Increasing incidence and mortality related to liver cancer in Australia: time to turn the tide

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Abstract

Objective: Assess national and jurisdictional incidence and mortality trends for primary liver cancer in Australia.

Methods: Analysis of Australian Cancer Incidence and Mortality data published in 2017 by the AIHW. Age-standardised rates (ASR) for 1982 to 2014/2015. Piecewise linear regression was used to assess temporal trends. For the purposes of comparison, data were also extracted for all cancers with greater burdens of disease (lung, colorectal, breast, prostate, pancreatic, and brain cancers and melanoma of the skin).

Results: Since 1982, the average annual percentage change (AAPC) for ASR incidence of liver cancer was 4.858% (95%CI 4.558-5.563). This marked a 306% increase from 1.822/100,000 persons (95%CI 1.586-2.058) in 1982 to 7.396/100,000 persons (95%CI 7.069-7.723) in 2014. AAPC for ASR mortality was 3.013% (95%CI 2.448-3.521): an increase of 184% from 2.323/100,000 persons (95%CI 2.052-2.594) in 1982 to 6.593/100,000 (95%CI 6.290-6.896) in 2015. ASR incidence and mortality were highest in the NT (12.607/100,000 persons), VIC (8.229/100,000) and NSW (7.798/100,000). In comparison to the other selected cancers, higher AAPC for both incidence and mortality of liver cancer were observed.

Conclusion: Incidence and mortality associated with liver cancer have increased substantially in the past three decades, in contrast to the improved outcomes observed for many other cancers. Jurisdictional incidence rates reflect higher prevalence of hepatitis B and C.

Implications for public health: In the context of Australian cancer prevention and care programs, liver cancer is an outlier. Strategies to mitigate risk factors and improve surveillance of liver health for at-risk groups are urgently required.

Key words: primary liver cancer, hepatocellular carcinoma, incidence, mortality, surveillance

Primary liver cancer is the sixth most commonly occurring cancer in the world and the third most common cause of cancer-related mortality.[1] In 2013, 20.9 million disability life years (DALYs) were attributed to liver cancer globally. While 86% of this burden of disease is experienced in developing countries,[1] there are clear indications that incidence of liver cancer is increasing in developed countries. In the US, the age-standardised incidence rate increased from 4.9 per 100,000 persons in 1999 to 8.3 per 100,000 in 2015.[2]

Similar trends have been observed for Australia. A recently published study reported age-adjusted incidence of hepatocellular carcinoma (HCC) – the most common form of primary liver cancer – increased from 1.38/100,000 persons in 1982 to 4.96/100,000 in 2014.[3] In Victoria, the second most populous state in Australia, incidence of HCC increased sixfold from 0.9/100,000 persons to 5.9/100,000 persons between 1982 and 2013.[4] An older study based on data from the New South Wales Central Cancer Registry reported incidence of HCC among people with chronic hepatitis B or C increased from 1.4/100,000 persons in 1990 to 2.8/100,000 persons in 2002, with the greatest burden for people born in Vietnam.[5] Further, age-standardised mortality rates have been projected to increase for males from 9.0/100,000 persons in 2014 to 11.8/100,000 persons in 2025; and for females, from 3.8/100,000 persons to 4.9/100,000 persons.[6]

The disease burden associated with HCC is highest in areas with endemic hepatitis B (HBV) (i.e. HBsAg prevalence > 6%), such as in sub-Saharan Africa and Asia, with HCC incidence rates of over 20 per 100,000 individuals.[7-9] In regions of high incidence, the most common cause is HBV transmitted at birth, i.e. vertical transmission. In comparison to North American and European populations – where the most common aetiology is hepatitis C (HCV) acquired later in life – diagnosis of HCC occurs approximately one decade earlier among populations with prevalent vertical transmission.[9,10] For example, the mean age interval at diagnosis of HCC in China is 55 to 59 years; in Europe and North America this range is 63 to 65 years, and among low-risk populations 75+ years.[10] HCC is more common in men than women as HBV, HCV, and alcohol consumption are more prevalent and possibly more carcinogenic in males.[11]

In 80 to 90% of cases, most (70-90%) HBV-related HCC develops in cirrhotic livers.[12] Cirrhosis due to HBV or HCV is the leading risk factor for HCC: in 80 to 90% of cases, HCC occurs in the setting of cirrhosis.[13] The

