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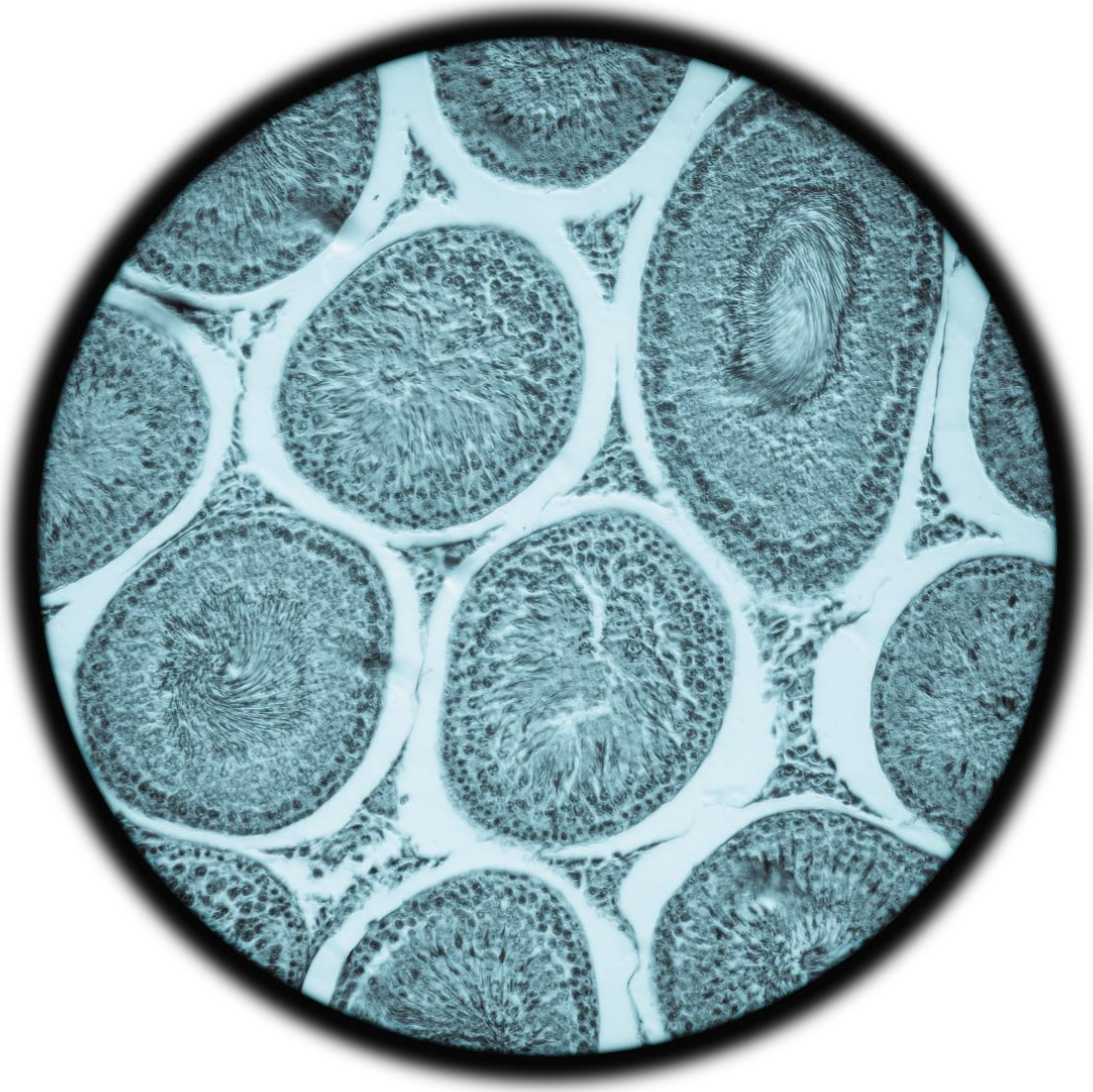

The Social and Economic Cost of
Primary Liver Cancer
Hepatocellular Carcinoma (HCC) in Australia

Liver Foundation

March 2021

Deloitte Access Economics

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The Liver Foundation is the peak not-for-profit community organisation in Australia for people affected by, or at risk of liver disease. The Liver Foundation's mission is to raise awareness and fund critical research into the prevention, detection and diagnosis, treatment, and cure of liver disease.

For more information, please visit our website www.liver.org.au

The Australian National Liver Cancer Collaborative (ANLCC) is a unified team of Physicians, Hepatologists, Scientists, Researchers, and Surgeons with the object to transform the prevention, diagnosis and delivery of health care to patients with liver cancer. The ANLCC is a registered division for tax and administration purposes of the Liver Foundation Limited.

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Glossary

Acronym	Description
ACD	Australian Cancer Database
ACIM	Australian Cancer Incidence and Mortality
AIHW	Australian Institute of Health and Welfare
AR-DRG	Australian refined diagnosis-related group
ASR	Age-standardised rate
CLD	Chronic liver disease
CT	Computed tomography
DALY	Disability adjusted life year
GP	General practitioner
HBV	Hepatitis B
HCC	Hepatocellular carcinoma
HCV	Hepatitis C
ICD-10	International Classification of Diseases 10
MRI	Magnetic resonance imaging
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NHMRC	National Health and Medical Research Council
NPV	Net present value
PEI	Percutaneous Ethanol Injection
TACE	Transarterial chemoembolization
RFA	Radiofrequency ablation
SIRT	Selective internal radiation therapy
VCR	Victorian Cancer Registry
VSLY	Value of a statistical life year
YLD	Years of life lost due to disability
YLL	Years of life lost due to premature mortality

Executive summary

Liver Cancer is developing at an unprecedented rate in the Western world. The Liver Foundation commissioned Deloitte Access Economics to produce this necessary paper to estimate the economic burden of liver cancer / hepatocellular carcinoma (HCC) in Australia given the increasing rates of incidence of liver cancer / HCC internationally and in Australia.

Key findings

- HCC has the second fastest growing incidence rate of all cancers, and is the fastest growing cause of cancer-related deaths in Australia.
- The health system cost per person with HCC is one of the highest and is the same to that of bowel cancer.
- HCC is overrepresented in Aboriginal and Torres Strait Islander people where it is the third most common cause of cancer-related death compared with seventh in the general Australian population.
- The total cost of HCC was calculated to be $4.8 billion in 2019-20.

About this report

Liver cancer is a serious chronic health condition that carries with it a high mortality rate, substantial economic costs and significant loss of wellbeing. There were 2,599 people diagnosed with primary liver cancer in Australia in 2019, with men accounting for 73% of new diagnoses.[1] The incidence of primary liver cancer has been on the rise over recent decades, with incidence rates increasing 378% between 1982 and 2019, making it the second fastest growing cancer in Australia.[2]

The most common type of primary liver cancer is hepatocellular carcinoma (HCC), accounting for 68% of all diagnoses in Australia.[3] Not only is the incidence growing at a fast rate, but HCC is also the fastest growing cause of cancer-related deaths in Australia. Across all diagnosed cases, just 19% are expected to survive beyond five years.[4] More broadly, primary liver cancer is responsible for the fourth largest number of cancer deaths worldwide.[5]

HCC is a unique condition in that its incidence is coupled with the frequency of its risk factors. These are broad and include viral hepatitis, excessive alcohol consumption, diabetes mellitus, aflatoxin exposure and non-alcoholic fatty liver disease (NAFLD). Despite improvements in survival rates over recent years due to improved diagnostic strategies, refinement of locoregional therapies, better and earlier identification of ideal transplant recipients and expanded availability of systemic therapies, the 5-year survival rate remains low.

Amid increasing rates of incidence in western countries due to increasing levels of obesity,[6] the Liver Foundation engaged Deloitte Access Economics to estimate the economic cost of HCC in Australia in 2019-20. This analysis considered the health system costs required to treat HCC, and the reduction

[1] Australian Institute of Health and Welfare 2019. Cancer in Australia 2019. *Cancer in Australia series no. 5. Cat. No. CAN 123*.
[2] Ibid.
[3] Wallace, M.C., Preen, D.C., Short, M.W., Adams, L.A., & Jeffrey, G.P. (2019) Hepatocelluar carcinoma in Australia 1982-2014: Increasing incidence and improving survival. *Liver International*, 39(3):522-530.
[4] Forman D., Bray F., Brewster D.H., Gombe, M.C., Kohler, B., Pineros, M., Steliarova-Foucher, E., Swaminathan, R., & Ferlay, J. (2014) Cancer incidence in five continents: Volume X, *IARC Scientific Publication No. 164*, Lyon: International Agency for Research on Cancer.
[5] World Health Organisation 2018, *Cancer: Key facts*, <https://www.who.int/news-room/fact-sheets/detail/cancer>.
[6] Wallace, M.C., Preen, D.C., Short, M.W., Adams, L.A., & Jeffrey, G.P. (2019) Hepatocelluar carcinoma in Australia 1982-2014: Increasing incidence and improving survival. *Liver International*, 39(3):522-530.

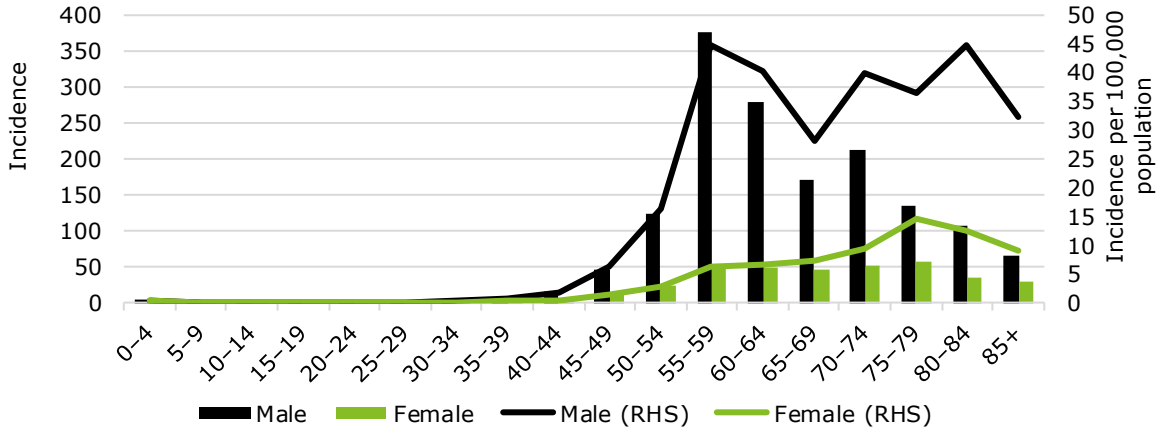
in productivity and wellbeing among people with HCC.[7] Our analysis found that **HCC cost a total of $4.8 billion in 2019-20**.

Epidemiology of HCC in 2019-20

To establish the incidence, 5-year prevalence and mortality of HCC in Australia, our analysis draws on data recorded in the Australian Cancer Database (ACD) by the Australian Institute of Health and Welfare (AIHW). This broad data collected for all primary liver cancers is combined with estimates of HCC incidence published by Wallace et al (2019) to estimate the number of new and total cases of HCC in Australia in 2019-20.

Chart i presents the number of incident cases of HCC in Australia in 2019-20, both total and per 100,000 population, by age and gender. As can be seen, almost all cases occurred after the age of 40, with 1,515 and 357 cases in males and females aged 45 and over, respectively. This compared to just 32 and 11 cases among males and females aged 44 or below, respectively. **Overall, there were an estimated 1,916 new cases of HCC in Australia in 2019-20,** equivalent to 6.46 cases per 100,000 population. When only considering cases in those aged 45 or over, **the rate per 100,000 population was 32.19 for males and 7.82 for females.**

Chart i: Incident cases of HCC in Australia, total and per 100,000 population, by age and gender, 2019-20



Source: Deloitte Access Economics analysis.

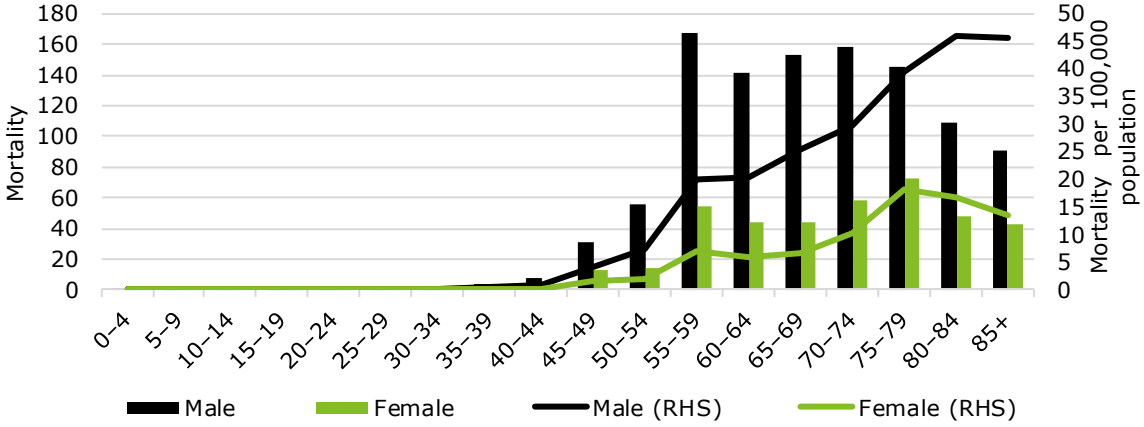
Prevalence refers to the total number of cases of a condition in a given time period. For the purposes of this report, the total number of people living with HCC in 2019-20 was defined as the 5-year prevalence of HCC. This includes newly recorded cases in 2019-20, as well as those who have been diagnosed since 2016 but have not yet died as a result of their liver cancer.

