JOURNAL OF MEDICAL ECONOMICS
2025, VOL. 28, NO. 1, 1023–1036
https://doi.org/10.1080/13696998.2025.2525006
Article /2525006

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

OPEN ACCESS Check for updates

Cost-effectiveness analysis of artificial intelligence (AI) in earlier detection of liver lesions in cirrhotic patients at risk of hepatocellular carcinoma in Italy

L. Maas[a,b], C. Contreras-Meca[a], S. Ghezzo[a], F. Belmans[a,c], A. Corsi[a], J. Cant[a], W. Vos[a], M. Bobowicz[d], M. Rygusik[d], D. K. Laski[e], L. Annemans[f] and M. Hiligsmann[b]; on Behalf of EuCanImage Working Group*

[a]Radiomics.bio, Liege, Belgium; [b]Department of Health Services Research, Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands; [c]Department of Imaging and Pathology, Biomedical MRI Unit, KU Leuven, Leuven, Belgium; [d]2nd Division of Radiology, Medical Univeristy of Gdańsk, Gdańsk, Poland; [e]Department of Oncological, Transplant and General Surgery, Medical Univeristy of Gdańsk, Gdańsk, Poland; [f]Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third most common cause of cancer-related death. Cirrhosis is a major contributing factor, accounting for over 90% of HCC cases. With the high mortality rate of HCC, earlier detection of HCC is critical. When added to magnetic resonance imaging (MRI), artificial intelligence (AI) has been shown to improve HCC detection. Nonetheless, to date no cost-effectiveness analyses have been conducted on an AI tool to enhance earlier HCC detection. This study reports on the cost-effectiveness of detection of liver lesions with AI improved MRI in the surveillance for HCC in patients with a cirrhotic liver compared to usual care (UC).

Methods: The model structure included a decision tree followed by a state-transition Markov model from an Italian healthcare perspective. Lifetime costs and quality-adjusted life years (QALY) were simulated in cirrhotic patients at risk of HCC. One-way sensitivity analyses and two-way sensitivity analyses were performed. Results were presented as incremental cost-effectiveness ratios (ICER).

Results: For patients receiving UC, the average lifetime costs per 1,000 patients were €16,604,800 compared to €16,610,250 for patients receiving the AI approach. With a QALY gained of 0.55 and incremental costs of €5,000 for every 1,000 patients, the ICER was €9,888 per QALY gained, indicating cost-effectiveness with the willingness-to-pay threshold of €33,000/QALY gained. Main drivers of cost-effectiveness included the cost and performance (sensitivity and specificity) of the AI tool.

ARTICLE HISTORY

Received 20 February 2025
Revised 27 May 2025
Accepted 23 June 2025

KEYWORDS

Cost-effectiveness analysis; hepatocellular carcinoma; artificial intelligence; cirrhosis; Markov; decision tree

JEL CLASSIFICATION CODES

I15; I18; O32; O31

CONTACT Lieke Maas lieke.maas@maastrichtuniversity.nl Radiomics.bio, Boulevard Patience et Beaujonc 3/3, 4000 Liège, Belgium

*EuCanImage Working Group: Karim Lekadir (Universitat de Barcelona (UB)), Kaisar Kushibar (Universitat de Barcelona (UB)), Philippe Lambin (Universiteit Maastricht (UM)), Henry Woodruff (Universiteit Maastricht (UM)), Martijn Starmans (Erasmus Universitair Medisch Centrum Rotterdam (EMC)), Josep Lluis Gelpi (Barcelona Supercomputing Center – Centro Nacional de Supercomputacion (BSC)), Jordi Rambla (Fundacio Centre de Regulacio Genomica (CRG)), Fred Prior (University of Arkansas (UAMS/TCIA)), Melanie Goisauf (Biobanks and Biomolecular Resources Research Infrastructure Consortium (BBMRI-ERIC)), Pilar Nicolas (Universidad Delpais Vasco/Euskal Herriko Unibertsitatea (UPV/EHU)), Davide Zaccagnini (Lynkeus (LYN)), Pär Kragsterman (Collective Minds Radiology AB (CMRAD)), Tobias Heimann (Siemens Healthcare Gmbh (SIE)), Peter Gordebeke (Eibir Gemeinnutzige Gmbh zur Forderung der Erforschung der Biomedizinischen Bildgebung (EIBIR)), Emanuele Neri (European Society of Oncologic Imaging – Esoi Europaische Gesellschaftfur Onkologische Bildebung (ESOI)), Jane Smith (European Association for Cancer Research (EACR)), Lorenzo Faggioni (Universita di Pisa (UNIPI)), Jordi Rimola (liver) (Fundacio Clinic per a la Recerca Biomedica (FCRB)), Xavier Bargalló (breast) (Fundacio Clinic per a la Recerca Biomedica (FCRB)), Katrine Riklund (Umea Universitet (UmU)), Maciej Bobowicz (Gdanski Uniwersytet Medyczny (GUMed)), Juozas Kupčinskas (Lietuvos Sveikatos Mokslu Universiteto Ligonine Kauno Klinikos (KAUNO)), Javier del Riego (The Institute for Research and Innovation Parc Taulí (Plaça Torre de l'Aigua, s/n 08208 Sabadell Spain)).

Supplemental data for this article is available online at https://doi.org/10.1080/13696998.2025.2525006.

www.tandfonline.com/ijme

Discussion: This study suggests that an AI-based approach to detect HCC earlier in cirrhotic patients can be cost-effective. By incorporating cost-effective AI-based approaches in clinical practice, patient outcomes and healthcare efficiency are improved.

1. Introduction

According to the Global Cancer Observatory, hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third most common cause of cancer-related death[1]. Cirrhosis, caused by excessive alcohol consumption, hepatitis B and C infections, obesity, and diabetes[2], contributes to over 90% of HCC cases[3] and increases the mortality rate further[4]. With cirrhosis present, the HCC incidence is about 5% per year in Italy[5].

With only 68% of cirrhotic patients surviving the first year after HCC diagnosis, earlier detection of HCC is critical[5,6]. Furthermore, unless diagnosed in a presymptomatic stage, HCC has a 5-year survival rate of less than 20%[7]. However, if found earlier, curative options remain, including radiofrequency ablation, surgical resection, and/or liver transplantation[8]. Biannual surveillance of small tumors in cirrhotic patients using abdominal ultrasounds has become common practice as it has been associated with earlier tumor detection and increased curative treatment intent and has shown to be cost-effective compared to no surveillance[8–10]. Nonetheless, ultrasounds can still miss one-third of early-stage HCC due to its suboptimal sensitivity often leading to other expensive diagnostic techniques (i.e. computed tomography (CT), magnetic resonance imaging (MRI), and liver biopsy) being required[10]. With additional imaging or invasive techniques, sensitivity is improved, but false positives remain in 20% of patients, with some patients undergoing repeated CT or MRI screening or invasive techniques such as liver biopsy[11].

Considering the high mortality rate of HCC and the lack of earlier HCC detection by the current diagnostic tools, artificial intelligence (AI) has the potential to improve lesion detection, patient quality-of-life, and efficient healthcare resource allocation. AI has already demonstrated favorable results, with AI models consistently outperforming clinicians in the interpretation of ultrasounds, CT, and MRI scans[12]. When added to MRI, AI could anticipate better sensitivity and specificity and make it more likely to identify small lesions (< 1 cm), ultimately leading to less usage of unnecessary invasive diagnostic techniques, in this case liver biopsies, or more extensive treatment due to delay in diagnosis. Nonetheless, AI is paired with additional costs, and it is therefore important to investigate whether the additional costs are worth the additional benefits when implementing AI in assessing diagnostic imaging results. However, to our knowledge, no cost-effectiveness analyses have been published on AI tools used to enhance earlier HCC detection[12].