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five-year cumulative risk of developing HCC for patients with cirrhosis ranges between 5% and 30%, depending on aetiology, region or ethnicity, and stage of cirrhosis.[12,14] The highest risks are observed for individuals with HCV infection, of Asian ethnicity, and with decompensated disease.[12,14] Further, non-alcoholic fatty liver disease (NAFLD) – associated with obesity, insulin resistance, and type 2 diabetes – is an increasingly recognised risk factor for HCC in developed countries.[15,16]

The recently released Australian Cancer Incidence and Mortality books by the Australian Institute of Health and Welfare (AIHW) have, for the first time, provided incidence and mortality data for a broad range of cancers by states and territories. The current study will extract data for primary liver cancers (no breakdown by type available), with the aim to i) assess temporal trends for incidence and mortality of liver cancer; ii) assess jurisdictional differences for liver cancer incidence and mortality; and iii) compare national incidence and mortality data for other types of cancers.

Methods

The AIHW publishes the Australian Cancer Incidence and Mortality books based on data supplied by Australian cancer registries and the National Mortality Database.[17] For the first time, in late 2017, the AIHW published a breakdown of this data by jurisdiction, i.e. for states and territories. Data for liver cancer was reported for all forms of liver cancer combined. Raw data and age-standardised rates (ASR) were extracted for liver cancer incidence (1982-2014) and mortality (1982-2015) (incidence data were not available for 2015) nationally and by jurisdictions. The AIHW did not report incidence data for: New South Wales for 2014, the Northern Territory for 1982-1994 and the Australian Capital Territory 1982-1985 due to "small numbers, confidentiality or concerns regarding data quality".[17] The ASRs were calculated by the AIHW using the Australian 2001 standard population.

For comparison, national incidence and mortality data were also extracted for the seven cancers that have greater burdens of disease than liver cancer. In this context, 'burden of disease' refers to the combined impact of fatal and non-fatal disease, as measured by disability adjusted life years (DALYs).[18] These cancers include: lung, colorectal, breast, prostate, pancreatic, brain and melanoma of the skin.[17] The National Cancer Institute's Joinpoint Regression software (version 4.6.0.0)[19] was used to assess trends of ASR incidence and mortality over time. The software identifies whether increases (or decreases) in rates are linear or fluctuate. For fluctuating rates, the model identifies statistically significant changes in the slope of the line (i.e. joinpoints) using Monte Carlo permutations.[19] Statistical significance was set at $p<0.05$. Average annual percentage change (AAPC) was calculated for the entire reporting period, and annual percentage change (APC) for each section between the joinpoints.

Table 1: Liver cancer ASR incidence and mortality: average annual percentage change (AAPC) and average percentage change (APC), 1982-2014/15.

		AAPC (%)	95%CI	*P* value	Joinpoint section	APC (%)	95%CI	*P* value
National	Incidence	4.858	4.558-5.159	<0.001	1982-2006	5.258	4.954-5.563	<0.001
					2006-2014	3.668	2.816-4.526	<0.001
	Mortality	3.013	2.448-3.581	<0.001	1982-1986	-0.474	-4.967-4.232	0.835
					1986-2015	3.504	3.356-3.652	<0.001
NSW	Incidence[a]	5.677	5.232-6.125	<0.001	n/a			
	Mortality	3.642	3.385-3.599	<0.001	n/a			
VIC	Incidence	4.593	4.226-4.961	<0.001	n/a			
	Mortality	2.845	2.563-3.128	<0.001	n/a			
QLD	Incidence	4.136	3.757-4.516	<0.001	n/a			
	Mortality	3.547	3.144-3.953	<0.001	n/a			
WA	Incidence	3.838	3.399-4.279	<0.001	n/a			
	Mortality	3.598	3.041-4.158	<0.001	n/a			
SA	Incidence	5.451	4.782-6.124	<0.001	n/a			
	Mortality	3.963	3.348-4.529	<0.001	n/a			
TAS	Incidence	4.069	3.203-4.943	<0.001	n/a			
	Mortality	2.672	1.713-3.639	<0.001	n/a			
ACT	Incidence[b]	3.538	2.079-5.017	<0.001	1986-1996	0.772	-1.515-3.112	0.494
					1996-2001	11.814	4.479-19.663	0.003
					2001-2014	2.636	1.852-3.426	<0.001
	Mortality	2.269	0.980-3.574	0.001	n/a			
NT	Incidence[c]	1.526	-2.032-5.214	0.405	1994-2003	-2.985	-5.570- -0.328	0.032
					2003-2007	-13.763	-25.236- -0.531	0.043
					2007-2011	30.018	15.757-46.037	0.001
					2011-2014	4.010	-3.941-12.620	0.296
	Mortality	0.692	-0.787-2.193	0.349	n/a			

