

Cost-Effectiveness of emicizumab prophylactic treatments Versus Recombinant Activated FVII On-Demand Therapy for Hemophilia A with Inhibitors in China

Ziyi Lin¹, Xuerong Ran², Yan Xia², Xin Liu², Christian Buhner³, Jianwei Xuan¹

¹Sun Yat-san University, Guangzhou, China. ²Shanghai Roche Pharmaceuticals Ltd., Shanghai, China. ³F. Hoffmann-La Roche Ltd., Basel, Switzerland

Introduction

✧Hemophilia A: an inherited coagulation disorder caused by mutation or defect of the FVIII gene on the X chromosome. Arthrorrhagia is the most common type of bleeding and can lead to disability in severe cases. Incidence: 1/5,000 ^[1].

✧Neutralizing antibodies (inhibitors) to FVIII occur after receiving FVIII treatment, which is the most serious complication of hemophilia A treatment. In China, the proportion of patients with inhibitors is 3.9%, and the prevalence of inhibitors in severe patients was 4.3% ^[2].

✧The main clinical burden associated with spontaneous and prolonged bleeding and the presence of FVIII inhibitors is the serious one. Hemophilia A also has a significant impact on patients' quality of life. The financial burden of the patients with inhibitors is more burdensome, with annual medical costs 3.3 times higher than those of patients without inhibitors ^[3].

✧As the world's first subcutaneous injection drug in the field of hemophilia, emicizumab is effectively reduce the number of bleeding patients with good safety and tolerability. However, the cost-effectiveness of emicizumab is unknown in China.

Objective

✧ Evaluating the cost-effectiveness of emicizumab prophylactic treatments versus rFVIIa on-demand therapy for HA patients with inhibitors in China.

Methods

- Population: hemophilia A patients with inhibitors
- Model structure: a Markov model with two states (hemophilia A with inhibitors and death) and two events (treated bleed and arthroplasty) (see Figure 1)
- Comparison: emicizumab prophylactic treatments versus rFVIIa on-demand therapy
- Perspective: the Chinese healthcare system and the societal and two scenarios: whole life years and 1-12 years.