The **5-year prevalence of HCC in Australia in 2019-20 was estimated to be 4,392 people**, 3,589 males and 803 females. The estimated 5-year prevalence of HCC in 2019-20 peaked between the ages of 55 and 59, where there are 899 males and 119 females living with HCC. This compares to just 108 and 41 cases in males and females, respectively, between the ages of 0 and 44.

[7] The scope of this report was restricted to consider health sector costs, productivity losses due to reduced employment and premature mortality, and the value of reduced wellbeing due to HCC. It is common for cost of illness analyses to also include costs of absenteeism, presenteeism, informal care costs, and other costs such as the efficiency losses associated with transfer payments. These have not been estimated here, although it is noted that these other costs outside the scope of the report would likely be minor compared to the costs included in this report.

Deaths due to HCC were estimated using data from AIHW and Wallace et al (2019).[8, 9] Chart ii presents the estimated number of deaths from HCC in Australia in 2019-20, stratified by age and gender. **It was estimated that 1,070 males and 396 females died from HCC in 2019-20, summing to a total of 1,466 deaths.** This was equivalent to a death rate per 100,000 population of 7.62 for males and 3.02 for females. By comparison, lung cancer had a mortality rate of 36 deaths per 100,000 population among males and 23 among females,[10] while bowel cancer was responsible for 23 deaths per 100,000 population in males and 15 among females.[11]

Chart ii: Estimated deaths due to HCC, by age and gender, 2019-20



Source: AIHW (2018), Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

Health system and productivity costs

Health system costs include inpatient costs for treatments such as ablation or surgical resection. Other costs include imaging for diagnosis and management of the condition, along with GP and medical specialist consultations that form part of the person's multidisciplinary care team. There are also research costs attributable to HCC. Health system costs are typically funded by government and supplemented by out-of-pocket payments and private health insurers.

In 2019-20, a total of $139.5 million in health system expenditure was attributed to HCC, or $31,775 per person with HCC. The largest component of this expenditure was inpatient hospital admissions ($116.1 million) followed by outpatient expenditure ($14.6 million) and other health system services ($6.1 million). Finally, $2.8 million was spent on HCC research in 2019-20. By comparison, bowel cancer and breast cancer are estimated to cost the health system $1.1 billion and $800 million per year in Australia.[12] These are equivalent to per person costs of $20,353 and $11,120 for bowel cancer and breast cancer, respectively,[13] meaning that **HCC costs the health system significantly more per case than breast cancer and bowel cancer.**

The analysis also considered productivity losses attributable to the reduced employment and premature mortality among people diagnosed with HCC. **The total productivity cost attributable**

[8] Australian Institute of Health and Welfare 2018. Australian Cancer Incidence and Mortality (ACIM) books: liver cancer. *Cancer Data in Australia*. *Cat. No. CAN 122.*

[9] Wallace, MC, Preen, DB, Short, MW, Adams, LA, and Jeffrey, GP, 'Hepatocellular carcinoma in Australia 1982-2014: Increasing incidence and improving survival' (2019), 39 *Liver International* 522.

[10] Cancer Australia 2019, *Lung cancer in Australia statistics*, Australian Government, Canberra. Available at: https://lung-cancer.canceraustralia.gov.au/statistics

[11] Cancer Australia 2019, *Bowel cancer in Australia statistics*, Australian Government, Canberra. Available at: https://bowel-cancer.canceraustralia.gov.au/statistics

[12] Goldsbury, D. E., Yap, S., Weber, M. F., Veerman, L., Rankin, N., Banks, E., Canfell, K., & O'Connell, D. L. (2018). 'Health services costs for cancer care in Australia: Estimates from the 45 and up study', *Plos One* 13(7):e0201552.

[13] Australian Institute of Health and Welfare (AIHW) 2019, *Cancer in Australia 2019*, Cancer series no.119. Cat. no. CAN 123. Canberra, AIHW.

to HCC in 2019-20 was estimated to be $382.5 million in 2019-20. This comprised $294.1 million due to premature mortality from HCC and a further $88.4 million due to reduced workforce participation among people living with HCC.

Lost wellbeing from HCC

In addition to the financial costs, HCC significantly reduces the wellbeing of people who are diagnosed with it. The value of reduced wellbeing was quantified using the burden of disease methodology, which is a non-financial valuation approach where life and health are measured in terms of disability adjusted life years (DALYs). DALYs include both years of healthy life lost due to disability (YLDs) and years of life lost due to premature mortality (YLLs). One DALY is equivalent to one year of healthy life lost.

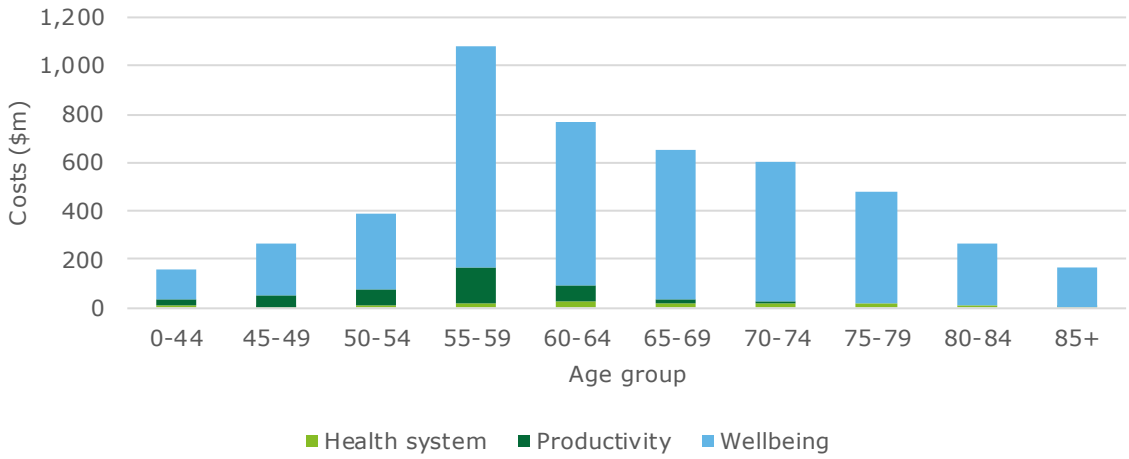
The YLDs attributable to HCC were estimated by multiplying the number of prevalent cases by disability weights and the average length of time for each stage of the cancer in 2019-20. YLLs were estimated by multiplying the number of deaths by the average expected years of life remaining at each age group. Finally, these DALYs (the sum of YLLs and YLDs) were multiplied by the value of a statistical life year (VSLY) to place a monetary value on the loss of wellbeing, which was assumed to be $216,626 in 2019-20 based on guidance from the Department of Prime Minister and Cabinet, adjusted for inflation.[14]

In 2019-20, it was estimated that 26,891 DALYs were due to HCC, comprising 551 YLDs and 26,340 YLLs. When future years of life were discounted at 3% per annum, there were an estimated 19,918 DALYs due to HCC in 2019-20. **The value of the lost wellbeing was estimated to be $4.3 billion**,[15] representing 90.2% of the total costs attributed to HCC. The loss of wellbeing is a non-financial cost (i.e. wellbeing is not measured within traditional measures of economic activity, such as gross domestic product).

Total cost of HCC in Australia in 2019-20

Overall, **the total cost of HCC was estimated to be $4.8 billion in 2019-20.** Most of these costs were due to cases in males ($3.5 billion). As shown in Chart iii, nearly $1.1 billion in costs accrued between the ages of 55 and 59, and a further $0.8 billion between the ages of 60 and 64.

Chart iii: Total cost of HCC in Australia in 2019-20, by age and cost component



Source: Deloitte Access Economics analysis.

[14] Department of Prime Minister and Cabinet 2019, *Best Practice Regulation Guidance Note: Value of Statistical Life*, Australian Government, Canberra, available at: <https://www.pmc.gov.au/sites/default/files/publications/value-of-statistical-life-guidance-note_0_0.pdf>

[15] Note that the value of lost wellbeing is estimated by applying the VSLY to the discounted DALYs, which have a discount rate of 3% applied.

HCC is a serious health condition with a complex and evolving aetiology, carrying with it a high mortality rate, substantial economic costs and significant loss of wellbeing. Despite improvements in diagnostics and available treatments in recent years, 5-year survival rates remain low. Moving into a new decade, it is imperative that investment is focused on preventative strategies, particularly for causes of growing concern such as non-alcoholic fatty liver disease.

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1 Background

1.1 Introduction

Liver cancer is a serious chronic health condition that carries with it a high mortality rate, substantial economic costs and significant loss of wellbeing. There were 2,599 people diagnosed with liver cancer in Australia in 2019, with men accounting for 73% of new diagnoses.[16] Across all diagnoses, just 19% are expected to survive beyond five years.[17]

Incidence rates for all primary liver cancer have increased 378% between 1982 and 2019, making it the second fastest growing cancer in Australia.[18] Over the same period, median survival increased from 2.1 months to over 12 months,[19] largely due to improvements in diagnostic strategies, refinement of targeted therapies (such as chemoembolism or thermal ablation), better and earlier identification of ideal transplant recipients and expanded availability of systemic therapies (including intravenous immune tyrosine kinase inhibitors).[20]

Nonetheless, survival rates remain poor in most cases, and the number of total cases continues to climb, largely due to changing risk factors such as the growing prevalence of non-alcoholic fatty liver disease (NAFLD), obesity and type 2 diabetes.

The most common type of primary liver cancer is hepatocellular carcinoma (HCC), accounting for 68% of primary liver cancers in Australia.[21] HCC occurs due to chronic liver inflammation, generally as a result of chronic viral hepatitis (B or C) or excessive exposure to toxins including alcohol or aflatoxin (e.g. contaminated food).

Amid these increasing rates of incidence, particularly in western countries,[22] the Liver Foundation engaged Deloitte Access Economics to estimate the economic cost of HCC in Australia in 2019-20. This analysis considered the health system costs required to treat HCC, and the reduction in productivity (excluding costs associated with absenteeism, presenteeism and informal care) and wellbeing due to HCC. Other costs, such as aids or transfer costs and the efficiency losses associated with transfer payments, were excluded from the scope of this report.

This report is structured in the following way:

- **Chapter 1** introduces this report, describes the causes and severity of HCC and its comorbidities, available treatments and care pathways, and the general prognosis for people diagnosed with HCC. Lastly, it provides an overview of the methodology used to estimate the costs of HCC in Australia in 2019-20.
- **Chapter 2** presents the epidemiology of HCC in Australia in 2019-20, covering the number of new cases expected, the prevalence of HCC and the mortality due to HCC. The epidemiology is a critical input underlying the cost estimates presented in subsequent chapters.
- **Chapter 3** provides estimates of the health system expenditure attributable to HCC in 2019-20. This includes costs such as inpatient and outpatient hospital expenditure, as well as specialists, GPs, allied health, imaging, pathology services, and other health costs.
- **Chapter 4** estimates the productivity losses that arise due to HCC, including the reduction in employment participation and the lost productivity from premature mortality due to HCC.
- **Chapter 5** presents the estimated loss of wellbeing due to HCC in 2019-20.

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[16] Australian Institute of Health and Welfare 2019. Cancer in Australia 2019. *Cancer in Australia series no. 5. Cat. No. CAN 123*.
[17] Ibid.
[18] Ibid.
[19] Wallace, M.C., Preen, D.C., Short, M.W., Adams, L.A., & Jeffrey, G.P. (2019) Hepatocelluar carcinoma in Australia 1982-2014: Increasing incidence and improving survival. *Liver International*, 39(3):522-530.
[20] Ibid.
[21] Ibid.
[22] Ibid.

1.2 Causes and comorbidities

Liver cancer typically develops as a result of liver damage caused by chronic infections affecting the liver, or certain biomedical and behavioural risks. The most common causes of HCC are hepatitis C virus (HCV, 41%), alcoholic liver disease (39%), hepatitis B virus (HBV, 22%) and fatty liver disease (14%).[23] Other key risk factors are type 2 diabetes, tobacco use and alcohol consumption, with 13% to 23% of HCC cases attributed to alcohol use.[24] These can lead to liver damage, which over time causes cirrhosis, whereby scarring develops and significantly reduces liver function.

