

Jessica Howell^{1,2,3,4*}

Troy Combo^{2*}

Paula Binks⁵ 

Kylie Bragg^{6,12}

Sarah Bukulatjpi^{5,7}

Kirsty Campbell⁸

Paul J Clark^{9,10} 

Melissa Carroll¹¹

Jane Davies^{5,8}

Teresa de Santis⁸

Kate R Muller^{9,12}

Bella Nguyen¹³

John K Olynyk^{13,14,15} 

Nicholas Shackel¹⁶

Patricia C Valery¹⁷ 

Alan J Wigg^{6,12} 

Jacob George^{18,19,20†} 

Stuart K Roberts^{21,4†} 

1 St Vincent's Hospital, Melbourne, VIC.

2 Burnet Institute, Melbourne, VIC.

3 University of Melbourne, Melbourne, VIC.

4 Monash University, Melbourne, VIC.

5 Charles Darwin University, Darwin, NT.

6 Southern Adelaide Local Health Network, Adelaide, SA.

7 Miwatj Health Aboriginal Corporation, Nhulunbuy, NT.

8 Royal Darwin and Palmerston Hospitals, Darwin, NT.

9 University of Queensland, Brisbane, QLD.

10 Princess Alexandra Hospital, Brisbane, QLD.

11 John Hunter Hospital, Newcastle, NSW.

12 Flinders University, Adelaide, SA.

13 Fiona Stanley Fremantle Hospital Group, Perth, WA.

14 Curtin University, Perth, WA.

15 Edith Cowan University, Perth, WA.

16 Launceston General Hospital, Launceston, TAS.

17 QIMR Berghofer Medical Research Institute, Brisbane, QLD.

18 Storr Liver Centre, Westmead Millennium Institute, Sydney, NSW.

19 Westmead Hospital, Sydney, NSW.

20 University of Sydney, Sydney, NSW.

21 Alfred Hospital, Melbourne, VIC.

*Equal first authors.

†Equal senior authors.

jess.howell@monash.edu

Overcoming disparities in hepatocellular carcinoma outcomes in First Nations Australians: a strategic plan for action

Every year, about 1800 Australians die of hepatocellular carcinoma (HCC), the most common type of primary liver cancer.¹

Aboriginal and Torres Strait Islander peoples of Australia (hereon respectfully referred to as First Nations Australians) are 2.5 times more likely to develop HCC and 1.4 times more likely to die from HCC than non-Indigenous Australians.²

First Nations Australians with HCC have a 9% five-year survival rate compared with 23% for non-Indigenous Australians,² and are half as likely to be diagnosed with early-stage HCC and receive curative therapy.² This is driven by First Nations Australians being adversely affected by social, cultural and commercial determinants of health stemming from colonisation, racism and remoteness.³

Chronic liver disease is the key cause of HCC and most chronic liver disease is preventable and treatable.^{4,5} First Nations Australians shoulder a disproportionate burden of chronic liver disease (Box 1).⁶ Alcohol-related liver disease is a leading cause of HCC in all Australians, including First Nations Australians.^{2,7,8} The prevalence of hepatitis B and C is two- to three-fold higher in First Nations Australians compared with non-Indigenous Australians.^{2,5} The most prevalent hepatitis B genotype in remote First Nations communities (genotype C4) is associated with more aggressive liver disease and increased HCC risk compared with other genotypes.^{9,10} Obesity and type 2 diabetes, both leading risk factors for metabolic-associated fatty liver disease, are twice as common in First Nations Australians than in non-Indigenous Australians.³ Importantly, First Nations Australians are more likely to have multiple cofactors driving liver injury,² warranting a multipronged approach to HCC prevention.

