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Cost-Effectiveness Analysis of Icosapent Ethyl (IPE) for the Reduction of the Severe Hypertriglyceridemia (HTG) in China

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BACKGROUND

- Severe hypertriglyceridemia (Severe HTG), defined as a triglyceride (TG) concentration ≥ 500 mg/dL (≥ 5.7 mmol/L), is not only associated with residual risk of cardiovascular disease (CVD) for patients with reduced low-density lipoprotein cholesterol[1], but also has been shown to be an independent risk factor for the severity and recurrence of hypertriglyceridemia-induced severe acute pancreatitis (HTG-SAP)[2].
- Icosapent ethyl (IPE; formerly AMR101), as a high-purity prescription form of eicosapentaenoic acid ethyl ester, could efficiently and safely diminish serum TG by 19.9% when compared to placebo in individuals with extremely high TG levels (5.6~22.3 mmol/L) in the Phase III randomized clinical trial (RCT) in China (CTR20170362)[3].This result validated the effectiveness and safety of IPE in a Chinese patient group, consistent with the findings of the MARINE trial (NCT01047683) [4] in the Western community.
- However, no studies have reported whether the IPE treatment is cost-effectiveness in China.

OBJECTIVE

- To compare the cost-effectiveness of IPE to placebo for long-term clinical benefit in patients with severe HTG from the perspective of Chinese health care system.

METHODS

Model structure and setting

- A cost-effectiveness analysis was conducted based on a twelve-state Markov model (Figure 1), whose health states included severe HTG, HTG, first event of ischemic stroke (IS), post IS, IS recurrence, first event of myocardial infarction (MI), post MI, MI recurrence, first event of HTG-SAP, post HTG-SAP, HTG-SAP recurrence, and death.
- A lifetime time horizon.
- Corrected by half-cycle correction
- 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: 3 times China's per capita GDP (¥257,094/QALY, 2022)

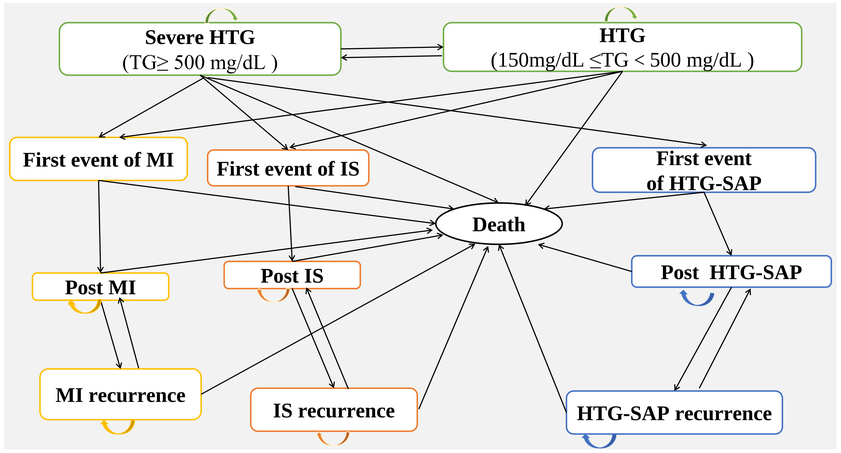

Figure 1. Markov Model

Study population

- The target population of this study was adults with severe HTG who had not previously had any CVD events or HTG-SAP events. The baseline characteristics of the simulated patients in the model were consistent with population in the Phase III RCT in China (CTR20170362) [3].

Intervention and control group

- The intervention group: IPE (4g/day, ¥50/day). The usage and dosage are consistent with its instructions. It is assumed that the number of days that the patient complies with the medication in a year is 80%. The control group: no intervention.

Model input

- **Effectiveness Parameters (Table 1,2,3)**
- As shown in the Table 1, effectiveness parameters of IPE and placebo were obtained from the Phase III RCT in China[3]. Other parameters about effectiveness were extracted from the published literature(Table 2 and 3).

Table 1. Annual probability of transitions between different health states

Event		Mean value	Event	Mean value
Severe HTG → HTG	Placebo	40.54%[3]	IS recurrence	12.50%[5]
	IPE Intervention	62.39%[3]	MI recurrence	2.50%[6]
HTG → Severe HTG	Placebo	31.11%[3]	HTG-SAP recurrence	1.36%[7]
	IPE Intervention	25.00%[3]	IS mortality in the general population	15.00%[8]
Severe HTG → HTG-SAP		4.86%[3]	MI mortality in the general population	7.90%[9]
			HTG-SAP specific mortality	33.00%[10]

Table 2. Annual probability of different event in the general population

Age	IS[11]	Age	All-cause mortality[13]
40-49	0.14%	45-49	0.20%
50-59	0.34%	50-54	0.32%
60-69	0.67%	55-59	0.53%
70-79	1.34%	60-64	0.78%
80+	2.75%	65-69	1.29%
Age	MI[12]	70-74	2.22%
45-54	0.06%	75-79	3.86%
55-64	0.13%	80-84	6.49%
≥65	0.36%	≥85	15.18%

Table 3. Relative risks (RRs) of the annual incidence of events

RRs for different patients v.s general population	IS	MI	All-cause mortality
Patients with HTG[14]	1.61	2.3	1.49
Patients with severe HTG[14]	2.3	1.61	3.08
Patients taking IPE[15]	0.72	0.69	-
Patients with IS[16]	-	-	1.49
Patients with MI[17]	-	-	3.08

- **Utility (Table 4)**
  - Utility values were sourced from the published literature[18-22].

