	5.45% (2.28–8.62)	β
Efficacy of LPT in reducing TBD incidence	0.59 (0.08–0.82)	β
Annual incidence of TBI in contacts of MDR/RR-TB	21.6% (16.70–27.40)	β
Annual incidence rate of TBD in MDR/RR-TB contacts	1.67% [1.42–2.30]	β
Proportion of secondary MDR/RR-TB	90% (65–100)	β
DS-TB treatment outcomes		
Mortality rate	7.20% (5.76–8.64)	β
Treatment success rate in surviving cases	80.82% (64.66–96.98)	β
LTFU rate in survivors of unsuccessful treatment	56.18% (44.94–67.42)	β
MDR/RR-TB treatment outcomes		
Mortality rate	16.90% (13.52–20.28)	β
Treatment success rate in surviving cases	74.09% (59.27–88.91)	β
LTFU rate in survivors of unsuccessful treatment	79.85% (63.88–95.82)	β
Annual TB relapse rate in successfully treated cases	3.72% (2.35–5.96)	β
Surgery rate among MDR-TB/RR-TB treatment failures	11.29% (9.03–13.55)	β
Mortality rate following lung surgery	8.36% (6.69–10.03)	β
Success rate among survivors after surgery	76.03% (60.82–91.24)	β
Annual mortality rate from untreated TB or LTFU	38.9% (31.12–53.20)	β
Probability of linking to treatment among LTFU	35.35% (28.28–42.42)	β
Utility inputs		
DS-TB treatment	0.69 (0.57–0.77)	Triangular
MDR/RR-TB treatment	0.51 (0.39–0.73)	Triangular
LTFU	0.34 (0.27–0.41)	Triangular
TBD treatment success	0.88 (0.67–1.00)	Triangular
Age of contacts to MDR-TB (years)	25 (12–43)	Triangular
Cost inputs per case ($)		
TBI treatment with LPT	321 (120–664)	γ
SAE management	1,343 (1,074–1,617)	γ
DS-TB treatment	509 (407–611)	γ
MDR/RR-TB treatment	3,132 (2,506–3,758)	γ
Lung surgery	9,172 (7,338–11,006)	γ
Palliative inpatient care	4,294 (3,435–5,153)	γ
TB-related hospitalization	5,180 (4,144–6,216)	γ

LTFU: lost to follow-up; LPT: levofloxacin preventive treatment; MDR/RR-TB: multidrug-resistant/rifampicin-resistant tuberculosis; SAE: severe adverse events; DS-TB: drug-sensitive tuberculosis; TBI: tuberculosis infection; TBD: tuberculosis disease; TB: tuberculosis

Results

Base-case analysis (LPT vs NPT)
- ICER: $3,610/QALY (below WTP threshold of $6,023/QALY)
- TB incidence reduction: 18%
- TB-related mortality reduction: 9.4%

Key influential parameters
- LPT efficacy in reducing TBD incidence [base-case: 59.00% (61.20–91.75)]
- Cost of LPT per case [Base-case: $321(120–664)]

Threshold Analysis (Fig.2)
- Minimum efficacy of LPT for cost-effectiveness: 42.80%
- Maximum LPT price for cost-effectiveness: $447

Probabilistic sensitivity analysis
- Cost-saving probability: 31.44% (in 10,000 Monte Carlo simulations) (Fig.3)
- Cost-effectiveness probability:74.00% at WTP threshold of $6,023/QALY (Fig.4)
- WTP thresholds for cost-effectiveness: $1,957/QALY

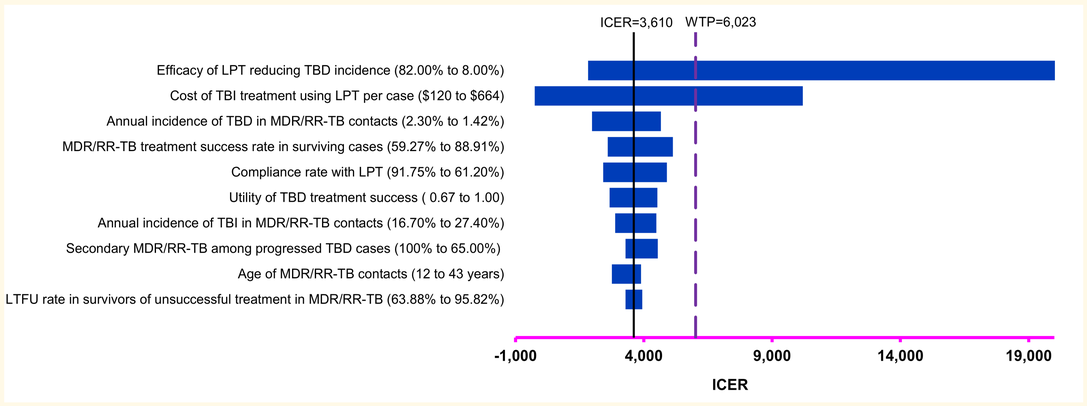
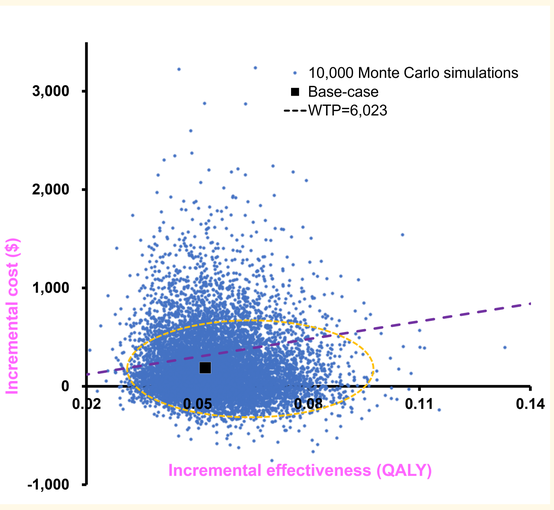


Fig. 2. Tornado diagram of primary analyses showing influential factors identified in a one-way sensitivity analysis of the ICER for LPT versus NPT



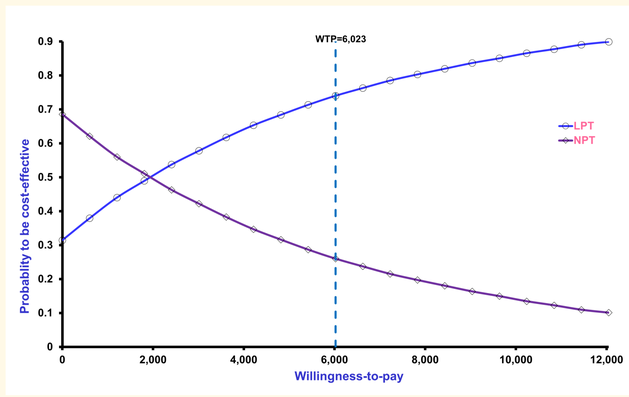


Fig. 3. Scatter plot of the incremental cost against QALY gained by LPT versus NPT

Fig. 4. Cost-effectiveness acceptability curves of LPT and NPT for TB prevention in MDR/RR-TB contacts

Conclusions

- LPT is a cost-effective strategy for MDR/RR-TB contacts in South Africa.
- It also significantly reduces TB incidence and mortality.
- Supports WHO guidelines and contributes to achieving End TB targets.

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