Notes:
a: 2013 data as no incidence data was reported for 2014.
b: First year reported: 1986.
c: First year reported 1994.

Results

Age-standardised incidence and mortality of liver cancer: 1982-2014/2015

The ASR for incidence of liver cancer has steadily increased since 1982 (Table 1). For all persons, piecewise linear regression identified one joinpoint: between 1982 and 2006, the APC was 5.258% (95%CI 4.954-5.563) and between 2006 and 2014, the APC was lower at 3.668% (95%CI 2.816-4.526) (Figure 1a). AAPC over the entire time period was 4.858% (95%CI 4.558-5.159). Overall, ASR incidence increased by 306%, from 1.822/100,000 (95%CI 1.586-2.058) persons in 1982 to 7.396/100,000 persons (95%CI 7.069-7.723) in 2014 (Table 2).

For males, the AAPC observed was 4.597% (95%CI 4.387-4.808), with no joinpoints identified (Figure 1, supplementary file). For females, one joinpoint was observed: between 1982 and 2005 the APC was 5.907% (95%CI 5.322-6.495) and between 2005 and 2014 the APC was 3.029% (95%CI 4.559-5.623) (Figure 2, supplementary file).

For ASR mortality (all persons), piecewise linear regression identified one joinpoint: between 1982 and 1986 APC was -0.474% (95%CI -4.967-4.232); subsequently, between 1986 and 2015 APC was 3.504% (95%CI 3.356-3.652) (Figure 1b). Across the entire reporting period, the AAPC was 3.013% (95%CI 2.448-3.581) (Table 1), and ASR mortality increased by 184% from 2.323/100,000 persons (95%CI

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2.052-2.594) in 1982 to 6.593/100,000 (95%CI 6.290-6.896) in 2015 (Table 2).

For males, no joinpoints were identified, with an AAPC of 3.150% (95%CI 2.972-3.327) observed (Figure 3, supplementary file). For females, the AAPC was 3.597 (95%CI 3.314-3.880), with no joinpoints identified (Figure 4, supplementary file).

Jurisdictional trends for ASR incidence and mortality of liver cancer

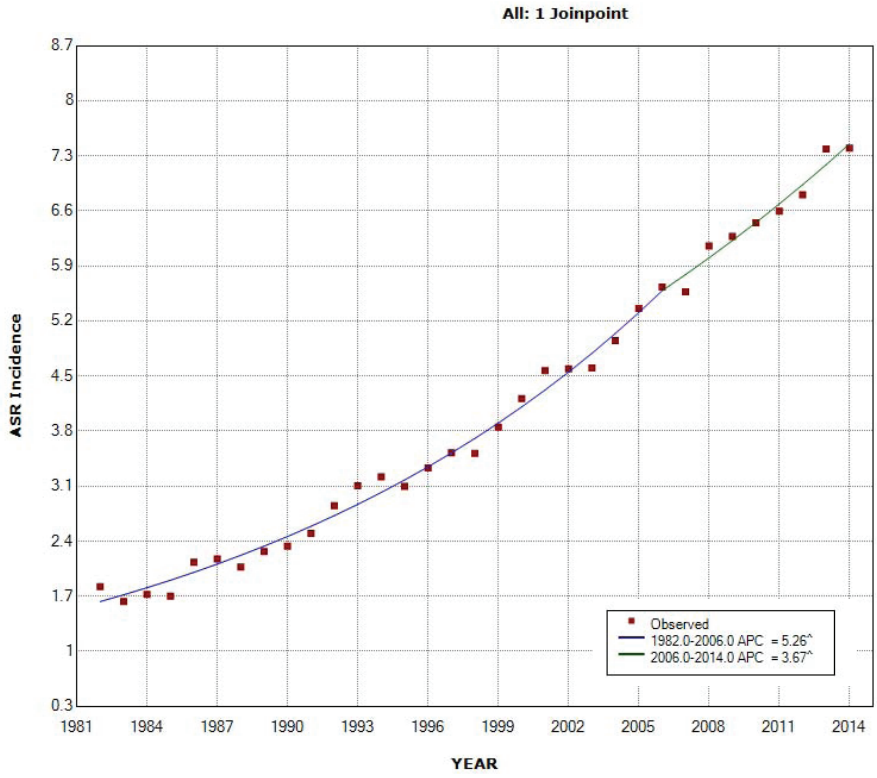
ASR incidence for all persons in 2014 was higher for the Northern Territory (NT) (12.607/100,000 persons; 95%CI 7.339-17.867) than the national rate (7.396/100,000; 95%CI 7.069-7.723), however, the wide 95%CI for the NT indicates this difference was not statistically significant (Table 2). For other jurisdictions, ASR incidence ranged between 5.766/100,000 persons (Tasmania (TAS); 95%CI 4.022-7.509) and 8.229/100,000 persons (Victoria (VIC); 95%CI 7.540-8.917).