Table 4. Utility

Utility	Base-case	Lower value	Upper value
Severe HTG[18-20]	0.857	0.686	1.000
HTG[20]	0.946	0.757	1.000
First event of IS or IS recurrence[21]	0.327	0.262	0.392
First event of MI or MI recurrence[21]	0.672	0.538	0.806
First event of HTG-SAP[22]	0.695	0.556	0.834
Post IS[21]	0.524	0.419	0.629
Post MI[21]	0.824	0.659	0.989
Post HTG-SAP[22]	0.798	0.638	0.958

- **Costs (Table 5)**
  - From the perspective of Chinese health care system, this study only includes direct medical costs and utility values were sourced from the published literature[23-25].

Table 5. Costs

Annual treatment costs	Base-case (¥)	Lower Value (¥)	Upper Value (¥)
IPE	14,600	11,680	17,520
First event of IS or IS recurrence[23]	50,392	40,313	60,470
First event of MI or MI recurrence[23]	40,020	32,016	48,025
First event of HTG-SAP[24]	77,236	61,789	92,683
Post IS[23]	9,548	7,638	11,457
Post MI[23]	8,941	7,153	10,729
Post HTG-SAP[25]	1,311	1,049	1,573

Sensitivity analysis

- **One-way sensitivity analysis:** The maximum and minimum values of the parameters in the model were their 95% confidence intervals or the range of 20% plus or minus the mean value of these parameter.
- **Probabilistic sensitivity analysis:** the model used the Gamma distribution to model costs, the Beta distribution to model probabilities, the Lognormal distribution to model parameters about relative risks.

RESULTS

Base-case analysis (Table 6)

- Compared with placebo, IPE resulted in a total incremental cost per patient of ¥149,980, but provided an additional 0.75 QALYs. The ICER was ¥198,939/QALY gained, indicating that IPE is cost-effective at the WTP threshold of ¥257,094 per QALY in 2022 (3 times of GDP in China).

Table 6. Results of base-case analysis

Index	IPE intervention	Placebo	Incremental
Total cost	¥ 187,868	¥ 37,888	¥137,511
QALYs	11.43	10.68	0.75
ICER	-	-	¥198,939/QALY

Sensitivity analysis

- **One-way sensitivity analysis (Figure 2)**
  - Top 3 parameters that have the greatest impact on the results were utility value of HTG and discount rate and utility of Severe HTG.

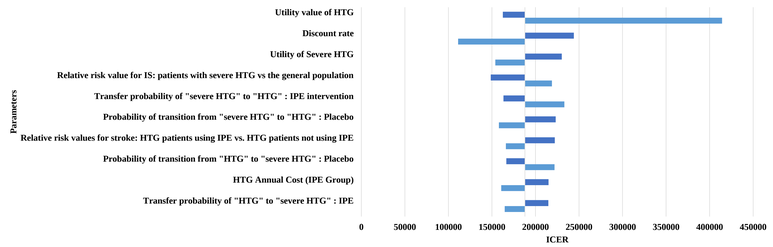

Figure 2. Tornado Diagram

- **Probabilistic sensitivity analysis (Figure 3,4)**
  - The probability of the IPE being cost-effective is 73% at the ¥257,094/QALY threshold.

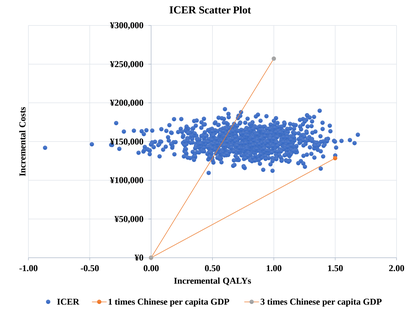

Figure 3. ICER Scatter Plot

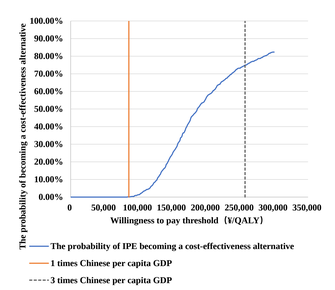

Figure 4. Cost-Effectiveness Acceptability Curve

CONCLUSIONS

- IPE is cost-effectiveness versus placebo for Chinese patients with severe HTG due to reducing the risk of CVD and HTG-SAP in the long-term.

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