The Australian Prevention
Partnership Centre
Systems and solutions for better health

Estimating the impact of public health interventions to prevent liver cancer

More data-informed evidence is needed to optimise interventions for liver cancer control

We estimated the impact of alcohol and obesity on liver disease and liver cancer in Australia

The health and economic estimates can help guide future liver cancer control interventions
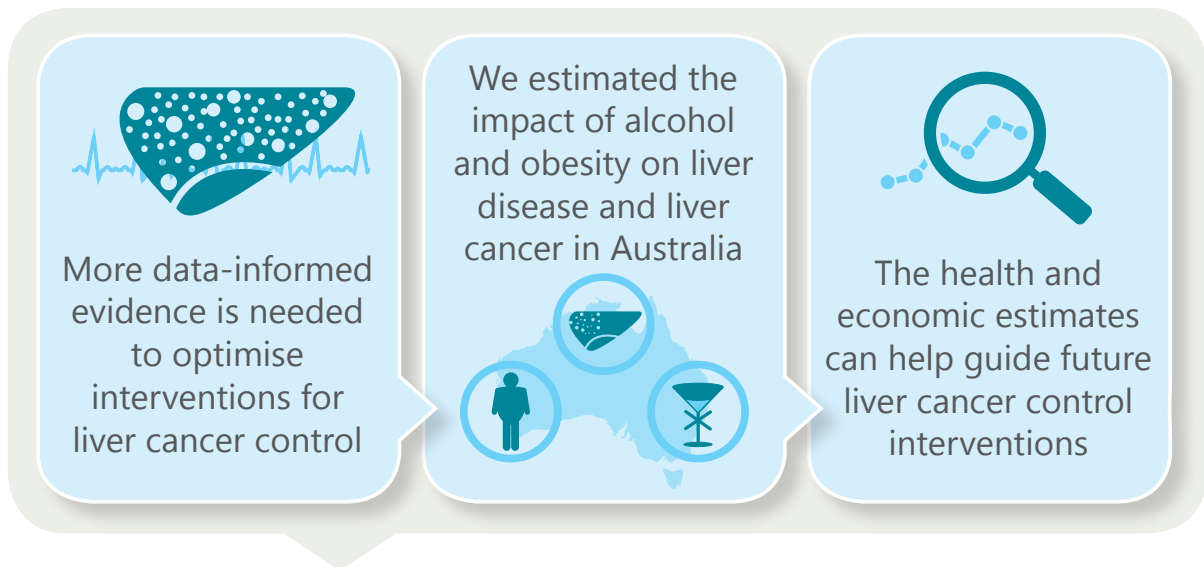
Key messages

- Liver cancer is the fastest growing cause of cancer death in Australia and more research is needed to better understand how we can help prevent this disease in people at highest risk.

- The most common type of liver cancer, hepatocellular carcinoma (HCC), often develops in people with underlying liver disease caused by modifiable risk factors, including excessive alcohol consumption, excess body fatness and the metabolic syndrome.

- The project aimed to estimate the impact of prevention activities on liver cancer outcomes, including reduction of excessive alcohol consumption, reduction of excess body fatness, and routine HCC surveillance, using an updated Australian liver cancer predictive model (Policy1-Liver).

- Predictive modelling estimated that evidence-based interventions could reduce HCC deaths in Australia by 100-500 deaths annually, with the highest reductions a result of combining primary and secondary prevention activities.

- The predictive model developed provides an evidence base to support recommendations for future local liver cancer control interventions, including health and economic estimates.

- This work shows that interventions designed to reduce the prevalence of alcohol consumption and excess body fatness have the potential to reduce the liver cancer burden, particularly when targeted at patients with reversible early-stage liver disease.

The Daffodil Centre

The project: Preventing liver cancer: Obesity and alcohol consumption
Project lead: Associate Professor Eleonora Feletto, The Daffodil Centre
Project start: February 2021 **Project end:** April 2023

Why is this issue important?

Liver cancer is one of the most rapidly growing cancer types in Australia in terms of incidence and mortality rates. The most common type of liver cancer, hepatocellular carcinoma (HCC), often develops in people with underlying liver disease caused by modifiable risk factors, including excessive alcohol consumption, excess body fatness and the metabolic syndrome.

