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BACKGROUND

- **Severe asthma** is a chronic disease requiring treatments with grade 4 or 5 drugs recommended by GINA, accounting for **3.4-8.3%** of asthma patients. 80% of severe asthma patients have type 2 inflammation. Medium-high doses of inhaled glucocorticoids combined with long-acting beta-2 receptor agonists or other control agents are used as **background therapy**.
- Guideline recommends **background therapy plus biologics** for uncontrolled severe asthma.
  - **Omalizumab** is the **world's first approved** biologic for the treatment of severe allergic asthma.
  - **Dupilumab** was **approved after omalizumab** for patients with uncontrolled type 2 severe asthma and oral glucocorticoid-dependent asthma ("OCS-dependent asthma").
- The comparative effectiveness of these two drugs in the treatment of severe asthma patients in China are still unclear.

OBJECTIVES

- To evaluate the economics of dupilumab versus omalizumab in additional treatments of severe asthma by Markov model from the perspective of the Chinese medical system.

METHODS

A cost-utility analysis method was used to simulate the medical costs and health outcomes of patients with severe asthma with dupilumab and omalizumab.

Model Structure

- Two treatment patterns, four health statuses, and two death statuses (Figure 1):

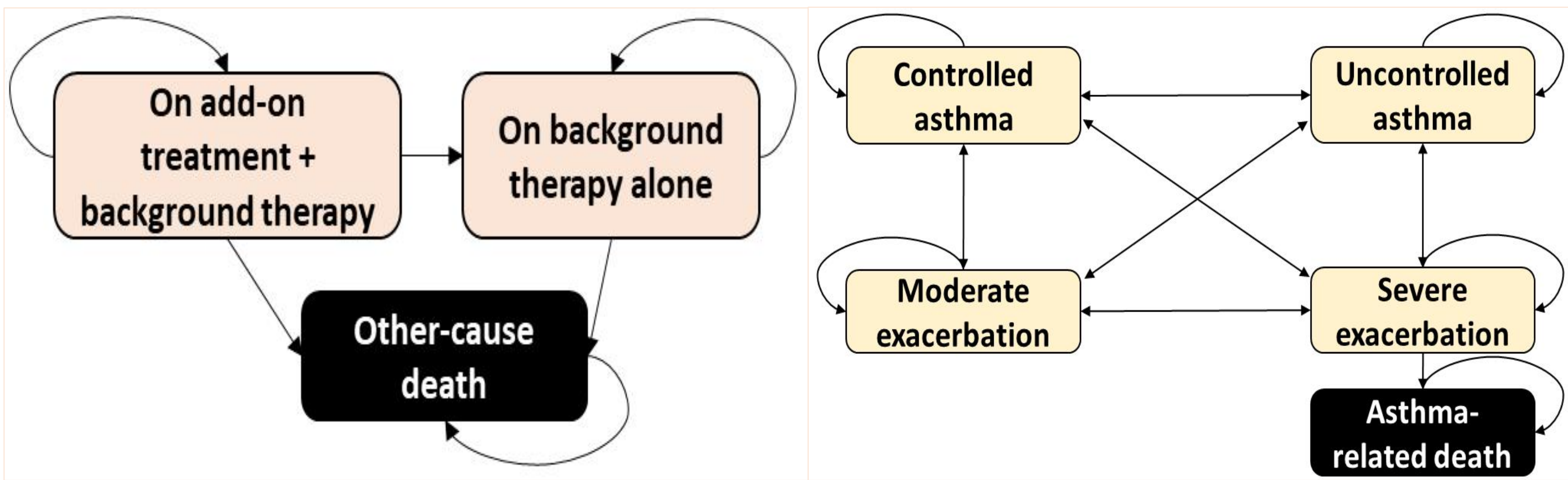


Figure 1. Markov model

Model Setting

- Perspective: China’s healthcare system.
- Corrected by half-cycle correction.
- Four-week cycle over and a lifetime horizon.
- Incremental cost-effectiveness ratios (ICERs) were expressed in CNY (¥) per QALY gained, with all costs and utilities discounted at 5% annually.
- Willingness to pay (WTP) threshold: 2 times China's per capita GDP (**¥178,716/QALY**, 2023)

Study Population

- The target population was consistent with the Chinese subgroup of patients in the Asian Phase III trial EFC13995 (NCT03782532).
- This study screened out patients from the dupilumab trial population (called "omalizumab-like population") according to the baseline characteristics of the omalizumab trial population.