Addressing this gap in knowledge on the economic impact of AI tools used to enhance earlier HCC detection is critical to limit false positive rates and the need for invasive diagnostic techniques, ultimately ensuring appropriate implementation of AI in health care within cirrhotic patients who have or will have developed HCC throughout their lifetime. To address this gap, a cost-effectiveness analysis will be performed to provide evidence-based guidance on whether AI-enhanced MRI should be integrated into routine HCC surveillance strategies for cirrhotic patients. Given the complexity of healthcare decision-making, model-based economic evaluations enable simulating lifelong effects and costs when comparing the implementation of AI in healthcare compared to the usual care (UC). This study is part of the European Cancer Image Platform Linked to Biological and Health Data for Next-Generation Artificial Intelligence and Precision Medicine in Oncology (EuCanImage) that represents a unique coalition of expertise developing a GDPR-compliant integrated platform for large scale cancer imaging that can significantly enhance the potential of AI in oncology[13].

2. Methods

2.1. Patient group

Our model evaluated the cost-effectiveness of implementing an AI-assisted MRI tool for more accurate HCC detection in patients who have been diagnosed with cirrhosis in the past and are adherent

to biannual screening appointment for possible HCC. Only cirrhotic patients at risk of developing HCC and who are adherent to the biannual screening procedures were considered. It is important to note that, throughout this article, more accurate HCC detection refers to the assumption that higher specificity and sensitivity of a diagnostic tool can lead to earlier detection of HCC. Earlier detection should not be confused with early-stage cancer. More specifically, earlier detection refers to the time when cancer is found whereas early-stage cancer describes how advanced the cancer is at diagnosis. While earlier detection can lead to diagnosing early-stage cancer, some cancers are detected earlier but already at an advanced stage. The Italian Medicines Agency's National guidelines for conducting economic evaluations was used[14]. The Consolidated Health Economic Evaluation Reporting Standards for Interventions That Use Artificial Intelligence 2024 (CHEERS-AI) was used to report our study (see Supplementary Table 1)[15]. A health economic plan was developed prior to data analysis (see Supplementary Table 2).

2.2. AI tool and setting

Based on the NICE digital health categories, the AI tool is classified as tier 3b as the AI tool aims to improve HCC diagnosis[16]. The AI tool was intended to be non-directive, retaining the healthcare professional's autonomy to make care decisions. The impact of the AI tool on the outcomes was determined through open discussion with the EuCanImage consortium clinical experts and AI engineers, which were noted down *via* field notes and validated with CCM, LA, and MH. The training dataset used to develop the AI tool was based on real-world cases from four clinics in Europe (Poland, Italy, Lithuania, and Spain). Due to limited country-specific data from most of these countries, data sources used to develop the economic model were based on existing literature on patient populations from Italy.

In summary, cirrhotic patients attended their biannual screening appointment, where they received an ultrasound. Additional diagnostic tools including a CT, MRI, or biopsy, were used, respectively, if needed based on the sensitivity and specificity of the previous imaging technology. Once diagnosed with HCC, care was based on the Barcelona Clinic Liver Cancer (BCLC) staging system[17] that classifies HCC based on tumor characteristics and liver function. For early-stage HCC, surgical resection or liver transplantation is recommended. If HCC is already at a progressive stage, transarterial chemoembolization (TACE) and systemic therapies like sorafenib are typically involved. The AI tool was developed to optimize MRI imaging reading by enhancing the conventional sensitivity and specificity of MRI semi-qualitative interpretation. However, no changes were made to the diagnostic and treatment patient management pathway. Figure 1 summarizes the comparison of AI to the usual care pathway.

Static models for segmentation and classification were based on 969 patients, each one containing imaging of T1 post-contrast and T2 MRI sequences (1,211 images in total). Performance evaluation was based on a held-out cohort of 30% of the total sample (363 images from 290 patients), stratified according to patient ID (so that images belonging to a certain patient were either used only for training or only for testing), center, gender, presence of chronic hepatitis or liver cirrhosis, and diagnosis (benign lesions or HCC). This study was part EuCanImage project under the European Union's Horizon 2020 Research and Innovation Programme, grant agreement No 952103.

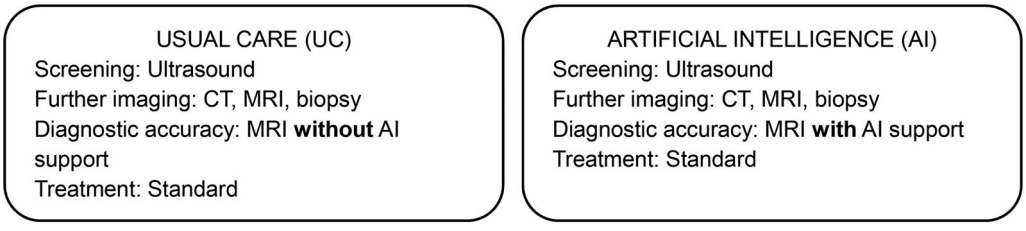

Figure 1. Comparison arms explained. UC, usual care; AI, artificial intelligence; CT computed tomography; MRI, magnetic resonance imaging.

2.3. Model structure

The model structure included a decision tree followed by a state-transition Markov model from a healthcare perspective using a lifetime horizon, in line with the Italian Medicines Agency's National guidelines for conducting economic evaluations[14]. The BCLC management guidelines were used as a foundation for our model. The model structure and patient management were further verified *via* semi-structured interviews with at least one clinician of each EuCanImage clinic. Due to availability constraints of the clinics, some clinicians opted for a digital questionnaire for model verification.

A decision tree with consecutive Markov models were employed to perform simulations based on existing literature. The decision tree provides information on the short-term effects of implementing an AI tool during HCC screening, including total screening costs, cancer detection rates, and rates of false and true positive or false and true negative HCC diagnosis. The two branches of the decision tree reflected whether patients received the AI tool or UC. The Markov models simulate then the long-term lifetime quality-adjusted life-years (QALYs) and costs of implementation of such an AI tool compared to standard of care. The analyses were conducted using R Studio version 2.4.3.

