The Disease and Economic Burden of Hepatocellular Carcinoma in Australia

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BACKGROUND

- Hepatocellular carcinoma (HCC) is the most common type of liver cancer, accounting for approximately 75% of total cases[1]
- Effective population health planning and resource allocation for HCC depend on accurate epidemiological and disease burden evidence, however these data are currently limited
- This study used an Australian population-based cancer registry to examine the incidence, mortality, and prevalence rate of HCC using relevant incidences from 2009–2018

OBJECTIVES

- To quantify the current incidence, prevalence, and mortality of HCC
- To project the life expectancy of patients diagnosed with HCC by examining the trend over the past 10 years
- To estimate the economic and psychosocial burden of HCC

METHODS

- Data were collected from the Australian Cancer Database, Australian Cancer Registries, and the National Mortality Database by the Australian Institute of Health and Welfare (AIHW) using pre-defined data fields
- Data from 4 Australian States/Territories (Victoria, Queensland, Tasmania, and the Australian Capital Territory) were included in the study
- HCC cases were identified using International Statistical Classification of Diseases (ICD-10-AM code C22.0) with a data cut-off of December 2018
- Incidence, prevalence, mortality, and associated trends were calculated using established methods, including linear regression and DisMod, as used in a recent Australian Institute of Health and Welfare report[2]
- Kaplan-Meier survival curves for overall survival were constructed with a maximum follow-up of 10 years (since 2009)
- A Cox proportional hazard model was used to calculate the hazard ratio (HR) for the difference in hazard rate between sex, age groups, and year of diagnosis
- All analyses were stratified by sex and age group where applicable. A *P*-value <0.05 was considered statistically significant
- Ethics exemption for this study was approved by the Deakin University Human Ethics Research Committee (DUHERC 2022-091 and the NSW Cancer Registry (2022/ETH01850)

Markov Model Structure

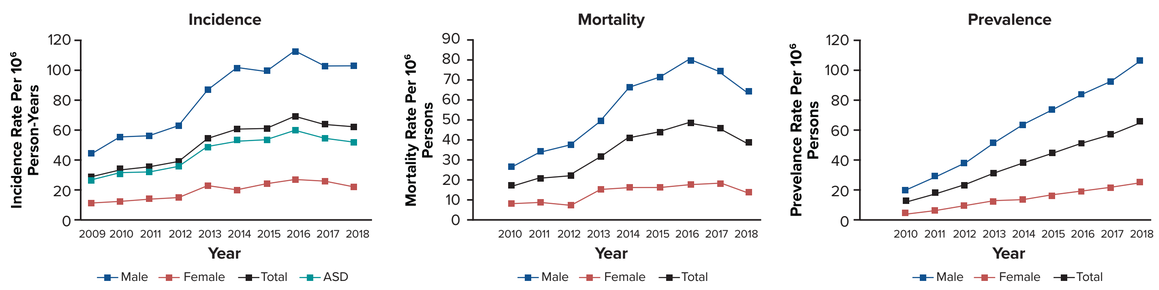
- A two-state Markov model was developed to simulate a hypothetical cohort of 10,000 patients over the lifetime horizon based on a yearly cycle length
- Patients entered the model in the alive health state after the index cancer diagnosis. In each cycle, they were assigned to either the survived or dead state
- The data were divided into three 3-year periods (2009–2011, 2012–2014, 2015–2017) to compare the differences in survival over the study period
- Model parameters were identified from the literature[3-8]

RESULTS

Incidence, Prevalence, and Mortality of Patients With HCC in Australia

- Data were analyzed for 5,993 patients with HCC in Australia. Demographic characteristics of the population are summarized in **Supplementary Table 1**, available for download by scanning the following Quick Response (QR) code at right
- The crude annual incidence of HCC (2009–2018) was estimated as 28.31–69.94 per 1,000,000 person-years (**Figure 1**)
  - Annual mortality was estimated as 17.23–48.92 per 1,000,000 person-years
  - Annual prevalence was estimated as 30.79–164.12 per 1,000,000 person-years
- There were increasing trends for the incidence, mortality, and prevalence of HCC over the study period, particularly for male patients (**Figure 1** and **Table 1**)
- Kaplan-Meier survival estimates were significantly different between the age groups assessed (**Figure 2**)
  - No statistically significant differences were observed in the Kaplan-Meier survival estimates for the sex, year of diagnosis, or study period subgroups assessed
- Statistically significant HRs for HCC for increased age groups were identified (**Table 2**)
  - HRs for patients by sex or year of diagnosis were not significantly different, with the exception of patients diagnosed in 2012 and 2017

Figure 1: Incidence, Mortality, and Prevalence Rate Per 10^6 Persons/Person-Years of Patients With HCC, 2009–2018



ASD, age standardized; HCC, hepatocellular carcinoma.