Intervention and Control Group

- The intervention group was dupilumab (200mg/300mg) plus background therapy.
- The reference group was set as omalizumab (150mg) plus background therapy.
  - ✓ The study used the average dose of 450mg/4weeks in the Chinese Phase III clinical trial of omalizumab (NCT01202903).

Model Parameters

- **Clinical Inputs (Table 1)**
  - ✓ Bucher ITC was used to compare the severe exacerbation rate between dupilumab trial population and omalizumab trial population.
  - ✓ All other parameters came from linical trial or expert consultations.

Table 1. Clinical Parameters of Markov Model

Parameters	Value (range)	Distribution
Long-term discontinuation (%)	7.8 (4,13)	Gamma
Reletive efficacy of severe exacerbation rate (oma vs. dupi)	2.5 (2.08, 3.13)	Lognormal
Reletive efficacy of moderate exacerbation/uncontrolled rate	1 (0.80,1.20)	Lognormal
Ajusted severe exacerbation rate after 24 weeks	1.35 (0.90,1.94)	Lognormal
Outpatient visits due to severe exacerbation (%)	18.8 (0.02,0.97)	Dirichlet
Emergency visits due to severe exacerbation (%)	55.84 (0.02,0.97)	Dirichlet
Hospitalization due to severe exacerbation (%)	25.34 (0.025,0.975)	Dirichlet

Utility Inputs (Table 2)

- ✓ All parameters were derived from the Chinese subgroup of dupilumab EFC13995 trial, the international LIBERTY ASTHMA QUEST and LIBERTY ASTHMA VENTUR clinical trials or published literatures.

Table 2. Utility Parameters of Markov Model

Utility	Value (range)	Distribution
Controlled asthma	0.974 (0.97,0.98)	Beta
Uncontrolled asthma	0.860 (0.84,0.88)	Beta
Moderate exacerbation	0.715	-
Outpatient visits or emergency visits	0.57 (0.42, 0.72)	Beta
Hospitalization	0.33 (0.05, 0.71)	Beta

Cost Inputs (Table 3)

- ✓ The unit price of drugs is based on the latest negotiated price of medical insurance and the average bid price of each province in the past year. The use and cost data of other medical resources came from the clinical expert consultations of five provinces and cities in China.

Table 3. Cost Parameters of Markov Model

Costs (CYN per 4 weeks)	Value (range)
<b>Drug costs:</b>	
Dupilumab (initial cycle)	3416.39 (2733.12, 3416.39)
Dupilumab (subsequent cycles)	2277.60 (1822.08, 2277.60)
Omalizumab	3612.00 (2889.60, 3612.00)
Background therapy	224.55
<b>Disease management costs:</b>	
Controlled asthma	460.51 (368.41,552.61)
Uncontrolled asthma	2,132.57 (1706.06,2559.09)
<b>Severe exacerbation costs:</b>	
Moderate exacerbation	1471.39 (1177.11,1765.67)
Outpatient visits due to severe exacerbation	1708.00 (1366.40,2049.60)
Emergency visits due to severe exacerbation	3206.99 (2565.59,3848.39)
Hospitalization due to severe exacerbation	14196.41 (11357.13,17035.69)

RESULTS

Base case results

- ✓ The incremental cost per QALY gained showed that dupilumab plus background therapy was **dominant**. (Table 4).

Table 4. Baes case results

Outcomes	Dupilumab + background therapy	Omalizumab + background therapy	increment
<b>Total costs (CNY)</b>	490,663	615,213	<b>-124,549</b>
Drug costs (CNY)	265,723	383,357	-117,634
Disease management costs (CNY)	168,403	165,121	3,282
Exacerbation costs (CNY)	56,537	66,734	-10,197
<b>Total LYs</b>	14.35	13.95	0.40
<b>Total QALYs</b>	13.11	12.68	<b>0.43</b>
<b>ICER (CNY/QALY)</b>	<b>dominant</b>		

Scenarios analysis results

- ✓ In this study, three additional scenarios were simulated (Table 5).

Table 5. Scenarios analysis results

Scenarios	Treatment plan	Costs /CNY	QALYs	ΔCosts	ΔQALY	ICER (CNY/QALY)
Omalizumab-like population was simulated	Dupilumab group	481,065	13.69	-123,020	<b>0.66</b>	<b>dominant</b>
	Omalizumab group	604,085	13.03			
Generic omalizumab + background therapy was used as the reference protocol	Dupilumab group	490,663	13.11	<b>-99,517</b>	0.43	<b>dominant</b>
	Omalizumab group	590,180	12.68			

Sensitivity analysis results

- ✓ ΔQALY-OWSA (Figure 2); Probabilistic sensitivity analysis (Figure 3).

