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Cost-Effectiveness Analysis of GAAD Algorithm for Hepatocellular Carcinoma Surveillance of Cirrhotic Patients using Italian Real-World Data

Porta C[1], Pradelli L[1], Cirotto G[2], Majorini MT[2], Garay OU[3], Calvaruso V[4], Fasano T[5], Napoli L[6], Foschi FG[6], Lampertico P[7,8]

[1] AdRes HE&OR, Turin, Italy, [2] Roche Diagnostics Spa, Monza, Italy, [3] Roche Diagnostics International, Rotkreuz, Switzerland, [4] Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), Section of Gastroenterology and Hepatology, University of Palermo, Palermo, Italy, [5] Intercompany Department for Integrated Activities in Laboratory Medicine and Pathological Anatomy (DIIMLAP) AUSL Modena, AUSL Modena, Modena, Italy, [6] Department of Internal Medicine, Ospedale per gli Infermi Faenza (RA) AUSL ROMAGNA, Faenza, Italy, [7] Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [8] CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

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Introduction

- In patients with compensated cirrhosis (CC), hepatocellular carcinoma (HCC) early diagnosis can improve prognosis.[1]
- European guidelines recommend surveillance every six months using ultrasound (US), with or without alpha-fetoprotein (AFP).[2] However, the performance of these methods remains suboptimal.
- The Elecsys ® GAAD algorithm (gender [biological sex], age, alpha-fetoprotein [AFP], protein induced by vitamin K absence-II [PIVKA-II]) demonstrated good performance for the prediction of early-stage HCC.[3]

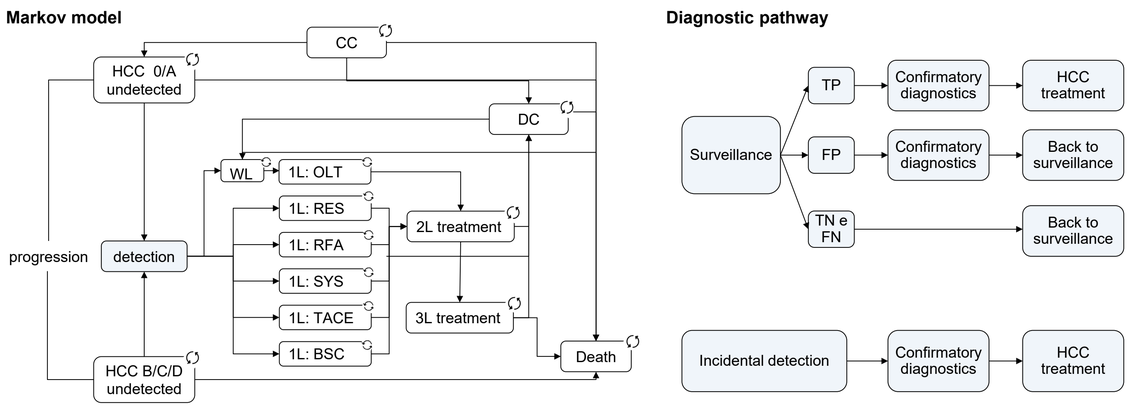
Objective

This study aimed to assess the cost-effectiveness of the GAAD algorithm for HCC surveillance in patients with CC in Italy, from the Italian Health Service perspective.

Methods

- A probabilistic micro-simulation Markov model[4] (*Figure 1*) was adapted to the Italian context to estimate lifetime clinical outcomes and costs of CC patients undergoing bi-annual surveillance with US, US+AFP, GAAD, and US+GAAD.

Figure 1. Model structure



Patients initially enter the model in the CC state. After each cycle, patients could either remain in the CC state, develop decompensated cirrhosis (DC), develop early-stage HCC, which could progress to late-stage HCC, or die. HCC stage was defined based on the Barcelona Clinic Liver Cancer (BCLC) staging system. HCC could be detected at any stage, either incidentally or by surveillance. Following the confirmed diagnosis of HCC, patients received one to three lines of therapies. Patients treated for HCC could transition to the DC state before death. Vice versa, from the DC state, patients could access the transplant WL.

- Clinical inputs were derived from published literature and integrated with real-world data collected at three Italian centres, which informed CC etiology and first-line HCC treatment patterns (*Figure 2 and 3*).