Piecewise linear regression was used to assess temporal trends in ASR incidence across jurisdictions (Table 1). In all states and territories, with the exception of the NT and the Australian Capital Territory (ACT), AAPC for ASR incidence increased steadily and significantly with no joinpoints identified. For the NT, three joinpoints were identified. Between 1994 and 2003, and 2003 and 2007, negative APCs were reported (-2.985% (p=0.032) and -13.763% (p=0.043) respectively). Subsequently, between 2007 and 2011, APC was 30.018% (p=0.001) and 4.010% (p=0.296) between 2011 and 2014. The overall AAPC was 1.526% (95%CI -2.032-5.214). For the ACT, two joinpoints were observed: between 1986 and 1996, the APC was 0.772% (p=0.494); between 1996 and 2001 the APC increased to 11.814%, however this rate was characterised by a wide 95%CI of 4.479-19.663. Subsequently, in 2001-2014 the APC was 2.636 (p<0.001). The overall AAPC was 3.538% (95%CI 2.079-5.017).

While ASR mortality was highest in the NT at 11.252/100,000 persons, this estimate was characterised by a wide 95% confidence interval of 5.739-16.766 (Table 2). The ASR for mortality for the remaining jurisdictions ranged between 5.924/100,000 persons (95%CI 4.132-7.715) (TAS) and 7.329/100,000 persons (95%CI 6.207-8.450) (South Australia (SA)).

Across the reporting period, ASR mortality increased steadily and statistically significantly for most jurisdictions, with

Figure 1a: ASR incidence liver cancer for all persons, Australia 1982-2014.

