

Jingwei Si^{1,2}, Yuyang Zhang^{1,2}, Yiling Jiang³, Xiaomin Duan⁴, Shitong Xie^{1,2*}

1 School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, China. 2 Institute of Health Economics and Policy, Tianjin University, Tianjin, China. 3 MSD (UK) Limited, London, UK. 4 MSD, China.

BACKGROUND

- Carbapenems are highly effective against a wide range of Gram-negative pathogens and are relatively stable to most β-lactam resistance mechanisms. Nevertheless, the global emergence of carbapenem-non-susceptible (CNS) Gram-negative (GN) bacteria has markedly limited therapeutic options and challenged clinical management.
- The novel triple-combination, imipenem/cilastatin/relebactam (IMI/REL), leverages relebactam to restore carbapenem activity against Carbapenem-resistant organisms (CROs) and is indicated for treating CNS GN infections.

OBJECTIVE

- To evaluate the cost-effectiveness of IMI/REL compared with CMS+IMI (colistin+imipenem/cilastatin) for the treatment of hospitalized adult patients with hospital-acquired bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VABP), complicated urinary tract infections (cUTIs), or complicated intra-abdominal infections (cIAIs) caused by CNS GN bacteria in China.

METHODS

A cost-utility analysis was conducted to simulate outcomes of hospitalized adult patients with CNS GN infection.

Model Structure

- Decision tree combined with three-state Markov model was performed (Figure 1).