Figure 2. CC etiology distribution

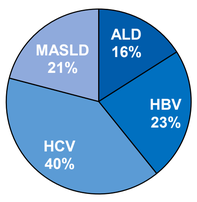
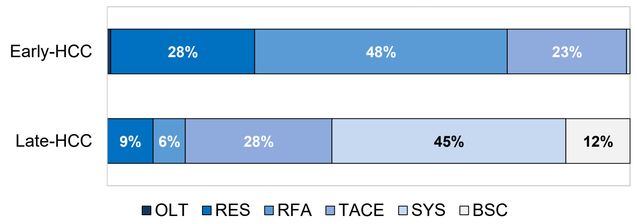
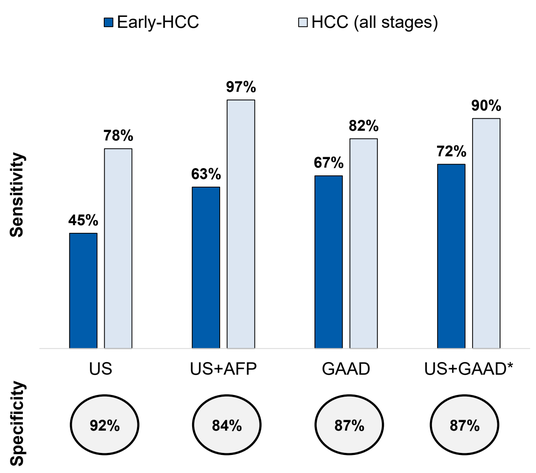


Figure 3. HCC treatment distribution by stage



- Diagnostic performance data were sourced from a meta-analysis and a clinical validation study (*Figure 4*). [4-6]
- Adherence to surveillance was assumed to be 70% based on local evidence.[7]
- Utility values were sourced from previously published health economics studies.[9-13]
- Direct healthcare costs were collected from Italian sources (*Table 1*).[14-18]

Figure 4. Diagnostic performance



Sensitivity and specificity values for all stages were used as a proxy for late-stages.
*Specificity was assumed to be equal to that of GAAD. Sensitivity was estimated by applying an absolute increase to the GAAD estimates, based on the findings reported by Huang et al.[8]

Table 1. Direct healthcare costs

Cost item	Value (€)	Source
Screening		
US	44.95	14
US+AFP	52.35	
GAAD	37.40	
US+GAAD	82.35	
Event costs		
CC (annual)	3,194.00	15
DC (annual)	5,273.02	
TP	379.00	14, clinical expert opinion*
FP	370.64	
Incidental diagnosis	240.20	
HCC follow-up (per cycle)	414.84	14, national guidelines
HCC Treatment		
OLT	66,092.76	16,17
Post-OLT year 1	15,962.19	18
Post-OLT year 2+ (per year)	5,186.29	
RES	9,558.00	16
RFA	5,040.00	17
TACE	4,085.00	16
BSC (per month)	763.75	Elaboration
SYS (per year)	99,972.07	Weighted average of 1L treatment cost

*Informed resource use for confirmatory diagnostics.

- Costs and health gains were discounted at an annual 3% rate.
- Probabilistic Sensitivity Analysis (PSA) was conducted to evaluate uncertainty in input parameters.

1L: first-line; 2L: second line; 3L: third line; AFP: alpha-fetoprotein; ALD: alcohol liver disease; BSC: best supportive care; CC: compensated cirrhosis; DC: decompensated cirrhosis; FP: false positive; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV: hepatitis C virus, MASLD: metabolic dysfunction-associated steatotic liver disease; OLT: orthotopic liver transplantation; RES: resection; RFA: radiofrequency ablation; SYS: systemic treatment; TACE: transarterial chemoembolization; TP: true positive; US: ultrasound.

