

# Cost-effectiveness of pretomanid-based regimen for treatment of highly drug-resistant tuberculosis in a high-income country

## Background

- **u** Tuberculosis (TB) is the leading deadliest infectious disease globally (1.6 million in 2021)<sup>1.</sup>
- Highly drug-resistant tuberculosis (HDR-TB) comprises pre-extensively or extensively drug-resistant tuberculosis (XDR-TB) and treatment-intolerant or nonresponsive multidrug-resistant tuberculosis (MDR-TB)<sup>1-3</sup>.
- **n** Treatment for HDR-TB with bedaquiline-linezolid-based regimen is costly, takes a long time to complete, and has life-threatening adverse effects <sup>2-4</sup>.
- Lower treatment success rate (59% for MDR-TB and 52% for XDR-TB)
- ◆ Treatment cost per case in the US (420,000 USD for MDR-TB and 801,000 USD for XDR-TB) <sup>5</sup>.
- Recent clinical findings reported improvement in clinical outcomes of HDR-TB with the pretomanid-based regimen (with shortened treatment duration) <sup>1,4</sup>.

### **Objective**

This study aimed to evaluate the cost-effectiveness of the pretomanid-based regimen for HDR-TB treatment from the perspective of healthcare provider in the US.

### Methods

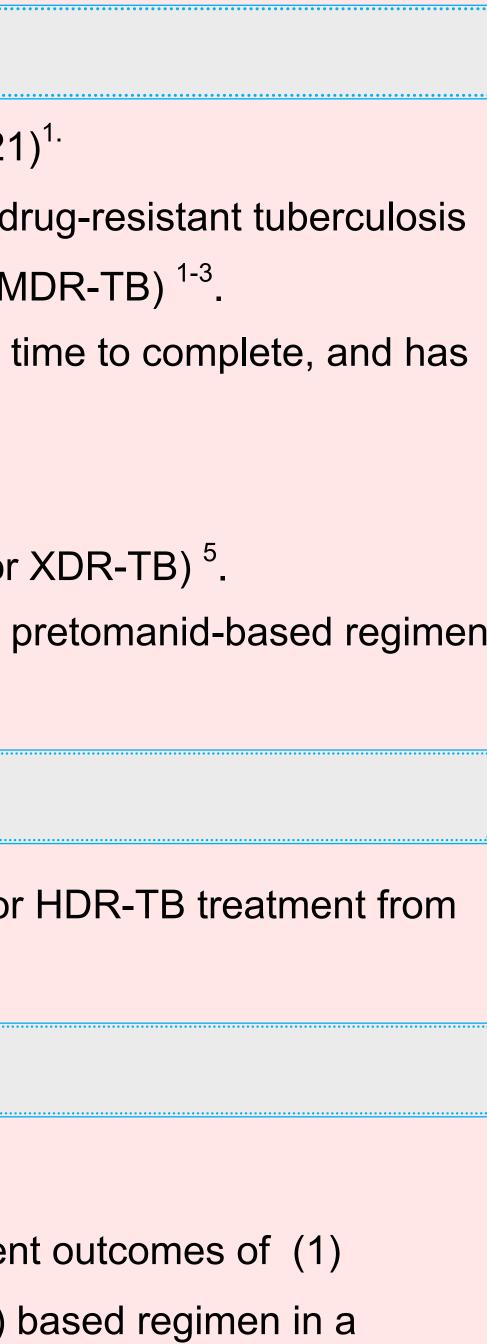
### **Decision model**

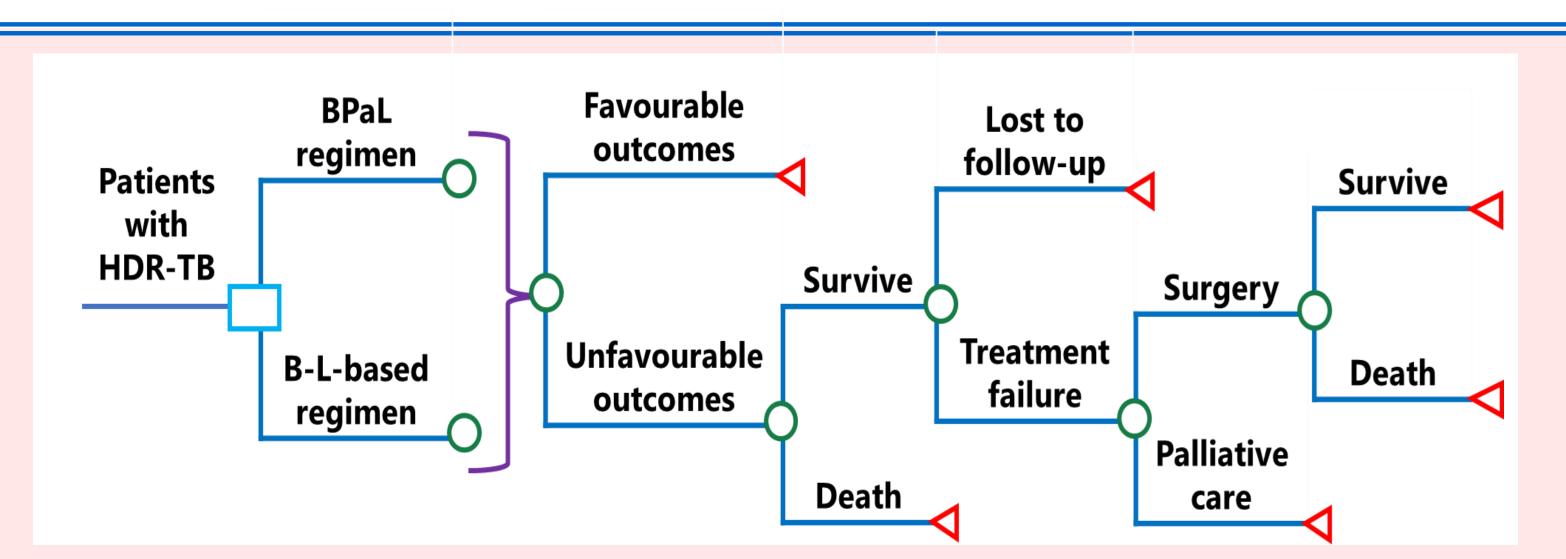
A 2-year decision-analytic model (Fig 1) was constructed to simulate potential treatment outcomes of (1) bedaquiline-pretomanid-linezolid (BPaL) regimen), and (2) bedaquiline-linezolid (B-L) based regimen in a hypothetical cohort of adult patients with HDR-TB.

Table 1 Model inputs <sup>5-20</sup>						
Parameters	Base-case value	Range	Distribution type			
<b>Clinical inputs</b>						
Favourable outcome rate of B-L-based regimen	65.12%	52.10%-78.14%	Beta			
Relative risk ratio of favourable outcome with BPaL versus B-L-based regimen	1.35	1.13-1.60	Lognormal			
Mortality rate among HDR-TB patients with unfavourable outcomes	55.00%	44.00%-66.00%	Beta			