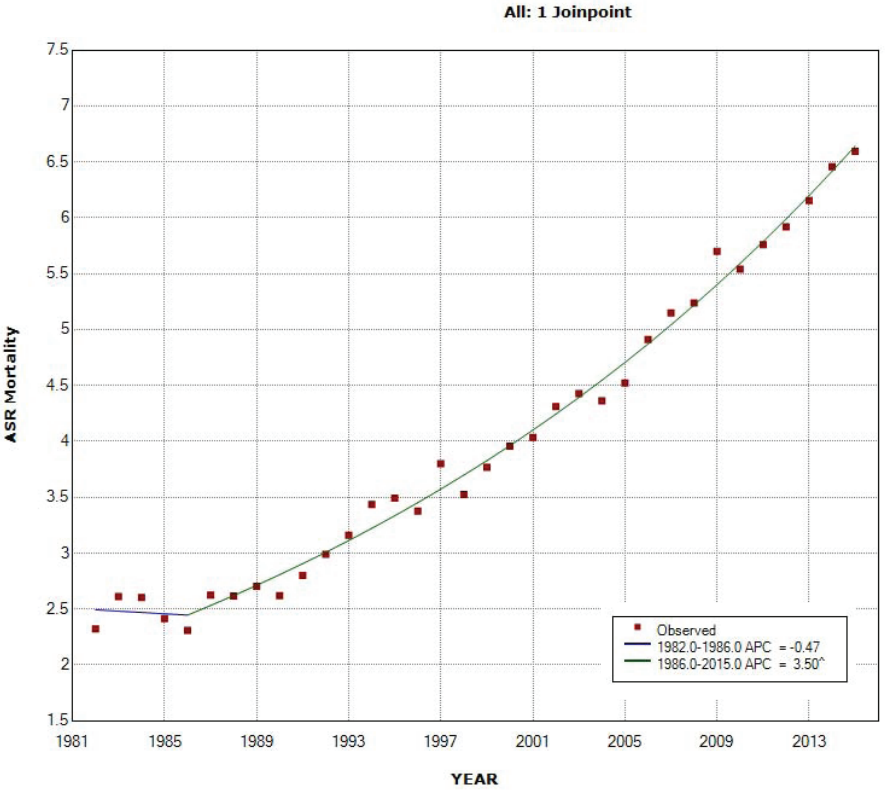


Notes:

^ Indicates that the Annual Per cent Change (APC) is significantly different from zero at the alpha=0.05 level.

Final Selected Model: 1 Joinpoint.

Figure 1b: ASR mortality liver cancer for all persons, Australia 1982-2015.



Notes:

^ Indicates that the Annual Per cent Change (APC) is significantly different from zero at the alpha=0.05 level.

Final Selected Model: 1 Joinpoint.

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AAPCs ranging between 2.269% for the ACT and 3.963% for SA. For the NT, the AAPC for mortality was 0.692% (p=0.349) (Table 1).

Changes in incidence and mortality of liver cancer compared with all cancers, cancers of the lung, colorectal, breast, prostate, pancreas, brain and melanomas of the skin: 1982-2014/2015

Table 3 provides AAPC and APC for incidence and mortality for each of the selected cancers and for all cancers combined. For all cancers combined, the AAPC for ASR incidence between 1982 and 2014 was 0.759% (95%CI 0.555-0.964). A decreased AAPC was observed for lung cancer (-0.376%, 95%CI -0.733- -0.017), and moderate increases for pancreatic cancer (0.496%, 95%CI 0.187-0.807), breast cancer (1.426%, 95%CI 1.085-1.769), melanomas of the skin (2.048%, 95%CI 1.540-2.558) and prostate cancer (2.672%, 95%CI 1.423-3.936). In comparison, a larger increase in incidence for liver cancer was observed, with an AAPC of 4.858% (95%CI 4.558-5.159).

For all cancers combined, the ASR mortality rate decreased between 1982 and 2015, with an AAPC of -0.780, 95%CI -0.843- -0.716). Negative AAPCs (indicating decreased mortality rates) were also observed for colorectal cancer (-2.302%, 95%CI -2.615- -1.987), lung cancer (-0.999, 95%CI -1.128- -0.869) and breast cancer (-1.425%, 95%CI -1.704- -1.145). Between 1982 and 2015, the ASR mortality for melanomas of the skin increased, with an AAPC of 0.514% (95%CI 0.007-1.024). In contrast, the AAPC for liver cancer mortality was 3.013% (95%CI 2.448-3.581).

Discussion

This paper provides an overview of the increasing burden of liver cancer experienced in Australia over the past three decades. Since 1982, ASR incidence for liver cancer increased by an average of 4.858% annually, and mortality by 3.013% annually. Over the entire reporting period, ASR incidence increased by 306% and mortality by 184%. These results are in keeping with a recently published study by Wallace and colleagues.[3] This study used data from the Australian Cancer Database to assess incidence and survival trends for HCC between 1982 and 2014. The authors reported a slightly lower AAPC for ASR incidence of 4.46% (95%CI 4.24-4.69 cf. 4.858% (95%CI 4.558-5.159)), however, this analysis was limited to HCC cases. For ASR incidence by sex, Wallace and colleagues reported an AAPC of 4.33% (95%CI 4.09-4.57) for males and 4.21% (95%CI 3.81-4.60) for females, similar to our estimates: 4.597% (95%CI 4.387-4.808) for males, but slightly lower for females (5.089%, 95%CI 4.559-5.623). Our inclusion of all primary liver cancers and Wallace's focus on HCCs likely explains these differences, along with different approaches to coding of cases.

