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In this section, eight cancer types are outlined briefly as a way of contextualising the analysis and highlighting cancer types that are important in Australia – either because of their public health programs or because of large incidence or mortality percentage changes – to illustrate how policy, programs or other changes may have affected these measures. These have been selected based on a combined list of the top five cancer sites for males and females in incidence and mortality according to IARC GLOBOCAN 2008 working estimates, and cancer types of national importance in Australia.\(^5\)

Firstly, trends in incidence and mortality for the cancer type are described – including data from the IARC GLOBOCAN project to illustrate global incidence and mortality working estimates for 2008 in individuals aged 74 years and under. Additionally, the most current survival data available for Australia from the AIHW are also provided.\(^3\) The AIHW survival data are presented to provide context rather than to facilitate a comparison between survival trends and our findings. However, the AIHW data were only available for all ages combined. The relative survival and five-year conditional relative survival data reported by the AIHW show the probability of surviving a given number of years, provided that an individual has already survived a specific amount of time after diagnosis.\(^3\)

A brief overview of current prevention strategies, screening programs and treatment methods in use globally and in Australia are also provided. The results of our analysis for the specific cancer type are then presented and discussed.

References


7.4 Liver cancer (C22)

7.4.1 Background
Liver cancer is the fifth most common cancer in males and the seventh most common in females. For individuals under the age of 75, incidence was 14.1/100,000 in males and 5/100,000 in females. Incidence rates are higher in developing countries and Southern Europe in comparison to other developed areas. In Western countries, liver cancer is more prevalent in people aged 75 or over, and more common in males than females, but in African countries this trend is variable. Worldwide, 70–80% of all liver cancers are associated with chronic hepatitis viruses B and C infection or liver cirrhosis. Mortality from liver cancer is 12.5/100,000 in males and 4.6/100,000 in females under the age of 75. Survival from liver cancer is low and, as a result, liver cancer is the third most common cause of death globally. Low survival leads to a higher burden from premature mortality than morbidity.

Approximately 80% of liver cancer cases are hepatocellular carcinomas, resulting from hepatocytes. The remaining 20% of cases are made up of intrahepatic cholangiocarcinoma (affecting the bile duct epithelium), hepatoblastoma (a malignant tumour in infants and children) and angiosarcoma (tumours arising in the liver’s blood vessels). Prognosis of the disease is often measured by the Child–Pugh score, which assesses the level of cirrhosis in the liver. It is often used to determine treatment requirements and need for transplantation.

In Australia, liver cancer is 3 times more common in males than in females, and relative survival is 16% for 5 years after diagnosis. The 5-year conditional relative survival was 38% at 1 year after diagnosis, and 75% at 5 years after diagnosis. Survival rates are similar for both genders but are higher in major cities. Changes from 1988–1993 to 2006–2010 indicated an improvement in survival from 7% to 16%.
7.4.1.1 Causes and risk factors

Chronic infection with hepatitis B and C viruses is responsible for approximately 80% of liver cancer cases worldwide. With hepatitis B, the progression to hepatocellular carcinoma can bypass the cirrhosis stage in approximately 30% of individuals, which makes hepatocellular carcinoma surveillance more challenging and less reliable. On the other hand, hepatitis C infection is mediated through liver fibrosis or cirrhosis, which makes cirrhosis screening a valuable indicator. HIV-1 has also been positively associated with liver cancer.

Liver cirrhosis is associated with hepatocellular carcinoma, especially in Western countries, with at least 80% of cases having a history of cirrhosis before tumour development. High alcohol intake is a significant contributing risk factor for liver cirrhosis and alcohol-related liver cancer. Although assumed to be beneficial, alcohol cessation has no clear association with reduced risk.

From 1982, hepatitis B vaccine was commercially available, but not immediately administered as part of a population-wide prevention program, because of the high associated cost, especially in the developing world. The hepatitis B vaccination is now part of the infant immunisation program in 179 countries. As the vaccine is not effective in people already infected, 350 million people worldwide are still at risk of developing hepatocellular carcinoma. In Australia, the prevalence of hepatitis B is relatively low, except in immigrants from countries where the prevalence is high. People with a large number of sexual partners and those who inject drugs with contaminated needles are also considered high-risk population groups for hepatitis B.