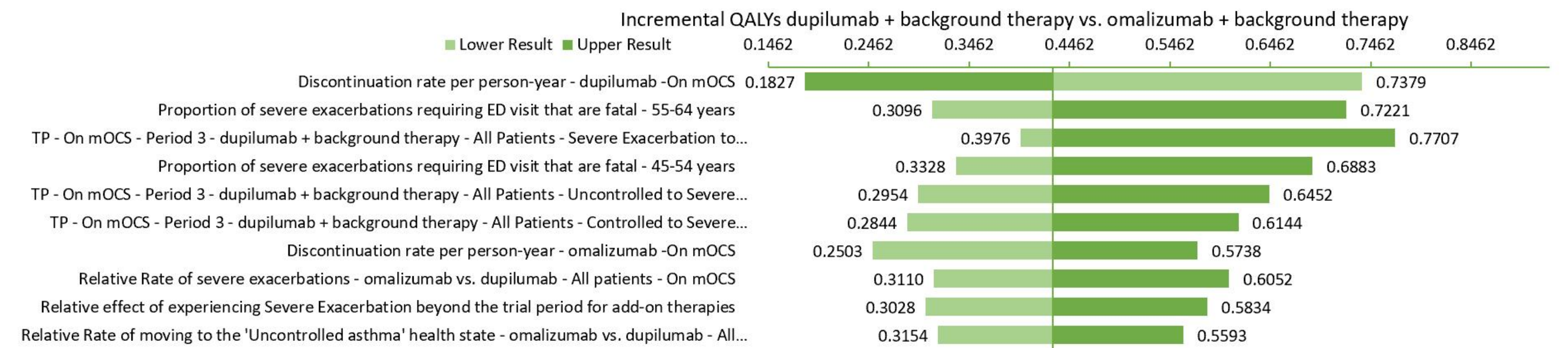


Figure 2. ΔQALY-OWSA tornado chart

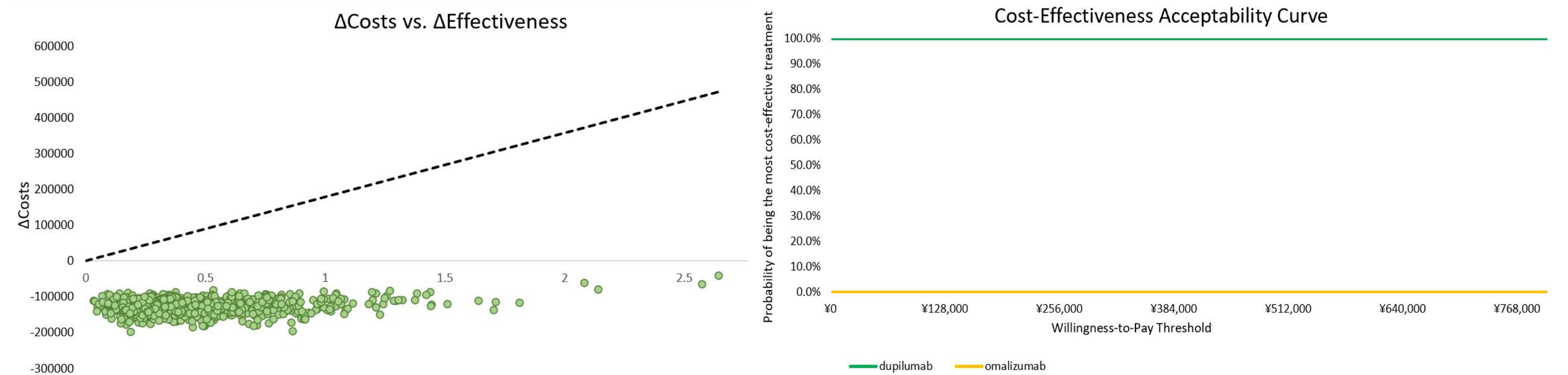


Figure 3. Scatter chart and CEAC

CONCLUSIONS

- As one of the biologics for severe asthma patients in China, dupilumab required the lowest annual drug costs among biologics. Compared with the first approved omalizumab, dupilumab was dominant in the treatment of severe asthma patients.

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