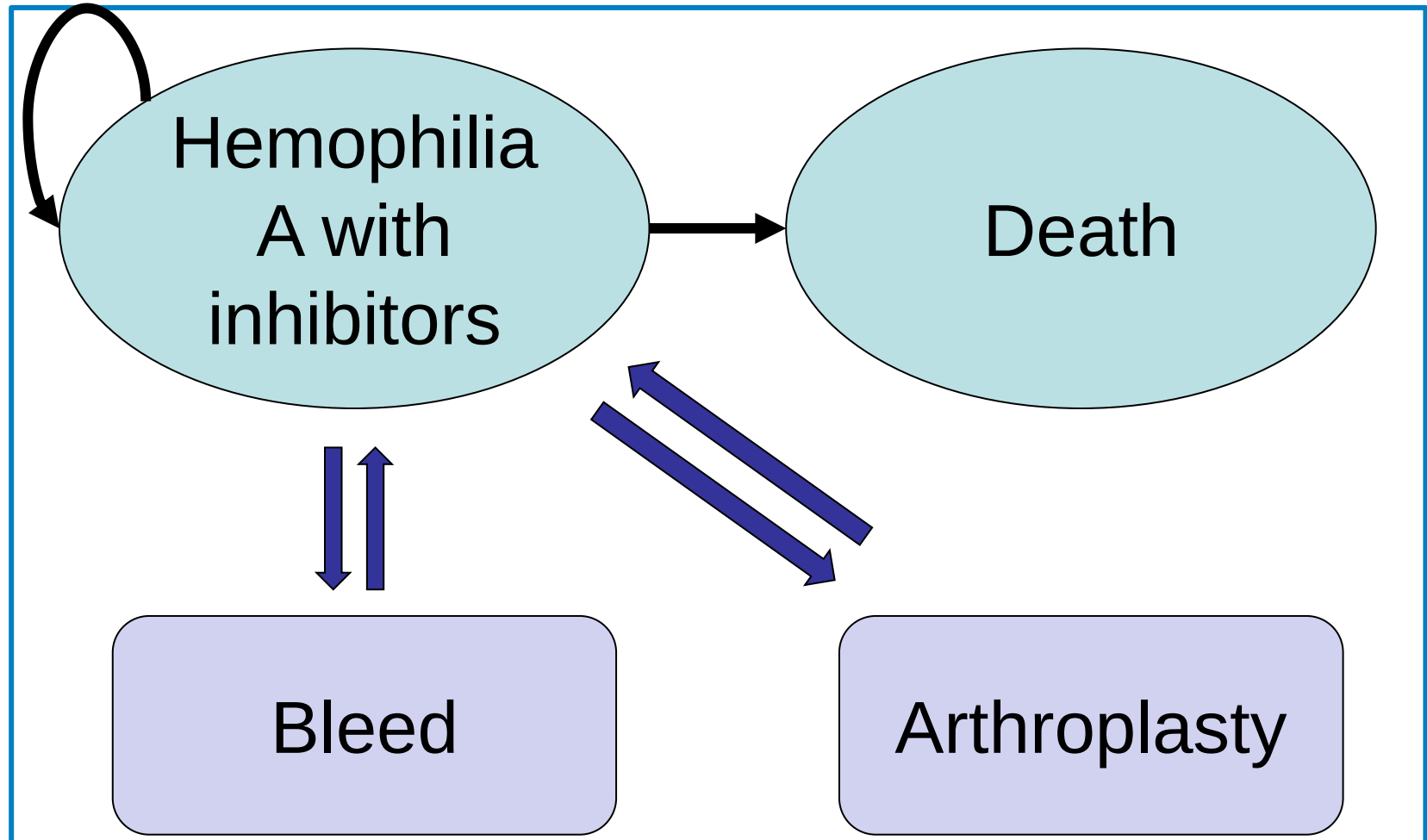


Figure 1 | Model structure

Model parameters Population characteristics

- The weight data used for dose calculation of patients aged 3-69 were obtained from the National Physical Fitness Monitoring Bulletin in 2014 ^[4].

Clinical Data

- Compare to on demand one, emicizumab prophylactic reduce 87% and is significant in > 12 years old group and reduce 99% in <12 years old group

Table 1: Annual number of bleeding with emicizumab prophylaxis versus on-demand treatment

Parameters	emicizumab prophylactic treatment	no prophylactic treatment
ABR* of >= 12 ^[5]	2.9	23.3
ABR of < 12 ^[6]	0.3	19.9

*ABR: annualised bleed rate

- Assume that patients with on-demand treatment would undergo two joint surgeries (age=25, sd=2.5; age=35, sd=3.5).

Cost Data

- The unit price of emicizumab is 270 yuan /mg. On bleeding, all patients need to be treated on demand with rFVIIa due to the inhibitor status.

Table 2: cost for two groups

	emicizumab prophylactic treatment	rFVIIa on-demand treatment
Unit price	CNY 270/mg	CNY 5500/mg
dosage	Loading: 3mg/kg qw for 4 weeks; Maintain: 1.5mg/kg qw ^[9]	0.295mg/kg (each bleeding)
Length of inpatient days	0	2.5
Daily cost of hospitalization	CNY 1800/day ^[10]	
Cost for hiring care worker	CNY 636.4/year	
Hours spend on informal care	465.47hours/year	761.27hours/year

- Cost of arthroplasty was assumed to equal to the cost of normal arthroplasty plus additional clotting drugs.
- The average length of hospital stay of two groups was based on the results of a Hemophilia Burden of Disease Study in China.
- Adverse event cost data come from clinical expert interview.
- Main parameters of costs were used in model could be presented in table 2.

Utility Data

- The utility of prophylactic and non-prophylactic treatment was derived from the HAVEN 1 clinical trial ^[5]. Assuming that the utility value decreases to 0 ^[11] after joint surgery for approximately 8.1 days ^[12].

