Hospitalisation Costs of Primary Liver Cancer in Australia: Evidence from a data-linkage study

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Abstract

Objectives. This study aimed to estimate the public hospital costs associated with Primary Liver Cancer (PLC) in the first and second years following the cancer diagnosis.

Methods. This study linked administrative datasets of patients diagnosed with PLC in Victoria, Australia from 01/2008 to 12/2015. The health system perspective was adopted to estimate the direct healthcare costs associated with PLC, based on inpatient and emergency costs. Costs were estimated for the first 12 month and 12 to 24 months after the PLC diagnosis and expressed in 2017 Australian dollars. The cost estimated was then extrapolated nationally. The linear mixed model with a Box-Cox transformation of the costs was used to explore the relationship between costs and patients' sociodemographic and clinical characteristics.

Results. For the first 12 months, the total and annual per-patient cost was $211.4 million and $63,664, respectively. Regarding the cost extrapolation to Australia, the total cost was $137 million for the first 12 months after notification and $42.6 million for the period from 12 to 24 months. Higher costs per episode of care were mostly associated with older age, Hepatocellular Carcinoma type of PLC, metropolitan hospitals, and Asian birth region.

Conclusion. This study showed the public hospital admission and emergency costs associated with PLC and the substantial economic burden this cancer has placed on the Australian Health System.

Keywords: Primary Liver Cancer, Hepatocellular Carcinoma, Cholangiocarcinoma, Health Economics, Data Linkage, Cost of illness, hospitalisation costs, emergency costs, cost extrapolation

1. Introduction

Primary liver cancer (PLC) is the sixth most common cancer[1] and third leading cause of death from cancer worldwide[2]. PLC is especially common in Eastern Asian and Sub-Saharan African countries[3]. However, the incidence and mortality rates are increasing in the USA[4] and in Northern and Central European countries[4, 5]. Similarly, in Australia, the age standardized incidence and mortality rates increased by 306% and 184% respectively from 1982 to 2014[6], making it the fastest increasing cause of cancer mortality in this country[7].

The economic burden of PLC is also substantial. In 2016, the hospitalisation costs of PLC for 31 hospitals in Beijing, China was USD16.2 million[8]. Meanwhile, in the USA, the annual-per-patient cost for hepatocellular carcinoma (HCC) – the most common PLC type[9] – was USD147,912[10]. For Australia, in 2012, the estimated hospitalisation costs associated with PLC was AUD50.2 million[11].

In Australia, the incidence of PLC is expected to continue increasing[12, 13] due to the increasing inflow of migrants from hepatitis B virus (HBV) endemic countries and prevalence of obesity and non-alcoholic fatty liver disease[14]: all of which are PLC risk factors . As such, the increasing incidence will contribute to greater demand for diagnosis and treatment for PLC. A precise estimation of healthcare costs will provide better understanding of the economic burden of the disease as well as optimal resource allocation for targeted screening programs, diagnosis, and treatment[10].

To date, studies on PLC in Australia have mostly focused on the epidemiology and health burden[6, 15-17] but not the economic burden of the disease, except one report[11]. This report only described the general costs to the health system of PLC as a part of an overview of many other liver diseases. Therefore, this study aimed to address this gap by estimating public

hospital costs associated with PLC. The secondary aim was to identify factors associated with these costs.

2. Methods

2.1 Study design and setting

This is an observational, retrospective study using linked population-based datasets of patients diagnosed with PLC in Victoria, Australia. The cohort was defined as all PLC notifications to the Victorian Cancer Registry (VCR) between 1/1/2008 and 31/12/2015.

2.2 Economic Analysis

The study adopted the health system perspective to estimate the direct costs associated with PLC, based on public hospital admissions (inpatient) and Emergency Department (ED)-related costs of the patients. Costs were expressed in 2017 Australian dollars and assessed in the first and second years following PLC notification to the VCR. Patients diagnosed with PLC at the time of their death were excluded from the cost estimations. Additional information regarding the data-linkage process, calculation of inpatient and ED costs are shown in the Supplementary Material 1.

The main outcomes estimated were the annual total and per-patient costs. Costs were reported by PLC types and estimated for the first 12-month period and 12-to-24-month period after the PLC notification.

The mean costs were used to extrapolate the cost of PLC nationally. The cost extrapolation in the first year after PLC diagnosis was estimated using the number of people diagnosed with PLC in Australia in 2017[18]. The first-year survival rate was then used to extrapolate the costs for the second year.