2.3.1. Decision tree model

The decision tree describing the possible outcomes is shown in Figure 2. Following initial screening *via* ultrasound, where it was assumed that all patients were adherent to the screening procedure, patients received additional diagnostic imaging techniques depending on the presence or size of the lesion. Patients either had a presence or absence of cancer, which was detected or missed by the imaging techniques (ultrasound, CT, MRI, biopsy). The need for multiple diagnostic imaging techniques was determined based on the sensitivity and specificity of their prior imaging scans. The patients entering the decision tree have the chance of entering one of four scenarios for their diagnosis: true positive, false negative, false positive, or a true negative diagnosis for HCC. All input variables are presented in Table 1. These variables were derived from a targeted review of published literature. Searches were conducted in PubMed and Google Scholar using keywords and search terms related to cost-effectiveness in cirrhosis and HCC. Articles were included if they reported on an original article reporting on either clinical outcomes, costs, utilities, cost-effectiveness analyses, or mortality rates relevant to the model

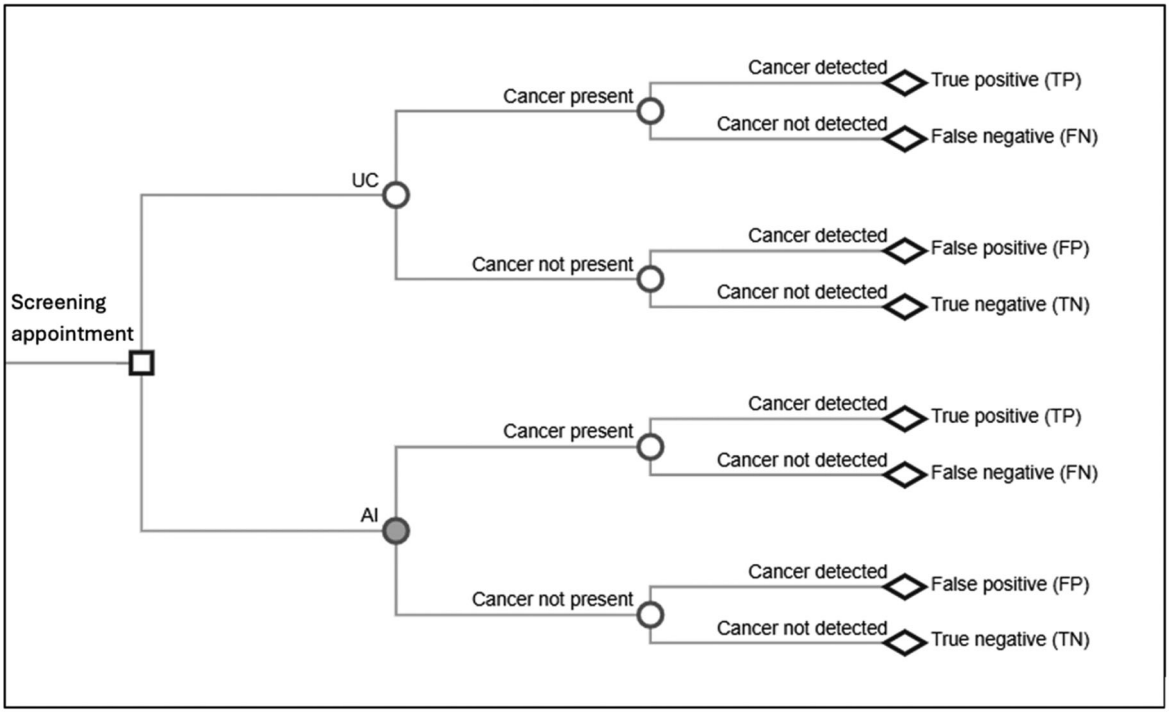

Figure 2. Decision tree structure that provides four possible scenarios for the state-transition Markov model. UC, usual care; AI, artificial intelligence.

Table 1. Input parameters.

Parameters	Parameter values	Literature
Patient probabilities and diagnostic accuracy		
HCC prevalence	0.56	18
Starting age	50	10
Sensitivity ultrasound	0.70	33
Sensitivity MRI	0.76	34
Sensitivity CT	0.63	34
Sensitivity biopsy	0.89	34
Sensitivity AI tool	0.90	–
Specificity ultrasound	0.94	33
Specificity MRI	0.78	34
Specificity CT	0.82	34
Specificity biopsy	0.93	34
Specificity AI tool	0.90	–
Transition and mortality rates		
Transition rate cirrhosis to diagnosed cancer	0.05	9
Transition rate diagnosed cancer to remission	0.26*	35
Transition rate remission to diagnosed cancer	0.19	36
Transition rate diagnosed cancer to cancer progression	0.15**	37
Mortality rate cirrhosis (6-year)	54%	20
Mortality rate HCC (1-year)	68%	6
Mortality rate undiagnosed HCC (1-year)	56%	22
Hazard ratio remission versus cirrhosis	0.95	21
Costs (2023 €)		
Ultrasound	57	38
MRI	238	38
CT	184	38
Biopsy	242	38
AI tool	300	–
Cirrhosis (yearly)	1950	5
False positive diagnosis (yearly)	1817	29,39
HCC cancer (yearly)	7638	27
False negative diagnosis consequences (yearly)	14865	31,40
Cancer progression (yearly)	7227	27
Remission (monthly)	195	28
Utilities		
Utility cirrhosis health state	0.78	1
Utility diagnosed cancer health state	0.64	18
Utility cancer progression health state	0.40	19
Disutility remission	0.13	24
Disutility extra screening false positive	0.01	1

Abbreviations: HCC, hepatocellular cancer; MRI, magnetic resonance imaging; CT, computed tomography.
*The average was taken between male and female reported data.
**Transition rate was taken from intermediate stage HCC cancer to advanced stage HCC cancers.

structure. The final parameters were selected based on relevance, data quality, and alignment with the model's requirements.

2.3.2. Markov models

To simulate lifelong effects in HCC diagnosis and following the decision tree, patients entered a Markov model. Each cycle consisted of 6 months, aligning with the biannual screening intervals and previous studies[5,8], with a maximum end age of 100 years old or death. Health states included cirrhosis, diagnosed cancer, cancer progression, remission, and death. No distinction was made between BCLC staging. Within each state, patients received treatment and were considered stable. Remission refers to cancer patients having received successful curative treatment. All patients entered the Markov model in either the diagnosed cancer or cirrhosis health state. Depending on whether their cancer detection was a true positive result or a false negative, patients would start in the diagnosed cancer health state and stayed there or transitioned to either the remission or cancer progression health state. Patients with a true negative or false positive result would start in the cirrhosis health state and had the possibility to stay here or still develop HCC in their lifetime, transitioning to the same possible health states as stated above, depicted in Figure 3. Patients in the false negative scenario started in the diagnosed cancer health state and received biannual screening during this state, due to the lacking information on transition rates to cancer progression, only the mortality rate and costs were adjusted for these patients. More specifically, patients with a false negative diagnosis had a higher mortality rate in the first year of

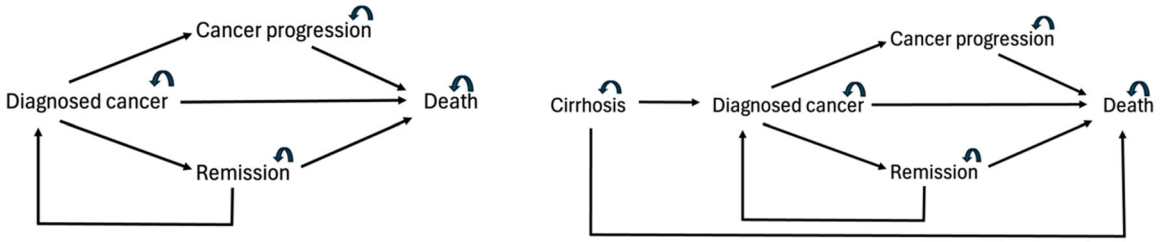

Figure 3. Markov model structure for true positive and false negative scenarios (left) and false positive and true negative scenarios (right).

the Markov model and contained additional costs due to late HCC diagnosis in the diagnosed cancer health state. Patients in the false positive scenario were different from true negative patients due to disutility and extra costs in the cirrhosis health state due to additional screening needed to determine the false positive diagnosis. Patients who entered the Markov model with a false negative diagnosis were assumed to have been correctly diagnosed with having HCC within 6 months after initial screening. Patients who entered the Markov model with a false positive diagnosis were assumed to have been correctly ruled out form having HCC within 6 months after initial screening. Once cancer progression occurred, no further improvement in survival was assumed. Patients in this health state were not considered eligible for remission at any point, and only stabilization of disease was deemed possible for which case they would remain in the cancer progression health state until death. Compared to patients in the diagnosed cancer health state, patients classified with cancer progression had higher costs and a lower quality-of-life score. Upon transitioning into the death state, all patients remained in this state indefinitely.

