

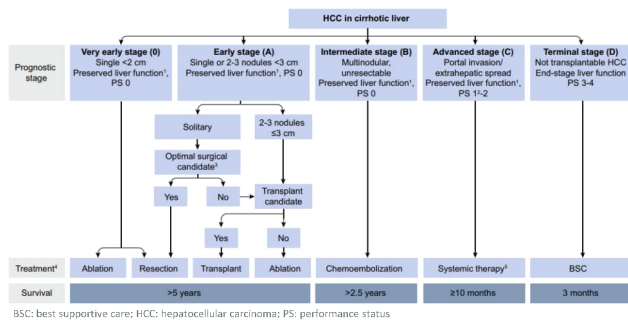
Disease Burden and Cost-of-Illness of Hepatocellular Carcinoma in Portugal: A Model-Based Analysis Considering the Barcelona Clinic Liver Cancer Disease Staging and Treatment Algorithm System

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1 – Objectives

- Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer, accounting for 90% of these tumors. It exerts a substantial socio-economic burden due to its high morbidity and mortality, costly treatment, and escalating general healthcare expenses over time.
- The clinical guidelines of the European Association for the Study of the Liver (EASL) recommend the classification of HCC based on the Barcelona Clinic Liver Cancer (BCLC) staging system for prognosis prediction and treatment decision-making at all stages of the disease (Figure 1) [1].



- The objective of this study was to assess the potential impact of fully adhering to the BCLC system – in terms of disease staging and treatment algorithm – on the disease burden and cost-of-illness associated with HCC in Portugal.

2 – Methods

- An individual-level, continuous-time, state-transition model was developed to simulate the progression of hypothetical HCC patients through the disease stages and corresponding treatment algorithms suggested by the BCLC system, in the Portuguese National Health Service (Figure 2). The model was validated by the physician co-authors, specialized in the treatment of liver cancer patients.

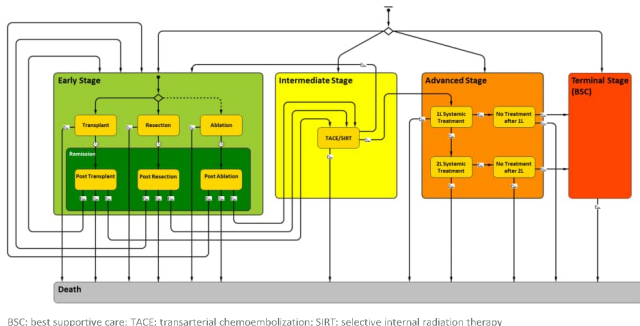


Figure 2. Model diagram of the model developed to simulate the progression of hypothetical HCC patients through the BCLC disease stages and corresponding treatment algorithms (Software: Anylogic®).

- A targeted literature review was conducted with the aim of identifying studies specifically conducted in the population of patients with HCC that could provide information about the transition probabilities between various health states in the model.
- A panel of 11 experts provided further insights into disease incidence, disease prevalence, and healthcare resource utilization at each disease stage. The composition of the panel sought to be representative, on one hand, of the various medical specialties involved in the care and treatment of patients with HCC throughout the course of the disease - internal medicine, gastroenterology, oncology, interventional radiology, and general surgery - and on the other hand, of the various institutions, geographically dispersed, where these patients are treated and monitored.
- Unit costs for healthcare resource utilization were collected from reliable national public sources. Together with the healthcare resource utilization data resulting from the expert panel, these gave rise to the annualized costs, associated with consultations, tests, exams, and hospitalizations in each health state of the model, presented in Table 1.

Table 1. Predicted number of HCC patients treated with each of the therapeutic options, conditional on fully adhering to the BCLC system.