Table 3 each state's utility

state	Mean value	95%CI	distribution
emicizumab prophylaxis	0.83	(0.77-0.89)	Beta
Non-prophylaxis	0.65	(0.57-0.73)	Beta
Joint surgery	0	-	-
death	0	-	-

Sensitive analyses

- Both the one-way sensitivity analyses (1WSA) and probabilistic sensitivity analysis (PSA) were conducted.

Results

Base case results

- Scenarios 1: For time horizon of all life, emicizumab prophylactic treatments could gain 4.03 QALYs, saved CNY 10.73 million from the health care system perspective and save about CNY 11 million from societal perspective.
- Scenarios 2: For time horizon of 12 years, emicizumab prophylactic treatments gained 1.72 more QALYs, saved CNY 2.5 million from the health care system perspective and save CNY 2.6 million from societal perspective.

Sensitivity analysis

- The ABR data and the discount rate for cost are the parameters with the most significant impact on the results.
- Through a 1000-iteration Monte Carlo simulation, the probability of emicizumab prophylactic treatment being cost-effective was found always greater than 90%

Table 3: cost-effectiveness analysis results for whole life

	emicizumab prophylaxis	rFVIIa on-demand treatment	difference
Number of bleeding	36	427	-390
QALY	16.68	12.65	4.03
Total cost (healthcare system perspective)	¥23,855,434	¥35,582,357	¥-10,726,923
Total cost (societal perspective)	¥24,354,162	¥35,364,337	¥-11,010,174
ICER	emicizumab prophylaxis dominates		

Table 4: cost-effectiveness analysis results under for 1-12 years

	emicizumab prophylaxis	rFVIIa on-demand treatment	difference
Number of bleeding	5	187	-182
QALY	7.70	5.98	1.72
Total cost (healthcare system perspective)	¥5,190,860	¥7,672,687	-¥2,481,827
Total cost (societal perspective)	¥5,374,782	¥7,977,523	-¥2,602,741
ICER	emicizumab prophylaxis dominates		

>12 ABR-OD
2-12 ABR-OD
Discount for cost
>12 ABR –Emi
Discount for effect
Utility-OD
Utility-Emi
SMR-OD
SMR-Emi
2-12 ABR-Emi