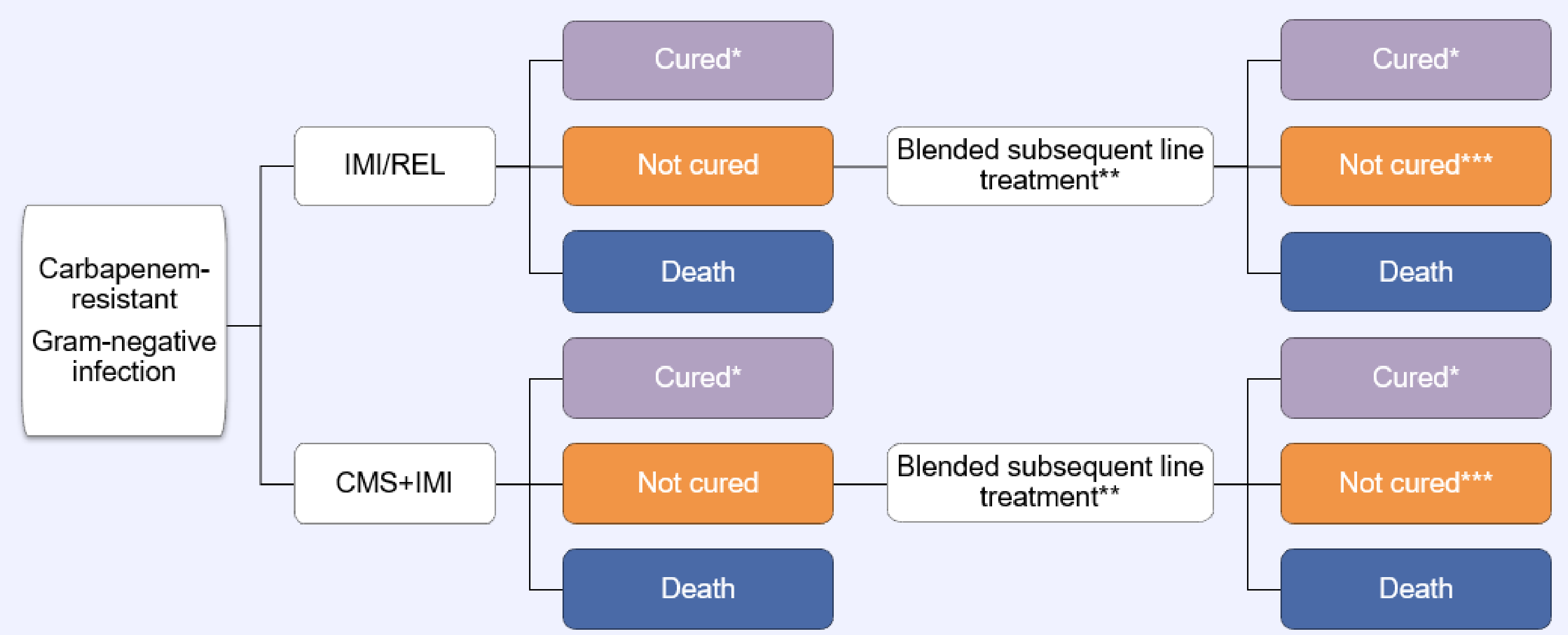


Figure 1. Decision tree model

Model Setting

- Perspective: Chinese healthcare system.
- Cycle length: 1 year.
- Time horizon: lifetime.
- Half-cycle correction.
- Discount rate: 5%
- Willingness to pay (WTP) threshold: 1 times China's per capita GDP (¥95,749/QALY, 2024).
- Key assumption: Uncured patients assumed to die within 1 year.