Methods

The two lead authors of this article, one First Nations Australian and one non-Indigenous Australian, established a nationally representative, diverse group of four First Nations Australian and 14 non-Indigenous Australian clinical and research leaders in the fields of HCC and chronic liver disease for the project. All authors have expertise in the provision of regional or remote models of HCC or chronic liver disease care, or both. First, an initial two-hour virtual meeting was held, where authors shared their thoughts and responses to two main topics: i) identifying unmet needs in prevention, diagnosis and treatment of HCC in First Nations Australians; and ii) identifying opportunities to address these unmet needs. All authors shared key evidence and their experiences and perspectives, representing the differing epidemiology, health resourcing, policy and legislative contexts

across all Australian states and territories. From this discussion, the lead authors developed a list of eight key action items using a positive, evidence-based approach that prioritised First Nations-led interventions and models of care. The aim was to retain action items that had 100% agreement across the author group; all eight action items were ratified by all authors.

Overcoming the challenges: steps for action

As a nationwide collaboration of First Nations and non-Indigenous health workers and researchers in HCC, we identified eight key action measures, which are listed below, that will help address disparities in HCC incidence and mortality in First Nations Australians that should be urgently prioritised for investment (Box 2, Box 3, Box 4).

Increase Indigenous community engagement and co-designed health promotion

Community engagement through partnership with First Nations Australians is the first step to improving HCC outcomes in Australia. The public health response to HCC in First Nations people should be determined and led by First Nations communities and Aboriginal Community Controlled Health Organisations (ACCHOs), supported by medical and community stakeholders. To sustain community engagement, we need more funding for effective First Nations co-designed, culturally safe health education resources in First Nations languages and health promotion programs,¹¹ Indigenous-led civil society organisations that promote liver health, and the strengthening of the First Nations peer workforce.¹²

Stigma and discrimination are critical barriers to liver disease diagnosis in First Nations Australians, amplified by intersectionality with social, cultural and economic factors.^{3,13} National approaches to improving community and health worker education are needed to overcome systemic discrimination and entrenched health disparities for First Nations Australians.

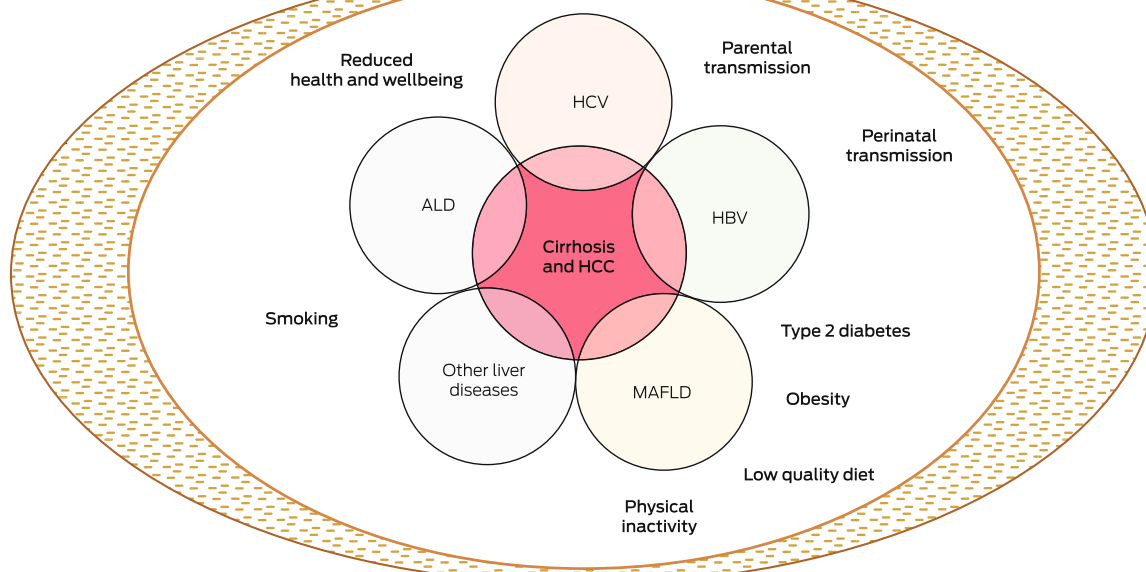
Create an enabling Indigenous health policy environment