Treatment failure rate among survived HDR-TB patients with unfavourable outcomes	38.89%	31.11%-46.67%	Beta			
Proportion of patients who underwent surgery among treatment failure patients	63.41%	50.73%-76.09%	Beta			
Mortality rate among patients who underwent surgery	7.69%	6.15%-9.23%	Beta			
Utility inputs						
Disutility						
HDR-TB	0.333	0.224-0.454	Triangular			
TB treatment success	0.120	0.096-0.144	Uniform			
Surgery	0.490	0.392-0.588	Uniform			
Palliative care	0.660	0.528-0.792	Uniform			
Lost to follow-up	0.660	0.528-0.792	Uniform			
HDR-TB patient age (years)	42	23-76	Triangular			
Cost inputs (USD)						
Drug (cost per treatment course)						
B-L based regimen	82,330	65,864-98,796	Gamma			
BPaL regimen	35,100	28,080-42,120	Gamma			
TB outpatient clinic visit (cost per visit)	83	66-100	Gamma			
Number of outpatient clinic visits (days)						
B-L-based regimen	20					
BPaL regimen	8					
Laboratory and imaging tests (cost per treatment course)						
B-L-based regimen	867	694-1,040	Gamma			
BPaL regimen	624	499-749	Gamma			
Cost per case						
Surgery	26,004	20,803-31,205	Gamma			
Palliative care	28,037	22,430-33,644	Gamma			
TB-related mortality	39,588	31,670-47,506	Gamma			

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### **Cost-effectiveness and sensitivity analyses**

- Primary model outputs were TB-related direct medical cost, disability-adjusted life-years (DALYs), and incremental cost per DALY averted (ICER).
- **n** The clinical, utility and cost parameters of the model retrieved from literature and public data are shown in Table 1.
- **B** Sensitivity analysis was performed to assess the robustness of base-case results.
- One-way sensitivity analysis: to identify influential factors with threshold values.
- Probabilistic sensitivity analysis: to evaluate the uncertainty of all variables simultaneously and was performed in 10,000 Monte Carlo simulations by randomly drawing each of model inputs.