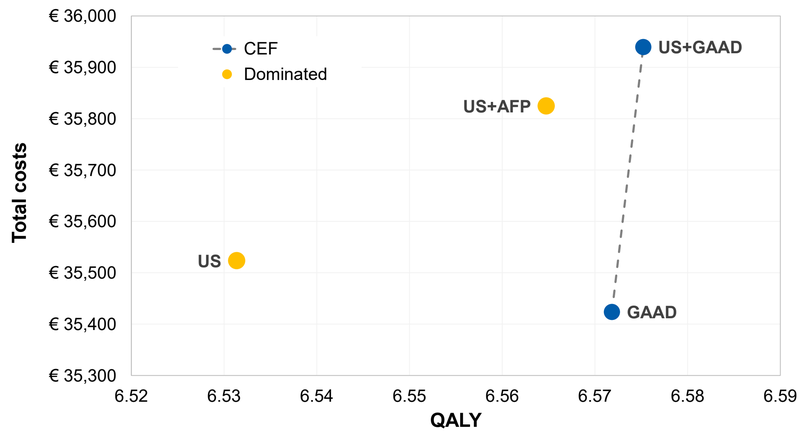
Results

- **US+GAAD** and **GAAD** were the **most effective strategies**, yielding 6.58 and 6.57 quality-adjusted life years (QALY) per patient at costs of €35,939 and €35,423, respectively (*Table 2*).
- Compared to US and US+AFP, **GAAD** was **dominant**, while **US+GAAD** was **cost-effective** (incremental cost-utility ratio [ICUR] of €9,482 and €10,951 per QALY gained, respectively).
- **GAAD** and **US+GAAD** were the most efficient strategies, forming the **cost-effectiveness frontier** (CEF) (*Figure 5*).
- PSA confirmed the robustness of results (*Figure 6*).

Table 2. Base case results

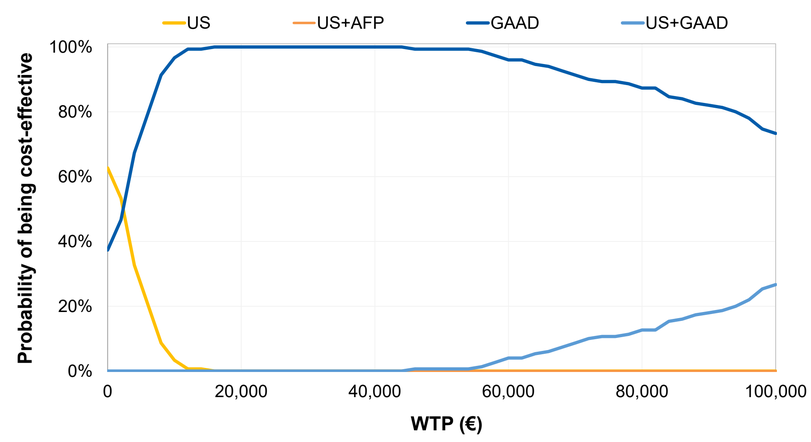
	US	US+AFP	GAAD	US+GAAD
Cost per patient	€ 35,524	€ 35,825	€ 35,423	€ 35,939
QALY per patient	6.531	6.565	6.572	6.575
Vs. US				
Incremental costs		€ 301	€ -100	€ 416
Incremental QALY		0.033	0.040	0.044
ICUR		€ 9,022	dominant	€ 9,482
Vs. US+AFP				
Incremental costs			€ -401	€ 115
Incremental QALY			0.007	0.010
ICUR			dominant	€ 10,951
Vs. GAAD				
Incremental costs				€ 516
Incremental QALY				0.003
ICUR				€ 152,658

Figure 5. Cost-effectiveness plane



The dotted lines indicate the CEF, and the slope of the frontier that connects two strategies is the ICUR. Points not lying on the CEF represent the alternatives that are not considered cost-effective.

Figure 6. Cost-effectiveness acceptability curve (CEAC)



*CEAC shows that GAAD was the **most cost-effective strategy**, with a 100% probability of CE at willingness to pay (WTP) of €30,000 per QALY gained.*

Conclusions

GAAD, either alone or in combination with US, is a **cost-effective strategy** for HCC surveillance in CC patients Italy, significantly **improving the detection of early-stage HCC**.

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Disclosures

- CP is an employee of AdRes. LP is a co-owner and employee of AdRes. AdRes conducted the study and received project funding from Roche Diagnostics. GC, MTM and OUG are employed by Roche Diagnostics.
- This study was funded by Roche Diagnostics International Ltd, Rotkreuz, Switzerland.
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