Historically, liver disease and HCC have not been included in Close the Gap initiatives,¹⁴ or the *National Aboriginal and Torres Strait Islander health plan*, despite being key drivers of premature mortality in First Nations Australians. For the first time, prevention and detection of primary liver cancer has been included in the National Aboriginal Community Controlled Health Services (NACCHO) and Royal Australian College of General Practitioners *National guide to a preventive health assessment for Aboriginal*

1 Driving causes of chronic liver disease and hepatocellular carcinoma (HCC)

Socio-economic inequity

Geographic inequity



ALD = alcoholic liver disease; HBV = hepatitis B virus; HCV = hepatitis C virus; MAFLD = metabolic associated fatty liver disease. Most causes of chronic liver disease lead to HCC through the interim step of cirrhosis development. However, chronic hepatitis B infection and MAFLD may cause HCC in the absence of cirrhosis. Additionally, 30–40% of First Nations Australians have more than one risk factor for HCC.² ◆

and Torres Strait Islander People,¹⁵ an important first step. Currently, many liver care programs for remote areas are unsustainably funded through research grants. Liver disease and HCC measures should be included in national key performance indicators for Aboriginal and Torres Strait Islander primary health care and funding leveraged from the \$230 million federal budget allocated to improve cancer outcomes in First Nations Australians.

Removing barriers to viral hepatitis test frequency, enabling reflex testing and the use of rapid point-of-care tests and dried blood spot testing would increase access to viral hepatitis testing for First Nations Australians.¹⁶ Governments should work closely with First Nations leaders to develop ambitious yet workable policy and legislation that focus on improved liver health for First Nations communities, such as improved alcohol policies and improved access and affordability of fresh unprocessed foods to reduce the risks of metabolic-associated fatty liver disease.

Expand First Nations Australian co-designed and led liver health services

ACCHOs are essential in providing culturally safe care. Convenience, acceptability and trusted relationships increase linkage and retention in care.¹⁶ Increased employment and training of Aboriginal and Torres Strait Islander health workers and peers builds a culturally safe health workforce and increases continuity of care on Country through greater staff retention. Expansion of the ACCHO health workforce should be leveraged for HCC models of care. However, a significant proportion of First Nations Australians do not access ACCHOs, therefore improving the cultural safety of health services more broadly will improve

access for all First Nations Australians. Specialist nurse support for ACCHO health workers and general practitioners, outreach multidisciplinary liver services and telehealth models of hub-and-spoke specialist care will improve rapid specialist care access and uptake for First Nations Australians,^{2,5} particularly in regional and remote areas.

Increase investment in chronic liver disease prevention and early diagnosis

Offering screening for chronic liver disease to all First Nations Australians, or a “healthy liver check”, is vital to ensure timely identification and treatment of chronic liver disease. Although alcohol abstinence rates are higher in First Nations Australians than in non-Indigenous Australians,¹⁷ active screening for harmful alcohol use and early linkage to First Nations community alcohol counselling and treatment services should be increased. High levels of hepatitis B vaccination coverage have been achieved in many remote communities,^{6,10} however, catch-up programs for First Nations Australian adults, particularly in regional areas, are needed. Funding for Close the Gap infant mortality reduction should be harnessed for perinatal hepatitis B transmission prevention within a “triple elimination” strategy.¹⁸ Timely diagnosis and treatment of people with hepatitis B is proven to reduce HCC risk.¹⁹ Increased access to needle and syringe exchange programs, opiate agonist therapy programs and timely test-and-treat models of hepatitis C care are vital to prevent further transmission.^{20,21} Embedding chronic liver disease screening and management within existing metabolic syndrome health programs for First Nations Australians, such as type 2 diabetes or childhood obesity, would optimise resource allocation and cost-effectiveness.