### **Base-case analysis**

**n** The BPaL regimen averted 2.5511DALYs and saved cost by USD53,502 when compared to the B-L-based regimen.

Table 2 Results of the base-case analysis					
Treatment strategy	Total direct cost (USD)	Incremental cost (USD)	DALYs	DALY averted	
BPaL regimen	39,283	- 53,502	1.5929	2.5511	
B-L-based regimen	92,785	-	4.1440	_	

### Sensitivity analysis

- **n** No influential parameter with threshold value was identified in the one-way sensitivity analysis.
- In the probabilistic sensitivity analysis, the BPaL regimen reduced DALYs by 2.2974 (95%CI: 2.2802-2.3146; p<0.001) with cost saving of USD53,072 (95%CI:USD51,366-USD54,778; p<0.001)
- **•** The BPaL regimen reduced DALYs at lower cost in 75.51% of the time, and averted DALYs at higher cost with ICER less than willingness-to-pay (WTP) threshold (100,000 USD/DALY) in 24.08% of the simulations (Fig 2)

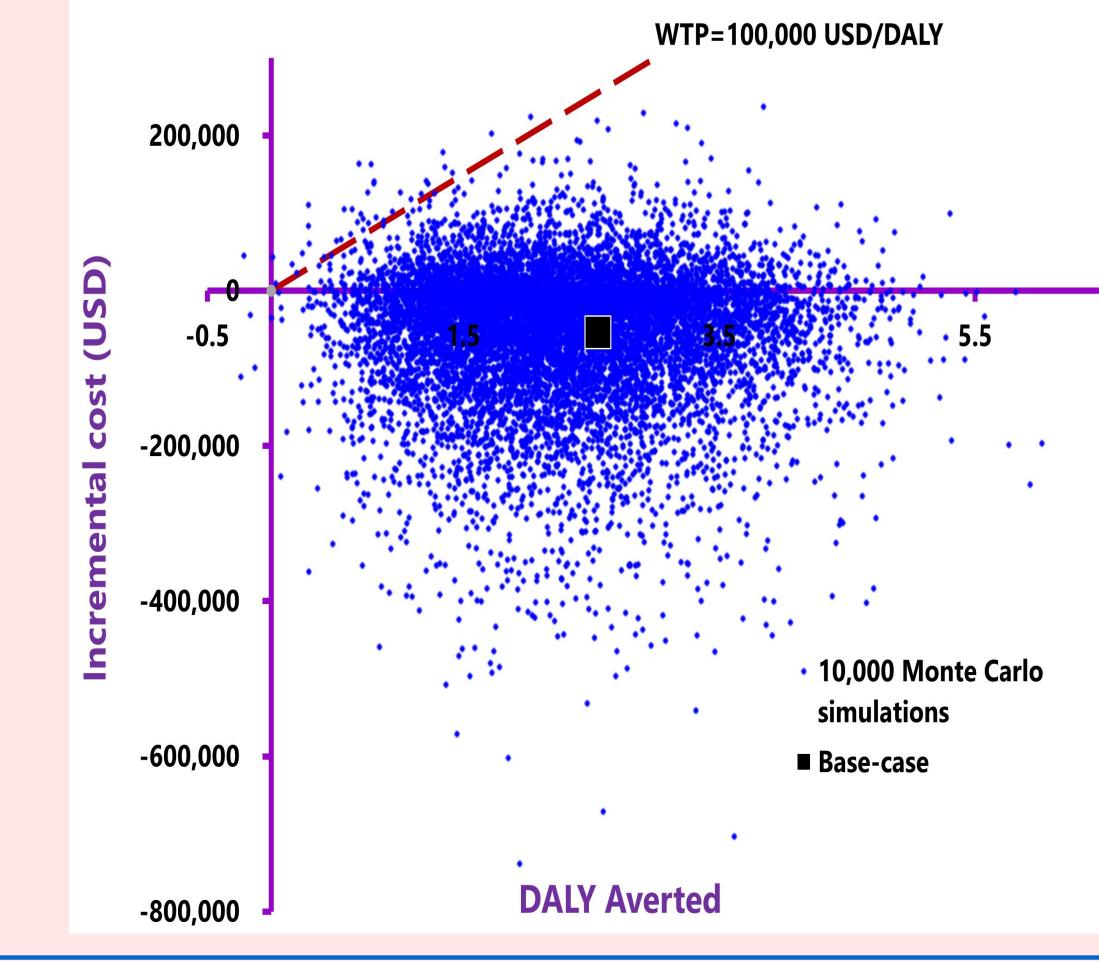


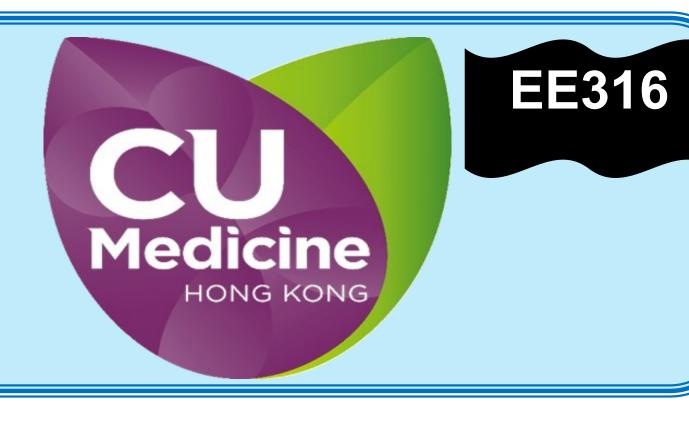
Fig 1 Simplified decisionanalytical model

### Results

Fig 2 Scatter plot of the incremental cost against DALY averted by the BPaL regimen versus the B-L-based regimen in

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- **•** The base-case analysis findings showed the BPaL regimen to save cost and avert DALYs in HDR-TB.
