

COST-EFFECTIVENESS ANALYSIS OF PROPHYLAXIS VS. ON-DEMAND TREATMENT FOR HAEMOPHILIA B CHILDREN WITHOUT INHIBITOR IN CHINA

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Background

- HaemophiliaB (HB) is a hereditary bleeding disorder caused by a deficiency of coagulation factor IX (FIX),which represents 15~20% of the hemophilia patients. Currently, replacement therapy is the dominant treatment, including on-demand(OD) and prophylaxis treatment. Clinical studies have demonstrated significant benefits of prophylaxis treatment versus OD treatment. However, these benefits are associated with an considerable costs, and most of Chinese HB pediatric patients are on OD treatment. Joint bleed is the most common bleeding manifestation in persons with hemophilia. The resulting joint disability is the most common complications in these patients receiving inadequate treatment.
- The objective of this study was to assess the cost effectiveness of prophylaxis treatment compared with OD treatment in HB children without inhibitors from the healthcare perspective

Methods

Model design

A Markov model was designed and populated. A year model cycle was used to estimate the cost and health effects for each treatment. Patients with HB entered into the model at 2 years of age, taking into consideration of international recommendation about the start treatment for prophylaxis. the base case model ran for 17 yearly cycles accounting for the life expectancy.

The primary outcome of interest was incremental cost-effectiveness ratio (ICER) of on-demand treatment compared with prophylactic treatment, which was defined as the difference in costs of on-demand treatment versus prophylaxis divided by the difference in effectiveness per Quality-adjusted life years (QALYs) gained. Clinical outcome was presented in terms of QALYs gained. A theoretical cost-effectiveness threshold of one up to three times the current gross domestic product (GDP) in Beijing per -capita in 2018 was set as decision rule, and the number is ¥193932.

Model structure

Patients in the model could experience four health states including Extra-articular bleeding, articular bleeding, joint damage or disabled.

