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Cost-effectiveness Analysis of Rosuvastatin and Ezetimibe Single Pill Combination (SPC) versus Free Combination Treatment (FCT) in Chinese hypercholesterolemia adult patients

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INTRODUCTION

- The prevalence of hypercholesterolemia is approximately 8.1% in Chinese adults. There are estimated 93.2% patients at high atherosclerotic cardiovascular disease risk did not reach 2023 Chinese Lipid Management Guidelines recommended targets for low-density lipoprotein cholesterol (LDL-C) of < 1.8 mmol/L.[1]
- Statins combined with ezetimibe was recommended by guidelines to achieve the LDL-C goal.

OBJECTIVES

- This study aimed to evaluate the cost-effectiveness of single pill combination (SPC) versus free combination treatment (FCT) of Rosuvastatin 10mg/Ezetimibe 10mg in Chinese moderate to very-high risk hypercholesterolemia adult patients whose LDL-C was not adequately controlled receiving statin monotherapy (2023 Chinese Lipid Management Guidelines, IA).

METHODS

- **Perspective**: Chinese public healthcare system
- **Target population:** Chinese moderate to very-high risk hypercholesterolemia adult patients whose LDL-C was not adequately controlled despite on statin monotherapy.
- **Model structure:** A Markov model with seven health states was developed to assess the cost effectiveness of SPC versus FCT of rosuvastatin10mg / EZE 10mg. Clinical events considered in the analysis included non-fatal coronary revascularization, non-fatal myocardial infarction, non-fatal ischemic stroke, and death. All patients entered the model started from "Event-free" state and moved to different health states depending on the clinical events occurred (Figure 1).
- **Time horizon:** The model is set with a cycle length of one year and an 18-year time horizon, which aligned with the life expectancy of 79 years for Chinese patients.
- **Methods and demographics**
  - The baseline characteristic/CV risk were obtained from a local database study based on hypercholesterolemia patients on statin monotherapy and still did not reach the LDL-C goal (Table 1-2).[2]
  - LDL-C reduction of SPC of Rosuvastatin 10mg/Ezetimibe 10mg was derived from a Chinese multicenter retrospective case registry study (Table 3).[3] The superior effectiveness of SPC may be attributed to improved treatment adherence. The reduction of LDL-C level was translated to risk reduction of major adverse cardiovascular events (MACE), defined as MI/IS/coronary revascularization/CV death, based on CTT 2010 (Table 4).[4]
  - Cost and utilities were obtained from literature (table 5-6,8).[5-8]
  - The CV risk of patients on SPC were adjusted based on the additional LDL-C reduction sourced from local multicenter observational study （Table 7）.[3]
  - The discount rate was 5% for both costs and health outcomes. The willingness-to-pay threshold was set at the 2023 one gross domestic product per capita of China (¥89,358).
- **Sensitivity analysis**
  - One-way sensitivity analysis (PSA) was conducted to test the uncertainty: clinical inputs were using 95% confidence interval, costs and health outcomes were using -20% to 20%. Probabilistic sensitivity analysis (PSA) was also adopted to verify the robustness.

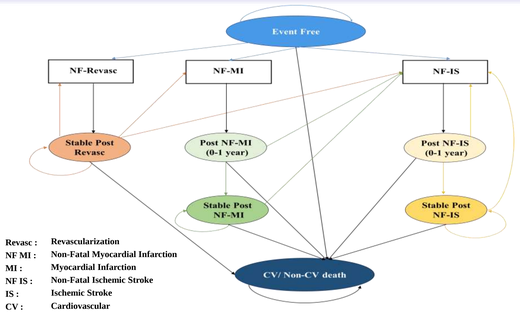

Figure 1 Markov model

Table 1 Baseline patient characteristics[2]

Parameter	Value
Initial age (years)	61
Baseline LDL-C (mmol/L) level	3.4
Proportion of males	52.94%

Table 2 Baseline event probabilities in patients[2]

		To event			
	Untreated patients	MI	IS	Revascularization	CV Death
From state	Event free	2.33%	4.82%	3.18%	1.16%
	Post non fatal MI (0-1 year)	7.02%	1.95%	16.76%	7.38%
	Stable post non fatal MI	0.40%	4.57%	0.48%	2.17%
	Post non fatal IS (0-1 year)	1.27%	27.76%	1.82%	3.50%
	Stable post non fatal IS	1.78%	0.57%	3.86%	2.04%
	Post Revasc	2.28%	1.90%	24.62%	2.45%

Table 3 Overall reduction in LDL-C from baseline for SPC and FCT[3]

Treatment	LDL-C Efficacy (% reduction in LDL-C)	Standard deviation	
SPC	43.17%	± 16.11%	P<0.01
FCT	29.14%	± 29.13%	

Table 4 Risk reduction rate by event type (which is ratio per 1 mmol/L reduction) inputs

	Events type (MACE)	Rate Ratio per 1.0 mmol/L reduction in LDL-C[4]
All years	Non-fatal MI	0.74
	Non-fatal IS	0.79
	Stable post Revasc	0.77
	CV death	0.88