2.4. Model input data

2.4.1. Patient sample

The starting age was 50 years old, and no difference was made in gender as clinical, cost, and effectiveness profiles within HCC do not significantly vary by gender and limited data could be found on input parameters stratified by gender. The prevalence of HCC was 56%[18] and the annual HCC incidence for patients with cirrhosis is about 5%[5]. The prevalence was aligned with previous studies, the consideration that the Italian population has higher rates of HCC risk factors such as chronic hepatitis C, hereditary hemochromatosis, and metabolic syndrome, and their higher levels of longevity and therefore possibility of risk accumulation over their lifetime[19].

2.4.2. Mortality

Mortality rates were calculated by health state. The cirrhosis mortality rate was based on the 6-year survival rate of Italian cirrhosis patients being 54%[20] (depicted in Table 1). Mortality rates for diagnosed cancer and cancer progression were assumed to be the same, with a 1-year mortality rate for Italian patients being 68%[6], and were appropriately converted using standard exponential formulas. The mortality rate for patients in the cancer remission health state was calculated based on the mortality rate of cirrhosis and the hazard ratio of death in remission versus cirrhosis[21]. For patients with a false negative cancer diagnosis, the first-year mortality rate was assumed to be similar to undiagnosed HCC patients[22].

2.4.3. Utility

Utility was based on several studies based on Italian populations[8,23], with remission being based on cirrhosis with a disutility adjustment of 0.127[24]. An additional disutility was used for false positive diagnosis due to additional screening or diagnostic testing required during the first cycle[8]. All utility values were calibrated to the 6-month cycle length.

2.4.4. Performance of diagnostic techniques

Performance of the imaging techniques included the ultrasound (sensitivity: 0.70, specificity: 0.94), CT (sensitivity: 0.63, specificity: 0.82), MRI (sensitivity: 0.76, specificity: 0.78), and biopsy (sensitivity: 0.89,

specificity: 0.93)[8]. Due to the fact that the AI tool was not yet developed within the study's timeframe, the performance (sensitivity and specificity) of the AI tool was aligned with previous estimates of Koh et al.[12] and validated by the EuCanImage developers of the AI tool. Several sensitivity analyses were conducted on the sensitivity and specificity of the AI tool. It was assumed that all patients were adherent to the screening procedures.

2.4.5. Diagnostic and treatment costs

All costs were based on the Italian Medicines Agency's National guidelines for conducting economic evaluations and adjusted to 2023 euros based on the consumer price index[14] and were calibrated to the 6-month cycle length. The additional per-patient cost of the AI tool was set at €300 based on the willingness-to-pay for diagnostic technologies and expert opinion from radiomics.bio[25]. Health state costs were based on cost studies based on Italian populations and adjusted for inflation to 2023 euros. Cirrhosis health state costs included inpatient and outpatient visits, diagnostic and laboratory testing, medications, and procedures. Diagnosed cancer health state costs were based on patients newly diagnosed with HCC and included all healthcare resource utilization costs such as pharmacy fills, inpatient stays, and health services which required hospital assistance, including surveillance appointments, pharmacy refills, and outpatient services[26]. Cancer progression costs included diagnosed cancer health state costs and additional progression costs (e.g. diagnostic exams, visits, hospitalization)[27]. The AI tool was solely used in the first cycle during the initial screening. Due to lacking information on costs based on the Italian national health service, the costs of patients in remission were based on Lillini et al.[28] Additional costs due to a false negative diagnosis were assumed to be associated with higher hospitalization costs[29,30], reflecting the increased resource utilization observed in cases where diagnostic delays lead to more advanced disease stages requiring intensive treatment. While specific data for HCC were limited, studies have demonstrated that diagnostic discrepancies can result in significantly longer hospital stays and increased healthcare costs[28]. Due to lacking information on estimated cost differences between true positive and false negative diagnoses, additional hospitalization costs were accounted for in patients with a false negative diagnosis due to late diagnosis. No costs were associated with death.

2.5. Analysis

To estimate the total costs of AI and UC, costs from the short-term and long-term disease costs were combined. The decision tree provided information on short-term diagnostic scenarios. The state-transition Markov model provided life-time simulation of cirrhotic and HCC patients. The overall results of the base-case analysis were presented as per patient average lifetime costs, accumulated quality-adjusted life years (QALYs), incremental costs and QALYs between the two arms, and the incremental cost-effectiveness ratio (ICER). The willingness-to-pay (WTP) threshold in Italy is not a set value, instead the average Italian WTP threshold/QALY gained was used of €33,000/QALY gained[31].

2.5.1. One-way sensitivity analyses to characterize parameter uncertainty

To characterize parameter uncertainty and explore potential differences across healthcare systems in Europe, several sensitivity analyses were performed. One-way sensitivity analyses included changing the following variables: (i) proportion of cirrhotic patients undergoing initial HCC surveillance 50% and 75%; (ii) discount rate for cost and benefits 0% and 5%; (iii) HCC prevalence ±25% and −50%; (iv) transition rates ±25%; (v) mortality rates ±25%; (vi) utility ±25%; (vii) costs diagnostic techniques ±25%; (viii) costs health states ±25%; (ix) costs AI tool ±25%; (x) false negative first-year HCC mortality rate ±25%; (xi) extra costs false negative ±25%; (xii) false positive disutility ±25%; (xiii) extra costs false positive ±25%; and (xiv) starting age 60, 70, and 80. Finally, a one-way sensitivity analysis was performed incorporating fixed costs associated with AI implementation in health care, including costs related to staffing, equipment, storage, and training resource utilization (312,400 euro)[32]. Although the reference study focuses on AI implementation in the United States, this intended to provide a preliminary estimation rather than precise cost projections.

2.5.2. Two-way sensitivity analyses

To explore potential differences in disease management within other healthcare systems, several two-way sensitivity analyses were conducted. These included (i) diagnostic and health state costs ±25%; (ii) performance (sensitivity and specificity) of all usual care diagnostic techniques ±25%; (iii) performance (sensitivity and specificity) of MRI, CT, and biopsy, ±25%; (iv) performance (sensitivity and specificity) of the AI tool at 0.80 and 0.85, respectively. Additionally, variation in screening costs (±25%) and variation in health state costs (±25%) were analyzed with each possible combination, as well as variation in performance (sensitivity and specificity) of the AI tool (±25%) and variation in costs of the AI tool (±25%) were analyzed with each possible combination.

3. Results

3.1. Diagnostic outcomes

The decision tree estimated the proportion of patients who received the different diagnostic scenarios in the UC arm compared to the AI arm. The AI arm had 0.1% more true positive and 0.1% less false negative cases, with an estimated cost difference of +€25 per patient for the AI arm. Additionally, the AI arm presented 0.004% less false positive and 0.004% more true negative cases, with a cost difference of +€3 for the AI arm (see Supplementary Table 3).

3.2. Overall outcomes

The base-case analysis (see Table 2) revealed a marginal increase in both costs and QALYs for the AI arm compared to UC. For patients receiving UC, the average lifetime costs for every 1,000 patients were €16,604,800 compared to €16,610,250 for patients receiving the AI approach. With an incremental QALY of 0.55 (2,226 vs. 2,227) and incremental costs of €5,450, the ICER was €9,888 per QALY gained, indicating cost-effectiveness with the average Italian WTP threshold of €33,000/QALY gained.