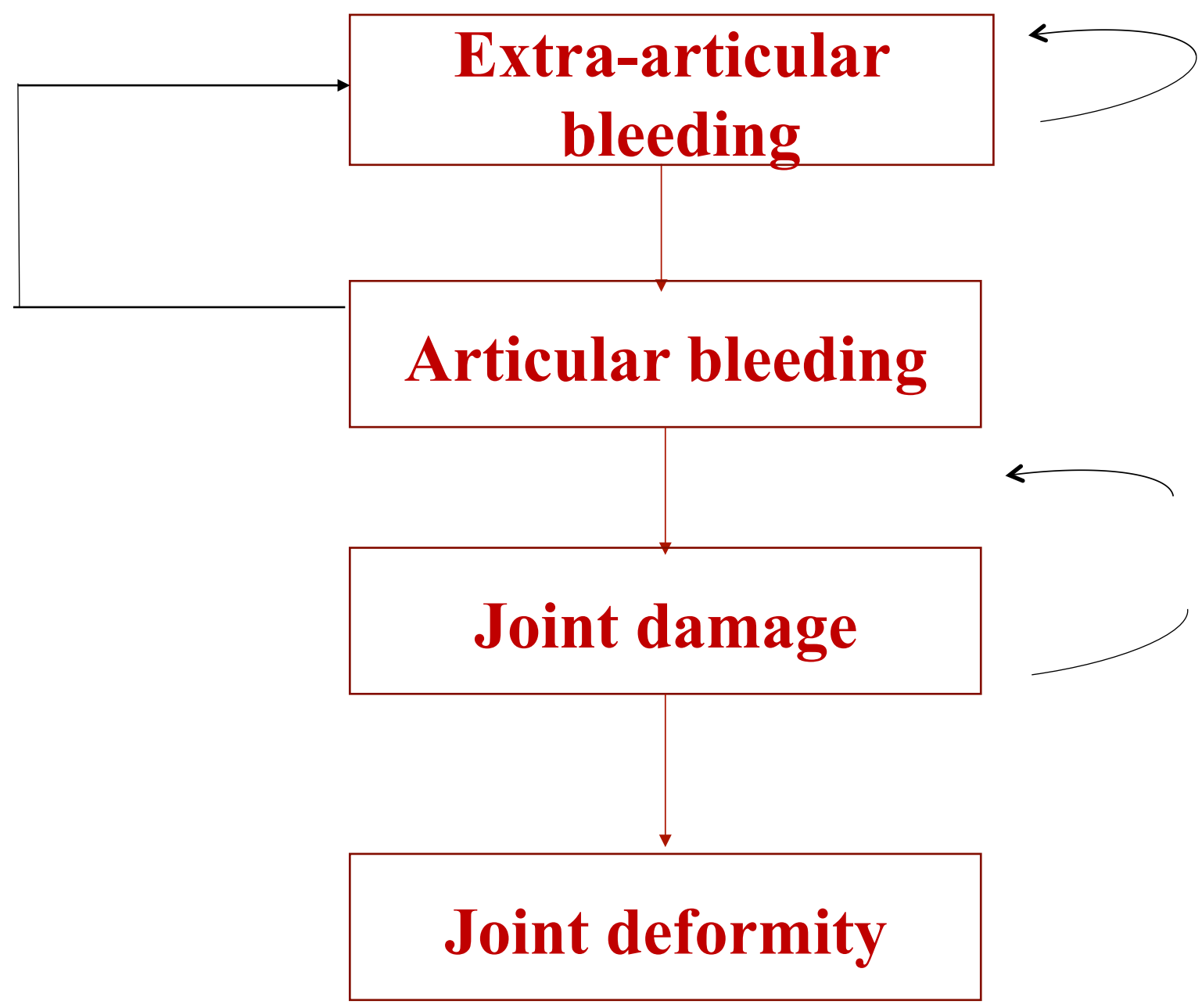


Figure 1. Markov model layout

Population

For this analysis, the patient population were from Beijing Children’s Hospital, Captital Medical University from Oct 2012 to Oct 2018. The cost data for 48 Hemophilia B children aged less than 18 years and without any inhibitors were enrolled.

Data source

Transition probability and utility

Transition probabilities and utilities were extracted from the published literature(**Table 1**).

Table 1. Transition probabilities and Utilities

Variable	Base case	Source
Probability		
On-demand		
Extra-articular bleeding to articular bleeding	0.800	Reference ⁴
Articular bleeding to Extra-articular	0.800	Calculated
Articular bleeding to joint damage	0.185	Reference ⁵
Joint damage to disabled	0.023	Reference ⁶
Prophylaxis		
Extra-articular bleeding to articular bleeding	0.094	Reference ^{4,7}
Articular bleeding to Extra-articular	0.964	Calculate
Articular bleeding to joint damage	0.036	Reference ⁵
Joint damage to disabled	0.007	Reference ⁶
Utility		
on-demand/ prophylaxis		
Normal	0.937	Reference ⁴
Joint bleeding	0.875	Reference ⁸
Joint damage	0.739	Reference ⁴
Disabled	0.190	Reference ⁶
Others		
Discount rate for costs	3%	Specified
Discount rate for utility	3%	Specified
Number of cycles	17	Specified

Cost

All relevant costs associated with clinical events included in the model were collected except the cost of the disabled, Annually cost per patient was computed. The total cost includes drug cost, and the other costs like hospitalization, examination, and treatment fee were used in this study. In addition, since no patients occurred disabled in both groups, the value for disabled was referred from the literature, and set the same in both groups. (**Table 2**).

Table 2. Costs summary included in the study

Annually Cost/per patient (¥)	Drug cost	Other cost
On-demand		
Extra-articular bleeding	1700.00	425.50
Articular bleeding	1400.00	350.00
Joint damage	2400.00	450
Disabled ¹¹	7663.99	34749.91
prophylaxis		
Extra-articular bleeding	24000.00	3000.00
Articular bleeding	45000.00	5000.00
Joint damage	2400.00	450.00
Disabled ¹¹	7663.99	34749.91

Results

Base case result

In the base case, the incremental cost-effectiveness ratio (ICER) calculated for PP versus OD treatment until 18 years old was ¥125919.86 per QALY gained, and considered cost-effective.

Table 3. Base case results

Strategy	Cost(¥)	Incremental cost	Effectiveness (QALYs)	Incremental effectiveness	ICER
On demand	45338.27		13.726		
prophylaxis	302076.76	256738.48	15.765	2.039	125919.86

Sensitivity analysis

One way and probabilistic sensitivity analysis (PSA) to estimate the impact of uncertainty of parameters and structural assumptions of the model in the cost-effectiveness results. the tornado result indicates that utility of Extra-articular bleeding is the most influential factor in the model(**Figure 2**).

