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COST-EFFECTIVENESS OF SUSTAINED-RELEASE DEXMETHYLPHENIDATE VERSUS PROLONGED-RELEASE METHYLPHENIDATE FOR PEDIATRIC ADHD: AN ANCHORED MAIC ANALYSIS

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BACKGROUND

Rising pediatric Attention-Deficit/Hyperactivity Disorder (ADHD) prevalence imposes substantial clinical and socioeconomic burdens worldwide. Newly approved in China, first generic sustained-release dexmethylphenidate (*d*-MPH-SR) offers potency and formulation advantages; yet its comparative pharmacoeconomic value remains unexamined.

OBJECTIVES

To evaluate the comparative efficacy and cost-effectiveness of ***d*-MPH-SR** versus the most prevalent stimulant, prolonged-release methylphenidate (**MPH-PR**), for **Chinese pediatric ADHD**.

METHODS

A hybrid short-term **decision tree** and long-term four-state **Markov model** simulated disease progression, quality-adjusted life-years (QALYs) and costs from **healthcare system** and **societal** perspectives.

- Lacking head-to-head trials, an **anchored matching-adjusted indirect comparison (MAIC)** integrating individual patient data (CTR20150202) and aggregate data from the Concerta study was performed to adjust for cross-trial heterogeneity and derive relative efficacy.
- Transition probabilities, costs and utilities were obtained from literature, public databases, clinician surveys and systematic reviews. Costs and QALYs were discounted at 4.5% annually.

Table 1 Model Input Parameters for Transition Probabilities, Utilities and Costs

Parameter		Value
Transition probabilities		
Optimal → Optimal, %		54.40
Optimal → Suboptimal, %		37.54
Optimal → Treatment modification/interruption, %		4.20
Optimal → Remission, %		3.86
Suboptimal → Optimal, %		17.70
Suboptimal → Suboptimal, %		72.89
Suboptimal → Treatment modification/interruption, %		8.43
Suboptimal → Remission, %		0.98
Treatment modification/interruption → Optimal, %		13.53
Treatment modification/interruption → Suboptimal, %		14.60
Treatment modification/interruption → Treatment modification/interruption, %		71.17
Treatment modification/interruption → Remission, %		0.71
Suboptimal	Medication adherence rate, %	79.56
Treatment modification/interruption	Medication switching, %	64.79
	Non-pharmacological therapy, %	23.81
	Treatment discontinuation, %	11.40
Resource utilization and direct cost data		
Days of medication use (non-adherent patients), days/month		19.19
Medication costs (monthly cost)		
Dexmethylphenidate - caps 12.87 mg daily, CNY (USD)		¥665.50 ($93.17)
Methylphenidate - tab 34.33 mg daily, CNY (USD)		¥1088.96 ($152.45)
Treatment modification/interruption (monthly cost)		
Medication switching, CNY (USD)	Dexmethylphenidate arm	¥794.93 ($111.29)
	Methylphenidate arm	¥118.64 ($16.61)
Non-pharmacological therapy, CNY (USD)		¥1301.90 ($182.27)
Treatment discontinuation, CNY (USD)		¥0 ($0)
Management cost		
Outpatient registration (monthly cost), CNY (USD)		¥29.97 ($4.20)
Diagnostic workup (per case), CNY (USD)		¥1842.78 ($257.99)
Follow-up visit (monthly cost), CNY (USD)		¥149.04 ($20.87)
Cost of adverse reaction (monthly cost)		
Headache, CNY (USD)		¥21.23 ($2.97)
Decreased appetite, CNY (USD)		¥104.89 ($14.68)
Insomnia, CNY (USD)		¥41.68 ($5.83)
Abdominal pain, CNY (USD)		¥369.79 ($51.77)
Nausea/Vomiting, CNY (USD)		¥108.63 ($15.21)
Asthenia, CNY (USD)		¥782.04 ($109.49)
Diarrhea, CNY (USD)		¥86.20 ($12.07)
Utility estimates for health states		
Utility for different health states		
Response		0.837
Non-response		0.773
Unable to tolerate		0.805
Optimal		0.820
Suboptimal		0.700
Treatment modification/interruption		0.650
Remission		1.000
Disutility for adverse reaction		-0.040