Prolonged excess alcohol consumption can cause liver damage and may lead to alcohol-related liver disease (ARLD), while excess body fatness and the metabolic syndrome are associated with an increased risk of metabolic-associated fatty liver disease (MAFLD, previously classified as non-alcoholic fatty liver disease or NAFLD).

There is potential for targeted prevention interventions to reduce the disease burden from liver cancer through alcohol cessation, weight loss interventions and routine HCC surveillance of patients at high risk to detect cancer earlier when curative treatment is possible.

Key terms

HCC   hepatocellular carcinoma (most common type of liver cancer)

ARLD   alcohol-related liver disease

MAFLD   metabolic-associated fatty liver disease; replaces previous classification of NAFLD

NAFLD   non-alcoholic fatty liver disease; replaced by the updated classification of MAFLD

What did we do?

The project team aimed to expand the scope of an Australian liver cancer predictive model (Policy1-Liver) developed by the Daffodil Centre. This model was used to further evaluate the impact of excessive alcohol consumption or obesity on liver cancer alongside HCC surveillance.

Predictive models are mathematical simulations that are simplified representations of the real world. Predictive modelling allows researchers to provide estimates for complex problems by bringing together a variety of evidence such as data, expert knowledge, and practice experience. The resulting model is a "what-if" tool which can simulate various intervention scenarios and estimate the differences in cancer cases, deaths, and costs.
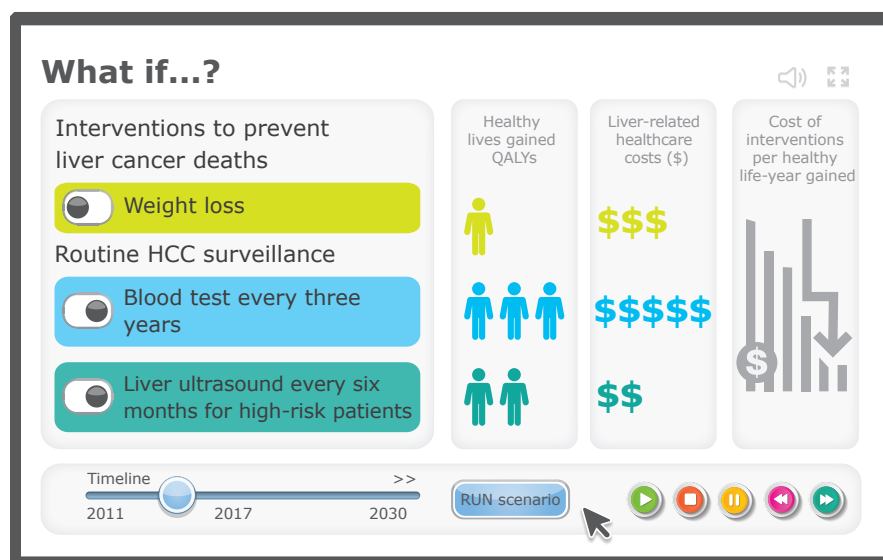
In this project, predictive modelling was used to compare the likelihood of an individual developing and/or dying from HCC with and without an intervention, such as routine HCC surveillance, weight loss, alcohol cessation, or a combination of these. This allowed us to calculate the potential benefit of these interventions, and weigh this against the potential increase in costs (both HCC surveillance costs and the cost of liver cancer treatment).

What did we find?

Predictive modelling estimated that evidence-based interventions could reduce HCC deaths in Australia by 100-500 deaths annually, with the largest reductions resulting from the combination of primary and secondary prevention activities.

Excess body fatness, metabolic syndrome and metabolic-associated fatty liver disease

If routine HCC surveillance using six-monthly ultrasound, with or without alpha-fetoprotein testing (a type of blood test), was provided to all MAFLD patients in Australia, this could prevent up to an estimated 150 MAFLD-related HCC deaths annually by 2045.

If all MAFLD patients undergo a once-off 10% weight reduction intervention in 2023 or at age 40, whichever occurs first, this would prevent up to an estimated maximum 417 MAFLD-related HCC deaths annually. If the weight loss intervention was combined with routine HCC surveillance, this would further increase to 485 deaths prevented annually.