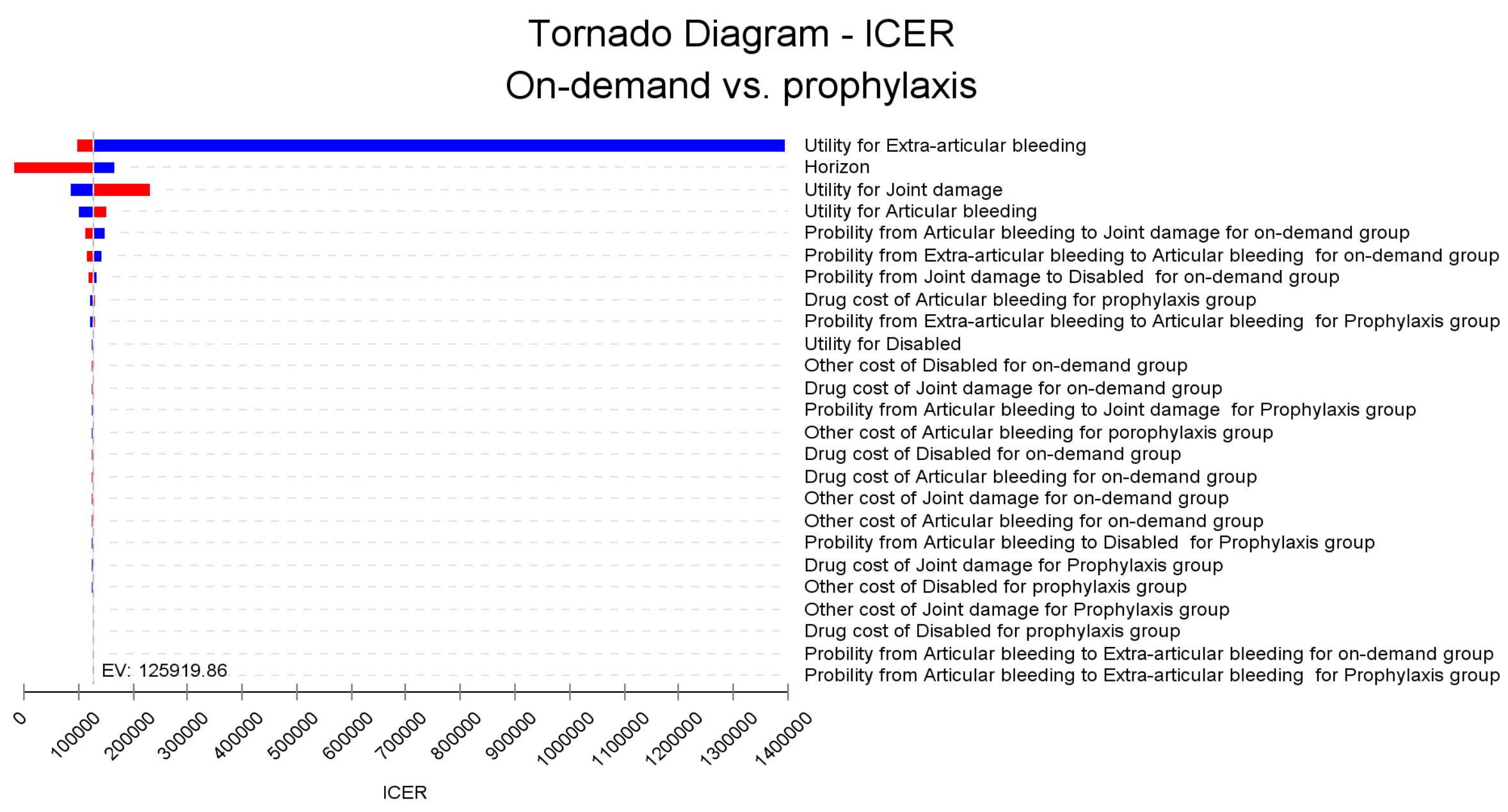


Figure 2. Tornado analysis

Probabilistic sensitivity analysis result demonstrates the probability of prophylaxis being cost –effective is 100% (**Figure 3**).