3.3. Sensitivity analyses

3.3.1. One-way sensitivity analyses

Most variables had limited impact on ICER values. For example, varying the discount rate between 0% and 5% demonstrated ICERs of €9,189 and €10,380, respectively (depicted in Table 3). Most variation in ICER values was seen in mortality rates, specific first-year mortality adjustments due to false negative diagnosis, and additional costs for the AI. More specifically, increasing and decreasing mortality rates by 25% presented variation in ICERs of €15,076 and €2,731, respectively. When adjusting solely the one-year higher mortality rate in patients with a false negative diagnosis, a 25% decrease and increase demonstrated an ICER value of −€643 and €13,767, respectively. The cost of the AI tool significantly influenced its cost-effectiveness, showing incremental cost-savings of −€135 with a 25% decrease in AI costs and an increase in incremental costs of €19,911 with a 25% increase in AI costs. An additional cost-saving scenario was when the performance of the UC diagnostic techniques decreased by 25%. Scenarios that did not lead to the AI-based approach being cost-effective were where the performance (sensitivity and specificity) of the AI was below 0.85 or the performance of the UC diagnostic techniques (ultrasound, MRI, CT) increased by 25% (performance of 0.85: €35,084, performance of 0.8: €123,359).

Table 2. Average lifetime costs, accumulated QALYs, incremental costs and QALY per 1,000 patients, and ICER of base-case analysis.

	UC	AI	Incremental
Costs	€16,604,800	€16,610,250	5,450 €
QALYs	2,226.7	2,227.3	0.55
ICER	–	–	9,888 €

Abbreviations: UC, usual care; AI, artificial intelligence; QALY, quality-adjusted life-years; ICER, incremental cost-effectiveness ratio.

Table 3. One-way and two-way sensitivity analyses, incremental costs and QALY per 1,000 patients, and ICER.

Parameters	Parameter alterations		Incremental costs	Incremental QALYs	ICER
Base case			5,450 €	0.55	9,888 €
One-way sensitivity analysis					
Proportion of cirrhotic patients undergoing initial surveillance	50%		3,962 €	0.28	14,308 €
	75%		7,753 €	0.80	9,710 €
Discount rate (cost and benefits)	0%		5,584 €	0.61	9,189 €
	5%		5,380 €	0.52	10,380 €
HCC prevalence	−25%		7,753 €	0.80	9,710 €
	−50%		3,962 €	0.28	14,308 €
	+ 25%		11,269 €	1.33	8,482 €
Transition rates	−25%		4,243 €	0.56	7,564 €
	+ 25%		6,409 €	0.54	11,879 €
Mortality rates	−25%		1,525 €	0.56	2,731 €
	+ 25%		8,034 €	0.53	15,076 €
Starting age	60		5,446 €	0.55	9,887 €
	70		5,446 €	0.55	9,887 €
	80		5,442 €	0.55	9,890 €
Costs AI tool	−25%		−74 €	0.55	−135 €
	+ 25%		10,966 €	0.55	19,911 €
False negative mortality rate in the first year	−25%		−205 €	0.32	−643 €
	+ 25%		10,425 €	0.76	13,797 €
False negative extra hospitalization costs	−25%		9,692 €	0.55	17,598 €
	+ 25%		1,199 €	0.55	2,177 €
False positive disutility	−25%		5,446 €	0.55	9,894 €
	+ 25%		5,446 €	0.55	9,882 €
False positive extra costs	−25%		5,463 €	0.55	9,918 €
	+ 25%		5,429 €	0.55	9,857 €
Performance AI	Sensitivity/specificity: 0.8		19,392 €	0.16	**123,359** €
	Sensitivity/specificity: 0.85		12,419 €	0.35	**35,084** €
Costs all diagnostic techniques	−25%		7,117 €	0.55	12,922 €
	+ 25%		3,775 €	0.55	6,854 €
Costs health states	−25%		7,933 €	0.55	14,405 €
	+ 25%		2,958 €	0.55	5,371 €
Utility all health states	−25%		5,446 €	0.41	13,173 €
	+ 25%		5,446 €	0.69	7,914 €
Per patient AI costs and fixed costs	€300 + €312,400		22,999,000 €	0.55	41,759,286 €
Two-way sensitivity analysis					
Performance of all usual care diagnostic techniques	Sensitivity/specificity: − 25%		−8,207 €	1.53	−5,340 €
	Sensitivity/specificity: +25%		7,881 €	0.13	**59,364** €
Performance and cost MRI	Sensitivity/specificity: − 25%	Costs: −25%	−908 €	0.79	−1,154 €
	Sensitivity/specificity: +25%	Costs: +25%	12,275 €	0.31	**39,008** €
Performance and cost CT	Sensitivity/specificity: −25%	Costs: −25%	7,340 €	0.69	10,661 €
	Sensitivity/specificity: + 25%	Costs: +25%	3,765 €	0.41	9,114 €
Performance and cost biopsy	Sensitivity/specificity: + 25%	Costs: +25%	3,518 €	0.69	5,110 €
	Sensitivity/specificity: + 25%	Costs: +25%	7,373 €	0.41	17,850 €
Performance and cost AI	Performance: 0.8	Costs: −25%	13,370 €	0, 16	**85,051** €
	Performance: 0.85	Costs: −25%	6,648 €	0,35	18,780 €
	Performance: 0.9	Costs: −25%	−74 €	0.55	−135 €
	Performance: 0.8	Costs: +25%	25,414 €	0,16	**161,667** €
	Performance: 0.85	Costs: +25%	18,190 €	0,35	**51,388** €
	Performance: 0.9	Costs: +25%	10,966 €	0.55	19,911 €
Diagnostic and health state costs	Diagnosis: −25%	Health states: −25%	9,605 €	0.55	17,439 €
	Diagnosis: −25%	Health states: +25%	4,629 €	0,55	8,405 €
	Diagnosis: +25%	Health states: −25%	6,262 €	0,55	11,370 €
	Diagnosis: +25%	Health states: +25%	1,287 €	0.55	2,337 €

Abbreviations: ICER, incremental cost-effectiveness ratio; HCC, hepatocellular cancer; AI, artificial intelligence; MRI, magnetic resonance imaging; CT, computed tomography.
In bold, scenarios that do not lead to cost-effectiveness.

3.3.2. Two-way sensitivity analyses

Combining changes in performance and costs of AI presented significant variability in ICER values. For example, a reduction in performance (sensitivity and specificity) of 0.85 with a reduction of AI costs by 25% resulted in an ICER of €18,780, however a performance of 0.80 with increased costs resulted in an ICER of €161,667. Two-way sensitivity analyses on varying diagnostic costs and costs by health state demonstrated marginal changes in ICER values but demonstrated the obvious compounding effect on ICER values when decreasing or increasing both variables (€2,337 vs €17,439), depicted in Table 3. An additional cost-saving scenario included when the cost of the AI tool decreased by 25% and its performance increased to 0.9.