The key drivers of both the observed and projected increases in incidence of liver cancer have been discussed by several authors.[20-23] These include an ageing population, increasing prevalence of metabolic syndrome, NAFLDs and type 2 diabetes, and increased migration from endemic HBV countries.[14,24-27] HCV infections have also been a key risk factor for HCC, however, the uptake of direct-acting antiviral treatments in Australia is expected to result in HCV becoming a less commonly observed risk factor.[3,28]

Universal vaccination for HBV, specifically for infants, is a cornerstone of the strategy to reduce prevalence, with 84% of infants globally having received a full schedule of vaccine doses as of 2015.[29] However, estimates suggest that globally, only 9% of HBV infected people have been diagnosed, and of this group, 8% have received antiviral treatment.[29] In the absence of treatment, the cumulative five-year incidence of cirrhosis for adults is 8-20%.[30] In turn, the annual risk for developing HCC for cirrhotic HBV patients is 2-8%.[31-33] The global burden of HBV and consequently HCC has been concentrated in developing countries, with >75% of HCC incidence occurring in Asian and sub-Saharan African countries.[34,35] With increasing migration occurring globally, it is essential that countries experiencing changing demographics, such as Australia, respond accordingly to these health issues.

In concert with global increases in prevalence of obesity, are increased prevalence rates for NAFLD, largely driven by metabolic syndrome.[16] NAFLDs include conditions of increasing severity of liver injury: simple steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis and complications of cirrhosis in the absence of competing etiologies.[16,36] These disorders are considered to represent hepatic manifestations of metabolic syndrome.[36] A large review recently reported the annual incidence of HCC amongst NAFLD patients was 0.44 per 1,000 person years (95%CI 0.29-0.66) and more specifically, for NASH the annual incidence rate was 5.29 per 1,000 person years (95%CI 0.75-37.56).[16] Global prevalence

Table 2: Changes in ASR incidence and mortality for liver cancer, 1982-2014/15

	Incidence					Mortality				
	1982		2014		Change over time	1982		2015		Change over time
	ASR incidence	95%CI	ASR incidence	95%CI		ASR mortality	95% CI	ASR mortality	95% CI	
NSW	1.273	0.948-1.597	7.798[a]	7.209-8.388	513%[a]	2.389	1.934-2.843	7.010	6.470-7.551	193%
VIC	1.991	1.518-2.464	8.229	7.540-8.917	313%	2.214	1.706-2.721	6.267	5.677-6.856	183%
QLD	2.292	1.598-2.985	6.468	5.774-7.161	182%	2.338	1.631-3.045	6.034	5.372-6.697	158%
WA	1.744	0.938-2.550	6.755	5.763-7.747	287%	1.730	0.908-2.553	6.523	5.556-7.489	277%
SA	2.464	1.567-3.360	7.071	5.932-8.210	187%	2.451	1.543-3.358	7.329	6.207-8.450	199%
TAS	1.752	0.350-3.153	5.766	4.022-7.509	229%	2.982	1.134-4.830	5.924	4.132-7.715	99%
ACT	2.176[b]	-0.047-4.822	6.190	3.603-8.777	184%[b]	2.923	0.385-6.231	5.990	3.593-8.386	105%
NT	9.375[c]	1.468-17.282	12.607	7.339-17.876	34%[c]	7.224	-0.951-15.399	11.252	5.739-16.766	56%
AUST	1.822	1.586-2.058	7.396	7.069-7.723	306%	2.323	2.052-2.594	6.593	6.290-6.896	184%

Notes:

a: 2013 data as no incidence data was reported for 2014.

b: First year reported: 1986.

c: First year reported 1994.

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of NAFLD has been estimated to be 25.24% (95%CI 22.10-28.65),[16] and prevalence often corresponds with rates of obesity.[25] Highest rates of NAFLD were reported for the Middle East (32%), South America (31%), Asia (27%), the USA (24%) and Europe (14%) – no data have been reported for the general Australian community.[16] With 63.4% of the adult Australian population overweight or obese,[37] studies are required to better understand the burden of NAFLD and NASH locally to inform responses.