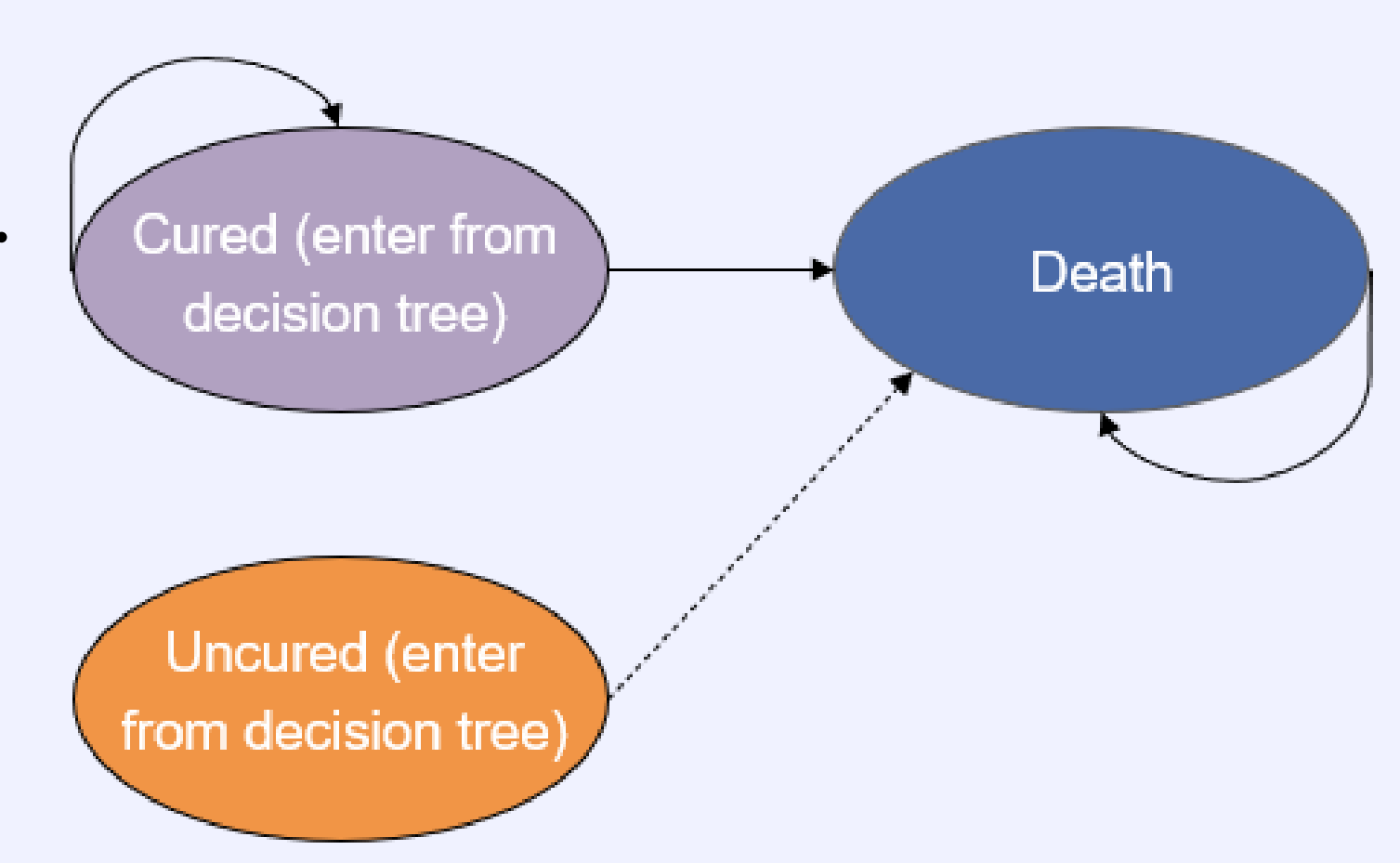


Figure 2. Markov model

Study population

- Patients from RESTORE-IMI 1, an international multicenter double-blind phase III trial, which enrolled adults with HABP/VABP, cUTIs, or cIAIs caused by CNS GN pathogens.

Intervention and Control Group

- Intervention group: IMI/REL, 1.25g (500mg/250mg) every 6 hours.

- Reference group: CMS+IMI, following RESTORE-IMI 1 dosage regimen.
 - ✓ loading dose (1st treatment): 900,000 IU CMS;
 - ✓ maintain dose (12h after 1st): 450,000 IU CMS every 12h, 1g IMI every 6h.

Model parameters

- Clinical Inputs (Table 1)

Table 1. Clinical transition parameters

Parameter	Treatment	Transition probability	Distribution
Initial treatment			
Response rate	IMI/REL	71.4%	Beta
	CMS+IMI	40.0%	Beta
Mortality	IMI/REL	9.5%	Beta
	CMS+IMI	30.0%	Beta

*From RESTORE-IMI 1.

- Cost Inputs (Table 2)

- ✓ Treatment cost, resource use cost, AE cost and monitoring cost were primarily obtained from provincial tender prices, published literature, and clinical expert opinion.

Table 2. Cost parameters

Model	Parameter	Value	Distribution
Decision tree	• IMI/REL	¥ 55,489.0	Normal
	• IMI/REL subsequent treatment	¥ 1,409.8	Normal
	• CMS+IMI	¥ 14,919.4	Normal
	• CMS+IMI subsequent treatment	¥ 865.7	Normal
Markov	• Cured	¥ 31,690.5	Normal
	• Uncured	¥ 53,873.9	Normal
	• Death	¥ 25,352.4	Normal
✓ Long-term monitoring cost yearly	¥ 1,170.5	Normal	

- Utility Inputs (Table 3)

- ✓ Short-term health state utilities (for patients in ICU and general wards) were derived from published literature.
- ✓ Long-term utilities were based on Chinese general population norms.

Table 3. Utility parameters

Health state	Utility	Distribution
Patients hospitalized in the ICU	0.23	Beta
Patients hospitalized in the general ward	0.25	Beta

RESULTS

Base case results

- ✓ Compared with CMS+IMI, IMI/REL was cost-effective, with an ICER of ¥11,149 per QALY, substantially below the WTP threshold (Table 4).

Table 4. Base case results

Outcomes	IMI/REL	CMS+IMI	Increment
Total cost	¥ 98,626.2	¥ 63,861.2	¥ 34,765.0
Treatment costs	¥ 55,757.1	¥ 15,179.1	¥ 40,577.9
Resource use costs	¥ 41,761.2	¥ 46,570.2	¥ -4,809.0
AE costs	¥ 308.8	¥ 1,541.3	¥ -1,232.5
Monitoring costs	¥ 799.2	¥ 570.6	¥ 228.6
Total QALYs	10.33	7.21	3.12
ICER (¥/QALY)			11,149.22

Scenario analysis results

- ✓ Six scenarios were simulated; results are summarized in Table 5.

Table 5. Scenarios analysis results

Setting	Scenario	IMI/REL		Incremental		ICER (¥/QALY)
		Cost	QALY	ΔCost	ΔQALY	
Time horizon	Change to 3 years	¥ 98,626.2	2.07	¥ 34,765.0	0.62	55,841.0
	Change to 15 years	¥ 98,626.2	7.56	¥ 34,765.0	2.28	15,245.1
Discounting	Change to 0%	¥ 98,666.2	19.43	¥ 34,776.4	5.87	5,927.7
	Change to 4%	¥ 98,633.9	11.52	¥ 34,767.2	3.48	9,996.5
Drug cost of CMS	Used cheaper price of Polymyxin B	¥ 98,562.0	10.33	¥ 43,406.8	3.12	13,920.7
Hospital length of stay	Not stratified by response status	¥ 94,648.1	10.33	¥ 36,119.2	3.12	11,595.2

Sensitivity analysis results

- ✓ ΔQALY-OWSA (Figure 3); Probabilistic sensitivity analysis (Figure 4).