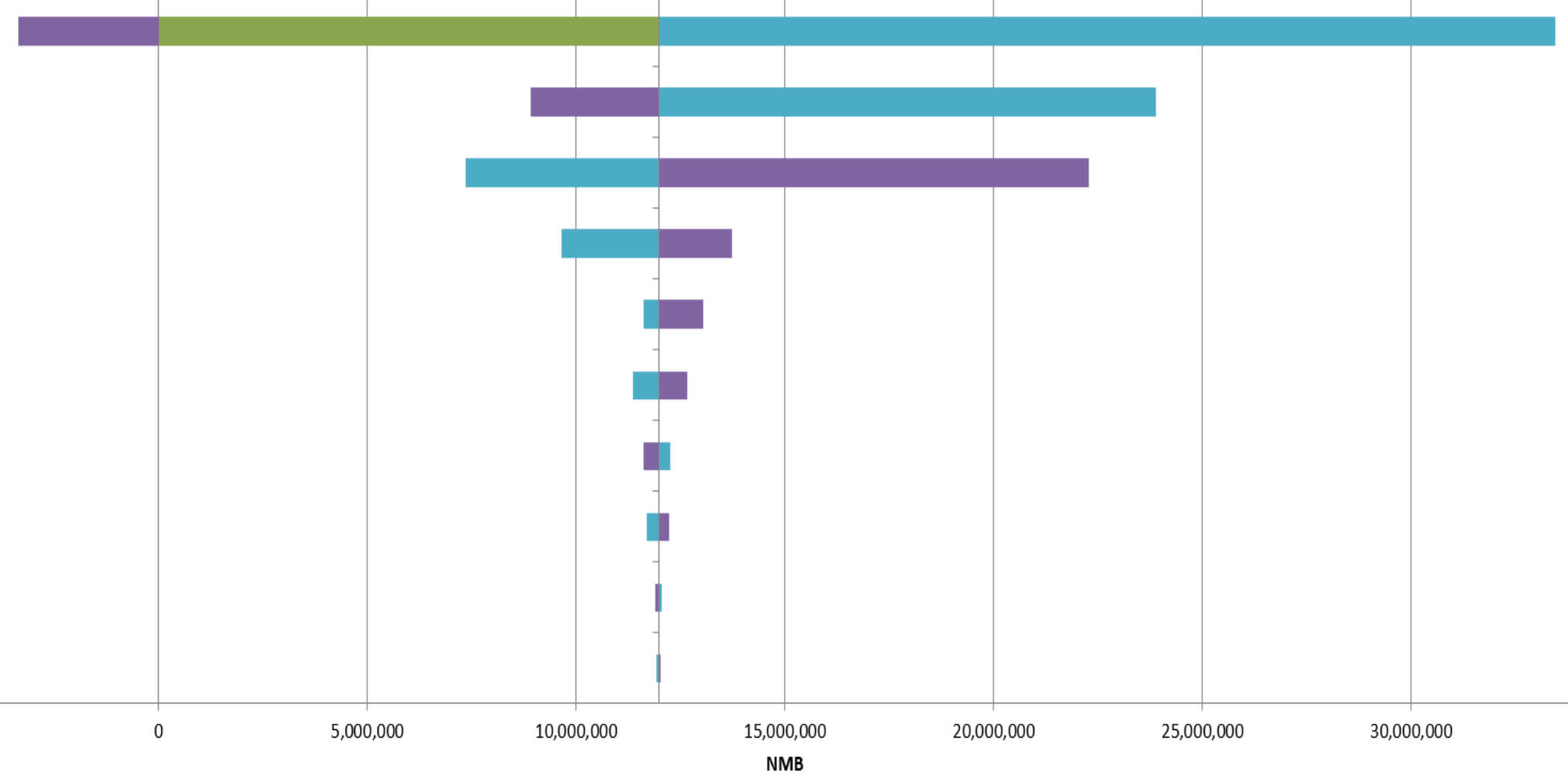


Figure 2 | tornado for whole life for 1WSA

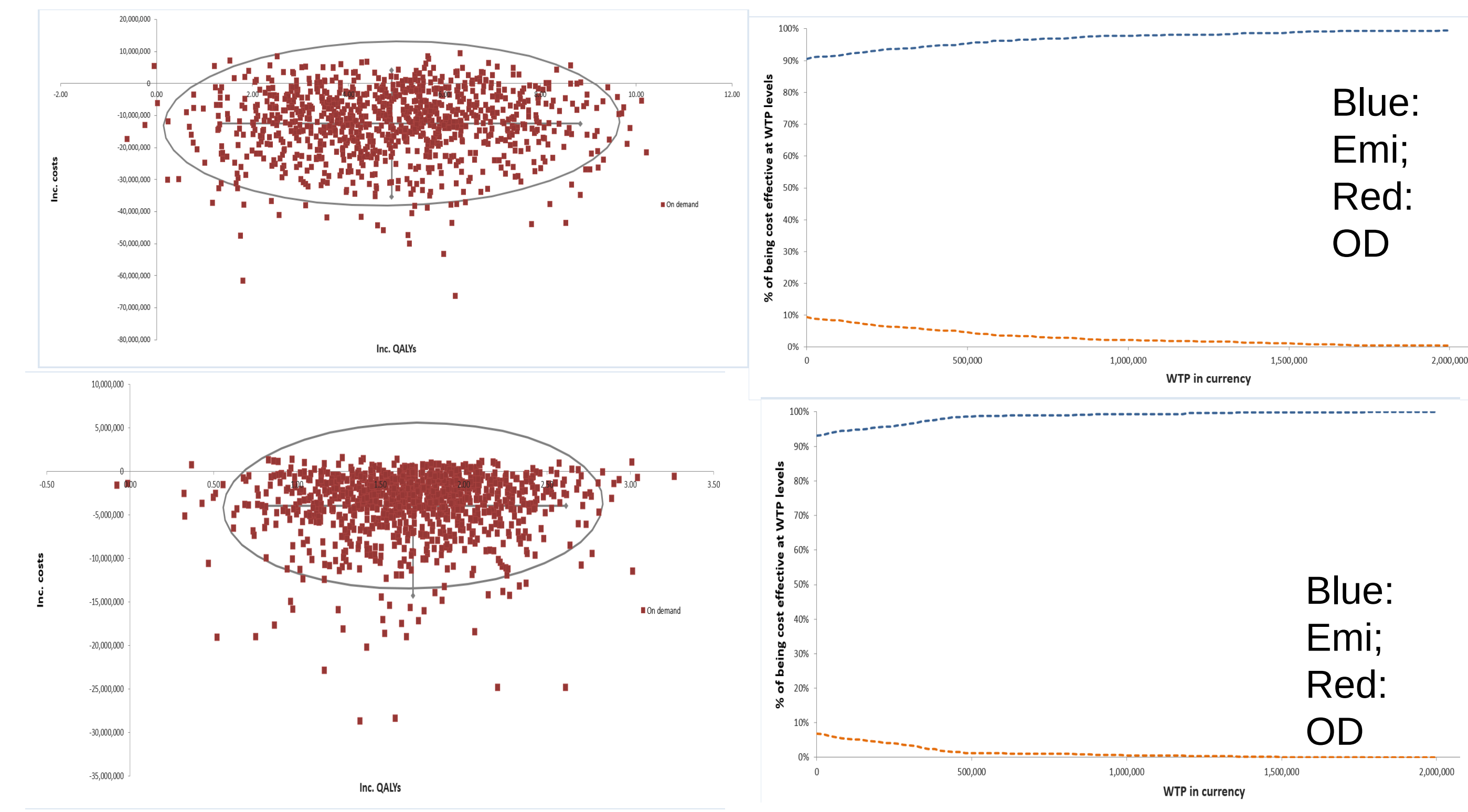


Figure 4 | Probabilistic sensitivity analysis for whole life (upper) and 1-12 years old (lower)