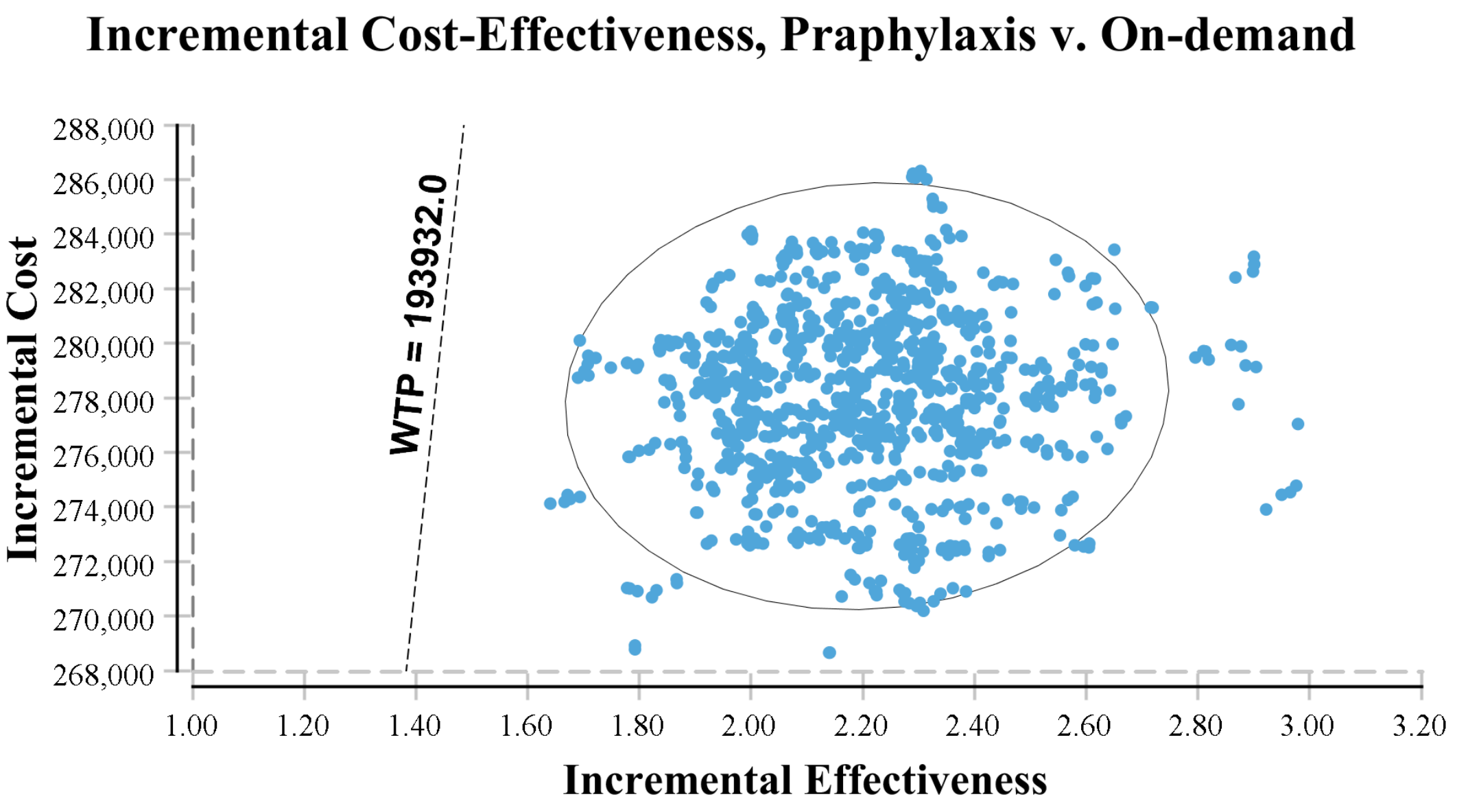


Figure 3. Probability sensitivity analysis result

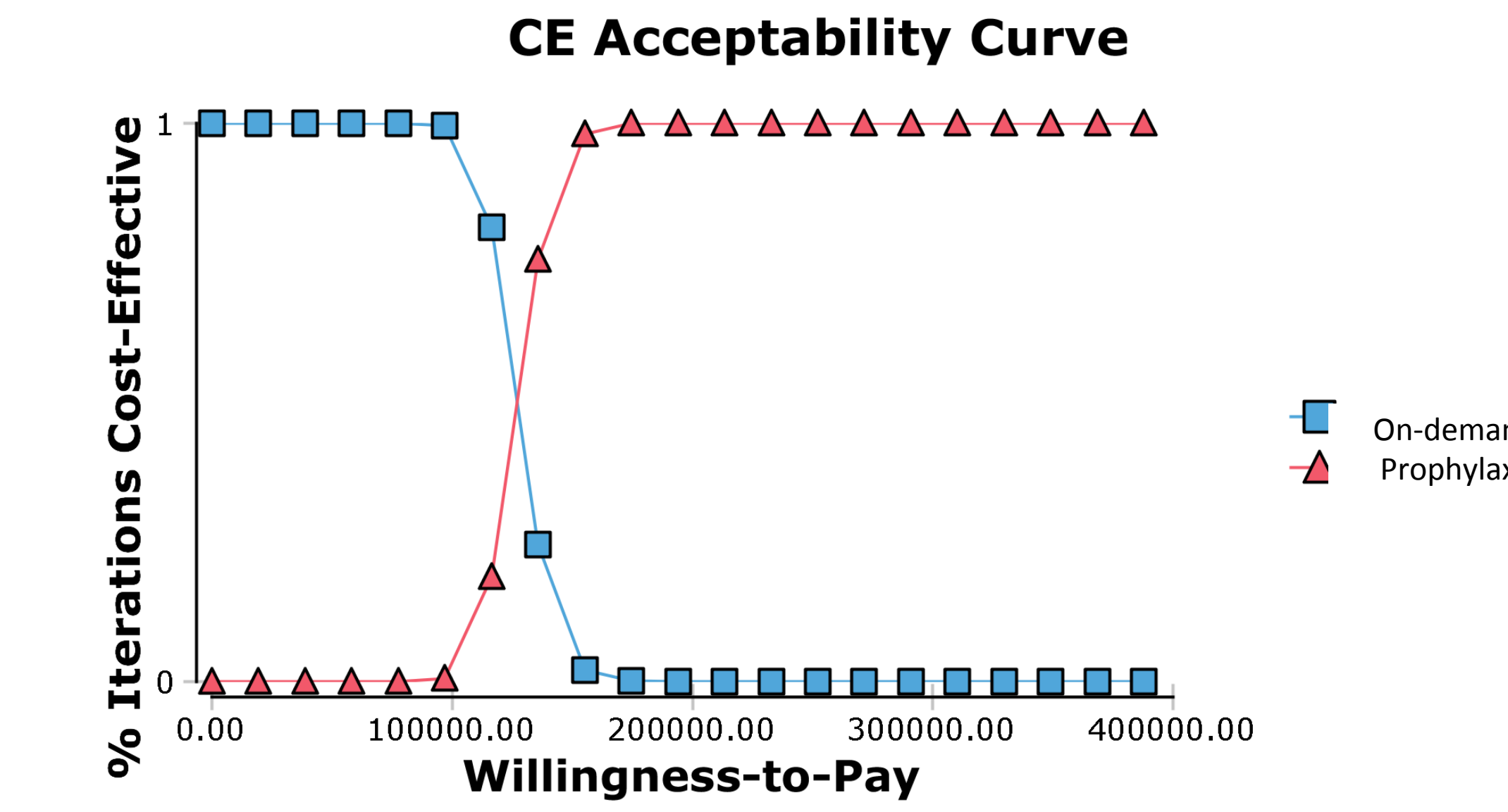


Figure 4. CE acceptability curve result

Discussion

The results showed that the patients received prophylaxis treatment improved their utilities compared with the patients received on-demand treatment. In addition, the ICER of prophylaxis treatment is less than willingness to pay, which means prophylaxis is a cost-effective treatment option.

Cost-effectiveness analysis in this study has some limitations. Firstly, the data included in this study focused on one hospital, more data should be assessed in the future. Secondly, transition probability is used from a literature, since it’s difficult to obtain the follow up data in China. Thirdly, utility is also referred to the values from the literature abroad.

Conclusion

In conclusion, using a decision rule of up to three times of China GDP per capita, PP would be considered as a cost -effective treatment option for HB patients in China.

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