No vaccine is as yet available against the hepatitis C virus. Hepatitis C infection prevention relies on the use of sterilised equipment in medical and on public health interventions, such as safe blood transfusions, safe injection practices, safe tattooing and adequate screening of blood and organ donors.

Coffee consumption has been associated with a reduced risk of liver cancer, but the evidence is not conclusive. A positive relationship has not been found with other caffeinated beverages such as green tea. Smoking has a causal relationship with hepatocellular carcinoma, with consistent findings across different geographic regions. Additionally, X- and γ-radiation are associated with increased risk of liver cancer, but the exact dose-response relationship is not clear. Combined oestrogen-progestogen oral contraceptive use has been linked to increased risk of liver cancer. There are also autoimmune and metabolic diseases associated with hepatocellular carcinomas. Research in iron metabolic disorders has suggested that iron overload is a risk factor.

Obesity and diabetes mellitus, both together and independently, have been linked to increased risk of fatty liver disease and hepatocellular carcinomas. Diabetes mellitus and liver cancer share similar risk factors, such as alcohol consumption and obesity, and diabetes has been suggested as a potential risk factor for liver cancer. Even after adjusting for confounders, the risk of hepatocellular carcinomas in diabetics was double that of non-diabetics. Other food- and nutrition-related evidence has only isolated fruit consumption as having a limited-suggestive association with decreased risk of liver cancer.

Exposure to aflatoxins through contaminated food consumption has been convincingly associated with liver cancer in developing tropical countries, especially in individuals with chronic hepatitis infections. Aflatoxins develop when mould develops on grains that are stored in poorly ventilated sites in hot and humid climates.

For intrahepatic cholangiocarcinomas, liver fluke infestation through consumption of raw or undercooked freshwater fish increases cancer risk; this occurs mainly in Thailand and South East Asia. An Italian case-control study showed that asbestos exposure increased the risk of intrahepatic cholangiocarcinoma; however, the number of cases was too small to confirm an association in all environments.
7.4.1.2 International prevention/screening/treatment programs

As the prognosis for liver cancer is poor, major emphasis is placed on prevention.7 Primary prevention strategies include hepatitis B infant immunisation programs, optimising grain storage to avoid aflatoxin contamination in the tropics, and public health campaigns addressing excessive alcohol consumption.196 Addressing excessive alcohol consumption could, theoretically, eliminate the incidence of alcohol-related liver disease, responsible for approximately 10.7% of deaths from liver cancer globally.202

The hepatitis B vaccine is available worldwide as part of many national immunisation programs. The initial immunisation approach targeting high-risk groups was found to be ineffective and, with falling costs of vaccination, universal vaccination became a reality.203

In Australia, the risk of liver cancer is high, and its management is challenging.215 The prevalence of hepatitis B is high in Australians born in countries where hepatitis B infection is endemic, and transmission occurs in the neonatal period and early infancy, such as in many Asian countries.204 Estimates for the year 2025 suggest that there will be an increase of hepatocellular carcinomas caused by hepatitis B in population groups from the Asia–Pacific region.204 The Australian Government has developed National Hepatitis B and C strategies to address these issues.216, 217 Programs such as Cancer Council NSW’s ‘B Positive’ Project, aim to raise awareness and educate these communities – and the health professionals who serve them – about the link between hepatitis B and liver cancer, and ensure regular follow-up and timely institution of antiviral therapy to prevent hepatocellular carcinomas.218

Population-wide screening programs for liver cancer are not recommended.219, 220 It is thought that it is more effective to identify high-risk patients via a relatively simple test for hepatitis B and C, or liver cirrhosis screening.219 Population-based hepatocellular carcinoma screening is not systematically practised in Australia, but expert groups recommend it in high-risk populations, including Asian-born individuals (commencing at age 40 for males and age 50 for females). African-born people aged over 20 years, people with cirrhosis, or those with a family history of liver cancer.221, 222 Screening, as well as diagnosis, can also be conducted in primary care facilities using ultrasounds.7, 219

Approximately half the cases of hepatocellular carcinomas have high fetal antigen α-fetoprotein levels, which could be used as a marker for screening in future.196