More recently, HCC has been linked to non-alcoholic fatty liver disease (NAFLD),[25] the hepatic response to obesity and other related metabolic disorders such as diabetes. NAFLD is a benign form of the disease where an accumulation of fat occurs in more than 5% of the hepatocytes histologically (a hepatocyte is a cell of the main parenchymal tissue of the liver, making up between 55% and 65% of the liver's total mass). Research has found that NAFLD is associated with higher overall and liver-related mortality in the general population.[26]

The link between NAFLD and HCC is of particular concern in developed countries due to the high prevalence of obesity and type 2 diabetes. In fact, NAFLD is the most common cause of liver disease in Australia, affecting approximately 30% of adults.[27] The burden of NAFLD is expected to increase over the next decade, with the number of prevalent cases projected to rise 25% from current levels by 2030.[28] While benign, NAFLD may progress to liver fibrosis, cirrhosis, decompensated liver disease and liver cancer.[29]

Cirrhosis is the most common comorbidity of liver cancer, present in 85% to 90% of cases in Australia.[30] Cirrhosis can develop due to the same risk factors as HCC. The presence of comorbidities can complicate or limit treatment options for HCC.[31] Success in treating and preventing HCC in the future will depend on the changing face of the risk factors of cirrhosis. For example, while Australia has been successful in finding and treating patients with hepatitis C and will likely have very low hepatitis C death rates in the near future,[32] non-alcoholic steatohepatitis (NASH) represents an increasing risk factor for HCC development. Recent analysis on the global burden of cirrhosis found the age-standardised mortality rates for hepatitis B, hepatitis C and alcohol-related liver disease

[23] Hong T.P., Gow P., Fink M., Dev A., Roberts S., Nicoll A., Lubel, J., Kronborg, I., Arachi, N., Ryan, M., Kemp, W., Knight, V., Farrugia, H., Thursfield, V., Desmond, P., Thompson, A.J., & Bell, S. (2016). Novel population-based study finding higher than reported hepatocellular carcinoma incidence suggests an updated approach is needed. *Hepatology*, 63(4):1205-12.
[24] Massarweh, N. N., & El-Serag, H. B. (2017). Epidemiology of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *Cancer Control*, 24(3).
[25] Dhamija, E., Paul, S. B., & Kedia, S. (2019). 'Non-alcoholic fatty liver disease associated with hepatocellular carcinoma: an increasing concern', *The Indian Journal of Medical Research*, 149(1):9-17.
[26] Ong, J., Pitts, A., & Younossi, Z. M. (2008). Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease'
[27] Iser, D., & Ryan, M. (2013). 'Fatty liver disease: a practical guide for GPs', *Australian Family Physician*, 42(6): 444-447.
[28] Adams, L. A., Roberts, S. K., Strasser, S. I., Mahady, S. E., Powell, E., Estes, C., Razavi, H., & George, J. (2020). 'Non-alcoholic fatty liver disease burden: Australia, 2019-2030', *Journal of Gastroenterology and Hepatology*, early view.
[29] Mahady, S. E., & Adams, L. A. (2018). 'Burden of non-alcoholic fatty liver disease in Australia', *Journal of Gastroenterology and hepatology*, 1:1-11.
[30] Hong T.P., Gow P., Fink M., Dev A., Roberts S., Nicoll A., Lubel, J., Kronborg, I., Arachi, N., Ryan, M., Kemp, W., Knight, V., Farrugia, H., Thursfield, V., Desmond, P., Thompson, A.J., & Bell, S. (2016). Novel population-based study finding higher than reported hepatocellular carcinoma incidence suggests an updated approach is needed. *Hepatology*, 63(4):1205-12.
[31] Massarweh, N. N., & El-Serag, H. B. (2017). Epidemiology of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *Cancer Control*, 24(3).
[32] Waheed, Y., Siddiq, M., Jamil, Z., & Najmi, M. H. (2018). Hepatitis elimination by 2030: progress and challenges. *World Journal of Gastroenterology*, 24(44):4959-4961.

decreased between 1990 and 2017, while the equivalent rate for NASH increased.[33] For people without cirrhosis, metabolic syndrome has been found to be a significant risk factor for HCC.[34]

Within Australia, there are also certain population subgroups that experience higher exposure to liver cancer risk factors. People at a higher risk of liver cancer include males (particularly older males) and Indigenous Australians. Liver cancer incidence peaks at ages 80-84 years for both sexes (ASR of 65.7 for males and 32.4 for females).[35] Indigenous Australians are 2.4 times more likely to be diagnosed with HCC compared to non-Indigenous populations due to a range of socio-economic and geographic factors.[36] These include higher rates of HBV HCV and alcohol abuse in Indigenous Australians.[37] [38] [39]

1.3 Diagnosis, treatment and care pathways

HCC often expresses nonspecific symptoms in the earlier stages and can be picked up as an incidental finding. Symptoms of HCC can include abdominal pain or discomfort, nausea, yellowing of the skin and eyes (jaundice), and fluid build-up around the abdomen. The presence of symptoms or key underlying risk factors may prompt a series of blood tests to check liver function and an ultrasound. Following these, liver cancer is diagnosed using a computed tomography (CT) scan or magnetic resonance imaging (MRI).[40]

An important development in the identification of HCC in recent years was the ability to diagnose HCC without histology. This has led to a much higher number of HCC diagnoses over recent decades, as well as a correction in the historic underreporting of HCC in Australian cancer registries. For example, a 2016 population-based study found that the number of cases recorded as HCC had been underreported in the Victorian Cancer Registry (VCR) by as much as 50%.[41] This underreporting had occurred due to a process where diagnoses were only classified as HCC if the case was histologically confirmed. Where this had not occurred, the case was recorded as unspecified primary liver cancer.

Retrospective analysis of cases between 1982 and 2014 found that 76% of those classified as unspecified primary liver cancer were in fact HCC.[42] These cases have subsequently been reclassified as HCC in the respective cancer registries in line with current diagnostic and management guidelines which no longer require biopsy for diagnosis.[43] More recent research found that two other state-based registries within Australia had similarly high proportions of unspecified primary liver cancer diagnoses (41% and 29%), while all other registries were reporting the expected number of

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[33] Sepanlou, S. G., et al. (2020). The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet. Gastroenterology and Hepatology*, 5(3), 245-266.
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[35] Australian Institute of Health and Welfare 2019. Cancer in Australia 2019. *Cancer in Australia series no. 5. Cat. No. CAN 123*.
[36] Australian Institute of Health and Welfare 2018. Australia's health 2018: in brief. *Australia's health 2018 series no.4. Cat. No. AUS 222*.
[37] Australian Institute of Health and Welfare 2020. *Alcohol, tobacco and other drugs in Australia. Cat. No. PHE 221.*
[38] Graham, S., MacLachlan, J. H., Gunaratnam, P., & Cowie, B. C. (2019). Chronic hepatitis B prevalence in Australian Aboriginal and Torres Strait Islander people before and after implementing a universal vaccination program: a systematic review and meta-analysis. *Sexual health*, 16(3), 201-211.
[39] Graham, S., Maher, L., Wand, H., Doyle, M., & Iversen, J. (2017). Trends in hepatitis C antibody prevalence among Aboriginal and Torres Strait Islander people attending Australian Needle and Syringe Programs, 1996–2015. *International Journal of Drug Policy*, 47, 69-76.
[40] Department of Health and Human Services Victoria 2014, *Optimal cancer care pathway for people with hepatocellular carcinoma*, <https://www.cancervic.org.au/for-health-professionals/optimal-care-pathways>.
[41] Hong, TP, Gow, P, Fink, M, Dev, A, Roberts, S, Nicoll, A, Lubel, J, Kronborg, I, Arachchi, N, Ryan, M, Kemp, W, Knight, V, Farrugia, H, Thursfield, V, Desmond, P, Thompson, AJ, and Bell, S, 'Novel population-based study finding higher than reported hepatocellular carcinoma incidence suggest an update approach is needed' (2016), 63(4) *Hepatology* 1205.
[42] Ibid.
[43] Carville, K., MacLachlan, J., Thursfield, V., and Cowie, B. 'Hepatocellular carcinoma over three decades in Victoria, Australia: epidemiology, diagnosis, and trends, 1984–2013' (2018)

HCC cases (0.5% to 7.2%).[44] To correct for the underreporting, this study assumed that all cases with this code were in fact HCC from 1982 to 2014, except in those under 5 years of age in which case the diagnosis was more likely to be hepatoblastoma.

Notwithstanding the improvements in diagnostics for HCC, prognosis is often poor due to the lack of specific symptoms early in the development of the cancer. Prognostic factors include tumour stage, tumour size, severity of liver disease, alpha-fetoprotein level, portal vein tumour thrombus and treatment response.

Despite poor survival outcomes for many of those diagnosed, specific treatments are more promising. While the one-, three- and 5-year survival rates are 63%, 29% and 19%,[45] respectively, the 5-year survival rate after a surgical resection is 25%. Furthermore, the 5-year survival rate after a liver transplant is 75%,[46] while treatment using percutaneous ethanol injection (PEI) has a 5-year survival rate of 35-75% and approximately 75% of patients respond to the treatment.[47]

1.3.1 Treatment options

A common treatment for people diagnosed with liver cancer is surgical resection. This surgery involves the removal of the cancerous part of the liver and is considered the best cure for tumours confined to the liver, allowing for removal while preserving function in the remnant liver. Evaluation of patients for surgery is based on liver function, portal hypertension and tumour characteristics.[48] If a patient is in early-stage HCC, a liver transplant may be considered, though this is usually for patients with a 5-year survival rate estimated to be greater than 50%.[49]

Ablative therapies are the most common treatment for HCC and are used when there is a small tumour (3cm or less), for people awaiting liver transplants or with unresectable disease.[50] PEI was the first ablative technique used to treat HCC, involving the injection of alcohol directly into the tumour. Radiofrequency ablation (RFA) also forms a critical role in overall treatment due to its efficacy, with a reported 5-year survival rate of 40% to 70%.[51] Evidence suggests that RFA may be more cost-effective than surgical resection for early-stage HCC.[52]

Transarterial chemoembolisation (TACE) is the primary non-ablative treatment for HCC. TACE involves the injection of chemotherapy and embolic material into hepatic artery branches of the tumour to control small lesions. Another treatment is selective internal radiation therapy (SIRT) which involves the administration of Yttirum-90 microspheres into hepatic arteries running to the tumour. SIRT can be considered in select patients with intermediate or locally advanced HCC.[53]

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[44] Wallace, MC, Preen, DB, Short, MW, Adams, LA, and Jeffrey, GP, 'Hepatocellular carcinoma in Australia 1982-2014: Increasing incidence and improving survival' (2019), 39 *Liver International* 522.
[45] op den Winkel, M., Nagel, D., Sappl, J., op den Winkel, P., Lamerz, R., Zech, C. J., Straub, G., Nickel, T., Rentsch, M., Stieber, P., Goke, B., & Kolligs, F. T. (2012). 'Prognosis of patients with hepatocellular carcinoma. Validation and ranking of established staging-systems in a large western HCC cohort', *Plos One* 7(10):e45066.
[46] Kim, W. R., Lake, J. R., Smith, J. M., Schladt, D. P., Skeans, M. A., Harper, A. M., Wainwright, J. L., Snyder J. J., Israni, K., & Kasiske, B. L., (2018). 'OPTN/SRTR 2016 Annual Data Report: Liver', *American Journal of Transplantation* 18(S1):172-253.
[47] op den Winkel, M., Nagel, D., Sappl, J., op den Winkel, P., Lamerz, R., Zech, C. J., Straub, G., Nickel, T., Rentsch, M., Stieber, P., Goke, B., & Kolligs, F. T. (2012). 'Prognosis of patients with hepatocellular carcinoma. Validation and ranking of established staging-systems in a large western HCC cohort', *Plos One* 7(10):e45066.
[48] Lubel, J. S., Roberts, S. K., Strasser, S. I., Thompson, A. J., Philip, J., Goodwin, M., Clarke, S., Crawford, D. H., Levy, M. T., Shackel, N. (2020), 'Australian recommendations for the management of hepatocellular carcinoma: a consensus statement', *Medical Journal of Australia*, https://doi.org/10.5694/mja2.50885.
[49] Ibid.
[50] Department of Health and Human Services Victoria 2014, *Optimal cancer care pathway for people with hepatocellular carcinoma*, <https://www.cancervic.org.au/for-health-professionals/optimal-care-pathways>.
[51] Facciorusso, A., Serviddio, G., & Muscatiello, N. (2016). 'Local ablative treatments for hepatocellular carcinoma: an updated review', *World Journal of Gastrointestinal Pharmacology and Therapeutics, 7(4):477-489.*
[52] Ibid.
[53] Lubel, J. S., Roberts, S. K., Strasser, S. I., Thompson, A. J., Philip, J., Goodwin, M., Clarke, S., Crawford, D. H., Levy, M. T., Shackel, N. (2020), 'Australian recommendations for the management of hepatocellular carcinoma: a consensus statement', *Medical Journal of Australia*, https://doi.org/10.5694/mja2.50885.

Ultrasound screening has been associated with early stage HCC diagnosis and improved patient survival outcomes. The pooled survival from four Australian studies suggested that ultrasound screening improved 2-year survival in people with HCC from 40% to 69%.[54]

Less common treatments include systemic therapy and endoscopic stent placements. Biological therapy involves a range of treatments that are designed to stop or limit the growth or function of cancer cells, or by aiding the body's immune system. This treatment is suitable for both primary and secondary liver cancers and may be used in conjunction with other treatments. Finally, in situations where the cancer has obstructed the bile duct, a stent may be recommended. This is designed to help drain a build up of bile and subsequently ease the symptoms being experienced.

1.3.2 Care pathways

Care for patients after diagnosis involves a multidisciplinary team which guides patients through the various stages of care.[55] The first stage involves prevention and early detection, including vaccinations for HBV and HCV and monitoring at-risk groups, such as those with NAFLD. The next step involves an assessment of symptoms and referral of the patient to specialists for further diagnosis. While clinicians may perform basic diagnostic tests such as an assessment of tumour markers, specialists are required in the next instance for CT and MRI scans to confirm the diagnosis.[56] Importantly, histology is no longer required to diagnose HCC, meaning that a far greater number of cases are now being accurately diagnosed.