Table 5 Event costs

Health states	Event costs	(0-1 year)	Stable (> 1 year)
Event free	¥0.00	¥0.00	¥0.00
NF-MI[5]	¥41,308.54	¥9,236.04	¥9,236.04
NF-IS[5]	¥18,017.88	¥9,367.62	¥9,367.62
Post Revasc[5]	¥72,975.69	¥9,236.04	¥9,236.04
CV death[5]	¥43,531.49	¥0.00	¥0.00
Non-CVdeath	¥0.00	¥0.00	¥0.00

Table 6 Drug costs of treatments

Treatment	Daily cost (¥)	PDC	Duration of treatment per year (days)	Annual cost (¥)
SPC	3.10	0.73	266	**826**
FCT	3.60	0.55	201	**722**

Table 8 Utilities

Health states	Utility (0-1 year)	Utility Stable (> 1 year)
Event free[6]	0.91	0.91
NF-MI[7]	0.67	0.82
NF-IS[7]	0.33	0.52
Post Revasc[8]	0.90	/
CV / Non-CV death	0.00	/

Table 7 The CV risk of patients on SPC

		To state							
	Health states	Post NF-MI (0-1 year)	Stable post NF-MI	Post NF-IS (0-1 year)	Stable post NF-IS	Event free	Post Revasc	CV death	Non-CV death
From state	Event free	1.50%	-	3.43%	-	Remainder	2.14%	0.96%	Age-Dependent
	Post NF-MI (0-1 year)	4.571%	Remainder	1.38%	-	-	-	6.16%	Age-Dependent
	Stable post NF-MI	0.26%	Remainder	3.26%	-	-	-	1.80%	Age-Dependent
	Post NF-IS (0-1 year)	-	-	20.55%	Remainder	-	-	2.91%	Age-Dependent
	Stable post NF-IS	-	-	0.40%	Remainder	-	-	1.69%	Age-Dependent
	Post Revasc	1.47%	-	1.35%	-	-	Remainder	2.04%	Age-Dependent
	CV death	-	-	-	-	-	-	100%	-
	Non-CV death	-	-	-	-	-	-	-	100%

RESULTS

Base case analysis

- Compared with FCT, patients treated with SPC was associated with cost savings of 8,232 RMB per patient, with an incremental greater quality-adjusted life years (QALY) of 0.177. The incremental cost effectiveness ratio (ICER, -46,508 ¥/QALY) below the willingness-to-pay threshold (2023 one gross domestic product per capita of China, ¥89,358). (Table 9)
- Compared to FCT, SPC reduces total MACE by 203 events per 1000 person, and Number Needed to Treat (NNT) was 4.93 (Table 10).

Table 9 Base case results

Treatment	Total costs/¥	Total QALY	ICER (¥/QALY)
SPC	99,938	8.316	
FCT	108,171	8.139	
Increment	-8,232	0.177	**-46,508 (Dominant)**

Table 10 Number of adverse events avoided per 1000 patients

	SPC	FCT	Increment
MI	247	278	-31
IS	569	626	-57
Revasc total	676	768	-92
CV death	307	330	-23
Total	1,799	2,002	-203
NNT		4.93	

Sensitivity analysis

- One way sensitivity analysis demonstrated that the three most influential factors were the unit cost of SPC at the minimum dosage, the risk reduction rate of any CV death, and the risk reduction rate of revascularization (Figure 2).
- PSA employed 1000 Monte Carlo simulations for parameters. Results showed SPC was dominant with higher QALY gains and lower costs over FCT. It further confirmed the robustness of the results (Figure 3).

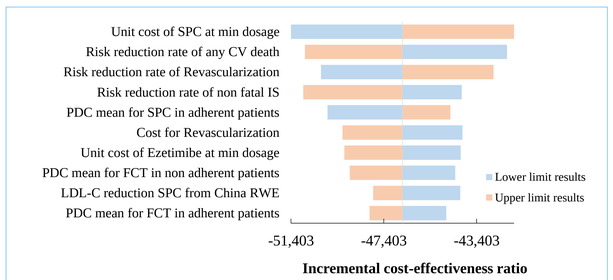

Figure 2 Tornado diagram

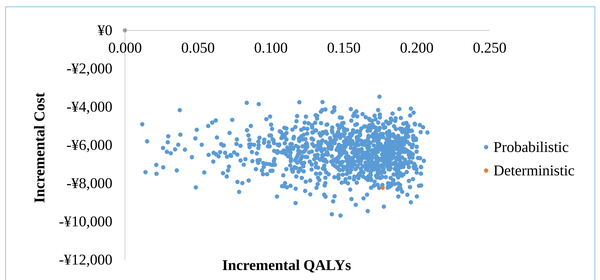

Figure 3 Incremental cost-effectiveness scatterplot

CONCLUSIONS

- SPC demonstrates dominant economic and health value than FCT of Rosuvastatin 10mg/Ezetimibe 10mg in hypercholesterolemia patients whose LDL-C still above target despite on statin monotherapy in China from public healthcare perspective.

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