Table 1: Regression Analysis Examining the Trend in Incidence, Mortality, and Prevalence Rate of Patients With HCC

	Male			Female			Total		
	Coefficient	SE	*P*-value	Coefficient	SE	*P*-value	Coefficient	SE	*P*-value
Incidence									
Constant	40.76	6.98	<0.0001	10.50	2.01	0.001	25.60	4.25	<0.0001
Year	7.67	1.12	<0.0001	1.73	0.32	0.001	4.65	0.69	<0.0001
Observations[a], n	10			10			10		
R^2	0.853			0.781			0.852		
RSD	10.21			2.94			6.23		
Mortality									
Constant	24.70	7.46	0.013	7.32	2.13	0.011	15.98	4.63	0.011
Year	6.27	1.32	0.002	1.24	0.38	0.014	3.72	0.82	0.003
Observations[a], n	9			9			9		
R^2	0.762			0.603			0.745		
RSD	10.26			2.94			6.38		
Prevalence									
Constant	19.86	2.66	<0.0001	3.72	0.82	0.003	11.70	1.36	<0.0001
Year	27.12	0.47	<0.0001	6.48	0.15	<0.0001	16.71	0.24	<0.0001
Observations[a], n	9			9			9		
R^2	0.998			0.996			0.999		
RSD	3.66			1.13			1.87		

[a]The regression analysis is based on 9 data points (mortality and prevalence rate) and 10 data points (incidence rate) for the annual rates between 2009 and 2018.
HCC, hepatocellular carcinoma; RSD, residual standard deviation (root error mean square); SE, standard error.

Economic Modelling of HCC Costs and Disease Burden in Australian Patients

- Base case analysis suggested a stable trend for remaining life expectancy over 15 years of model time horizon (**Table 3**)
  - The increased life expectancy in Period 3 (2015–2017) compared with Period 1 (2009–2011) was 0.131 years
- A stable trend for quality-adjusted life years (QALY) and disability-adjusted life years (DALY) was observed over the model time horizon (**Table 3**)
  - QALY and DALY were increased by 0.093 and 0.373 years, respectively, in Period 3 compared with Period 1
- The average cost per patient was $121,545.68 Australian dollars (AUD) in Period 3 (**Table 3**)
  - The increased cost in Period 3 compared with Period 1 was $4,093.20 AUD

CONCLUSIONS

- These data showed that the incidence of HCC in Australia has increased over the last decade while corresponding QALY, DALY, and costs have remained stable
- The incidence and mortality rates identified in this study were lower than those reported by the AIHW[2]
  - A possible explanation for this is the inclusion of only code C22.0 for hepatocellular carcinoma and the exclusion of codes for other types of liver cancer, such as C22.2–C22.9
- Although prevalence was a secondary outcome calculated from incidence and mortality, our estimation had a similar trend to a Deloitte report for the Liver Foundation[9]
- The costs identified in this study are similar to those reported by Nguyen et al. 2022 for HCC[10]

Figure 2: Kaplan-Meier Survival Estimates in Patient Subgroups With 10 Years of Follow-Up