The treatment of liver cancer is largely dependent on disease stage and the existence of other associated liver diseases. Liver resection is a commonly used technique, with portal vein embolisation if there is little remaining liver.7 Liver transplantation is also a possibility for patients.7 In the case of hepatocellular carcinomas, liver resection and transplantation are the only two curative treatment options available.221 If liver failure is likely, the cancer can be treated with radiofrequency ablation (RFA) or cryoablation.7 RFA is considered a safe treatment option with low mortality; however, there is a high chance of disease recurrence associated with the technique.223 Additional regional therapies, such as transarterial chemoembolisation, have shown more promising results when used in combination with RFA.224, 225 Hepatocellular carcinomas are resistant to radiotherapy, thus limiting its use in treatment.7 However, chemotherapy can be used, despite little evidence to suggest resulting improvement in survival.7 Sorafenib, a molecular-targeted drug, is the first agent to show improvements in survival of advanced hepatocellular carcinoma and is now more commonly used in treatment programs.198

7.4.2 Incidence and mortality rates in Australia 1987–2007

Liver cancer incidence and mortality rates have both increased over two decades (Figure 7–7 and Figure 7–8). Overall, there has been a 70% rise in mortality, which was slightly higher in males than females, and incidence increased by 132% in comparison to expected estimates (Table 7–7). This increase was higher in males, increasing by 165% over this period. Mortality and incidence results were statistically significant for both genders and overall (Table 7–8). The substantial burden of undiagnosed chronic hepatitis B infections in some Asian-born Australians, coupled with the natural history of chronic hepatitis B infection in populations where the infection is acquired early in life,217 contribute to about half of the increasing mortality and incidence in Australia.96
Table 7–7  
Liver cancer deaths and incident cases in Australia 1987–2007

<table>
<thead>
<tr>
<th></th>
<th>Deaths</th>
<th>Incident Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Observed in 2007 (O)*</td>
<td>460</td>
<td>189</td>
</tr>
<tr>
<td>Expected in 2007 (E)**</td>
<td>265</td>
<td>117</td>
</tr>
<tr>
<td>Difference (O-E)</td>
<td>195</td>
<td>72</td>
</tr>
<tr>
<td>Change in (O-E)/E (%)</td>
<td>73</td>
<td>62</td>
</tr>
</tbody>
</table>

*An average of the observed rates for 2006 to 2008 was applied to the 2007 population to calculate the observed number of deaths and incident cases for 2007.
**An average of the observed rates for 1986 to 1988 was applied to the 2007 population to calculate the expected number of deaths and incident cases for 2007.
†All figures have been rounded to the nearest whole number.

Table 7–8  
Liver cancer: average annual percentage change (AAPC)

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AAPC</td>
<td>Confidence Interval (95%)</td>
</tr>
<tr>
<td>Male</td>
<td>2.3</td>
<td>1.9, 2.7</td>
</tr>
<tr>
<td>Female</td>
<td>2.7</td>
<td>2.0, 3.3</td>
</tr>
<tr>
<td>Persons</td>
<td>2.4</td>
<td>2.1, 2.7</td>
</tr>
</tbody>
</table>

Figure 7–7  
Liver cancer: age-standardised cancer mortality rates in Australia 1987–2007, 0–74 years

Hepatocellular carcinoma patients have poor quality of life in comparison to the general population, specifically in physical aspects.187 Particular treatment courses, such as sorafenib, can have significant adverse effects which impede a patient’s ability to continue treatment and also affect their physical wellbeing.188 Fan et al188 found that the emotional functioning of these patients was higher than that of other cancer sufferers, proposed to be due to their resolve in combating their illness. Liver transplantation occurs more often in younger patients, and their quality of life post-transplant has been studied.190, 191 Transplant recipients have lower quality of life than their healthy peers, with physical and psychosocial health being lower than average in the healthy population, especially in school functioning.192

From 1988, the Australian Government began integrating the hepatitis B vaccination into the National Immunisation Program. It is now provided in infancy through a general practitioner.193 National strategies focusing on a reduction in transmission of hepatitis B and C have been developed in partnership with the community sector.194, 195 Additionally, public health campaigns to curb excessive alcohol consumption address one of the main risk factors for liver cancer, thus working towards disease prevention. Globally, governments are encouraged to take a harder stance on preventing alcohol-attributed harm through public health initiatives, taxation and legislation restricting alcohol availability.196 High-risk groups with higher rates of hepatitis B and C infections are a key focus of the national strategies, as well as NGOs such as Hepatitis Australia and Cancer Council to further reduce liver cancer incidence and mortality.197, 198
7.4 Liver Cancer (C22)

References


