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Cost-effectiveness Analysis of GAAD Algorithm on Hepatocellular Carcinoma Screening in Patients with Chronic Hepatitis B in China

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INTRODUCTION

- China had 410,000 new cases of hepatocellular carcinoma (HCC) in 2020, accounting for 45.3% of the world, most of which originated from chronic hepatitis B (CHB)[1-3].
- When clinically diagnosed as HCC in China, 70%-80% of patients are in the advanced stage and have no opportunity for radical treatment[4]. The 5-year survival rate in Chinese HCC patients was only 14.1%[5]. Meanwhile, treating for advanced HCC causes significant increases in costs. Accordingly, regular screening has been proposed as an important method to improve early diagnosis of HCC as well as patients' prognosis.
- Elecsys® GAAD is an approved in-vitro diagnostic digital tool that combines patient gender (sex) and age plus Elecsys® alpha-fetoprotein (AFP) and Elecsys® protein induced by vitamin K absence-II (PIVKA-II) assay results to aid in the early detection of HCC. Elecsys® GAAD measurements were validated for the Cobas system
- Currently, several screening strategies have been clinically employed, but early diagnosis of HCC is still limited. The emerging Elecsys® GAAD algorithm has demonstrated better performance on HCC screening, whereas its cost-effectiveness in China is unclear.

OBJECTIVE

To evaluate the cost-effectiveness of serological tests or ultrasound (US) alone versus their joint use with or without multivariate index algorithm for HCC screening in CHB patients in China.

METHODS

- A discrete event simulation model combining a decision tree and Markov structure was developed to simulate the CHB cohort with the age of over 40 years on a lifetime horizon. Each model cycle consisted of 6 months and Chinese healthcare system perspective was adopted.
- Patients of the simulated cohort were assumed to be screened with seven different strategies, US, AFP, PIVKA-II, US+AFP, AFP+PIVKA-II, GAAD, or GAAD+US per 6 months.
- The decision tree model (Figure 1) was used to simulate the results of above screening strategies. Patients detected as positive would receive confirmatory imaging tests (computed tomography (CT) or magnetic resonance imaging (MRI)). Patients confirmed by CT/MRI would receive corresponding treatment, while patients diagnosed as negative (either true or false) would be followed up or continue previous treatment.
- The Markov model (Figure 2) was used to simulate the natural history of CHB with 8 health states, including CHB, compensatory liver cirrhosis (CLC), decompensatory liver cirrhosis (DCLC), early HCC undetected, advanced HCC undetected, early HCC detected, advanced HCC detected, and death. Based on the Barcelona Clinic Liver Cancer (BCLC) staging system, early HCC includes BCLC (0) and BCLC (A) patients, while late HCC includes BCLC (B), BCLC (C) and BCLC (D) patients. The screening strategies in decision tree works in each cycle of Markov model until HCC diagnosis.