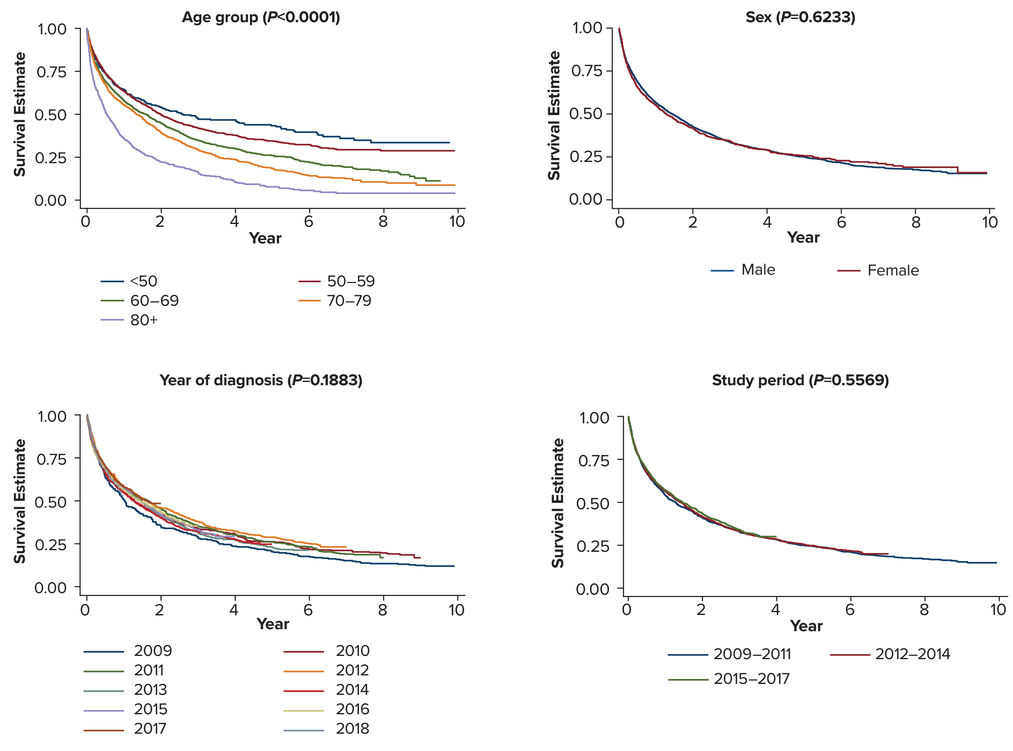


Table 2: Hazard Ratio of HCC by Sex, Age Group and Year of Diagnosis

	Hazard Ratio	*P*-value	95% CI
Age group			
<50		Reference group	
50–59	1.18	0.037	1.01–1.38
60–69	1.47	<0.0001	1.26–1.71
70–79+	1.71	<0.0001	1.46–1.99
80+	2.74	<0.0001	2.33–3.21
Sex			
Male		Reference group	
Female	0.97	0.400	0.89–1.05
Year			
2009		Reference year	
2010	0.90	0.218	0.76–1.06
2011	0.89	0.159	0.75–1.05
2012	0.82	0.022	0.70–0.97
2013	0.93	0.390	0.80–1.09
2014	0.93	0.361	0.80–1.08
2015	0.90	0.197	0.78–1.05
2016	0.88	0.111	0.76–1.03
2017	0.83	0.021	0.70–0.97
2018	0.91	0.333	0.76–1.10

CI, confidence interval; HCC, hepatocellular carcinoma.

Table 3: Results of the Markov Model Simulated on a Hypothetical Cohort of 10,000 Patients, 2009–2014

	LY	Increased LY	QALY	Increased QALY	Cost[a]	Increased cost[a]	YLL	DLY	DALY	Increased DALY
Base case analysis										
Period 1 (2009–2011)	3.762	-	2.677	-	$117,452.48	-	16.795	1.427	18.222	-
Period 2 (2012–2014)	3.802	0.040	2.705	0.028	$118,695.12	$1,242.64	17.005	1.442	18.447	0.225
Period 3 (2015–2017)	3.893	0.131	2.770	0.093	$121,545.68	$4,093.20	17.118	1.477	18.595	0.373
Sensitivity analysis (g gamma distribution)										
Period 1 (2009–2011)	3.766	-	2.679	-	$117,577.37	-	16.791	1.429	18.219	-
Period 2 (2012–2014)	3.814	0.049	2.714	0.035	$119,091.64	$1,514.27	16.992	1.447	18.439	0.220
Period 3 (2015–2017)	3.904	0.138	2.777	0.098	$121,876.64	$4,299.27	17.107	1.481	18.588	0.369
Sensitivity analysis (6 years observed data)										
Period 1 (2009–2011)	2.446	-	1.740	-	$76,372.13	-	18.110	0.928	19.038	-
Period 2 (2012–2014)	2.478	0.032	1.763	0.023	$77,377.48	$1,005.35	18.328	0.940	19.268	0.230

[a]Costs given in Australian dollars.
DALY, disability-adjusted life years; DLY, disability life years; LY, life years; QALY, quality-adjusted life years; YLL, years of life lost.

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DISCLOSURES

LG, **DN**, and **SBM**: Nothing to disclose; **BT** and **FLZ**: Employed and hold stock at BeiGene.

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