2.3 Statistical Analysis

To explore the relationship between inpatient and ED costs, with the sociodemographic and clinical characteristics of the patients reported, a linear mixed regression model was used with a Box-Cox transformation of the cost variables.

The model coefficients were reported in cost ratios and the statistically significant level was set at $p<0.05$. A random intercept for each individual was used to take account of the correlated observations and the model fit (factors associated with inpatient costs) was further improved whilst allowing a random slope for the hospital region (Metro vs Rural) indicator. All analyses were performed using STATAv.15 (Stata Corp., TX, USA). The reporting of this study followed CHEERS guidelines (Supplementary Material 2).

3. Results

3.1 Demographic characteristics

Between 01/01/2008 and 31/12/2015, 3,647 PLC notifications were made to the VCR. Table 1 provides the characteristics of these patients. Males represented the majority of patients, with a male to female ratio of 2.6:1. Half of the patients were 60-79 years old at the time of PLC diagnosis. Almost 30% of the patients were in the most disadvantaged Socioeconomic Indexes for Areas (SEIFA) quintile. More than half of the patients had a diagnosis of HCC, and the one-year survival rate was 41.2%.

3.2 Inpatient and ED costs

Table 2 describes the inpatient and ED costs for the 12 months subsequent to PLC diagnosis and 12 to 24 months after this.

Between 2008-2015, the total inpatient cost was $207.0 million. The annual cost was $25.9 million, and the annual per-patient cost was $62,679. The total ED cost between 2008-2015 was $4.5 million for 2,176 patients. The annual cost was $557,982, and the annual per-patient cost was $2,051.

For the period from 12 to 24 months after PLC notification, the total inpatient cost was $48.2 million. The annual cost was $6.9 million, and the annual per-patient cost was $46,869. For ED presentations, the total cost between 2008-2015 was $1.2 million. This resulted in an annual cost of $169,734 and an annual per-patient cost of $1,919.

3.3 Cost extrapolation to Australia

Table 3 shows the cost extrapolation to Australia in 2017. For the first 12 months post-diagnosis, the inpatient and ED costs were $132.6 million and $4.3 million, respectively (total $137 million). For the period from 12 to 24 months, the total extrapolated cost was $42.6 million.

3.4 Factors associated with costs

Tables 4 provides the factors associated with inpatient costs. For both post-diagnosis periods, patients younger than 40 years incurred lower costs than those older than 40 years. Patients treated in metropolitan hospitals exhibited significantly higher costs than those treated in rural hospitals. Lower costs were observed for cholangiocarcinoma patients compared to HCC patients. Furthermore, survival duration less than one year was correlated with higher costs compared to survival more than one year. For the first 12 months post-diagnosis, the costs for treating patients from the most disadvantaged SEIFA quintile were significantly higher than for those in the least disadvantaged quintile. Notably, Asian birth region was correlated with higher treatment costs than those born in Australia and New Zealand.

Table 5 shows the factors associated with ED costs. The ED costs of patients residing in the most advantaged SEIFA quintile were higher than that of those in the most disadvantaged area. Patients who did not survive beyond the first year after PLC notification were significantly correlated with higher ED costs than those who survived the first year.

4. Discussion

This is the first study to estimate the PLC costs in Australia using linked administrative data. Overall, PLC placed a heavy financial burden on the Victorian public hospital system as the first 12-month cost over the study period was approximately $211 million. In the second year after PLC notification, the costs reduced substantially to $49 million.

The cost reduction in the second year could be due to more intense treatments being conducted in the first year. For patients receiving liver resection and transplant, the costs in the one-year post operation period have been reported to be much lower than that of the operation period[19, 20]. Other options such as ablation and transarterial-chemoembolisation are also used more frequently to treat PLC in the first year after diagnosis than in years afterwards[21, 22]. The average number of hospital admission was also higher in the first year than in the second year (Supplementary Table 3)

The lower cost could also be explained by the substantial number of patients leaving the cohort due to death. The first-year survival rate in our study was 41.2%, which illustrates the poor outcomes for many patients diagnosed with PLC. Our data reflects the national figure from 2007 to 2011, which reported the one-year survival to be 40%[23].