Upon diagnosis with HCC, treatment plans are developed, and the relevant treatment(s) would be administered. After treatment is administered, the focus turns to addressing the underlying liver disease to improve quality of life. A follow-up care plan is provided which includes managing the effects of the treatment and an explanation of the required follow-up tests. Routine check-ups are also done to ensure the disease is being managed. Lastly, palliative care is considered, and an advanced care plan is enacted if prognosis is poor.

1.4 Methodology to estimate the costs of HCC

Estimating the cost of HCC in Australia in 2019-20 requires an understanding of its epidemiological profile and the costs incurred by people living with HCC.

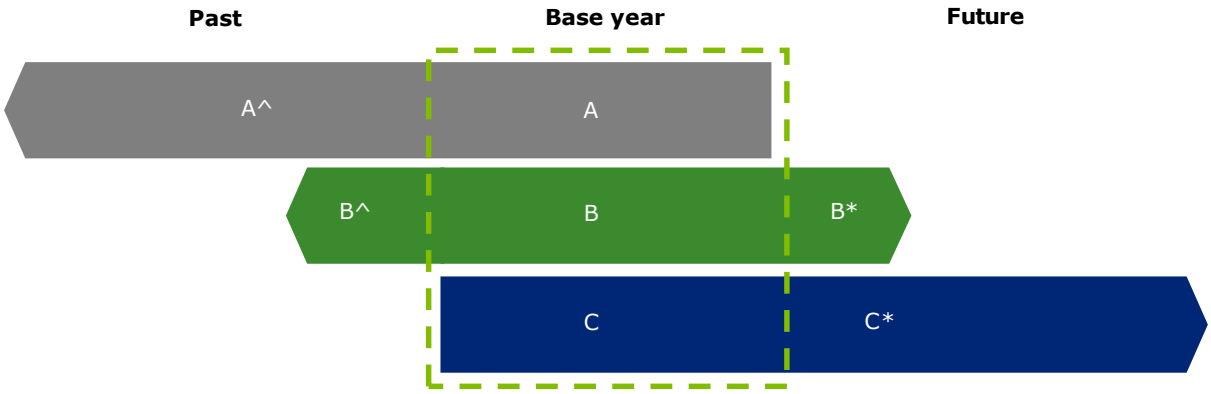
The costs of HCC were estimated for the financial year 2019-20 using a prevalence-based approach to cost estimation. A prevalence approach measures the number of people living with a condition (in this case, HCC) at a given point in time and estimates the costs incurred due to HCC for a period (in this case, 2019-20). Figure 1.1 presents a conceptual model of the differences in the cohort base used to estimate costs under incidence and prevalence approaches.

Figure 1.1 considers three different cases of people with HCC:

- A, where a person living with HCC was diagnosed in the past and have incurred the associated costs up to the year in question, with associated lifetime costs of A^ + A.
- B, where a person living with HCC was diagnosed in the past and has incurred the associated costs in 2019-20 as well as in the past and future, with associated lifetime costs of B^, B and B*.
- C, where a person living with HCC was diagnosed in 2019-20, with lifetime costs of C and C*.

[54] Jeffrey, Gary P., Louisa Gordon, and Grant Ramm. 'Hepatocellular carcinoma surveillance in Australia: time to improve the diagnosis of cirrhosis and use liver ultrasound.' *The Medical Journal of Australia* 212, no. 7 (2020): 297-299.
[55] Department of Health and Human Services Victoria 2014, *Optimal cancer care pathway for people with hepatocellular carcinoma*, <https://www.cancervic.org.au/for-health-professionals/optimal-care-pathways>.
[56] Ibid.

Figure 1.1: Conceptual differences between incidence and prevalence approaches to measurement of annual costs



Source: Deloitte Access Economics.

A prevalence-based approach to cost estimation considers only the annual cost incurred in the base year by all people living with HCC in 2019-20, or A, B and C per Figure 1.1. Alternatively, an incidence-based approach would consider the annual costs in the base year along with the present value of future costs (C + C*), based on the number of incident cases in 2019-20.

The prevalence-based approach was used in this analysis to estimate the cost of HCC in Australia in 2019-20, including financial costs to the Australian health system, productivity losses (e.g. reduced employment and/or reduced output due HCC),[57] and the loss of wellbeing due to HCC. Prevalence can be taken to have two broad meanings:

- **Point prevalence**, which refers to the cumulative number of HCC patients diagnosed prior to 2019-20 but have not yet died. This was estimated by multiplying the incidence of HCC in each of the past five years by the corresponding survival rate for the number of years required to live to survive until the base year.
- **Active prevalence**, which refers to the cumulative number of HCC patients diagnosed prior to 2019-20 and who have not yet died, but on the basis of probability will die from their HCC (thus they require health care for active HCC).

For the purposes of this report, the prevalence-based approach is based on 5-year prevalence estimates to account for the costs incurred in 2019-20 from people diagnosed with HCC in previous years. The approach to estimate 5-year prevalence is detailed in Section 2.2.

A 5-year period was chosen as survival rates for HCC at this point are approximately 12% on average, meaning that most people with HCC will have died by the end of 5 years.

Using 5-year prevalence as the basis for cost estimation may be conservative as there will still be some people incurring costs as a result of HCC who were diagnosed more than five years ago – for example, they may still be out of the workforce due to HCC but otherwise be cured of cancer and thus may not require active treatment. This approach is also more likely to conservatively estimate the average costs per person compared to an active prevalence approach.

However, it is also possible that using 5-year prevalence may overstate some costs as people diagnosed with HCC in the past may have been cured and therefore may no longer be incurring costs. In part, these challenges were addressed by choosing appropriate data sources. For example, it would not be appropriate to derive health system estimates based on a study that estimates health costs in the year after diagnosis using a 5-year prevalence approach.

[57] This analysis does not consider additional productivity costs associated with informal care required for people living with HCC, or the likely absenteeism and/or presenteeism arising due to HCC.

2 Epidemiology of HCC in Australia

Key findings

- In 2019-20, there were an estimated **1,916 new cases of HCC in Australia**, equivalent to 6.46 cases per 100,000 population. When only considering cases in those aged 45 or over, **the rate per 100,000 population is 32.19 for males and 7.82 for females.**
- The **5-year prevalence of HCC in Australia in 2019-20 was estimated to be 4,392 people**, with 3,589 males and 803 females.
- It was estimated that **1,070 males and 396 females died from HCC in 2019-20**, summing to a total of 1,466 deaths.

2.1 Incidence of HCC

The incidence of HCC refers to the total number of cases first diagnosed or reported in a given period (e.g. in a year). For the purposes of this report, our analysis estimated the total number of cases first diagnosed or reported in the year 2019-20.

Incidence data for primary liver cancer has been recorded by the AIHW in the Australian Cancer Database (ACD) from 1982 to 2016.[58] This database provides age- and gender-specific incidence rates. Cases are recorded under the International Classification of Diseases (ICD-10) three-character code for primary liver cancers, C22. This covers all sub-classifications of primary liver cancers, including:

- C22.0 (liver cell carcinoma)
- C22.1 (intrahepatic bile duct carcinoma)
- C22.2 (hepatoblastoma), C22.3 (angiosarcoma of liver)
- C22.4 (other sarcomas of liver)
- C22.7 (other specified carcinomas of liver)
- C22.8 (malignant neoplasm of liver, primary, unspecified as to type)
- C22.9 (malignant neoplasm of liver, not specific as primary or secondary).

The analysis in this report focuses on C22.0, or HCC, only, meaning that the number of incident cases classified as C22.0 were estimated from all primary liver cancer cases.

In order to estimate incidence to HCC and to consider the issues around underreporting in some of the cancer registries highlighted in Section 1.3.2, our analysis has derived incidence rates of HCC from the number of cases reported by Wallace et al (2019) as a proportion of the total number of primary liver cancer cases reported by AIHW.[59, 60] Wallace et al (2019) identified cases of HCC in the ACD for those aged 45 and above over a 32-year period spanning 1982 to 2014, adjusting for underreporting by assuming that actual incidence in those aged five or above followed that of the VCR.

To determine the number of cases likely to have been HCC, age- and gender-specific proportions (see Appendix A) were applied to recent AIHW incidence data for all primary liver cancers. The most recent 10 years of actual data (2006 to 2015) were used to account for the low single-year incidence

[58] Australian Institute of Health and Welfare 2018. Australian Cancer Incidence and Mortality (ACIM) books: liver cancer. *Cancer Data in Australia*. *Cat. No. CAN 122.*
[59] Ibid.
[60] Ibid.

in 5-year age groups between 5 and 29 years. In total, 74.7% of all cases between 1982 and 2014 were HCC for males compared to 48.3% for females, for an overall proportion of 67.4%.

The subsequent incidence rates (per 100,000 population) between 2006 and 2015 were adjusted by the 5-year average annual growth in incidence from 2010 to 2015 to account for expected growth in the number of incident cases between 2016 and 2020. This is presented in Table 2.1.

Overall, it was estimated that **there are 1,916 new cases of HCC in Australia in 2019-20, comprised of 1,547 male cases and 368 female cases**. This is equivalent to 10.25 cases of HCC per 100,000 males in 2019-20, substantially higher than the 2.68 cases per 100,000 females. The incidence rate is shown to peak at the age of 80-84 for males and 75-79 for females, with 44.84 and 14.51 cases per 100,000 persons, respectively. The total rate of incidence is estimated to be 6.46 per 100,000 population in 2019-20. **When only considering cases in those aged 45 or over, the rate per 100,000 population was 32.19 for males and 7.82 for females.**

As discussed in Section 1.2, the incidence of HCC in Australia over the coming years will depend on success at treating and preventing its primary risk factors. Australia has been successful in finding and treating patients with hepatitis C and will likely have very low hepatitis C death rates in the near future.[61] However, as the impact of hepatitis B and C is increasingly attenuated, the impact of NASH is expected to continue worsening.

Chart 2.1 provides an illustration of the number of new cases and incidence rate per 100,000 population for 2019-20.

[61] Waheed, Y., Siddiq, M., Jamil, Z., & Najmi, M. H. (2018). Hepatitis elimination by 2030: progress and challenges. *World Journal of Gastroenterology*, 24(44):4959-4961.

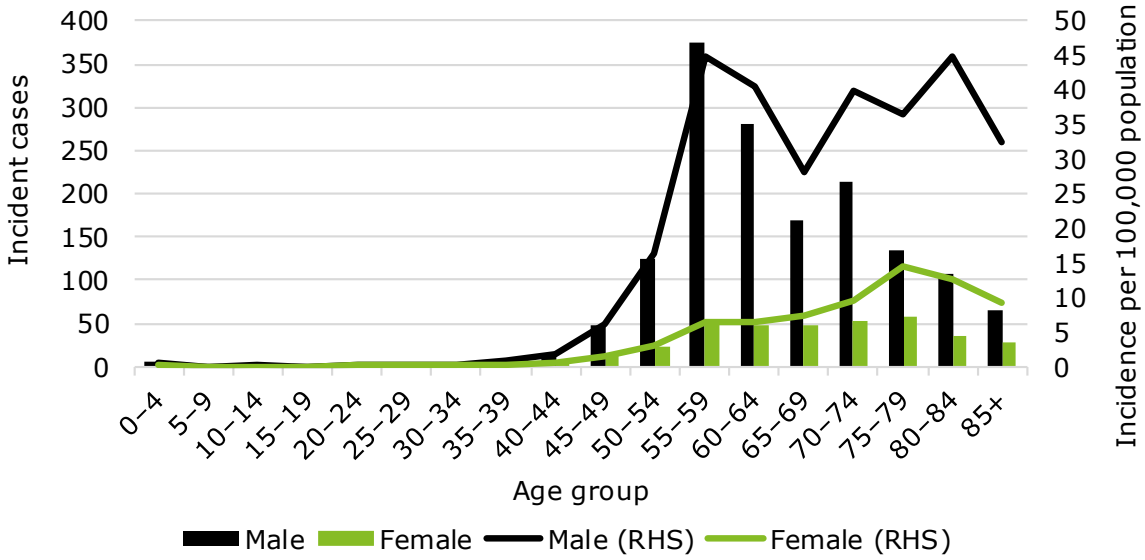
Table 2.1: Method for estimating the rate of HCC per 100,000 persons in 2019-20

Age / gender	Incident cases (2006-15)	Per 100,000 persons (2006-15)	Incidence trend, 2010-15 (%)	Incident cases (2019-20)	Per 100,000 persons (2019-20)
Male					
0-44	294	0.42	0.00	32	0.42
45-49	467	6.2	0.15	47	6.20
50-54	1,070	14.7	2.16	124	16.36
55-59	1,391	21.1	16.30	376	44.81
60-64	1,237	21.2	13.80	280	40.41
65-69	1,184	25.1	2.41	170	28.27
70-74	1,112	31.6	4.77	213	39.83
75-79	1,031	39.0	-1.24	135	36.64
80-84	682	36.8	4.01	106	44.84
85+	382	28.0	2.97	65	32.41
Male total	*8,850*	*8.02*	*5.04*	*1,547*	*10.25*
Female					
0-44	101	0.15	0.00	11	0.15
45-49	88	1.13	6.44	12	1.55
50-54	159	2.15	6.24	23	2.91
55-59	211	3.14	15.50	51	6.45
60-64	232	3.93	10.77	48	6.56
65-69	252	5.26	6.98	47	7.38
70-74	311	8.38	2.39	53	9.43
75-79	303	9.94	7.85	58	14.51
80-84	274	11.05	2.52	36	12.51
85+	221	8.57	1.15	29	9.08
Female total	*2,153*	*1.94*	*6.65*	*368*	*2.68*
Total	**11,003**	**4.96**	**5.84**	**1,916**	**6.46**

Source: Wallace et al (2019), AIHW (2018), Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

Chart 2.1: Incident cases of HCC in Australia, total and per 100,000 population, by age and gender, 2019-20



Source: Deloitte Access Economics analysis.