Utility-EMI
>12 ABR-Emi
Discount for effects
2-12 ABR-Emi
SMR-OD
SMR-Emi

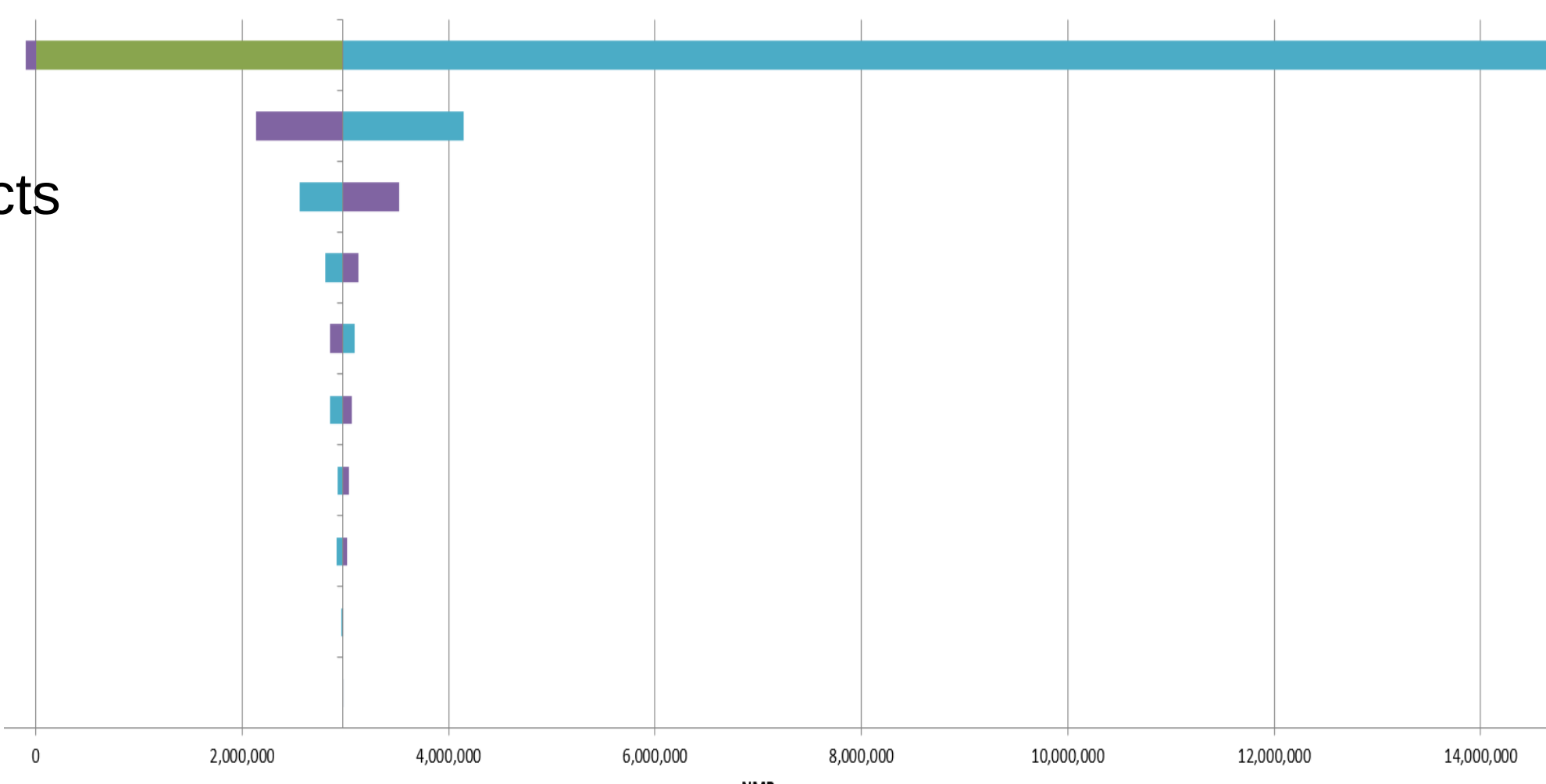


Figure 3 | tornado for 1-12 years old for 1WSA

Limitation

95% CI of the ABRs is wide due to the sample size in the clinical trials, which may change the original conclusion. However, the uncertainty around the ABRs was confirmed to have little probability of affecting the conclusion according to the sensitivity analyses.

Conclusion

emicizumab prophylactic treatments is a dominant option over rFVIIa on-demand treatment for HA with inhibitors in China, with increased QALYs and less total costs.

References

1. Thrombus and Hemostasis Group, Chinese Society of Hematology, Chinese Medical Association. Chinese Journal of Hematology. 2017; 37 (5) : 364-370.
2. Wang XF et al. Haemophilia. 2010; 16 (4) : 632-639.
3. Rocha P et al. BMC Heal Serv Res. 2015; 15:484.
- 4.State general administration of sports. http://www.sport.gov.cn/n16/n1077/n1227/7328132.html. Published 2015. Accessed out 16, 2019.
- 5.Oldenburg J et al. N Engl J Med. 2017; 377 (9) : 809-818.
6. Young G et al. [J BloodVolume 132, Issue S1. 2018. PP 632-6322018.
- 7.Farrugia A et al. Haemophilia. 2013. Doi: 10.1111 / hae. 12121
8. Knight C et.al. Haemophilia. 2003. Doi: 10.1046/1365-2516.2003.00783. J. x 9.
9. Roche. Instructions for emicizumab injection.
10. Happy Life Tech. Real-World Data from Chinese Tertiary Hospitals.; 2019.
- 11.Fitzgerald JD et al. Arthritis Care Res (Hoboken). 2010.1002 doi: 2004 / art. 20090
12. Zhang J. Journal of Clinical Military Medicine. 2017; 45 (8).