- **n** The study findings were consistent with cost-effectiveness analysis of the BPaL regimen (against the current standard of care) for the treatment of XDR-TB in high-burden epidemiological settings (South Africa, Georgia, and Philippines)<sup>21</sup>.
- treatment with BPaL.
- Lower the odds of treatment failure, loss to follow-up and mortality cases.
- The cost-saving of the BPaL regimen was primarily due to:
- Reduction in costs of drug acquisition, outpatient clinic visits and laboratory follow-up.
- Reduction in health service utilization from reduced cases of unfavourable treatment outcomes required to treat treatment failure cases and TB-related mortality costs.
- Inconclusion, the BPaL therapy appeared to be effective and cost-saving for HDR-TB treatment from the perspective of US healthcare provider.

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**The probability of the BPaL regimen to be cost-effective was higher than the B-L-based regimen throughout the** variation of WTP, and it was 99.59% at the WTP threshold of 100,000 USD/DALY (Fig 3).

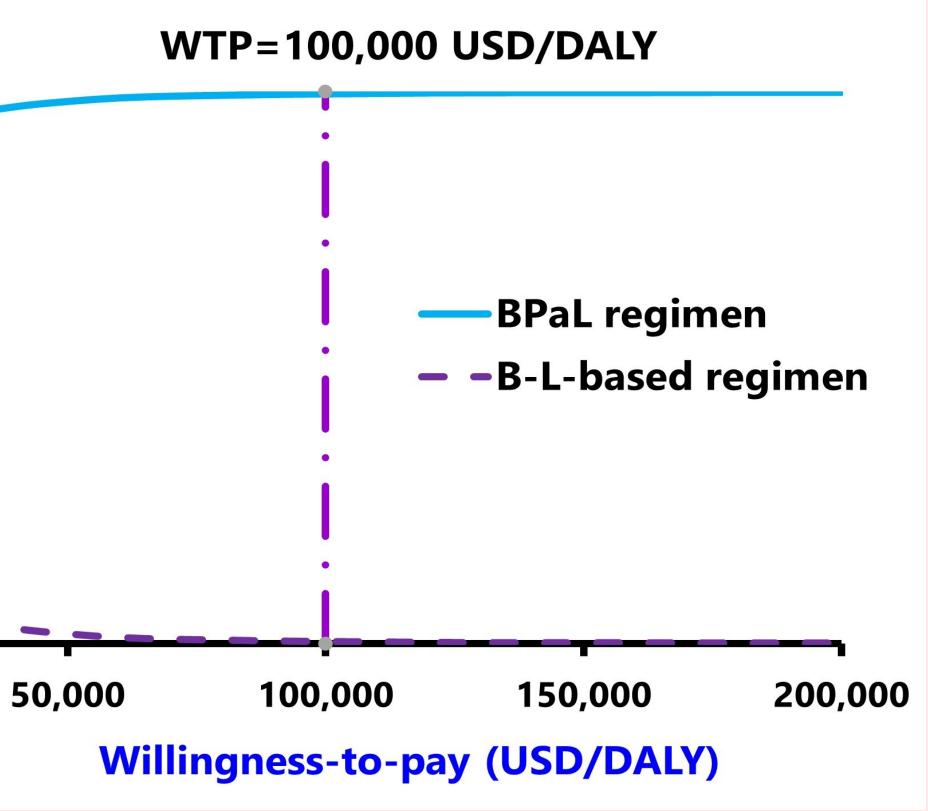


Fig 3 Acceptability curves of the BPaL regimen and the B-L-based regimen to be cost-effective

### **Discussion and Conclusion**

**B** The averted DALY with the BPaL regimen translated from higher clinical improvement (1.35-fold) of HDR-TB

Refere	nce	<b>?S</b>		
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