2.2 5-year prevalence of HCC

Prevalence refers to the number of cases of a condition in a given time period. For the purposes of this report, the prevalence of HCC was defined using a definition of 5-year prevalence which includes people who are newly diagnosed in 2019-20 and people who were diagnosed since 2016 but who are still alive. This 5-year prevalence was used as the basis for estimating the health system, productivity and other financial costs of HCC in Australia in 2019-20.

The 5-year prevalence of HCC in 2019-20 was estimated based on the number of incident cases in each year between 2016 and 2020.[62] The incident cases for each year between 2016 and 2020 were estimated by applying the calculated rate of incidence (per 100,000 population) in 2016 to the age-gender specific population in each given year. As outlined in Section 2.1, these incident cases were adjusted up or down to reflect the observed trend between 2010 and 2015, as it was expected that the direction of the trend will remain the same between 2016 and 2020.

For each of these incident cases, there are two possible outcomes: survival or death. Our modelling draws on 5-year survival rates published by the AIHW for all primary liver cancers to estimate relative survival rates for each year between 2016 and 2020. Survival rates were supplemented by the SEER US cancer data for age groups below 40 years of age (see Appendix A).[63, 64] The SEER US cancer data were used in cases where the AIHW has not published death rates due to the low number of cases in Australia in these ages.

The calculated survival rates for each age-gender cohort used in this analysis are presented in Table A.2. As an example, a male aged 55 to 59 diagnosed in 2016 has a 73% chance of surviving one year to 2017 but just a 28% chance of being alive in 2020. Overall, it was estimated that 13% of males and 11% of females survive five or more years after an HCC diagnosis, with an average of 12% for all persons.

[62] Survival is only considered over five years in this report as this is the common convention in cancer reporting and just 19% of those diagnosed with liver cancer survive beyond five years.
[63] Australian Institute of Health and Welfare 2018. Australian Cancer Incidence and Mortality (ACIM) books: liver cancer. *Cancer Data in Australia*. *Cat. No. CAN 122.*
[64] Surveillance, Epidemiology, and End Results (SEER) Program (2018), *Mortality - All COD, Aggregated With State, Total U.S. (1969-2016)*. National Cancer Institute, DCCPS, Surveillance Research Program.

All other people living with HCC are expected to have died at some point during the period 2016 to 2020. The method for estimating the number of deaths due to HCC is discussed in greater detail in Section 2.3.

Table 2.2 presents the estimated 5-year prevalence of HCC by age and gender in 2019-20. Overall, it was estimated that **there were 4,392 people living with HCC in 2019-20**,[65] which comprised **3,589 males and 803 females**.

Table 2.2: 5-year prevalence of HCC in Australia, by age and gender, 2019-20

Age	Male	Female	Persons
0-44	108	41	150
45-49	139	33	172
50-54	343	62	405
55-59	899	119	1,019
60-64	640	110	749
65-69	398	103	501
70-74	460	125	585
75-79	269	97	366
80-84	204	62	266
85+	127	51	179
Total	**3,589**	**803**	**4,392**

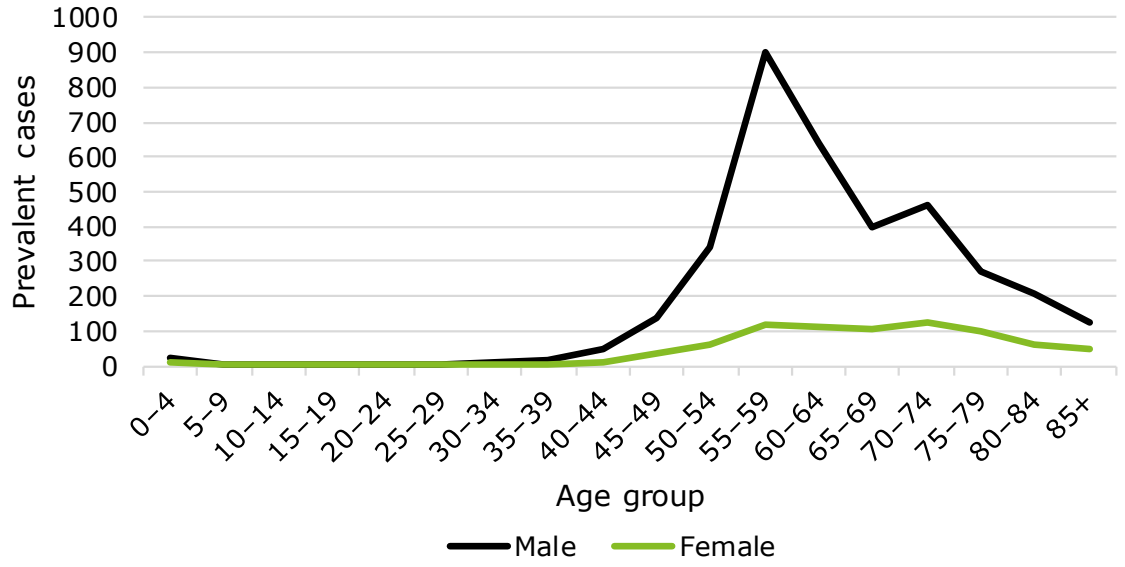
Source: Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

Chart 2.2 presents the 5-year prevalence estimates by age and gender, showing that very few cases occurred before the age of 45 and 5-year prevalence was consistently higher in males than females. The number of active cases peaked between the ages of 55 and 59, where there were 899 males and 119 females living with HCC. This compares to just 108 male cases and 41 female cases between the ages of 0 and 44. The number of cases was comparatively lower in ages above 65, likely due to the high mortality rate (meaning that not many people living with HCC survive until older ages). This finding may also be confounded by the high growth in cases in people aged between the ages of 55 and 59 (16.3%), compared to between the ages of 65 and 69 (2.4%).

[65] Again, this is based on incident cases between 2016 and 2020. Aside from those who died during this period, some of the cases may actually be cured, meaning that their cancer is not active.

Chart 2.2: 5-year prevalence of HCC in Australia, by age and gender, 2019-20



Source: Deloitte Access Economics analysis.

2.3 Mortality due to HCC

2.3.1 Risk of mortality

Despite advances in treatment and earlier detection of HCC over the past two decades, the prevalence of HCC has been on the rise, particularly in developed countries. It remains the fourth most common cause of cancer-related mortality worldwide.[66] In Australia, just 19% of those diagnosed with any liver cancer survive beyond five years.[67] In fact, while liver cancer was ranked 15th in terms of incident cases in 2019, it was ranked 7th in terms of mortality.[68] Combining AIHW and SEER US cancer data, our analysis found that the 5-year survival rate for HCC alone was 12%.

Deaths due to HCC were estimated using data from AIHW and Wallace et al (2019).[69, 70] The AIHW has recorded detailed data on cancer incidence and mortality for 5-year age groups by gender from 1982 to 2017.

To estimate deaths from HCC in 2020 for those aged 0 to 44, 10-year mortality rates between 2007 and 2016 were calculated to adjust for the low single-year mortality rates across these age groups and high year-on-year variation. Given the higher rate of mortality in ages above this, raw data from the most recent year was used as the basis for the analysis.

These mortality rates (per 100,000 population) between 2007 to 2016 were inflated to 2019-20 by applying a 5-year average annual trend in mortality from 2011 to 2016 to account for the expected growth in the number of deaths.

Table 2.3 presents the estimated number of deaths due to HCC by age and gender. Overall, it was estimated that **1,466 deaths were attributable to HCC in Australia in 2019-20, 1,070 of whom were males and 396 of whom were females**.

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[66] World Health Organisation 2018, *Cancer: Key facts*, <https://www.who.int/news-room/fact-sheets/detail/cancer>.
[67] Australian Institute of Health and Welfare 2019. Cancer in Australia 2019. *Cancer in Australia series no. 5. Cat. No. CAN 123*.
[68] Ibid.
[69] Australian Institute of Health and Welfare 2018. Australian Cancer Incidence and Mortality (ACIM) books: liver cancer. *Cancer Data in Australia*. *Cat. No. CAN 122.*
[70] Wallace, MC, Preen, DB, Short, MW, Adams, LA, and Jeffrey, GP, 'Hepatocellular carcinoma in Australia 1982-2014: Increasing incidence and improving survival' (2019), 39 *Liver International* 522.

Table 2.3: Estimated deaths due to HCC, by age and gender, 2019-20

Age	Male	Female	Persons
0-44	16	6	22
45–49	31	13	44
50–54	56	14	70
55–59	167	55	222
60–64	141	44	185
65–69	153	44	197
70–74	159	58	217
75–79	146	72	218
80–84	109	48	157
85+	91	43	135
Total	**1,070**	**396**	**1,466**

Source: AIHW (2018), Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

As with the recognised underreporting in the number of incident cases of HCC in Australia over past decades, it is possible, too, that the number of deaths from HCC have not been accurately recorded. There is evidence to suggest that some deaths that should be recorded with the underlying cause being HCC have instead been attributed to cirrhosis.

For example, a study of the cause of death in patients with HCC in Barcelona found that tumour progression was only recorded as the immediate cause of death in approximately 40% of cases.[71] In the Australian context, a study into HCC deaths using the WA Cancer Registry **found that around 75% of deaths among those with HCC were recorded as being due to HCC**.[72] The remainder were attributed to other cancer, liver disease, cardiovascular disease, and other or unknown causes.

Assuming that this recording pattern was consistent across all cancer registries across Australia, it is possible that the total deaths from HCC only account for around 75% of the actual figure. This has been used as a measure of sensitivity analysis (in chapter 6) to investigate how much higher the productivity costs and losses of wellbeing may be if the ABS cause of death data are not accurate.

[71] Dip Borunda, A. K., Campos Gomez, S., & Huitzil Melendez, F. D. (2011). Cause of death with hepatocellular carcinoma (HCC) according to Barcelona Clinic Liver Cancer System (BCLC): Tumor versus nontumor-related mortality, *Journal of Clinical Oncology*, 29(15):e14594.

[72] Wallace, M. (2017). HCC in WA: 1984-2013. A data linkage study. University of Western Australia, presentation delivered in November 2017.

3 Health system costs

Health system costs due to HCC include inpatient hospital services, imaging for the diagnosis and management of the condition, and consultations with medical specialists and GPs that form part of the person's multidisciplinary care team. There are also research costs attributable to HCC as, in the absence of the condition, the money funding research could be spent elsewhere. Health system costs are typically funded by government and supplemented by out-of-pocket payments and third-party private health insurers.

Key findings

- **Total health system expenditure attributed to HCC in 2019-20 was estimated to be $139.5 million**, or $31,775 per person with HCC.
- The largest component of health system expenditure was **inpatient hospital admissions ($116.1 million)** followed by **outpatient expenditure ($14.6 million)** and **research ($2.8 million)**. **Other health system costs totalled $6.1 million.**

3.1 Inpatient expenditure

The cost of admitted patient expenditure was estimated by deriving the number of hospital separations, which was then multiplied by the weighted average cost of a hospital admission for liver cancer.

Data on the number of hospital separations were retrieved from the Australian Institute of Health and Welfare (AIHW) principal diagnosis data cubes for the C22.0 ICD code.[73] In 2017-18 there were 3,998 separations (4,171 separations in 2019-20 adjusted for demographic changes).

It is understood that there are additional hospital separations due to HCC where HCC was not recorded as the principle diagnosis. In the UK in 2018-19, there were 8,929 inpatient hospitalisations with HCC as the principle diagnosis. This increased to 17,040 when HCC as an additional diagnosis was included. According to this data, for every 1 recorded inpatient admission for HCC, there was an additional 0.91 admissions where HCC was an additional diagnosis. This rate is greater in the US, where for every hospitalisation with a primary diagnosis of HCC there were an additional 2.1 hospitalisations with HCC as a secondary diagnosis.

Other literature indicates that the rate of hospitalisations per person with HCC ranges from 2-4 hospitalisations per year. A study of Australian patients with HCC found that in the year before liver transplantation, patients were hospitalised on 4.23 occasions.[74] One limitation of this study was that the patients were people who went on to receive a liver transplant, which is not necessarily reflective of the resource utilisation of a person who does not require a liver transplant. Other studies suggest the rate of hospitalisations per person per year may be closer to two.[75]

To account for additional hospital admissions where HCC may be the secondary diagnosis, it was assumed that there were an additional 0.91 hospital admissions for every primary diagnosis, as has been observed within the UK. It was estimated that there were 7,960 inpatient hospital admissions, or 1.81 hospitalisations per active case of HCC in 2019-20.

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[73] Australian Institute of Health and Welfare, 'Principal diagnosis data cubes' (2019) <https://www.aihw.gov.au/reports/hospitals/principal-diagnosis-data-cubes/contents/data-cubes>.
[74] McElroy, H. J., Roberts, S. K., Thompson, A. J., Angus, P. W., McKenna, S. J., Warren, E., & Musgrave, S. (2017). Medical resource utilization and costs among Australian patients with genotype 1 chronic hepatitis C: results of a retrospective observational study. Journal of medical economics, 20(1), 72-81.
[75] Thein, H. H., Isaranuwatchai, W., Campitelli, M. A., Feld, J. J., Yoshida, E., Sherman, M., ... & Earle, C. C. (2013). Health care costs associated with hepatocellular carcinoma: a population-based study. Hepatology, 58(4), 1375-1384.