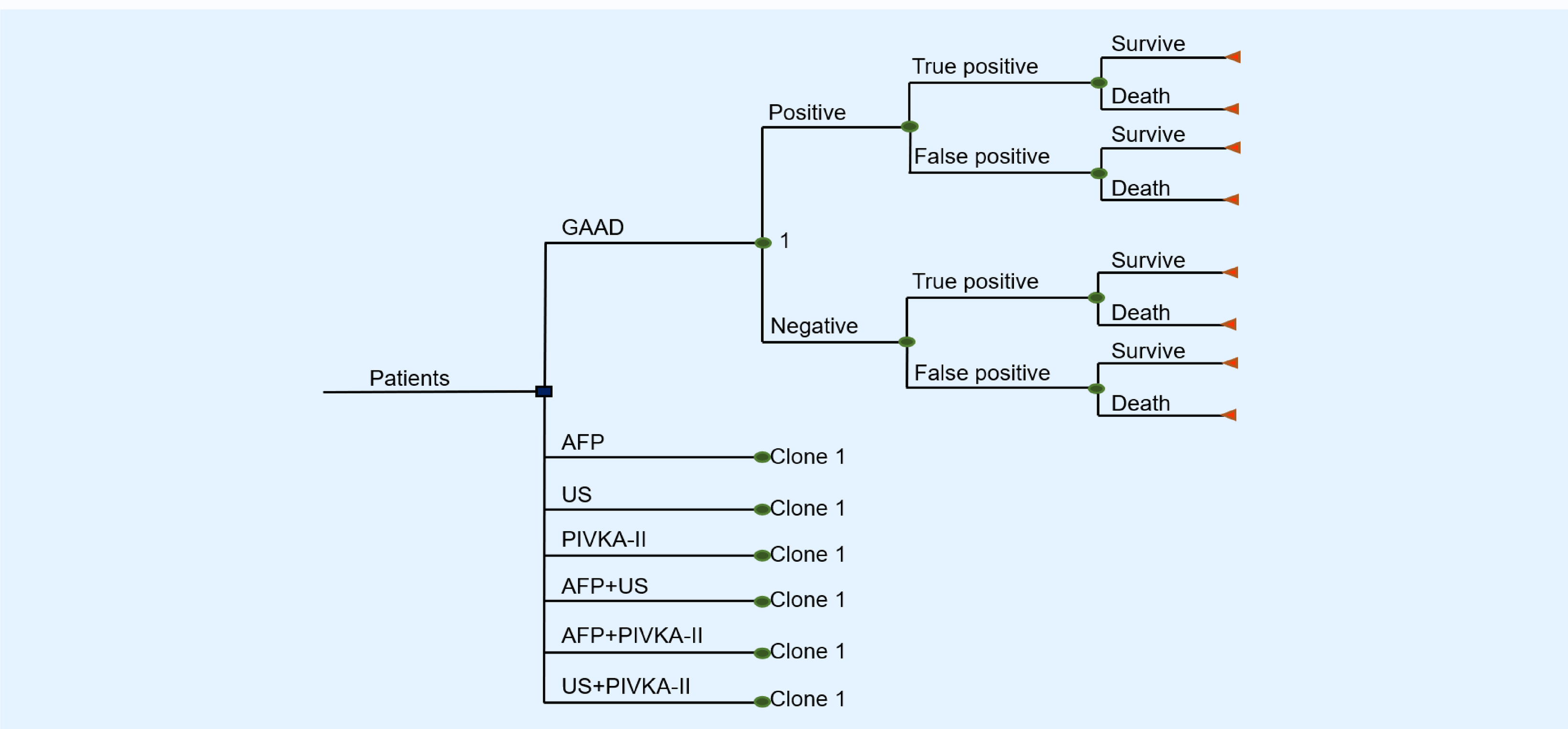

Figure.1 Decision tree

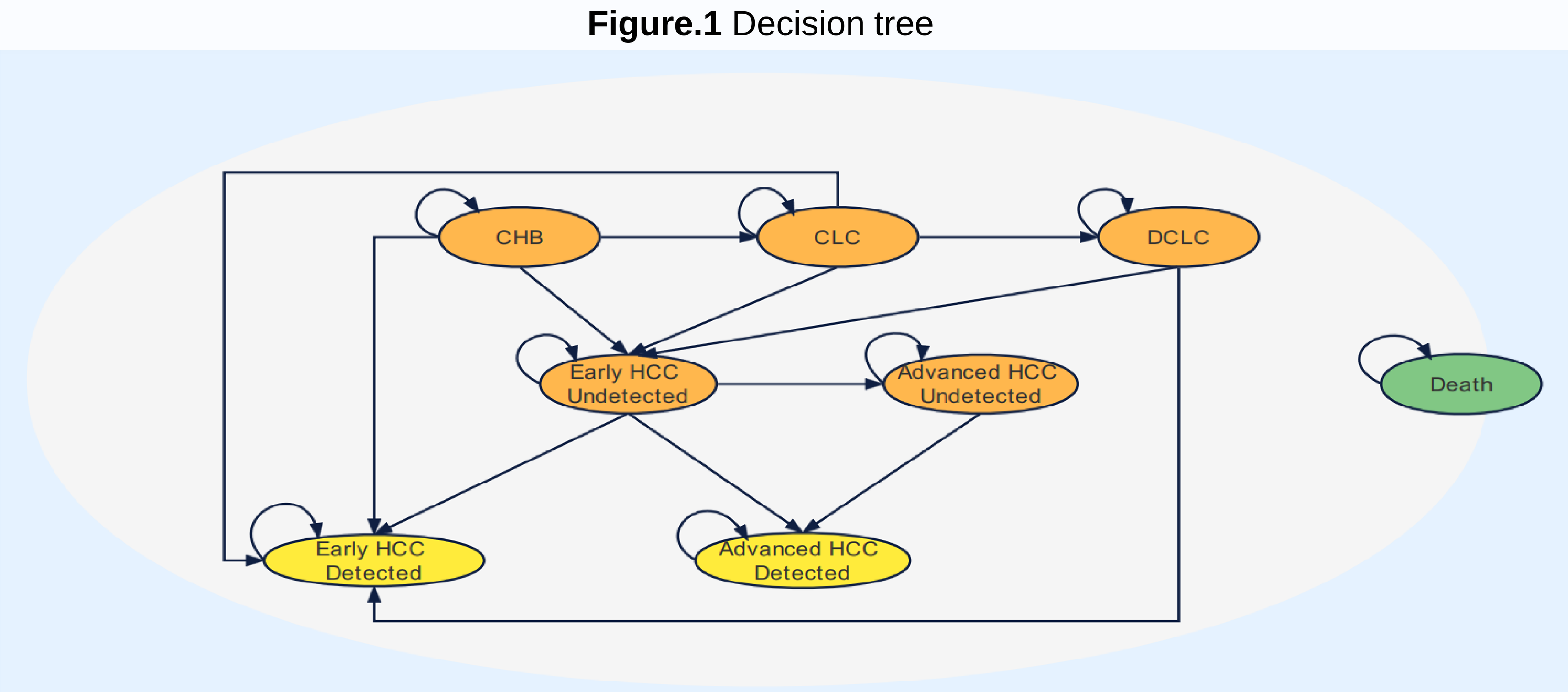

Figure.2 Markov model

METHODS (cont'd)

- Epidemiologic, clinical performance (Table 1), utility, and cost data were obtained from literature, interviews, and real-world data. Direct costs including screening costs and treatment costs were considered.
- Calculation of costs, quality-adjusted life years (QALYs), and incremental cost effectiveness ratio (ICER) were carried out. All costs and outcomes were discounted at an annual rate of 5%. Results based upon the simulation of 5000-patient cohort were reported.
- Uncertainties on key parameters were explored through deterministic and probabilistic sensitivity analyses.

Table.1 Clinical performance of each screening strategy

HCC stage	Screening strategy	Sensitivity	Specificity	HCC stage	Sensitivity	Specificity
Early HCC	AFP[6]	65.0%	81.0%	Advanced HCC	63.0%	83.0%
	US[7]	45.0%	92.0%		84.0%	92.0%
	PIVKA-II[6]	64.0%	87.0%		68.0%	90.0%
	GAAD[8]	78.9%	91.4%		92.9%	91.4%
	AFP+US[7]	63.0%	84.0%		97.0%	84.0%
	AFP+PIVKA-II[9]	76.1%	90.4%		85.3%	90.4%
	GAAD+US[10]	88.5%	88.7%		96.3%	88.7%