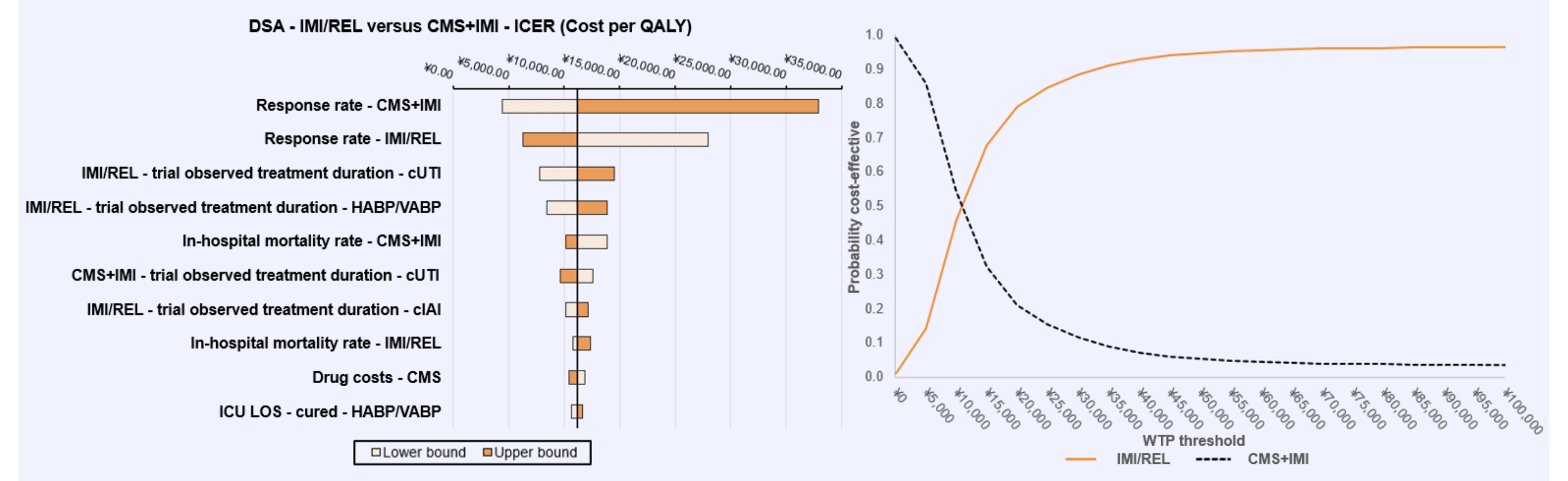


Figure 3. ΔQALY-OWSA tornado diagram

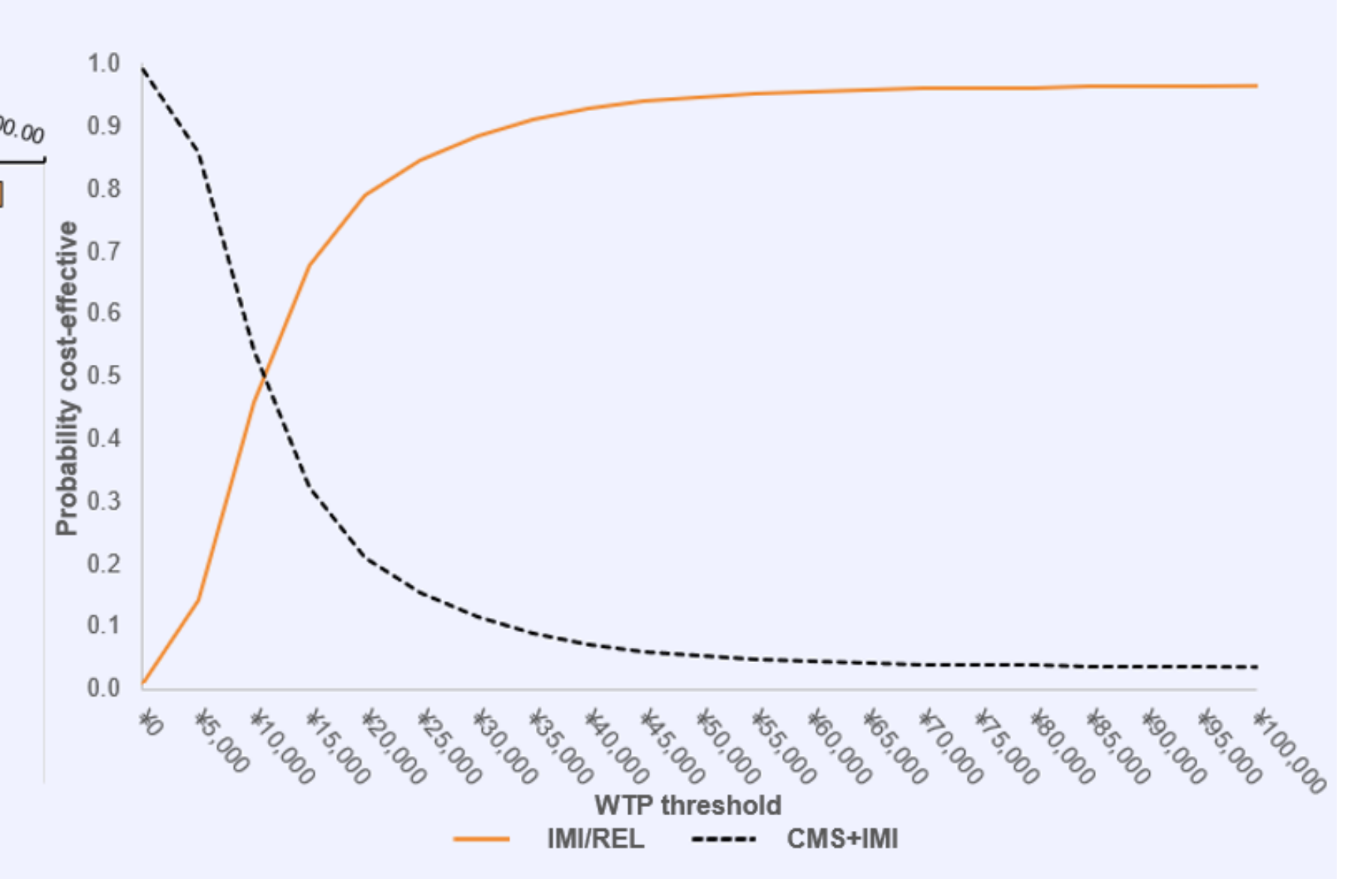


Figure 4. CE acceptability curve

CONCLUSIONS

- IMI/REL is a cost-effective strategy compared with CMS+IMI for adult patients in China with HABP/VABP, cUTIs, or cIAIs caused by GNS GN bacteria.

Reference

- [1] Wang J, Liu F, Tartari E, et al. The Prevalence of Healthcare-Associated Infections in Mainland China: A Systematic Review and Meta-analysis. Infect Control Hosp Epidemiol. 2018 Jun;39(6):701-709.
- [2] Zhen X, Lundborg C, Sun X, et al. Clinical and economic burden of carbapenem-resistant infection or colonization caused by Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii: a multicenter study in China [J]. Antibiotics (Basel).2020,9(8):514.
- [3] Motsch J, Murta de Oliveira C, Stus V, et al. RESTORE-IMI 1: A Multicenter, Randomized, Double-blind Trial Comparing Efficacy and Safety of Imipenem/Relebactam vs Colistin Plus Imipenem in Patients With Imipenem-nonsusceptible Bacterial Infections. Clin Infect Dis. 2020 Apr 15;70(9):1799-1808.
- [4] Xie S, Wu J, Xie F. Population Norms for SF-6Dv2 and EQ-5D-5L in China. Appl Health Econ Health Policy. 2022 Jul;20(4):573-585.
- [5] Du X, Han Y, Jian Y, et al. Clinical Benefits and Cost-Effectiveness of Moxifloxacin as Initial Treatment for Community-Acquired Pneumonia: A Meta-Analysis and Economic Evaluation. Clin Ther. 2021;43(11):1894-1909.e1.