The average cost per separation was estimated using selected AR-DRG codes related to HCC. The selected codes and assumed likelihood of occurrence were informed from McElroy et al (2017).[76] These codes and the respective cost weights reported by the Independent Hospital Pricing Authority are provided in Table A.3.[77] The average cost per separation was calculated to be $12,757 in 2016-17. Adjusted to 2019-20 terms (using AIHW health costs inflation data), this was $13,390.

Liver transplants were also informed by the Independent Hospital Pricing Authority using code H09Z 'Liver Transplants'. In 2016-17 there were 301 liver transplants, which was estimated to be 317 in 2019-20. According to the Australia and New Zealand Liver and Intestinal Transplant Registry, 18.7% of all liver transplants were attributable to HCC in 2018. It was assumed that this proportion remained consistent in 2019-20. It was estimated that there were 59 liver transplants due to HCC in 2019-20.

To calculate the average cost of inpatient admissions, the weighted average cost of transplants and all other admissions was calculated. It was estimated that the average cost of an inpatient admission due to HCC was $14,587 in 2019-20.

The number of HCC separations (7,960) was multiplied by the average cost of $14,587. **It was estimated that the total cost of HCC inpatient admissions was $116.1 million in 2019-20, or $26,438 per person.**

3.2 Other health system services due to HCC

The AIHW's disease expenditure report provides estimates of health system costs including GP, specialist and outpatient visits, imaging, pathology and pharmaceuticals, for nearly 200 conditions in 2015-16. This includes costs for liver cancer by age, gender and cost component. These costs were then adjusted for health inflation and demographic changes since 2015-16.

An additional adjustment was made reflecting that HCC represents a subset of total liver cancers. The proportion of liver cancer costs attributable to HCC was assumed to be 74.7% for males and 48.3% for females.[78] Accounting for the health system costs attributable only to HCC, the estimated health system cost was $14.3 million in 2015-16. After adjusting for inflation and demographic changes, it was estimated that this cost increased to $20.7 million in 2019-20. Table 3.1 provides a breakdown of other health system costs by component.

[76] McElroy, H. J., Roberts, S. K., Thompson, A. J., Angus, P. W., McKenna, S. J., Warren, E., & Musgrave, S. (2017). Medical resource utilization and costs among Australian patients with genotype 1 chronic hepatitis C: results of a retrospective observational study. Journal of medical economics, 20(1), 72-81.
[77] Underlying AIHW disease expenditure data covers several years to minimise the variability across conditions. Weights were created for each year to account for changes in population structure between the year of data and 2015.
[78] Based on the incidence of HCC from 1982-2014 compared to all liver cancer 1982-2014 in Australia. Wallace, MC, Preen, DB, Short, MW, Adams, LA, and Jeffrey, GP, 'Hepatocellular carcinoma in Australia 1982-2014: Increasing incidence and improving survival' (2019), 39 *Liver International* 522.

Table 3.1: Other health system costs by cost component, 2019-20

Component	Cost ($ million)	Cost per person ($)
Outpatient	14.6	3,316
Allied health expenditure	0.1	19
GP	1.1	258
Medical specialists (other than GPs)	2.6	595
Imaging and Pathology	1.2	271
Pharmaceuticals	1.1	249
Total other expenditure	**20.7**	**4,709**

Source: AIHW (2019), Deloitte Access Economics analysis.

3.3 Research

Research costs attributable to HCC were estimated based on the number of grants provided by the National Health and Medical Research Council (NHMRC). Examples of liver cancer research during this period include the development of a diagnostic serological test for extrahepatic biliary atresia and a study of the effectiveness of regular surveillance for HCC in patients with haemochromatosis and cirrhosis.

Data were available for all NHMRC funded research into cancer and other neoplasms from 2000-2014. In 2014, $181.7 million in funding was provided for cancer research, of which $1.7 million was funded directly towards liver cancer. Further to this $1.7 million, it was estimated that $103.0 million in research was funded towards non-specific cancer research. Based on 2019 incidence of liver cancer relative to all cancers, it was assumed that an additional $1.2 million of non-specific cancer research was attributable to liver cancer. As such, **it was estimated that there was $2.8 million in research grants attributable to HCC in 2019-20**.

3.4 Total health system expenditure

In total, it was estimated that **$139.5 million in health system expenditure was attributable to HCC** in 2019-20. This is presented by cost component in Table 3.2.

Table 3.2: Health system costs attributable to HCC by cost component, 2019-20

Cost component	Male	Female	Persons
Inpatient ($ million)	94.7	21.4	116.1
Outpatient and other costs ($ million)	12.8	7.9	20.7
Research ($ million)	2.3	0.5	2.8
Total cost ($ million)	**109.7**	**29.8**	**139.5**
Cost per person ($)	**30,571**	**37,156**	**31,775**

Source: Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

By comparison, Lang et al (2009) found that HCC was responsible for approximately USD$406 million in health system expenditure in the United States in 2009.[79] The total cost per

[79] Lang, K., Danchenko, N., Gondek, K., Shah, S., & Thompson, D. (2009). The burden of illness associated with hepatocellular carcinoma in the United States. Journal of hepatology, 50(1), 89-99.

patient was estimated to be US$29,354. Another paper from the US found the median cost per month to be $4,802 (non-transplant patients) and $7,492 (transplant patients).[80] One study conducted in Canada, found that HCC had an average cost per person over five years of CAD$77,000, which was equivalent to around CAD$15,400 per person annually.[81] In an Australian context, one paper found mean total costs of $55,092 over a 24 month period.[82] Another Australian study found health system costs in the pre-transplant population to be $31,221 in 2015.[83] Approximately 75% of health system costs are incurred in the first year after diagnosis,[84] which indicates that **the annual cost in the year after diagnosis is approximately $54,600 per person with HCC** (=$139.5 million * 75% / 1,916 incident cases). These costs are greater than the costs in the first year after diagnosis for breast cancer and comparable to the first-year cost of bowel cancer.[85]

With respect to the breakdown of health system costs, literature indicates that inpatient expenditure accounts for the majority of costs.[86] One study indicated that the number of outpatient visits per person could be significantly greater than the present estimate, which would suggest higher outpatient costs.[87] However, the estimated outpatient costs fall broadly in line with other Australian literature.[88]

It should be noted that these per person costs may not be directly comparable to those estimated in this report, given the basis for our analysis is 5-year prevalence and it is likely that some of these individuals are not receiving active treatment. This emphasises that the per person costs may be significantly higher, particularly for people recently diagnosed with HCC. Nonetheless, it does provide some indicative comparisons of the cost of treating HCC globally.

[80] Tapper, E. B., Catana, A. M., Sethi, N., Mansuri, D., Sethi, S., Vong, A., & Afdhal, N. H. (2016). Direct costs of care for hepatocellular carcinoma in patients with hepatitis C cirrhosis. Cancer, 122(6), 852-858.
[81] Thein, H. H., Isaranuwatchai, W., Campitelli, M. A., Feld, J. J., Yoshida, E., Sherman, M., ... & Earle, C. C. (2013). Health care costs associated with hepatocellular carcinoma: a population-based study. Hepatology, 58(4), 1375-1384.
[82] Hong, T. P. (2019). An Australian population-based study of the incidence and outcomes of hepatocellular carcinoma: the Hepatomas of Melbourne Epidemiological Research (HoMER) study (Doctoral dissertation).
[83] McElroy, H. J., Roberts, S. K., Thompson, A. J., Angus, P. W., McKenna, S. J., Warren, E., & Musgrave, S. (2017). Medical resource utilization and costs among Australian patients with genotype 1 chronic hepatitis C: results of a retrospective observational study. Journal of medical economics, 20(1), 72-81.
[84] Goldsbury, D. E., Yap, S., Weber, M. F., Veerman, L., Rankin, N., Banks, E., Canfell, K., & O'Connell, D. L. (2018). 'Health services costs for cancer care in Australia: Estimates from the 45 and up study', *Plos One* 13(7):e0201552.
[85] Goldsbury, D. E., Yap, S., Weber, M. F., Veerman, L., Rankin, N., Banks, E., Canfell, K., & O'Connell, D. L. (2018). 'Health services costs for cancer care in Australia: Estimates from the 45 and up study', *Plos One* 13(7):e0201552.
[86] Ibid.
[87] Nguang, S. H., Wu, C. K., Liang, C. M., Tai, W. C., Yang, S. C., Ku, M. K., ... & Hsu, P. I. (2018). Treatment and Cost of Hepatocellular Carcinoma: A Population-Based Cohort Study in Taiwan. International journal of environmental research and public health, 15(12), 2655.
[88] Hong, T. P. (2019). An Australian population-based study of the incidence and outcomes of hepatocellular carcinoma: the Hepatomas of Melbourne Epidemiological Research (HoMER) study (Doctoral dissertation).

4 Productivity costs

HCC is likely to place a significant burden on the individual, limiting their ability to engage in the workplace. Productivity costs are typically measured by reduced employment, presenteeism and absenteeism. For the purposes of this analysis, the effects of HCC on an individual's likelihood of employment and the reduced production as a result of premature mortality were considered. Absenteeism and presenteeism potential impacts were excluded for scope reasons.

Key findings

- The total **productivity cost attributable to HCC in 2019-20 was estimated to be $382.5 million in 2019-20**.
- This comprised **$294.1 million from the premature mortality** of those of working age and a further **$88.4 million attributable to the reduction in employment** among those living with HCC.

4.1 Reduced employment participation

Following a diagnosis of HCC, an individual may be unable to maintain their current level of employment due to the impact of the disease, or it may lead them to self-select out of the workforce entirely. There is likely to be a significant effect of HCC on employment, with the symptoms and subsequent treatment required to treat the condition limiting the person's ability to participate in the workforce. The productivity loss that results from HCC was captured through the lost wages that the individual otherwise would have gained if not for their condition. It is noted that HCC may cause productivity losses for some people even before it is diagnosed. This potential cost was not considered in the analysis as HCC incidence, prevalence and mortality were estimated based on diagnosed cases.

While there is a reasonable body of international literature investigating the impact of cancer on employment, research specifically looking at liver cancer is limited.

Choi et al (2007) investigated the impact of cancer diagnosis on employment status in South Korea.[89] The study followed a cohort of 396 male patients diagnosed with cancer, 117 of whom had liver cancer. While all patients were employed at the commencement of the study, 53% had lost their job at some point over the following two years. Liver cancer patients were the most likely to lose their job, with **63.2% experiencing job loss following their diagnosis. They were also the least likely to become re-employed within two years, with just 13.5% regaining employment following their initial job loss.** Approximately 87% of all cancer patients within the cohort who lost their jobs did so within 3 months of diagnosis. It was noted that other recent studies reported varying effects upon employment.[90] This may have been due to differences in baseline characteristics. Choi et al (2007) reported a mean age of 55 years, with 23.7% of cases classified as a stage 3 diagnosis and 28.9% of cases were stage 4.

[89] Choi, K, Kim, E, Lim, J, Kim, S, Lim, M, Park, J, and Park, E, 'Job loss and reemployment after a cancer diagnosis in Koreans – a prospective cohort study' (2007), 16 *Psycho-Oncology* 205.

[90] See e.g Park J, Park, E, Park, J, Kim, S, and Lee, S, 'Job loss and re-employment of cancer patients in Korean employees: A nationwide retrospective cohort study' (2008), 26(8) *Journal of Clinical Oncology* 1302; Park, J, Park, J, and Kim, S, 'Effect of cancer diagnosis on patient employment status: a nationwide longitudinal study in Korea' (2009), 18(7) *Psycho-Oncology* 691; Stepanova, M., De Avila, L., Afendy, M., Younossi, I., Pham, H., Cable, R., & Younossi, Z. M. (2017). Direct and indirect economic burden of chronic liver disease in the United States. Clinical Gastroenterology and Hepatology, 15(5), 759-766.

Park et al (2008) reported 26% of people with liver cancer lost their job in the year of diagnosis and a median time to job loss of 48 months. Stepanova et al (2016) reported 80.6% of people with liver cancer experienced unemployment, though it was unclear how many people were employed prior to diagnosis.

Due to the data limitations which prevented proper comparison between studies and the limited amount of available evidence,[91] it was assumed that Choi et al (2007) was the most representative source available. It was further assumed that a 63.2% reduction in employment probability following diagnosis would also apply in Australia.[92]

The employment reduction refers only to immediate job loss within one year of diagnosis. People diagnosed more than one year ago may have returned to work if they received successful treatment, which was captured by accounting for the probability of employees with HCC returning to work (as shown in Table 4.1). Therefore, people diagnosed in 2018 (but still alive in 2020) were assumed to experience a 54.7% reduction in employment in 2020 (as they are 2 years post diagnosis).[93]

Table 4.1: Percentage reduction in employment and time since diagnosis

Years after diagnosis	0	1	2	3	4
Employment reduction*	-63.2	-59.0	-54.7	-54.7	-54.7

Source: Choi et al (2007), Deloitte Access Economics analysis.