Excessive alcohol consumption and alcohol-related liver disease (ARLD)

By 2045, an estimated maximum 108 ARLD-related HCC deaths could be prevented annually through routine HCC surveillance in Australia. This is likely to increase beyond 2045, as long-term participation in routine HCC surveillance increases the likelihood of early detection of HCC.

HCC surveillance in Australia

Currently, routine HCC surveillance using six-monthly ultrasound with or without alpha-fetoprotein testing is only recommended for patients with chronic hepatitis B or cirrhotic patients. Its use and application are relatively new for patients with suspected MAFLD or ARLD. This study demonstrated that using non-invasive technologies, such as blood tests (FIB-4) every three years or annual transient elastography (a test to measure liver stiffness), for routine HCC surveillance can be effective for Australians with MAFLD or ARLD, with patients found to be at high-risk subsequently referred to ultrasound. This triaged surveillance would be nearly as effective in preventing HCC deaths as using ultrasound alone, while being more affordable, less burdensome for patients, and relieving pressure on already limited ultrasonography resources in Australia.

Excess body fatness and alcohol consumption are major determinants of many other health outcomes in addition to liver disease and are key health concerns in Australia. HCC prevention would be one of the many benefits of weight loss and alcohol cessation initiatives.

Estimated deaths prevented from routine HCC surveillance and primary prevention interventions

150

Providing routine HCC surveillance to people with metabolic-associated fatty liver disease could prevent up to **150 liver cancer deaths** every year in Australia

108

Providing routine HCC surveillance to people with alcohol-related liver disease could prevent up to **108 liver cancer deaths** every year in Australia

417

Weight loss interventions* could prevent up to **417 liver cancer deaths** every year in Australia

(*once-off 10% weight reduction at age 40)

What did we produce?

This work provides an evidence base to support recommendations for future local liver cancer control interventions, including health and economic estimates. The robust predictive model developed allows us to take a more comprehensive view of liver cancer control and guide long-term planning for liver cancer. This project will continue to produce peer-reviewed publications and other resources beyond its funding end date. For a list of the most current publications, visit: preventioncentre.org.au/research projects

Why does it matter?

Excess body fatness and alcohol consumption are major determinants of many health outcomes including liver disease and are key health concerns in Australia. Over 2017–18, 79% of Australian adults drank, with 6.3% consuming excessive amounts of alcohol, and 67% carried excess body weight. Interventions designed to reduce the prevalence of alcohol consumption and excess body fatness have the potential to reduce the liver cancer burden, particularly when targeted at patients with reversible early-stage liver disease. In patients with more advanced liver disease, routine HCC surveillance can help improve the likelihood of detecting cancers early and improving cancer survival outcomes.

Next steps

As liver cancer rates continue to rise in Australia, ongoing research and clearer understanding in these areas is crucial. Based on modelled estimates, recommendations could be made for at-risk groups based on their estimated health outcomes, including HCC surveillance recommendations for individuals with pre-cirrhotic liver disease. This could guide future investment in liver cancer control and reduce the burden in Australia.

Future reviews could seek to identify evidence regarding the interplay between risk factors for chronic liver disease and primary liver cancer and extend the predictive modelling platform. In future work, predictive modelling will be extended to explore the use of non-invasive testing to identify patients with metabolic-associated steatohepatitis (MASH), a more developed form of MAFLD, and estimate whether routine HCC surveillance would be more cost-effective for MASH patients compared to MAFLD patients.
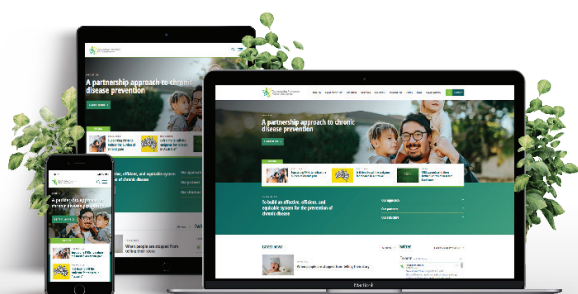
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