Analysis of jurisdictional data showed that ASR incidence was highest in the NT (12.607/100,000 persons), VIC (8.229/100,000) and NSW (7.798/100,000). Accordingly, these states experience the highest burden of HBV and, with the exception of VIC, HCV. The National Notifiable Diseases Surveillance System provides estimates of unspecified (i.e. not incident) cases for HBV and HCV. In 2017, the rate of unspecified HBV infections was highest in NT (38.0/100,000), NSW (29.2/100,000) and VIC (27.5/100,000).[38] For HCV unspecified cases, the rates were highest for the NT (59.0/100,000) and NSW (50.8/100,000).

The national incidence and mortality data presented in this paper are in stark contrast to the trends observed for the seven cancers with a greater burden of disease in Australia than liver cancer (lung, colorectal, breast, prostate, pancreatic, brain, melanomas of the skin) and for all cancers combined. Similar findings have been reported in other recently published papers[3,4] showing that in the context of Australian cancer prevention and care programs, liver cancer is an outlier.[39] Two recommendations for surveillance for liver cancer have been published, both stating that people at high risk (albeit different definitions) of developing liver cancer should undergo six-monthly liver health checks, as prognosis is highly dependent on timing of diagnosis.[40,41] However, the five-year survival rate of 18.5%[42] suggests most liver cancers are diagnosed late in their development, in the absence of regular surveillance.[43]

National screening programs have contributed to improved outcomes for many patients. For example, BreastScreen Australia, which targets women aged 50-74 years, has contributed to a 32% decrease in mortality over the past two decades, and the National Cervical Screening Program has contributed to a 60% reduction in mortality since it commenced in 1991.[44] However, screening programs for cancer can carry risks, such as

Table 3: Average annual percentage change (AAPC) and average percentage change (APC) in ASR incidence and mortality for lung, colorectal, breast, prostate, pancreatic, brain, melanomas and all cancers combined, 1982-2014/15

		AAPC (%)	95%CI	*p* value	Joinpoint section	APC (%)	95%CI	*p* value
Lung cancers	Incidence	-0.376	-0.733–-0.017	0.040	1982-2003	-0.472	-0.582–-0.362	<0.001
					2003-2006	1.372	-2.423–5.315	0.469
					2006-2014	-0.770	-1.155–-0.384	<0.001
	Mortality	-0.999	-1.128– -0.869	<0.001	1982-1994	-0.509	-0.819–-0.198	0.002
					1994-2015	-1.278	-1.395–-1.160	<0.001
Colorectal cancers	Incidence	-0.120	-0.365–0.126	0.339	1982-1997	0.711	0.444–0.979	<0.001
					1997-2010	-0.277	-0.581–0.029	0.074
					2010-2014	-2.679	-4.140–-1.196	0.0014
	Mortality	-2.302	-2.615–-1.987	<0.001	1982-2000	-1.305	-1.519–-1.091	<0.001
					2000-2006	-5.648	-7.024–-4.252	<0.001
					2006-2015	-2.013	-2.616–-1.407	<0.001
Breast cancers	Incidence	1.426	1.085–1.769	<0.001	1982-1995	2.702	2.237–3.169	<0.001
					1995-2011	0.149	-0.131–0.429	0.285
					2011-2014	2.801	-0.097–5.784	0.058
	Mortality	-1.425	-1.704–-1.145	<0.001	1982-1994	-0.160	-0.490–0.174	0.333
					1994-1999	-3.523	-5.126–-1.893	<0.001
					1999-2014	-1.705	-1.511–-17.899	<0.001
Prostate cancers	Incidence	2.672	1.423–3.936	<0.001	1982-1990	3.118	0.990–5.290	0.006
					1990-1994	20.105	12.251–28.509	<0.001
					1994-1998	-9.895	-15.093–-4.379	0.002
					1998-2008	5.989	4.975–7.014	<0.001
					2008-2014	-4.869	-6.281–-3.436	<0.001
	Mortality	-0.375	-0.981–0.235	0.228	1982-1994	2.758	2.299–3.220	<0.001
					1994-1997	-4.411	-10.271–1.832	0.154
					1997-2010	-1.056	-1.412–-0.699	<0.001
					2010-2015	-3.480	-4.701–-2.243	<0.001
Pancreatic cancers	Incidence	0.496	0.187–0.807	0.002	1982-2002	0.077	-0.104–0.258	0.390
					2002-2007	2.521	0.772–4.301	0.006
					2007-2014	0.266	-0.382–0.918	0.407
	Mortality	0.047	-0.125–0.219	0.590	1982-1998	-0.218	-0.510–0.075	0.139
					1998-2015	0.298	0.084–0.511	0.008
Brain cancers	Incidence	-0.002	-0.319–0.317	0.992	1982-2011	0.298	0.174–0.423	<0.001
					2011-2014	-2.852	-6.041–0.445	0.087
	Mortality	-0.125	-1.104–0.863	0.803	1982-2002	0.276	-0.057–0.609	0.100
					2002-2005	-4.208	-14.032–6.738	0.421
					2005-2015	0.325	-0.470–1.127	0.409
Melanomas of the skin	Incidence	2.048	1.540–2.558	<0.001	1982-1987	7.205	4.181–10.317	<0.001
					1987-2002	1.865	1.404–2.329	<0.001
					2002-2014	0.196	-0.259–0.654	0.384
	Mortality	0.514	0.007–1.024	0.047	1982-1987	3.304	0.872–5.795	0.010
					1987-2000	-0.096	-0.635–0.444	0.715
					2000-2011	1.363	0.759–1.970	<0.001
					2011-2015	-3.188	-5.278–-1.053	0.005
Liver cancers	Incidence	4.858	4.558–5.159	<0.001	1982-2006	5.258	4.954–5.563	<0.001
					2006-2014	3.668	2.816–4.526	<0.001
	Mortality	3.013	2.448–3.581	<0.001	1982-1986	-0.474	-4.967–4.232	0.835
					1986-2015	3.504	3.356–3.652	<0.001
All cancers	Incidence	0.759	0.555–0.964	<0.001	1982-1990	1.154	0.873–1.436	<0.001
					1990-1994	3.536	2.390–4.695	<0.001
					1994-1998	-1.274	-2.295–-2.584	0.018
					1998-2008	1.052	0.877–1.227	<0.001
					2008-2014	-0.699	-0.981–-0.416	<0.001
	Mortality	-0.780	-0.843–-0.716	<0.001	1982-1994	-0.024	-0.178–0.130	0.753
					1994-2015	-1.209	-1.265–-1.153	<0.001