The total per-patient cost in the first 12 months post-PLC-diagnosis was $63,664. The figure for the subsequent 12 to 24 months was $46,751. These results were comparable to that of the "Australian 45 and Up study", which reported the mean excess cost of all cancer types to be $33,944 in the first 12 months post-diagnosis and $8,796 in 12-24 months post-diagnosis[24]. In terms of international studies, our results are comparable with two studies from the USA that reported the annual per-patient cost of HCC to be around USD33,000 (in 2009 USD)[25, 26]. A cost-of-illness study in Japan reported a total cost (opportunity and mortality costs included) of 607.2 billion Japanese Yen (JPY) for 126,949 HCC patients in year 2014[27], which was equivalent to an annual per-patient cost of A$55,627.5 in 2017 (A$1= JPY85.983, 2017

value[28]). However, comparisons across health systems are problematic due to different health systems, costing approaches and other cultural and regulatory factors.

The national extrapolated hospitalisation costs in 2017 were around $137 million in the first 12 months post-diagnosis and $43 million in the next 12 months. This is substantially higher than the estimate in a 2019 AIHW report: PLC costs for public hospital admissions and ED presentations were estimated to be35.2 million and $38,203, respectively[29]. The difference is largely related to different costing methods. The AIHW's estimations were not based on actual costs incurred by a specific disease but rather the allocation of total expenditure to each health condition based on service use data[29]. Meanwhile, our cost extrapolation was based on a bottom-up approach, in which annual costs per patient were applied to incidence estimates. Our costs considered all admission after PLC diagnosis, which were assumed to be related to PLC.

For patients originating from Asia, higher inpatient costs were observed compared to those born in Australia and New Zealand. We speculate that the costs for patients born in Asian countries were higher as they may have had lower rates of cirrhosis and thereby be better candidates for more expensive curative treatments. However, we have no evidence for this and suggest further work to investigate the epidemiology and treatment of different PLC stages amongst patients of different birth regions.

For inpatient admissions, lower costs were associated with the highest SEIFA quintile, whilst the opposite was observed for ED presentations. The lower costs for inpatient admissions may be associated with patients in higher SEIFA quintiles receiving treatment in private hospitals. One of the limitations of our study is that we were unable to access data for private hospitals.

Patients in metropolitan hospitals incurred higher inpatient costs than patients in rural hospitals. This is largely due to the types of treatments available in different settings. It was estimated that more than one-third of rural hospitals have no medical oncology service and only 6% have a resident surgical oncologist[30]. Additionally, liver transplantation-the most expensive PLC treatment, is only available in major hospitals in Australia[31]. Therefore, patients living in rural areas were much more likely to travel to major healthcare centres for complex cancer treatments[32, 33].

Higher cost per episode of care was associated with older age, but younger patients were shown to have higher annual per-patient cost (Supplementary Table 4). Younger patients were shown to have higher median and average number of hospital admission in both period after cancer notification (Supplementary Table 3), which resulted in higher annual per-patient cost for this cohort.

The costs associated with HCC were significantly higher than for cholangiocarcinoma. Cholangiocarcinoma was shown to have much lower survival time than HCC[34-37]. It is often detected at a later stage than HCC[36] and has a higher propensity for regional and distant metastases[35]. In turn, this can lower the possibility for curative treatment, and patients with cholangiocarcinoma are further burdened with a lack of choices of effective systemic therapy[35].

Our study had several limitations. First, as costs were calculated from the healthcare system perspective, the indirect costs were not measured. Additionally, we were unable to report the expenditure for allied and primary health, general practitioner, specialists, and pathology services or costs incurred in private hospitals. Therefore, our results underestimated the true costs of PLC, had the societal perspective been considered. Second, our study assumed any hospitalisations or ED presentations after PLC diagnosis were due to the PLC *per se*. This

might not be true for all the episodes of care and may have led to overestimation of the true PLC-related costs. However, as our results are similar to other robust published literature, we expect this to be a low risk. Third, the size and number of tumours, which are amongst the most important factors affecting PLC survival[38], were not considered in our study. Administrative datasets do not routinely record this information. Fourth, all hospital admitted episodes were estimated based on the NHCDC's average costs for acute care type. This might result in inaccurate estimation of costs because the hospital admissions also included sub-acute and non-acute episodes. However, we expect the inaccuracy to be low, as the acute care types accounted for the vast majority of hospital admissions in our study (Supplementary table 2). Additionally, other information regarding the morphology of the tumour(s) is not recorded in many cases. This occurs as many PLC patients are diagnosed at late/end stage, in which investigations are unnecessary due to limited treatment options. Therefore, histological data are not collected.

5. Conclusion

In conclusion, our study showed the public hospital admission and ED costs associated with PLC and the substantial economic burden this type of cancer has placed on the Australian Health System through the linkage of several administrative population-based datasets.