The **total cost due to reduced employment was estimated to be $88.4 million in 2019-20**. Males incurred 90% of the total reduced employment costs, with males aged 55-59 incurring 39.5% of the total costs. This was driven by the underlying prevalence of HCC, although there are also differences in the expected earnings of males and females in different age groups. Table 4.2 presents a breakdown of productivity losses due to reduced employment participation in 2019-20.

Table 4.2: Productivity losses due to reduced employment ($ millions), 2019-20

Age	Male	Female	Persons
15-44	3.3	0.8	4.1
45-49	5.9	1.0	7.0
50-54	14.4	1.7	16.1
55-59	34.9	3.0	37.9
60-64	16.6	1.8	18.4
65-69	2.5	0.3	2.8
70-74	2.0	0.1	2.1
Total	**79.6**	**8.9**	**88.4**

Source: Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

[91] Park et al (2008) reported no patients aged older than 55 years (no mean age reported). No data were available regarding the stage of cancer at time of diagnosis.

[92] Based on the findings reported in Choi et al (2007).

[93] It was assumed that of the 63.2% of people who lose their job in the year of diagnosis, 13.5% regain employment after 2 years. 54.7% = 63.2 - (0.135*63.2%) The reduction in employment estimated in year 1 was assumed to be the average difference between the year of diagnosis and 2 years post diagnosis, 59% = (63.2% + 54.7%)/2.

It should be noted that the approach of using 5-year prevalence may have been conservative as it was likely that there were people living with HCC who were diagnosed more than five years ago but remained unemployed in 2019-20. These costs were not included in the analysis.

4.2 Premature mortality

There are also substantial productivity losses due to premature mortality from HCC, where future earnings are forgone due to the death.

There were an estimated 1,466 deaths from HCC in 2019-20. The productivity lost due to these premature deaths was calculated by multiplying the number of deaths in the working age population by the age-gender specific employment rates and remaining expected lifetime earnings at the time of death, assuming that people with HCC would have the same employment rates and earnings as the general population in the absence of HCC. These calculations assume that people enter the workforce at the age of 15 and may remain in the workplace until the age of 74.[94] The remaining years of employment were calculated by starting at the midpoint of each working age cohort at the time of death. Finally, all lifetime costs were discounted by 3% per annum to derive the net present value (NPV) of future potential earnings that were not realised due to premature mortality. No rate of real wage growth was applied to future earnings.

The **total annual cost associated with premature mortality from HCC was estimated to be $294.1 million in 2019-20**. Table 4.3 presents the estimated productivity losses from premature mortality by age and gender.

Table 4.3: Productivity losses due to premature mortality from HCC in 2019-20 ($ millions)

Age	Male	Female	Persons
15-44	21.0	5.7	26.7
45-49	32.4	9.1	41.4
50-54	44.7	7.1	51.8
55-59	90.7	18.6	109.2
60-64	38.4	7.1	45.5
65-69	12.0	1.4	13.5
70-74	5.4	0.4	5.8
Total	**244.5**	**49.5**	**294.1**

Source: Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

4.3 Total productivity costs

The total **productivity costs attributable to HCC were estimated to be $382.5 million** in 2019-20. This is presented by cost component in Table 4.4.

The majority of productivity costs were borne by males, accounting for 84.7% of the total costs. The largest cost component was premature mortality, representing 76.9% of the total costs. It was estimated that productivity costs were $87,093 per person alive with HCC in 2019-20.

[94] This follows the labour force distribution reported by ABS, where there are a percentage of people in the non-HCC population aged 70-74 who are employed. As such, it was assumed that an equivalent share of people with HCC at this age will also be employed.

Table 4.4: Total productivity cost by component in 2019-20 ($ millions)

Component	Male	Female	Persons
Reduced employment	79.6	8.9	88.4
Premature mortality	244.5	49.5	294.1
Total cost	**324.1**	**58.4**	**382.5**
Per person cost ($)	**90,300**	**72,753**	**87,093**

Source: Deloitte Access Economics calculations.

Note: Components may not sum to totals due to rounding.

5 Loss of wellbeing

There are substantial losses of wellbeing due to HCC in Australia, which arises from the suffering and premature death associated with the condition. The reduction in wellbeing was quantified using the burden of disease methodology.

Key findings

- In total, it was estimated that **there were 26,891 DALYs (undiscounted) due to HCC in 2019-20**, which was made up of 551 YLDs and 26,340 YLLs. When future years of life lost were discounted at 3% per annum, the loss of wellbeing was equivalent to 19,918 DALYs.
- **The value of the lost wellbeing was estimated to be $4.3 billion** based on the discounted DALYs, of which $3.1 billion is attributable to males and the remaining $1.2 billion to females.

5.1 Valuing life and health

The burden of disease methodology is a non-financial approach to quantifying the loss of wellbeing, where life and health are measured in terms of DALYs. DALYs account for both YLDs and YLLs, and one DALY is equivalent to one year of healthy life lost.

Disability weights are assigned to various health states, where zero represents perfect health and one is equivalent to death. Other health states are given a weight between zero and one to reflect the loss of wellbeing from a particular condition relative to perfect health. For example, a disability weight of 0.2 is interpreted as a 20% loss in wellbeing relative to perfect health for the duration of the condition.

DALYs can be converted into a dollar figure using an estimate of the value of a statistical life year (VSLY), an estimate of the value society places on an anonymous life. The Department of Prime Minister and Cabinet (2019) estimated the net VSLY (that is, subtracting financial costs borne by individuals) to be $213,000 in 2019 dollars.[95] This is valued at approximately $216,626 when inflated to 2019-20 dollars. This dollar value was applied to the discounted DALYs to estimate the value of the lost wellbeing due to HCC.

5.2 Estimating the loss of wellbeing from HCC

People living with HCC experience significant reductions to their wellbeing, and this depends on the stage at which their condition has progressed to. Cancer diagnoses are typically disaggregated into four stages which, for the purposes of this analysis, are as follows:

- Stage 1: Diagnosis and treatment
- Stage 2a: Cured
- Stage 2b: Remission
- Stage 3: Disseminated/metastatic
- Stage 4: Terminal

There are two outcomes for people living with HCC: survival or death. Each person living with HCC commences in Stage 1, with a diagnosis and initial treatment for their condition. In some cases, diagnosis will occur early and treatment will be successful, meaning that they are considered cured (Stage 2a). In the remainder of cases, diagnosis will occur too late and the individual may not be responsive to treatment, meaning that while they may be in remission for some time (Stage 2b),

[95] Department of Prime Minister and Cabinet, *Best Practice Regulation Guidance Note: Value of Statistical Life*, Australian Government, Canberra (2019) <https://www.pmc.gov.au/sites/default/files/publications/value-of-statistical-life-guidance-note_0_0.pdf>

their condition gradually progresses to Stage 3. Finally, as their condition deteriorates, the individual moves into the terminal phase (Stage 4).

The loss of wellbeing experienced during each of these stages can be quantified through disability weights, which describe the severity of a condition relative to perfect health. This is a key input used to calculate the YLDs attributable to HCC. These disability weights were taken from the Global Burden of Disease study,[96] and were as follows:

- Stage 1: 0.288
- Stage 2: 0.049 (applies to both 2a and 2b)
- Stage 3: 0.451
- Stage 4: 0.540

It is also important to consider how long each patient is expected to spend in each phase of treatment to accurately determine the loss of wellbeing experienced by patients in 2019-20. The average duration spent in each phase was taken from Akinyemiju et al (2017) who estimated that cancer patients tend to spend approximately 4 months in diagnosis and treatment, 2.5 months in the metastatic phase and 1 month in the terminal phase.[97] The remaining amount of time was allocated to either Stage 2a or Stage 2b, depending on whether the individual is expected to die or be cured. As an example, for those who are cured, the disability weight for diagnosis and treatment was applied for 0.333 years while the disability weight for the cured phase was applied for the remaining 0.667 years. A similar approach was taken for those who were newly diagnosed with HCC in 2019-20 but were expected to die, while people who had been diagnosed with HCC before 2019-20 but were still alive were considered to be cured (i.e. a disability weight of 0.049 for the duration of the year).

The YLLs due to HCC were estimated by multiplying the number of deaths in each age and gender group by the expected years of life remaining at the age of death. Average life expectancy data were obtained from the Australian Burden of Disease Study.[98] A discount rate of 3% was applied to the calculations while no age weighting was applied to the estimates of YLLs or YLDs.

Table 5.1 presents the age and gender breakdown of YLDs, YLLs and total DALYs, both undiscounted and discounted, attributable to HCC in Australia in 2019-20. It also presents the monetary value of the loss of wellbeing for each age-gender cohort, derived by applying the VSLY to the discounted DALYs.

In total, it was estimated that there were 26,891 DALYs (undiscounted) attributable to HCC in 2019-20, comprised of 551 YLDs and 26,340 YLLs. When future years of life lost were discounted by 3% per annum, this was equivalent to 19,918 DALYs. **The value of the lost wellbeing, based on the discounted DALYs, was estimated to be $4.3 billion**. Of the total reduction in wellbeing, $3.1 billion was borne by males and $1.2 billion was borne by females.

[96] Global Burden of Disease Collaborative Network. *Global Burden of Disease Study 2017 (GBD 2017) Disability Weights*. Seattle, United States: Institute for Health Metrics and Evaluation (IHME) (2018).
[97] Global Burden of Disease Liver Cancer Collaboration, Akinemiju T, Abera, S, et al. 'The Burden of Primary Liver Cancer and Underlying Etiologies from 1990 to 2015 at the Global, Regional, and National Level: Results from the Global Burden of Disease Study 2015', 3(12) *JAMA Oncology* 1683.
[98] Australian Institute of Health and Welfare (AIHW) 2019, 'Australian Burden of Disease Study: impact and causes of illness and death in Australia 2015', cat. no. BOD 22, AIHW, Canberra.

Table 5.1: DALYs attributable to HCC in Australia in 2019-20, by age and gender

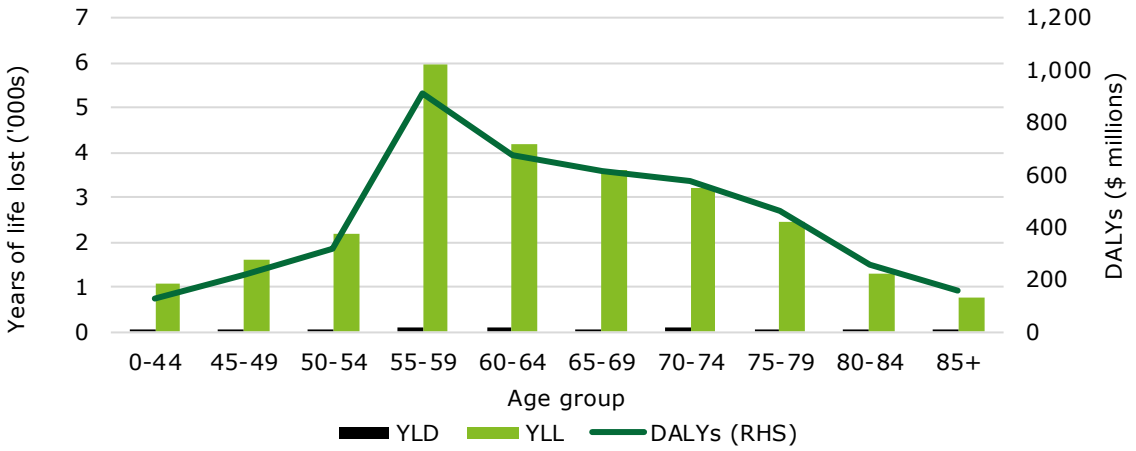
Age / gender	YLDs	YLLs	DALYs (undiscounted)	DALYs (discounted)	DALYs (discounted, $ millions)
Male					
0-44	10	741	751	404	87.6
45–49	14	1,101	1,115	695	150.6
50–54	34	1,705	1,738	1,150	249.1
55–59	95	4,374	4,469	3,127	677.4
60–64	71	3,094	3,165	2,340	506.8
65–69	52	2,728	2,781	2,165	468.9
70–74	59	2,237	2,297	1,884	408.1
75–79	42	1,554	1,596	1,372	297.2
80–84	32	846	878	787	170.5
85+	23	501	524	485	105.0
Male total	*433*	*18,880*	*19,313*	*14,408*	*3,121.2*
Female					
0-44	4	333	337	168	36.3
45–49	4	506	510	304	65.8
50–54	7	472	479	303	65.5
55–59	17	1,609	1,626	1,086	235.3
60–64	15	1,093	1,108	785	170.0
65–69	14	896	910	683	148.0
70–74	18	949	966	767	166.2
75–79	18	899	918	768	166.4
80–84	12	432	444	391	84.6
85+	10	269	279	255	55.3
Female	*118*	*7,459*	*7,578*	*5,510*	*1,193.5*
Total	**551**	**26,340**	**26,891**	**19,918**	**4,314.7**

Source: Deloitte Access Economics analysis.

Note: Components may not sum to totals due to rounding.

Chart 5.1 presents the estimated YLDs, YLLs and associated cost of the total DALYs by age in 2019-20. As can be seen, the burden of is much higher after the age of 50, peaking between the ages of 55 and 59, before a gradual decline. This profile is due to the relatively late onset of the condition and high mortality rate, meaning that those diagnosed tend not to survive for long and leading to the decline after the peak age where incident cases occur.

Chart 5.1: YLDs, YLLs and value of lost wellbeing from HCC in 2019-20



Source: Deloitte Access Economics analysis.