4. Discussion

This study pioneers in presenting the economic impact of AI as a tool for more accurate and, therefore, earlier detection of HCC in cirrhotic patients. Although there is a marginal impact on QALYs, the results of this study indicate that, even in a progressive disease like HCC where mortality rates are high, an AI tool for earlier detection is cost-effective. The small incremental benefits observed in this study suggest that cost-effectiveness of AI in this context may be limited by broader systemic factors, such as the specific imaging technique that the AI is designed for, and at which stage this imaging technique is used. For example, having an AI that is designed for the first imaging technique used would have a greater clinical and economic impact than an AI designed for an imaging technique that is usually used as a last approach. Although this study demonstrated little benefits of the AI tool, it is important to note the secondary synergistic effects of AI on usual care. For example, a radiologist using an AI tool as a first or second reader achieves higher accuracy compared to one who does not utilize an AI tool[41].

While the AI tool was demonstrated to be cost-effective, the marginal differences in QALYs highlight an important consideration. Due to the progressive nature of HCC and the high mortality rate in the first year of diagnosis, the burden of HCC may not be substantially mitigated solely by earlier detection[42]. Further advancements in therapeutic options and strategies to improve utilization rather than in improving performance of diagnostic tools alone might provide greater potential for improving patient outcomes[43]. Therefore, the AI's benefit might be more pronounced in other stages of the treatment pipeline or in diseases with lower mortality rates. Moreover, this AI tool was specifically developed for integration with MRI, a costly diagnostic technique that is typically reserved for cases where ultrasound and CT yield inconclusive results. In this case, the AI's impact is further limited by its confined role and narrow patient subset. As the analysis of economic impact was performed after the AI was developed, the alignment with economic opportunities during the design phase might have been overlooked[44]. Besides the high mortality rate, our study demonstrated that the cost of AI was another pivotal economic driver within earlier detection of HCC. By solely fluctuating the cost of AI by 25%, although cost-effective, the ICER varied from being cost-saving to €19,911/QALY. This emphasizes the importance of optimizing AI development and application costs to ensure economic feasibility. Lastly, it is important to note that the variation of HCC occurrence within cirrhotic patients varies between countries[45]. For example, a French and Belgian cohort observed an annual HCC incidence of 2.9%[46], while the Italian incidence rises to 5%[5]. The Italian population further distinguishes itself due to its large proportion of patients having risk factors that significantly impact the chance of developing HCC, namely chronic hepatitis C, hereditary hemochromatosis, and metabolic syndrome and the higher levels of longevity, further elevating the accumulated risk. For example, for patients who have cirrhosis due to hereditary hemochromatosis, a 5-year cumulative HCC risk of 21% has been reported[47].

Besides providing information to policymakers on the feasibility and value of an AI tool for HCC detection in cirrhotic patients, the results of this model shed light on several broader implications. First, due to the marginal benefits demonstrated in this study and assessing literature, the controversial discussion on the focus of improving earlier detection rather than other strategies such as increasing screening utilization is further confirmed in this study[42]. Second, this study highlights the importance and need of robust economic evaluations of AI in healthcare and the currently disproportionally low numbers of economic evaluations on AI applications in healthcare settings compared to the research published on AI developments for clinical use[48,49] with the number of trials on AI having more than

doubled since 2021[50]. A crucial point highlighted by our study is the importance of health economic involvement in the early stages of AI development to more effectively guide the impact of AI and ensure alignment with economic and clinical considerations needed to maximize AI's value in clinical application. Last, this study pinpoints the areas where AI development should be improved. Shifting the perspective on economic evaluations from proving a summative judgement in the form of expected cost-effectiveness to utilizing economic evaluations for the purposes of exploring possible costs and outcomes in the form of informative guidance could revolutionize healthcare resource allocation[51].

This study holds several limitations. First, due to limited gender-specific utility and cost data, the model did not incorporate more elaborate disease stages such as in-depth adjustments of transition rates, mortality rates, costs, and utility based on the Barcelona classification (stages 0, A, B, C, D) or based on gender. Including these stages or gender differences could provide a more nuanced understanding of the economic and clinical impact of AI-based HCC detection. Additionally, due to the study's timeframe, the effect of risk factors that impacts the chance of developing HCC, such as chronic hepatitis C, hereditary hemochromatosis, and metabolic syndrome, were not included in this study. Second, assumptions made within the false negative diagnostic scenario might have led to under- or overestimation of benefits. An additional cost was attributed to late detection of HCC within this scenario, generally due to the higher hospitalization rate and need for more intensive care for these patients. Nonetheless, one-way sensitivity analyses did not demonstrate a significant impact on the overall cost-effectiveness conclusions drawn from the model. Third, the model is also not directly translating to other European countries due to the reliance on country-specific data needed for this model. For example, other countries require an additional societal perspective, which was not included in this study. Furthermore, although a probabilistic sensitivity analysis would have tested the uncertainty of our model to a greater extent, due to lacking information on the parameter confidence intervals and the consequent need to rely heavily on assumptions, a probabilistic sensitivity analysis was not performed in this study. Nonetheless, the two-way sensitivity analyses aim to provide general information for application in other countries with, for example, higher patient costs or lesser performance of tools. Fourth, an important equity consideration is that MRI access is limited to more privileged healthcare settings. The added benefit is that AI-enhanced MRI may therefore preferentially impact patient populations with better access to advanced imaging and thereby potentially widen existing disparities in disease surveillance and diagnosis. It is further important to note that the costs of the AI were solely the per-patient cost for usage. These costs did not include fixed implementation costs such as software integration, staff training, and infrastructure, which may represent significant expenses during initial implementation. By including fixed costs published by Afshar et al. in 2025[32], our sensitivity analyses show that the AI would not be cost-effective under these conditions. The impact of fixed costs could particularly affect smaller centers where fewer patients are scanned annually, potentially diminishing the cost-effectiveness of the AI tool due to limited ability to benefit from economies of scale.

Specifically, within the field of HCC, future research should entail robust cost calculations of HCC healthcare costs based on disease progression. Additionally, uncertainty on mortality rates of HCC progression should be further investigated to increase the reliability of this analysis. Future research should assess the cost-effectiveness of the AI tool based on risk factors such as chronic hepatitis C, hereditary hemochromatosis, and metabolic syndrome through, for example, a microsimulation model. Lastly, additional attention should be paid to the geographic and socioeconomic disparities in access to surveillance and follow-up treatment which influence disease progression and surveillance effectiveness. Furthermore, our model assumes that all cirrhotic patients who receive the screening invite undergo surveillance. Future research could explore the comparative cost-effectiveness of AI-based improvements in diagnostic performance compared to interventions designed to improve adherence to existing surveillance protocols. On a broader perspective, further research should focus on exploring different applications of AI, such as treatment prediction and response monitoring, aiming to understand the full potential impact of AI when integrated into clinical care. Expanding the application to different stages in the patient's trajectory, diverse disease context, and screening modalities could create a more comprehensive understanding of the AI's role on patient outcomes and healthcare efficiency, which may also help reduce disparities in detection by increasing access in under-resourced settings.

Conclusion

The findings of this study demonstrate that an AI-based approach to earlier detection of HCC in cirrhotic patients is cost-effective at €10,000/QALY at a willingness-to-pay threshold of €33,000/QALY gained. The findings further highlight important considerations for integrating AI into clinical practice. Although it remains cost-effective despite varying key economic drivers, such as AI cost and mortality rates, the value of AI may be constrained by the mortality-driven and progressive nature of HCC. Additionally, integrating health economic evaluations in the early stages of AI development can ensure that its applications are aligned with areas that provide most substantial economic and clinical benefits for patient and society. Future research should focus on analyzing different applications of AI.