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those observed for prostate cancer using prostate specific antigen testing.[45] As such, new initiatives require careful consideration of the clinical, public health and health economics aspects.

A strength of our study was use of national and jurisdictional data on cancer incidence and mortality. In Australia, notifications to cancer registries for most cancer diagnoses are legislated. The AIHW collates these data and has published more than three decades of incidence and mortality data for a range of cancers. An important limitation of this study is the potential for misclassification of cancer diagnoses. A study by Hong and colleagues[46] compared capture of HCC diagnoses by the Victorian Cancer Registry with data collected from several tertiary hospitals and other health service providers. They reported incidence from the hospitals/service providers was two-fold higher than reported from the Cancer Registry. This difference was largely due to the Registry's use of histology as a basis for classification, whereas the researchers used diagnostic criteria from the American Association for the Study of Liver Diseases (AASLD) for this. In response the Victorian Cancer Registry reassessed all liver cancer diagnoses for the 1982-2014 period using clinical diagnostic guidelines, thereby reducing or eliminating under-reporting.[4] As such, the data reported in this study, particularly for other jurisdictions, may reflect an underestimate of the true number of liver cancer cases.

Liver cancer has been a low-prevalence cancer in developed countries including Australia. The demographic changes and increasing prevalence of overweight and obesity will likely contribute to increases in incidence in coming decades. The poor survival rates associated with liver cancer further contribute to the need for a greater focus on reducing this burden of disease. While substantial advances are being made regarding immunotherapy treatments for liver cancer, early diagnosis will likely remain a key factor in prognosis for several years to come. Current Australian recommendations for HCC surveillance differ and should be synthesised so health practitioners have a clear understanding of surveillance. Novel approaches are required to increase uptake and adherence to surveillance among at-risk groups, including people who have migrated from endemic HBV countries.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Supplementary Figure 1: ASR incidence liver cancer for males, Australia 1982-2014.

Supplementary Figure 2: ASR incidence liver cancer for females, Australia 1982-2014.

Supplementary Figure 3: ASR mortality liver cancer for males, Australia 1982-2014.

Supplementary Figure 4: ASR mortality liver cancer for females, Australia 1982-2014.

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