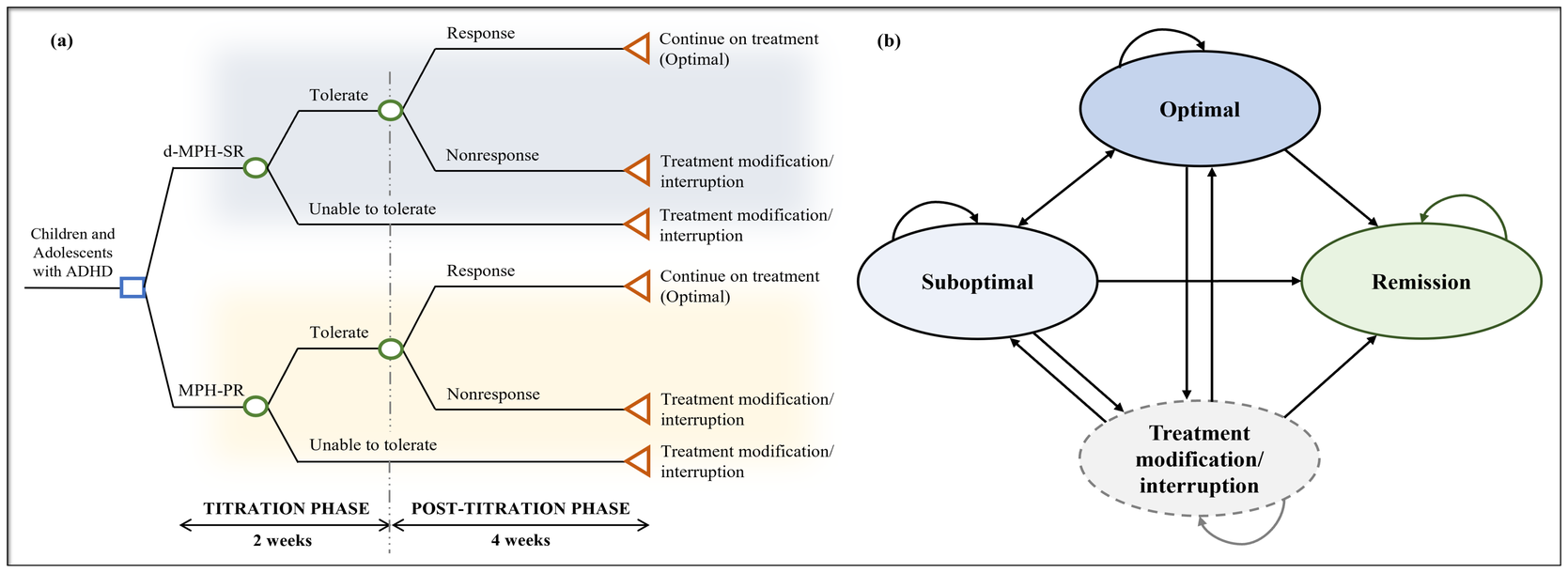

Fig.1 Decision tree (a) and Markov model (b)

Variables	Method	d-MPH-SR (mean)	MPH-PR (mean)	RD (95%CI)	*P* value
Tolerability, %	Naïve ITC	99.69	97.87	1.82 (-3.00 to 6.63)	0.459
	MAIC	100.00	97.87	2.14 (-1.12 to 5.40)	0.200
Improvement, %	Naïve ITC	49.14	46.70	2.44 (-10.21 to 15.09)	0.704
	MAIC	51.40	46.70	4.70 (-4.84 to 14.25)	0.337
AE, %	Naïve ITC	44.28	42.30	1.98 (-11.40 to 15.35)	0.771
	MAIC	37.60	42.30	-4.70 (-13.24 to 3.84)	0.277
Headache, %	Naïve ITC	8.44	14.40	-5.96 (-10.43 to -1.50)	**0.009**
	MAIC	6.94	14.40	-7.46 (-10.42 to -4.51)	**<0.001**
Abdominal pain, %	Naïve ITC	5.80	6.70	-0.90 (-5.68 to 3.87)	0.710
	MAIC	7.77	6.70	1.07 (-4.25 to 6.38)	0.696