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339 **Table 1.** Patient Characteristics at the time of PLC diagnosis

Patient characteristics (n=3,647)	n (%)
Sex	
Male	2,645 (72.5%)
Female	1,002 (27.5%)
Age group	
00-39	84 (2.3%)
40-59	972 (26.7%)
60-79	1,831 (50.2%)
80+	760 (20.8%)
SEIFA Quintile	
1 (most disadvantaged)	1,079 (29.6%)
2	744 (20.4%)
3	657 (18.0%)
4	639 (17.5%)
5 (least disadvantaged)	506 (13.9%)
Type of primary liver cancer (ICD-10-AM)	
Liver cell carcinoma (C220)	1,893 (51.9%)
Intrahepatic bile duct carcinoma (C221)	945 (25.9%)
Other PLC types (C222 - 229)	809 (22.2%)
Years of survival after diagnosis	
< 1 year	2,143 (58.8%)
1 – 2 years	635 (17.4%)
> 2years	869 (23.8%)
Years of survival after diagnosis	
Australia and New Zealand	1,863 (51.1%)
Europe	1,063 (29.1%)
Asia	499 (13.7%)
Africa	149 (4.1%)
America	34 (0.9%)
Unknown	39 (1.1%)
Length of Hospital admission (days)	
Mean (SD)	3.8 (7.6)
Median (IQR)	1 (1 – 4)
Min - Max	1 - 307
Length of ED stay (minutes)	
Mean (SD)	417.9 (302.3)
Median (IQR)	339 (211 - 531)
Min - Max	1 – 2,800
Number of hospitalisations per patient	
Mean (SD)	40.8 (78.4)
Median (IQR)	16 (7 – 34)
Min – Max	1 – 452
Number of ED presentations per patient	
Mean (SD)	7.1 (6.7)
Median (IQR)	5 (3 – 9)
Min – Max	(1 – 39)

340 *ED, Emergency Department; ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification; PLC,*

341 *Primary Liver Cancer; SD, Standard Deviation; SEIFA, Socioeconomic Indexes for Areas; IQR, inter-quartile range*

342 **Table 2.** Inpatient + ED costs by different types of liver cancer, 2008 - 2015

	12 months after notification			12 - 24 months after notification		
	Total costs from 2008 to 2015	Annualized cost	Annual cost per patient (SD)	Total costs from 2009 to 2015	Annualized cost	Annual cost per patient (SD)
All patients						
Inpatient cost		**n = 3,302**			**n = 1,028**	
	206,965,040	25,870,630	62,679 (60,018)	48,181,440	6,883,063	46,869 (58,583)
ED cost		**n = 2,176**			**n = 619**	
	4,463,855	557,982	2,051 (1,800)	1,188,137	169,734	1,919 (1,624)
Total cost		**n = 3,321**†			**n = 1,056**	
	211,428,895	26,428,612	63,664 (60,645)	49,369,577	7,052,797	46,751 (58,871)
HCC patients (C220)						
Inpatient cost		**n = 1,718**			**n = 611**	
	114,488,224	14,311,028	66,640 (61,986)	27,780,226	3,968,604	45,467 (60,041)
ED cost		**n = 1,097**			**n = 370**	
	2,205,073	275,634	2,010 (1,835)	683,890	97,699	1,848 (1,689)
Total cost		**n = 1,732**			**n = 635**	
	116,693,297	14,586,662	67,375 (62,625)	28,464,116	4,066,303	44,825 (60,073)
Cholangiocarcinoma patients (C221)						
Inpatient cost		**n = 885**			**n = 219**	
	54,256,736	6,782,092	61,307 (51,233)	9,401,149	1,343,021	42,928 (48,373)
ED cost		**n = 577**			**n = 118**	
	1,178,135	147,267	2,042 (1,583)	232,098	33,157	1,967 (1,505)
Total cost		**n = 887**			**n = 221**	
	55,434,871	6,929,359	62,497 (51,771)	9,633,247	1,376,178	43,589 (48,851)
Other types of liver cancer (C222-229)						
Inpatient cost		**n = 699**			**n = 198**	
	38,220,076	4,777,510	54,678 (64,456)	11,000,063	1,571,438	55,556 (63,561)
ED cost		**n = 502**			**n = 131**	
	1,080,647	135,081	2,153 (1,952)	272,149	38,878	2,077 (1,537)
Total cost		**n = 702**			**n = 200**	
	39,300,723	4,912,591	55,984 (65,206)	11,272,212	1,610,316	56,361 (64,207)