Transparency

Declaration of funding

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 952103. The funding body had no role in the design of the study, collection, analysis, interpretation of data, or writing of the manuscript.

Declaration of financial/other interests

The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this study. Mickaël Hiligsmann received research grants from Radius Health, radiomics.bio, and Angelini Pharma (paid to institution), lecture fees from IBSA (paid to institution), was grant advisor for Pfizer (paid to institution), and consultant for Grunenthal (paid to institution). LA received consultancy fees from radiomics.bio. LM, CCM, SG, FB, AC, JC, and WV are employed by radiomics.bio. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose. The Editors in Chief helped with adjudicating the final decision on this paper.

Author contributions

LM, CCM, AC, WV, LA, and MH contributed to the study design and interpretation of findings. LM, CCM, and MH contributed to the writing of the manuscript. All authors contributed to proofreading of the manuscript and approved the final version of the manuscript for submission.

Acknowledgements

We would like to thank all collaborators and institutions that contributed to this study. More specifically, we would like to thank the clinicians of the institutions of Kaunas Klinikos in Lithuania, Medical University of Gdansk in Poland, Pisa University Hospital in Italy, and Umeå University in Sweden for providing invaluable clinical expertise. We acknowledge the support of the EU-funded EuCanImage project, which provided us with the resources and a collaborative research environment that were crucial for this work. We also extend our appreciation to our colleagues and research partners for their valuable insights and discussions during the consortium meetings. Lastly, we want to thank the patients and healthcare professionals whose experiences and data have informed this research, ultimately contributing to the advancement of cost-effective strategies in HCC management.

ORCID

L. Maas http://orcid.org/0000-0002-0032-0712
C. Contreras-Meca http://orcid.org/0009-0002-2241-2260
S. Ghezzo http://orcid.org/0000-0002-7765-6759
F. Belmans http://orcid.org/0000-0002-8944-6898
A. Corsi http://orcid.org/0000-0003-3954-303X
J. Cant http://orcid.org/0000-0002-0772-252X
W. Vos http://orcid.org/0000-0003-0827-421X
M. Bobowicz http://orcid.org/0000-0002-3608-1960
M. Rygusik http://orcid.org/0009-0003-6352-0927
D. K. Laski http://orcid.org/0000-0002-1177-4541
L. Annemans http://orcid.org/0000-0001-8305-7210
M. Hiligsmann http://orcid.org/0000-0003-4274-9258

References

[1] International Agency for Research on Cancer. [Internet]. Cancer Today. [cited 2025 Mar 2]. Available from: https://gco.iarc.fr/today/en/dataviz/tables?mode=cancer&types=1&group_populations=1&multiple_populations=1&populations=903_904_905_908_909_935

[2] Cirrhosis [Internet]. [cited 2024 Sep 12]. Available from: https://www.mayoclinic.org/diseases-conditions/cirrhosis/symptoms-causes/syc-20351487

[3] Parikh ND, Singal AG, Hutton DW, et al. Cost-effectiveness of hepatocellular carcinoma surveillance: an assessment of benefits and harms. Am J Gastroenterol. 2020;115(10):1642–1649. doi: 10.14309/ajg.0000000000000715.

[4] Lee CH, Kang HJ, Yu SY, et al. Initial treatment response and short-term mortality of spontaneous bacterial peritonitis in cirrhotic patients with hepatocellular carcinoma. Sci Rep. 2023;13(1):6067. doi: 10.1038/s41598-023-32006-8.

[5] Cucchetti A, Trevisani F, Cescon M, et al. Cost-effectiveness of semi-annual surveillance for hepatocellular carcinoma in cirrhotic patients of the Italian Liver Cancer population. J Hepatol. 2012;56(5):1089–1096. doi: 10.1016/j.jhep.2011.11.022.

[6] Mazzucco W, Vitale F, Mazzola S, et al. Does access to care play a role in liver cancer survival? The ten-year (2006–2015) experience from a population-based cancer registry in Southern Italy. BMC Cancer. 2021;21(1):307. doi: 10.1186/s12885-021-07935-0.

[7] Erratum. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2020;70(4):313–313.

[8] Farhang Zangneh H, Wong WWL, Sander B, et al. Cost effectiveness of hepatocellular carcinoma surveillance after a sustained virologic response to therapy in patients with hepatitis C virus infection and advanced fibrosis. Clin Gastroenterol Hepatol. 2019;17(9):1840–1849.e16. doi: 10.1016/j.cgh.2018.12.018.

[9] Andersson KL, Salomon JA, Goldie SJ, et al. Cost effectiveness of alternative surveillance strategies for hepatocellular carcinoma in patients with cirrhosis. Clin Gastroenterol Hepatol. 2008;6(12):1418–1424. doi: 10.1016/j.cgh.2008.08.005.

[10] Goossens N, Singal AG, King LY, et al. Cost-effectiveness of risk score–stratified hepatocellular carcinoma screening in patients with cirrhosis. Clin Transl Gastroenterol. 2017;8(6):e101. doi: 10.1038/ctg.2017.26.

[11] Atiq O, Tiro J, Yopp AC, et al. An assessment of benefits and harms of hepatocellular carcinoma surveillance in patients with cirrhosis. Hepatology. 2017;65(4):1196–1205. doi: 10.1002/hep.28895.

[12] Koh B, Danpanichkul P, Wang M, et al. Application of artificial intelligence in the diagnosis of hepatocellular carcinoma. eGastroenterology. 2023;1(2):e100002. doi: 10.1136/egastro-2023-100002.

[13] EuCanImage [Internet]. 2024. Available from: https://eucanimage.eu/

[14] Linee guida per la compilazione del dossier a supporto della domanda di rimborsabilità e prezzo di un medicinale [Internet]. Agencia Italiana del Farmaco; [cited 2024 Dec 11]. Available from: https://www.aifa.gov.it/documents/20142/1307543/2021.01.22_estratto_linee_guida_sezione_E.pdf

[15] Elvidge J, Hawksworth C, Avşar TS, et al. Consolidated Health Economic Evaluation Reporting Standards for interventions that use artificial intelligence (CHEERS-AI). Value Health. 2024;27(9):1196–1205. doi: 10.1016/j.jval.2024.05.006.

[16] Risk-Based Digital Health Classification by NICE [Internet]. 2019 [cited 2024 Dec 11]. Available from: https://www.centivis.com/news/2019/1/4/risk-based-digital-health-classification-by-nice

[17] Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. J Hepatol. 2022;76(3):681–693. doi: 10.1016/j.jhep.2021.11.018.

[18] Cococcia S, Dutta P, Moghim M, et al. The fate of indeterminate liver lesions: what proportion are precursors of hepatocellular carcinoma? BMC Gastroenterol. 2022;22(1):118. doi: 10.1186/s12876-022-02135-x.

[19] Nousbaum JB, Pol S, Nalpas B, et al. Hepatitis C virus type 1b (II) infection in France and Italy. Ann Intern Med. 1995;122(3):161–168. doi: 10.7326/0003-4819-122-3-199502010-00001.

[20] D'Amico G, Morabito A, Pagliaro L, et al. Survival and prognostic indicators in compensated and decompensated cirrhosis. Dig Dis Sci. 1986;31(5):468–475.

[21] Xu X-S, Chen W, Miao R-C, et al. Survival analysis of hepatocellular carcinoma: a comparison between young patients and aged patients. Chin Med J (Engl). 2015;128(13):1793–1800. doi: 10.4103/0366-6999.159356.