RESULTS

- Screening with US was associated with lowest costs of ¥41,100 and yielded lowest number of QALYs (13.177), while GAAD+US had highest costs of ¥58,089 and generated greatest number of QALYs (13.518) (Table 2).
- With 3 times China 2021 GDP per capita (¥242,928) as the threshold, the 3 strategies of US, GAAD, and GAAD+US formed the cost-effectiveness frontier, in which GAAD+US brought the best health outcomes. The ICER of GAAD over the US and GAAD+US over GAAD were ¥33,586 per QALY and ¥179,529 per QALY respectively.
- Figure 4&5 showed one-way and probabilistic sensitivity analysis of GAAD versus US respectively. Both of them proved the stability of the results.

Table 2. Base case results

No.	Strategy	Costs	QALYs	Comparison	ICER
1	US	¥41,100	13.177	-	-
2	PIVKA-II	¥48,948	13.369	2 VS 1*	¥40,967
3	AFP+US	¥50,186	13.354	-	-
4	AFP	¥50,601	13.374	4 VS 2	¥290,630
5	AFP+PIVKA-II	¥51,079	13.463	5 VS 2 5 VS 1*	¥22,544 ¥34,881
6	GAAD	¥51,267	13.480	6 VS 5 6 VS1	¥11,281 ¥33,586
7	GAAD+US	¥58,089	13.518	7 VS 6	¥179,529

*: AFP+PIVKA-II and PIVKA-II were extended dominated by GAAD, thus being excluded.