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344 *† Excluded: 200 patients diagnosed with PLC at the time of their death, 97 patients did not have any hospital admissions or ED presentations within 2 years post diagnosis*

345 *and 29 patients only had hospital admissions or ED presentations in 2nd year post diagnosis*

346 *ED, Emergency Department; HCC, Hepatocellular Carcinoma; SD, Standard Deviation*

347 **Table 3.** Extrapolation of cost to Australia in 2017

Period after PLC diagnosis	**12 months**	**12 – 24 months**
Incident cases in 2017 [18]	2,116	873†
Per-patient admission costs	$62,679	$46,869
Per-patient ED costs	$2,051	$1,919
Total inpatient costs	$132,628,764	$40,899,689
Total ED costs	$4,339,916	$1,674,593
Total hospital costs	$136,968,680	$42,574,282

348 *† 1-year survival rate of 41.2%*

349 *ED, Emergency Department; PLC, Primary Liver Cancer*

Table 4. Factors associated with inpatient costs

Patients' characteristics	Inpatient cost 12 months after notification				Inpatient cost 12-24 months after notification			
	Univariable		Multivariable		Univariable		Multivariable	
	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )
Average cost per episode (95% CI)			4,791.98 (4,757.67 – 4,826.28)				2,932.09 (2,899.76 – 2,964.43)	
Sex (Ref: female)								
Male	1.19***	(1.12 – 1.26)	1.05	(0.99 – 1.11)	1.22**	(1.08 – 1.35)	1.08	(0.97 – 1.19)
Age group (Ref: <40)								
40-59	1.35**	(1.13 – 1.58)	1.29**	(1.10 – 1.48)	1.63*	(1.19 – 2.07)	1.59*	(1.19 – 1.98)
60-79	1.28*	(1.07 – 1.49)	1.32**	(1.13 – 1.51)	1.57*	(1.16 – 1.99)	1.59*	(1.19 – 1.99)
>79	1.32*	(1.09 – 1.54)	1.42**	(1.20 – 1.64)	1.49	(1.07 – 1.91)	1.56*	(1.14 – 1.99)
SEIFA Quintile (Ref: 1- most disadvantaged)								
2	0.93*	(0.86 – 1.00)	0.97	(0.90 – 1.03)	0.94	(0.80 – 1.07)	0.93	(0.82 – 1.04)
3	0.92*	(0.84 – 0.99)	0.96	(0.89 – 1.02)	1.00	(0.85 – 1.14)	1.02	(0.89 – 1.14)
4	0.96	(0.88 – 1.04)	0.95	(0.88 – 1.02)	0.98	(0.84 – 1.12)	0.98	(0.86 – 1.10)
5 (least disadvantaged)	0.89**	(0.81 – 0.96)	0.88***	(0.81 – 0.94)	0.95	(0.81 – 1.09)	0.95	(0.83 – 1.07)
Hospital region (Ref: Rural)								
Metro	1.51***	(1.43 – 1.60)	1.38***	(1.29 – 1.47)	1.33***	(1.19 – 1.47)	1.22**	(1.09 – 1.36)
Types of liver cancer (Ref: HCC)								
Cholangiocarcinoma	0.60***	(0.56 – 0.63)	0.65***	(0.61 – 0.69)	0.70***	(0.62 – 0.78)	0.77***	(0.69 – 0.85)
Other types	0.93*	(0.86 – 0.99)	0.92**	(0.86 – 0.98)	1.06	(0.93 – 1.19)	1.08	(0.97 – 1.20)
Survival year			Ref: < 1 year				Ref: 1 – 2 years	
1 – 2 years	0.82***	(0.77 – 0.88)	0.83***	(0.78 – 0.88)				
>2 years	1.03	(0.96 – 1.10)	0.94*	(0.89 – 0.99)	0.88**	(0.80 – 0.97)	0.84***	(0.77 – 0.91)
Birth region (Ref: ANZ)								
Europe	1.08*	(1.01 – 1.14)	0.98	(0.92 – 1.03)	1.10	(0.98 – 1.22)	1.03	(0.93 – 1.13)
Asia	1.40***	(1.27 – 1.53)	1.13**	(1.04 – 1.22)	1.21	(1.03 – 1.40)	1.10	(0.96 – 1.25)
Africa	1.16	(0.99 – 1.32)	1.02	(0.90 – 1.15)	1.07	(0.81 – 1.33)	0.99	(0.79 – 1.19)
America	0.77*	(0.57 – 0.97)	0.73***	(0.57 – 0.89)	0.98	(0.54 – 1.42)	1.01	(0.63 – 1.40)
Other	0.91	(0.65 – 1.17)	0.86	(0.64 – 1.08)	0.99	(0.46 – 1.53)	1.08	(0.57 – 1.59)