[22] Giannini EG, Farinati F, Ciccarese F, et al. Prognosis of untreated hepatocellular carcinoma. Hepatology. 2015;61(1):184–190. doi: 10.1002/hep.27443.

[23] Thompson Coon J, Rogers G, Hewson P, et al. Surveillance of cirrhosis for hepatocellular carcinoma: a cost–utility analysis. Br J Cancer. 2008;98(7):1166–1175. doi: 10.1038/sj.bjc.6604301.

[24] Tromme I, Devleesschauwer B, Beutels P, et al. Health-related quality of life in patients with melanoma expressed as utilities and disability weights. Br J Dermatol. 2014;171(6):1443–1450. doi: 10.1111/bjd.13262.

[25] Lin PJ, Cangelosi MJ, Lee DW, et al. Willingness to pay for diagnostic technologies: a review of the contingent valuation literature. Value Health. 2013;16(5):797–805. doi: 10.1016/j.jval.2013.04.005.

[26] Petta S, Ting J, Saragoni S, et al. Healthcare resource utilization and costs of nonalcoholic steatohepatitis patients with advanced liver disease in Italy. Nutr Metab Cardiovasc Dis. 2020;30(6):1014–1022. doi: 10.1016/j.numecd.2020.02.016.

[27] Cammà C, Cabibbo G, Petta S, et al. Cost-effectiveness of sorafenib treatment in field practice for patients with hepatocellular carcinoma. Hepatology. 2013;57(3):1046–1054. doi: 10.1002/hep.26221.
[28] Lillini R, De Lorenzo F, Baili P, et al. Out-of-pocket costs sustained in the last 12 months by cancer patients: an Italian survey-based study on individual expenses between 2017 and 2018. Eur J Health Econ. 2023;24(8): 1309–1319. doi: 10.1007/s10198-022-01544-9.
[29] Geh D, Rana FA, Reeves HL. Weighing the benefits of hepatocellular carcinoma surveillance against potential harms. J Hepatocell Carcinoma. 2019;6:23–30. doi: 10.2147/JHC.S159581.
[30] Hautz WE, Kämmer JE, Hautz SC, et al. Diagnostic error increases mortality and length of hospital stay in patients presenting through the emergency room. Scand J Trauma Resusc Emerg Med. 2019;27(1):54. doi: 10.1186/s13049-019-0629-z.
[31] Russo P, Zanuzzi M, Carletto A, et al. Role of economic evaluations on pricing of medicines reimbursed by the Italian National Health Service. Pharmacoeconomics. 2023;41(1):107–117. doi: 10.1007/s40273-022-01215-w.
[32] Afshar M, Resnik F, Joyce C, et al. Clinical implementation of AI-based screening for risk for opioid use disorder in hospitalized adults. Nat Med. 2025;31(6):1863–1872. doi: 10.1038/s41591-025-03603-z.
[33] Singal A, Volk ML, Waljee A, et al. Meta-analysis: surveillance with ultrasound for early-stage hepatocellular carcinoma in patients with cirrhosis. Aliment Pharmacol Ther. 2009;30(1):37–47. doi: 10.1111/j.1365-2036.2009.04014.x.
[34] Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. 2018;67(1):358–380. doi: 10.1002/hep.29086.
[35] Dal Maso L, Guzzinati S, Buzzoni C, et al. Long-term survival, prevalence, and cure of cancer: a population-based estimation for 818 902 Italian patients and 26 cancer types. Ann Oncol. 2014;25(11):2251–2260. doi: 10.1093/annonc/mdu383.
[36] Frager SZ, Cooper W, Saenger Y, et al. Treatment of recurrent hepatocellular carcinoma following liver resection, ablation or liver transplantation. World J Meta-Anal. 2023;11(2):47–54. doi: 10.13105/wjma.v11.i2.47.
[37] Chung W, Jo C, Chung WJ, et al. Liver cirrhosis and cancer: comparison of mortality. Hepatol Int. 2018;12(3): 269–276. doi: 10.1007/s12072-018-9850-5.
[38] Le modalità ed i criteri per la definizione delle tariffe massime delle prestazioni sanitarie [Internet]. [cited 2024 Oct 10]. Available from: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2023&codLeg=95791&parte=1%20&serie=null
[39] Lafata JE, Simpkins J, Lamerato L, et al. The economic impact of false-positive cancer screens. Cancer Epidemiol Biomarkers Prev. 2004;13(12):2126–2132. doi: 10.1158/1055-9965.2126.13.12.
[40] Di Nardo F, De Waure C, Longhi S, et al. Hospitalization costs of hepatitis B in Italy. Eur J Public Health. 2013; 23(suppl_1):ckt124.111. doi: 10.1093/eurpub/ckt124.111.
[41] Leibig C, Brehmer M, Bunk S, et al. Combining the strengths of radiologists and AI for breast cancer screening: a retrospective analysis. Lancet Digit Health. 2022;4(7):e507–e519. doi: 10.1016/S2589-7500(22)00070-X.
[42] Yang JD. Detect or not to detect very early stage hepatocellular carcinoma? The western perspective. Clin Mol Hepatol. 2019;25(4):335–343. doi: 10.3350/cmh.2019.0010.
[43] Arvind A, Redmon K, Singal AG. Persisting challenges in the early detection of hepatocellular carcinoma. Expert Rev Anticancer Ther. 2025;25(3):1–12. doi: 10.1080/14737140.2025.2467184.
[44] Partington A, Crotty M, Laver K, et al. Preparing early economic evaluations for the development and management of health service interventions. Int J Technol Assess Health Care. 2024;40(1):e47. doi: 10.1017/S0266462324000539.
[45] Poli E, Martin D. E. Progression of liver disease and associated risk of hepatocellular carcinoma. Hepatoma Res [Internet]; 2024 Mar 28 [cited 2025 Apr 4]; Available from: https://parjournal.net/article/view/2394-5079.2023.101
[46] Ganne-Carrié N, Chaffaut C, Bourcier V, et al. Estimate of hepatocellular carcinoma incidence in patients with alcoholic cirrhosis. J Hepatol. 2018;69(6):1274–1283. doi: 10.1016/j.jhep.2018.07.022.
[47] Fracanzani AL, Conte D, Fraquelli M, et al. Increased cancer risk in a cohort of 230 patients with hereditary hemochromatosis in comparison to matched control patients with non–iron-related chronic liver disease. Hepatology. 2001;33(3):647–651. doi: 10.1053/jhep.2001.22506.
[48] Dunning L, Kreif N, Gumbs P. ISPOR: the place of artificial intellingece in HTA and HEOR [Internet]. [cited 2024 Oct 12]. Available from: https://www.ispor.org/docs/default-source/euro2023/206the-place-of-artificial-intelligence-in-hta-and-heorfinal.pdf?sfvrsn=7b0eb2c3_0
[49] Kastrup N, Holst-Kristensen AW, Valentin JB. Landscape and challenges in economic evaluations of artificial intelligence in healthcare: a systematic review of methodology. BMC Digit Health. 2024;2(1):39. doi: 10.1186/s44247-024-00088-7.
[50] Han R, Acosta JN, Shakeri Z, et al. Randomised controlled trials evaluating artificial intelligence in clinical practice: a scoping review. Lancet Digit Health. 2024;6(5):e367–73–e373. doi: 10.1016/S2589-7500(24)00047-5.
[51] Leys M. Health care policy: qualitative evidence and health technology assessment. Health Policy. 2003;65(3): 217–226. doi: 10.1016/s0168-8510(02)00209-9.