6 Summary

Total costs of HCC

HCC is a serious health condition that carries with it a high mortality rate and substantial economic costs. There were an estimated 1,916 new cases and 4,392 prevalent cases of HCC (over 5 years) in Australia in 2019-20. Overall, **the total cost of HCC was estimated to be $4.8 billion in 2019-20.** Table 6.1 summarises the total cost attributable to HCC, disaggregated by age, gender and cost component.

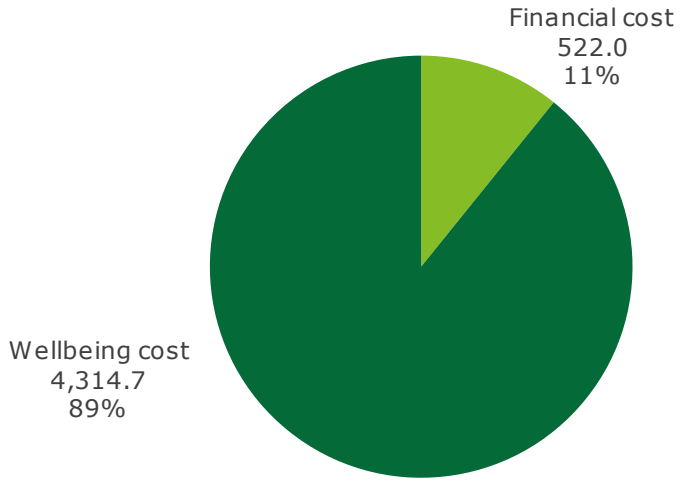
Table 6.1: Total cost of HCC in Australia in 2019-20 ($ millions)

Age/gender	Health system	Productivity	Wellbeing	Total
Male				
0-44	4.1	24.3	87.6	116.0
45-49	3.1	38.3	150.6	192.0
50-54	7.5	59.0	249.1	315.6
55-59	17.6	125.6	677.4	820.5
60-64	20.5	55.0	506.8	582.3
65-69	18.0	14.5	468.9	501.5
70-74	15.9	7.4	408.1	431.4
75-79	12.3	0.0	297.2	309.5
80-84	7.0	0.0	170.5	177.4
85+	3.8	0.0	105.0	108.8
Male total	*109.7*	*324.1*	*3,121.2*	*3,555.0*
Female				
0-44	2.4	6.5	36.3	45.3
45-49	1.2	10.1	65.8	77.0
50-54	2.2	8.9	65.5	76.6
55-59	4.1	21.6	235.3	261.0
60-64	4.3	9.0	170.0	183.2
65-69	4.4	1.8	148.0	154.2
70-74	3.5	0.6	166.2	170.2
75-79	3.7	0.0	166.4	170.2
80-84	2.2	0.0	84.6	86.8
85+	1.9	0.0	55.3	57.2
Female total	*29.8*	*58.4*	*1,193.5*	*1,281.7*
Person total	**139.5**	**382.5**	**4,314.7**	**4,836.8**

Source: Deloitte Access Economics analysis.

Most of the costs of HCC were due to cases in males ($3.6 billion). The total cost comprised financial costs ($522.0 million) and wellbeing costs ($4.3 billion). The breakdown of total costs by component is provided in Chart 6.1.

Chart 6.1: Total cost of HCC in 2019-20, by component ($ millions, %)



Source: Deloitte Access Economics analysis.

The financial costs in this report included health system expenditure required to treat and manage HCC cases and the losses of productivity attributable to the reduced employment among those living with the condition and those who died prematurely but were of working age.

Health system costs amounted to $139.5 million in 2019-20, accounting for approximately 2.9% of the total cost. This comprised $109.7 million for males and $29.8 million for females. In addition, **losses of productivity were estimated to cost $382.5 million**, $88.4 million of which was due to reduced employment. Premature mortality accounted for the remaining $294.1 million. These productivity costs accounted for 8.0% of the total costs due to HCC.

Sensitivity analysis to account for potential underreporting of deaths

As noted in section 2.3, it is possible that the number of deaths from HCC have not been accurately recorded where the cause of death was listed as cirrhosis. The number of deaths due to HCC could be approximately 33% higher as a result (=1/0.75-1).

This higher number of deaths has implications for the estimated productivity costs relating to premature mortality and the wellbeing losses related to YLLs. The number of deaths due to HCC estimated in section 2.3 was multiplied by 1.33 to determine the overall impact on total costs of HCC.

In this scenario, **the total deaths attributable to HCC in 2019-20 would have been 1,955 instead of 1,466**. Of the new total deaths under this scenario, 1,426 occurred in males and 529 in females.

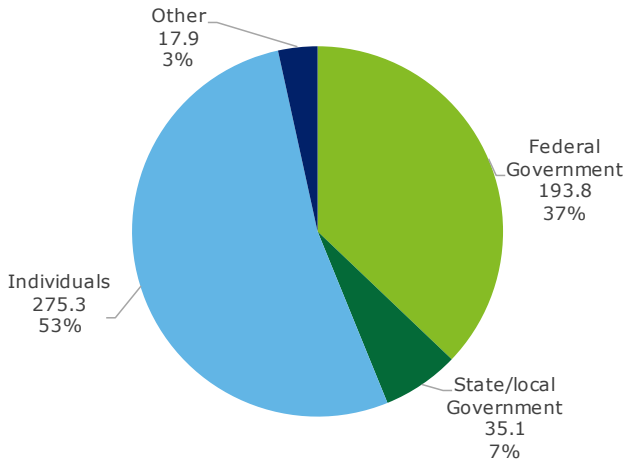
When calculated with the revised number of deaths as the base, the productivity cost from premature mortality rose from $294.1 million to $392.1 million, bringing the total productivity losses to $480.5 million. This represents an increase of 22.5%. Likewise, the number of YLLs rose from 26,340 to 35,120 (undiscounted), or 19,367 to 25,822 (discounted). When multiplied by the VSLY, this translated to an additional cost of approximately $1.4 billion, bringing the total financial value of the loss of wellbeing to $5.7 billion. Under this scenario, **the total cost of HCC in Australia in 2019-20 rises from $4.8 billion to nearly $6.3 billion, an increase of 31.7%.**

Costs by payer

The burden of financial costs mainly fell upon individuals, who bore 53% of financial costs (or $275.3 million). The remainder of the costs were borne by Federal Government (37%,

$193.8 million), State/Territory Governments (7%, $35.1 million) and other payers (3%, $17.9 million). The breakdown of financial costs by payer is provided in Chart 6.2.

Chart 6.2 Total financial costs of HCC in 2019-20, by payer ($ millions, %)



Source: Deloitte Access Economics analysis.

Outside of these financial costs are losses of wellbeing, and these accounted for the majority of the total cost of HCC in 2019-20. **Lost wellbeing was estimated to cost $4.3 billion** in 2019-20, equivalent to 90.2% of the total cost of HCC. The majority of this was due to premature mortality due to HCC.

Costs to the individual dwarfed the costs borne by other payers in society. Individuals bore $4.6 billion or 95.7% of the total cost, while government bore an estimated $193.2 million or 4.0%. The remaining costs were borne by other payers ($11.3 million or 0.2%).

In conclusion, HCC is a serious health condition with a complex and evolving aetiology, carrying with it a high mortality rate, substantial economic costs and significant loss of wellbeing. Despite improvements in diagnostics and available treatments in recent years, 5-year survival rates remain low. Moving into a new decade, it is imperative that investment is focused on preventative strategies, particularly for causes of growing concern such as non-alcoholic fatty liver disease.

Appendix A : Supplementary data and methodology

A.1. HCC cases as a proportion of all primary liver cancer

Table A.1 presents the estimated number of HCC and the total number of primary liver cancer cases between 1982 and 2014.

Table A.1: Cases of HCC and all primary liver cancer in Australia, 1982 to 2014

Age/gender	HCC	Primary liver cancer	HCC cases (%)
Male			
0-44	714	1,064	67.1
45-49	829	984	84.2
50-54	1,545	1,837	84.1
55-59	1,893	2,358	80.3
60-64	2,014	2,632	76.5
65-69	2,239	2,915	76.8
70-74	2,175	2,897	75.1
75-79	1,803	2,515	71.7
80-84	1,046	1,615	64.8
85+	519	963	53.9
Male total	*14,777*	*19,780*	*74.7*
Female			
0-44	240	526	45.6
45-49	157	274	57.3
50-54	249	446	55.8
55-59	314	586	53.6
60-64	369	724	51.0
65-69	449	851	52.8
70-74	569	1,091	52.2
75-79	543	1,093	49.7
80-84	430	988	43.5
85+	325	969	33.5
Female total	*3,645*	*7,548*	*48.3*
Total	**18,422**	**27,328**	**67.4**

Source: Deloitte Access Economics estimates based on Wallace et al (2019) and AIHW 2018.

A.2. 5-year survival rates for HCC

Table A.2 presents the survival rates for people living with HCC by age and gender, from one year up to five. For males, survival rates peak at 84% for one-year survival among those aged 0 to 44, while just 4% of those aged 75 and over are expected to survive for five years. Similarly, for females, survival rates are at the highest among those aged 0 to 44, with 87% expected to survive for at least one year, declining to just 2% for 5-year survival among those aged 75 years or older.

Table A.2: One to 5-year survival rates for people living with HCC, by age and gender

Age/gender	1	2	3	4	5
Male					
0-44	84%	72%	62%	54%	47%
45-49	74%	54%	40%	29%	21%
50-54	72%	52%	37%	27%	19%
55-59	73%	53%	39%	28%	20%
60-64	69%	48%	33%	23%	16%
65-69	63%	39%	25%	16%	10%
70-74	61%	38%	23%	14%	9%
75-79	54%	29%	16%	8%	4%
80-84	54%	29%	16%	8%	4%
85+	54%	29%	16%	8%	4%
Male total	*67%*	*45%*	*30%*	*20%*	*13%*
Female					
0-44	87%	76%	66%	58%	51%
45-49	74%	54%	40%	29%	21%
50-54	73%	54%	39%	29%	21%
55-59	71%	50%	35%	25%	17%
60-64	68%	46%	31%	21%	14%
65-69	62%	38%	24%	15%	9%
70-74	66%	43%	29%	19%	12%
75-79	46%	21%	10%	4%	2%
80-84	46%	21%	10%	4%	2%
85+	46%	21%	10%	4%	2%
Female total	*64%*	*41%*	*26%*	*17%*	*11%*
Total	**66%**	**43%**	**28%**	**19%**	**12%**

Source: Deloitte Access Economics estimates based on AIHW 2018 and SEER 2018.

Note: Age-specific survival rates only available up to 74 years, so survival rates for 75+ years have been applied to 75-79, 80-84 and 85+.

Table A.3: AR-DRG separations and cost weights ($) for HCC related separations, 2019-20

AR-DRG code	description	Separations per year	Cost weight, 2019-20
H09Z	Liver Transplant	0	174,370
B71A	Cranial and Peripheral Nerve Disorders, Major Complexity	0	5,973
E73A	Pleural Effusion, Major Complexity	0.03	15,224
E73B	Pleural Effusion, Intermediate Complexity	0	7,239
G12A	Other Digestive System GIs, Major Complexity	0	38,552
G66A	Abdominal Pain and Mesenteric Adenitis, Major Complexity	0.03	3,725
G66B	Abdominal Pain and Mesenteric Adenitis, Minor Complexity	0.03	1,949
G70A	Other Digestive System Disorders, Major Complexity	0	8,869
G70B	Other Digestive System Disorders, Intermediate Complexity	0	3,981
H01A	Pancreas, Liver and Shunt Procedures, Major Complexity	0.24	69,429
H01B	Pancreas, Liver and Shunt Procedures, Intermediate Complexity	0.15	29,792
H06A	Other Hepatobiliary and Pancreas GIs, Major Complexity	0.18	44,383
H06B	Other Hepatobiliary and Pancreas GIs, Intermediate Complexity	0.48	17,187
H60A	Cirrhosis and Alcoholic Hepatitis, Major Complexity	0	23,610
H60B	Cirrhosis and Alcoholic Hepatitis, Intermediate Complexity	0.96	9,159
H61B	Malignancy of Hepatobiliary System and Pancreas, Minor Complexity	0.3	4,835
H63A	Other Disorders of Liver, Major Complexity	0.24	14,405
H63B	Other Disorders of Liver, Intermediate Complexity	0.18	4,759
L61Z	Haemodialysis	0	604
L63A	Kidney and Urinary Tract Infections, Major Complexity	0.03	7,956
Q61A	Red Blood Cell Disorders, Major Complexity	0.03	2,998
Q61B	Red Blood Cell Disorders, Intermediate Complexity	0.06	5,743
T62A	Fever of Unknown Origin, Major Complexity	0	1,687
T63B	Viral Illnesses, Minor Complexity	0	2,492
Z40Z	Other Contacts W Health Services W Endoscopy	0.12	1,692
Z61A	Signs and Symptoms, Major Complexity	0.09	7,546
Z61B	Signs and Symptoms, Minor Complexity	1.05	2,361
Z64B	Other Factors Influencing Health Status, Minor Complexity	0.03	1,675
Average			**13,390**

Source: Independent Hospital Pricing Authority (2019) and Deloitte Access Economics analysis.

Limitation of our work

General use restriction

This report is prepared solely for the use of the Liver Foundation. This report is not intended to and should not be used or relied upon by anyone else and we accept no duty of care to any other person or entity. The report has been prepared for the purpose of estimating the social and economic impact of primary liver cancer in Australia. You should not refer to or use our name or the advice for any other purpose.

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