**P<0.05, **P<0.01, ***P<0.001*

ANZ, Australia and New Zealand; CI, confidence interval; HCC, Hepatocellular Carcinoma; SEIFA, Socioeconomic Indexes for Areas

Table 5. Factors associated with ED cost

Patients' characteristics	ED cost 12 months after notification				ED cost 12-24 months after notification			
	Univariable		Multivariable		Univariable		Multivariable	
	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )	Ratio of means	95% CI ( )
Average cost per ED presentation (95% CI)			878.26 (817.84 – 938.69)				852.01 (728.37 – 975.64)	
Sex (Ref: female)								
Male	0.99	(0.97 – 1.01)	1.00	(0.98 – 1.02)	1.00	(0.94 – 1.05)	1.01	(0.96 – 1.06)
Age group (Ref: <40)								
40-59	0.96	(0.91 – 1.02)	0.95	(0.90 – 1.01)	0.95	(0.83 – 1.07)	0.95	(0.84 – 1.06)
60-79	0.98	(0.93 – 1.03)	0.96	(0.91 – 1.01)	1.01	(0.89 – 1.14)	1.00	(0.88 – 1.12)
>79	0.99	(0.93 – 1.05)	0.96	(0.90 – 1.01)	1.00	(0.87 – 1.13)	0.98	(0.85 – 1.11)
SEIFA Quintile (Ref: 1- most disadvantaged)								
2	1.03	(1.00 – 1.05)	1.02	(1.00 – 1.05)	0.99	(0.93 – 1.06)	0.97	(0.91 – 1.03)
3	1.02	(0.99 – 1.05)	1.02	(0.99 – 1.05)	1.03	(0.97 – 1.09)	1.01	(0.95 – 1.07)
4	1.04*	(1.01 – 1.07)	1.03*	(1.01 – 1.06)	0.99	(0.93 – 1.06)	0.98	(0.92 – 1.04)
5 (least disadvantaged)	1.03	(1.00 – 1.07)	1.04*	(1.01 – 1.07)	1.06	(0.99 – 1.12)	1.05	(0.99 – 1.12)
Types of liver cancer (Ref: HCC)								
Cholangiocarcinoma	1.03*	(1.00 – 1.05)	1.01	(0.99 – 1.03)	1.09**	(1.03 – 1.14)	1.06*	(1.00 – 1.12)
Other types	1.03*	(1.00 – 1.05)	1.01	(0.99 – 1.04)	1.02	(0.97 – 1.07)	1.02	(0.97 – 1.07)
Survival year		Ref: < 1 year				Ref: 1 – 2 years		
1 – 2 years	0.93***	(0.91 – 0.96)	0.93***	(0.91 – 0.96)				
>2 years	0.90***	(0.87 – 0.92)	0.90***	(0.87 – 0.92)	0.90***	(0.86 – 0.93)	0.89***	(0.85 – 0.93)
Birth region (Ref: ANZ)								
Europe	1.02	(0.99 – 1.04)	1.02	(1.00 – 1.04)	1.00	(0.95 – 1.05)	1.01	(0.96 – 1.06)
Asia	0.99	(0.96 – 1.02)	1.00	(0.97 – 1.03)	1.03	(0.96 – 1.10)	1.04	(0.98 – 1.11)
Africa	1.04	(0.99 – 1.09)	1.05*	(1.00 – 1.09)	1.00	(0.90 – 1.10)	1.01	(0.91 – 1.10)
America	0.99	(0.88 – 1.10)	1.00	(0.91 – 1.10)	0.91	(0.72 – 1.11)	0.90	(0.71 – 1.08)
Other	1.12*	(1.02 – 1.22)	1.11*	(1.02 – 1.21)	0.92	(0.65 – 1.20)	0.97	(0.71 – 1.23)

**P<0.05, **P<0.01, ***P<0.001*

ANZ, Australia and New Zealand; CI, confidence interval; ED, Emergency Department; HCC, Hepatocellular Carcinoma; SEIFA, Socioeconomic Indexes for Areas