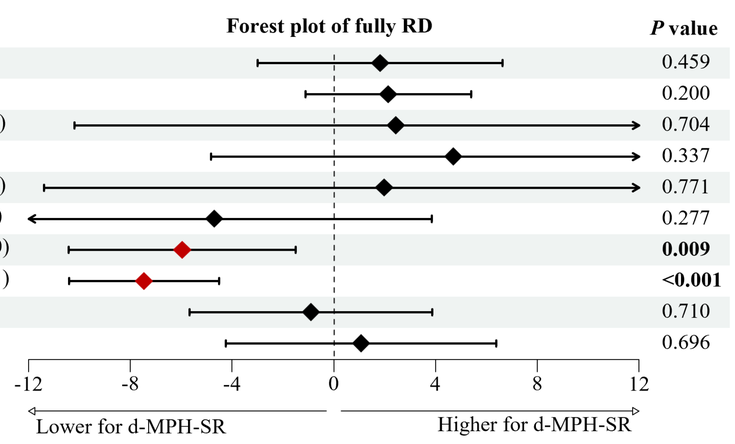

Fig.2 Forest Plot of Efficacy and Safety Outcomes for *d*-MPH-SR Versus MPH-PR Before and After MAIC Adjustment

Target population Variables	MPH-PR (N=185)	*d*-MPH-SR Before matching (N=214)		*d*-MPH-SR After matching (ESS=143)
	Mean/%	Mean/%	P value	Mean/%
Age				
Mean, years (SD)	8.85 (NA)	9.12 (2.23)	0.082	8.85
Aged 6-9 years, N (%)	120 (64.9)	125 (58.4)	0.058	64.9
Male, N (%)	149 (80.5)	182 (85.1)	0.067	80.5
Presence of comorbidity, N (%)	84 (45.4)	27 (12.6)	<0.001	45.4
History of prior treatment, N (%)	146 (78.9)	100 (46.7)	<0.001	78.9

- **Time horizon:** from childhood to adulthood
- **Cycle length:** monthly cycle

Model validation, scenario analyses and sensitivity analyses assessed robustness.

RESULTS

Base case: *d*-MPH-SR dominated MPH-PR

Table 3 Base-Case Results (Discounted)

	d-MPH-SR	MPH-PR	Difference
Remission rate, %	84.49	84.45	0.05
Total QALYs per patient	6.4886	6.4779	0.0107
Total costs per patient, CNY (USD)	¥85116.54 ($11916.24)	¥94698.72 ($13257.74)	-¥9582.17 (-$1341.50)
ICER, CNY/QALY (USD/QALY)	—	—	Dominate
Net monetary benefit, CNY (USD)	—	—	¥10647.25 ($1490.61)

Similar results were obtained in sensitivity *analysis*.

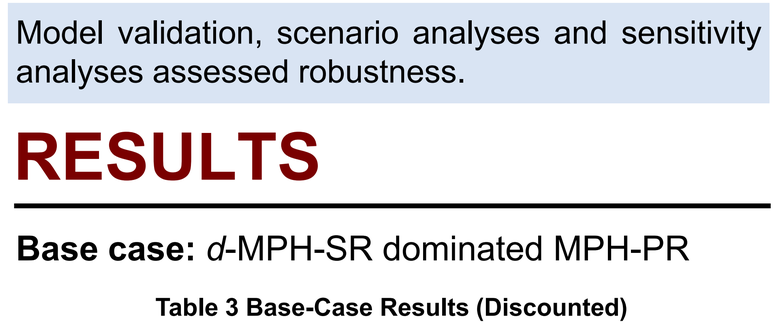

Fig.3 Tornado Diagram of One-Way Sensitivity Analysis

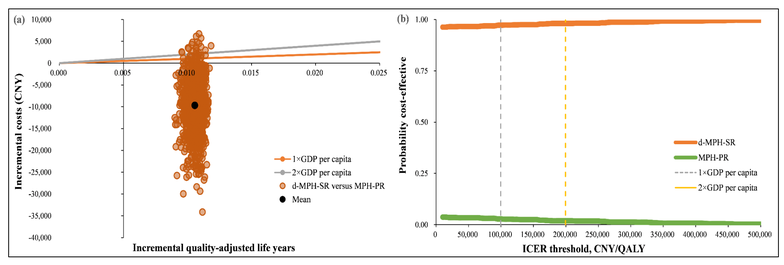

Fig.4 Probabilistic Sensitivity Analysis of *d*-MPH-SR Versus MPH-PR

CONCLUSION

This study presents the first cost-effectiveness evaluation of *d*-MPH-SR for ADHD. *d*-MPH-SR was demonstrated cost-effective compared to MPH-PR among Chinese children and adolescents.