Model Health State	Consultations	Test	Exams	Hospitalizations
Transplant	1.470,67 €	4.692,28 €	2.306,38 €	331.822,44 €
Resection	936,04 €	4.393,22 €	2.311,11 €	90.722,91 €
Ablation	1.143,06 €	4.385,43 €	2.276,45 €	22.919,47 €
Remission, post-transplant	728,24 €	842,80 €	381,84 €	1.881,73 €
Remission, post-resection	680,40 €	781,95 €	400,46 €	1.364,21 €
Remission, post-ablation	899,30 €	781,95 €	400,46 €	363,26 €
Intermediate	890,06 €	749,56 €	480,87 €	3.150,22 €
1L Systemic Treatment	1.432,81 €	1.084,66 €	487,24 €	2.999,76 €
2L Systemic Treatment	1.657,77 €	1.014,56 €	461,96 €	3.908,48 €
No treatment after 1L	1.455,37 €	629,84 €	389,03 €	3.473,14 €
No treatment after 2L	1.410,90 €	598,22 €	378,26 €	4.055,63 €
Terminal	1.455,72 €	390,84 €	270,67 €	9.741,15 €

1L: first line; 2L: second line

3 – Results

- Fully adhering to the BCLC system, the annual prevalence of HCC (including patients in remission) could be expected to keep increasing over the next five-year period, from 4.151 patients in 2023 to 4.851 patients in 2027 (Figure 3).

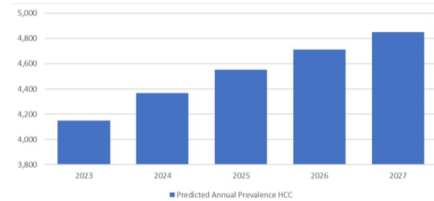


Figure 3. Predicted annual prevalence of HCC in Portugal, conditional on fully adhering to the BCLC system.

- Annual mortality rates could slightly decrease from 29.8% in 2023 to 28.7% in 2027, however still leading to a total of 120,314 years of life lost due to premature mortality (Figure 4).

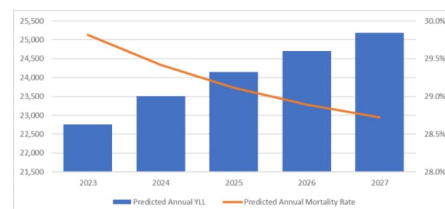


Figure 4. Predicted years of life lost (primary axis) and mortality rates (secondary axis) due to HCC in Portugal, conditional on fully adhering to the BCLC system.

- In Table 2 the potential number of patients treated with each of the treatment options included in the model are presented for the years 2023 to 2027.

Table 2. Predicted number of HCC patients treated with each of the therapeutic options, conditional on fully adhering to the BCLC system.

Treatment	2023	2024	2025	2026	2027
Transplant	191	197	202	206	210
Resection	181	187	193	197	202
Ablation	296	306	315	323	330
TACE/SIRT	333	352	368	381	393
1L Systemic Treatment	827	841	854	867	879
2L Systemic Treatment	103	105	106	108	110

1L: first line; 2L: second line

- Over the considered five-year period, HCC could account for 367,187,683€ in health-care system costs, 44.3% of which attributable to systemic treatment related costs and 29.0% to liver transplantation related costs (Figure 5).

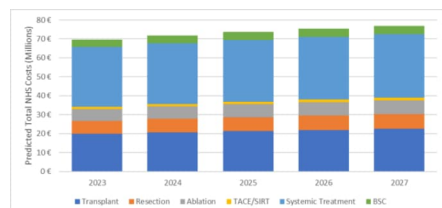


Figure 5. Predicted total NHS costs due to HCC in Portugal, related to each of the therapeutic options, conditional on fully adhering to the BCLC system.

4 – Conclusions

- ➔ This study provides valuable insights into the potential disease burden and cost-of-illness of HCC in Portugal, under the assumption of full adherence to the BCLC disease staging and treatment algorithm system.
- ➔ These findings can inform healthcare researchers on future investigation pathways and policymakers on resource allocation decisions, allowing for the effective management of HCC and potentially leading to improved patient outcomes.

[1] Galle, P.R., et al., EASL clinical practice guidelines: management of hepatocellular carcinoma. Journal of hepatology, 2018. 69(1): p. 182-236.

[2] World Health Organization. WHO methods and data sources for global burden of disease estimates 2000-2019. 2020; Available from: <https://tinyurl.com/2xcya9rd>.

[3] Instituto Nacional de Estatística. Tábua Completa de Mortalidade para Portugal 2017-2019 (Ambos os sexos). 28 de maio de 2020; Available from: <https://tinyurl.com/449z2cua>.