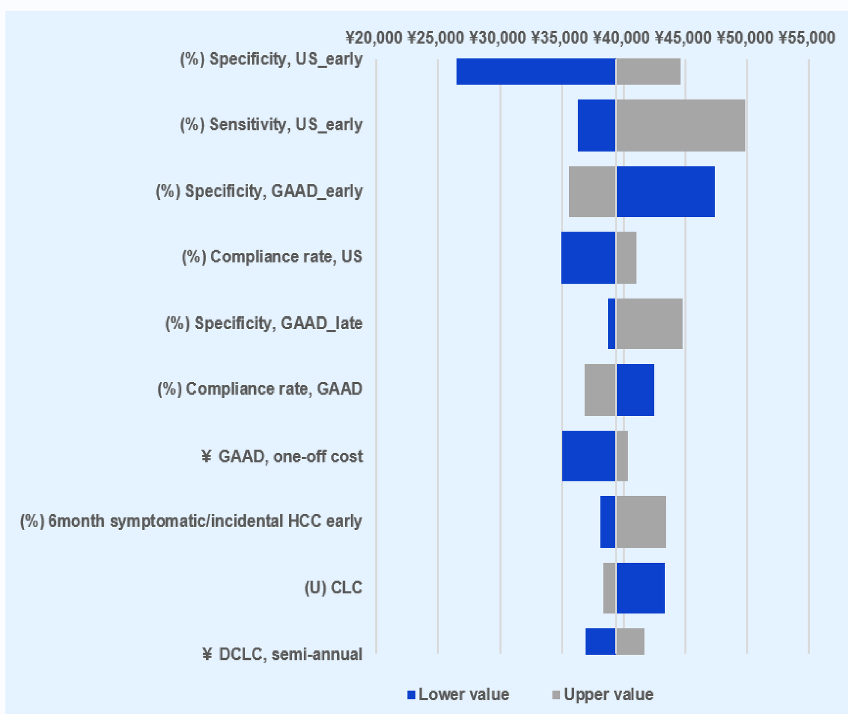

Figure 4. One-way sensitivity analysis

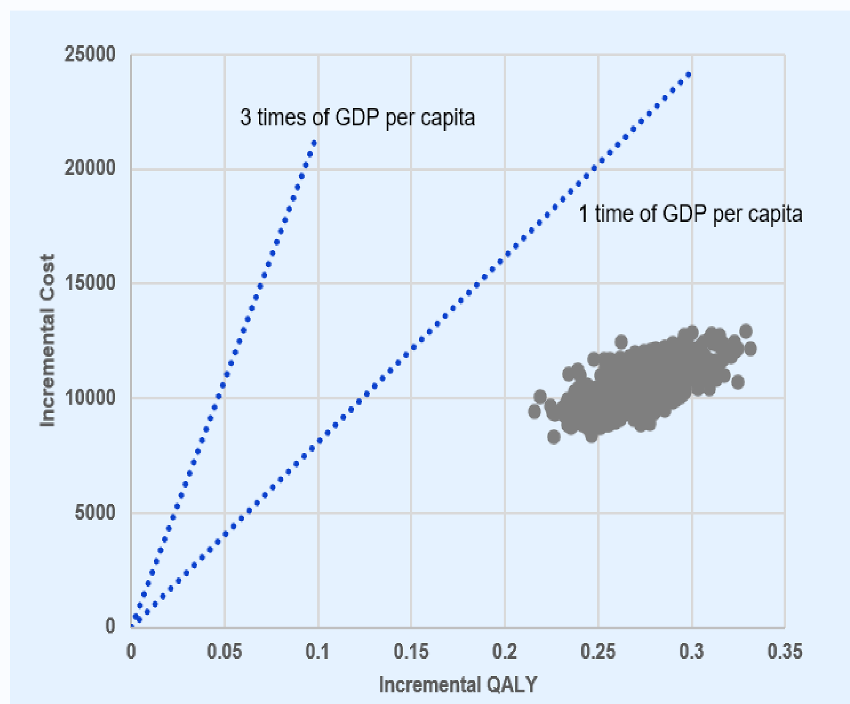

Figure 5. Probabilistic sensitivity analysis

CONCLUSION

With 3 times China GDP per capita as the threshold, the GAAD+US has been demonstrated the most cost-effective screening strategy for HCC among CHB patients with the age of over 40 years in China.

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