2 Hepatocellular carcinoma (HCC) action plan for First Nations Australians

Steps for action	Aims	Actions
Health promotion	Increase Indigenous community engagement and culturally sensitive health promotion	<ul style="list-style-type: none"> Engage Indigenous community elders to co-design and lead the response to HCC Indigenous community co-design of HCC programs Fund Indigenous community-led liver and cancer organisations Co-design liver disease and HCC resources in First Nations languages Invest in Indigenous peer workforce Fund community events eg, “Healthy liver yarning” days Invest in stigma/discrimination education and reduction United stakeholder advocacy to government, funding bodies, philanthropic organisations
Policy	Create an enabling Indigenous health policy environment	<ul style="list-style-type: none"> Increase resource allocation and funding for Indigenous health Increase travel allowances for medical services Include chronic liver disease and HCC key performance indicators in Close the Gap Include HCC in Indigenous preventive health assessments by general practitioners Create MBS item for “healthy liver check” general practitioner assessments Enable reflex testing for viral hepatitis through Medicare Fast-track TGA approval and Medicare funding for point-of-care tests for viral hepatitis Validate and fund dried blood spot testing for remote areas Enable nurse-led models of specialist liver care Enable task-shifting of existing health programs for liver disease (eg, type 2 diabetes) Legislate alcohol and sugar control policies (eg, sugar tax) Leverage Close the Gap funding for prevention of infant mortality from mother to child hepatitis B transmission, healthy diet interventions Law reform to reduce disproportionate incarceration of Indigenous Australians
Models of care	Expand Indigenous co-designed and led health services	<ul style="list-style-type: none"> Expand Aboriginal controlled health services via NACCHO Increase cultural safety and Indigenous support in primary care clinics and health services Support nurse-led and peer-led models of care Support telehealth models of community–specialist shared care
Prevention	Increase investment in liver disease prevention and early diagnosis	<ul style="list-style-type: none"> Increase hepatitis B vaccination coverage including birth dose Support “triple elimination” in infants, including administration of tenofovir in third trimester Increase funded access to needle syringe programs, opiate agonist therapy, hepatitis C test-and-treat models of care Active screening and treatment for risky alcohol consumption Obesity and type 2 diabetes prevention, including in children MBS item for holistic “healthy liver checks” by general practitioners Embed liver disease screening and assessment within MBS funded diabetes or cancer prevention health assessments
Risk identification	Fund diagnosis of cirrhosis and facilitate rapid linkage to specialist care	<ul style="list-style-type: none"> Educate and support health workers to exclude cirrhosis using the fibrosis-4 index or the aspartate aminotransferase to platelet ratio index scores Fund transient elastography via MBS item and national rollout Fund Enhanced Liver Fibrosis and Hepascore tests nationally via MBS item number Fund nurse-led models of cirrhosis care
Surveillance	Increase access to timely HCC surveillance	<ul style="list-style-type: none"> Invest in novel models of outreach HCC surveillance Provide TGA approval and Medicare funding of GAAD testing (gender, age, alpha-fetoprotein, des-carboxyprothrombin) for HCC surveillance in remote areas
Management	Provide streamlined pathways to HCC services and treatment	<ul style="list-style-type: none"> Develop and fund streamlined pathways for HCC care, from surveillance to multidisciplinary team review to specialist care Increase virtual multidisciplinary team access for local health workers Upskill local services in systemic HCC therapy provision and management of side effects Invest in outreach HCC radiological services Establish co-designed Indigenous palliative care services for liver disease and HCC
Research	Support key research priorities to address gaps in knowledge	<ul style="list-style-type: none"> Expand and upskill Indigenous research capacity Annual HCC incidence, stratified by age group, gender, aetiology including concurrent liver risk factors Validation of cirrhosis and HCC biomarkers Quantify surveillance uptake, and barriers and enablers to surveillance for First Nations Australians Genetic profiling of HCC in First Nations Australians and personalised HCC treatment allocation Validation of Indigenous-specific quality of life and stigma/discrimination assessment scores









MBS = Medicare Benefits Schedule; NACCHO = National Aboriginal Community Controlled Health Services; TGA = Therapeutic Goods Administration. ◆

3 Two-, five- and ten-year health policy action plan to reduce hepatocellular carcinoma (HCC) in First Nations Australians

Timeline	Actions
2 years	<ul style="list-style-type: none"> • Fund a First Nations Australians HCC health summit to kickstart priority setting and health solution co-design • Include chronic liver disease and HCC key performance indicators in Close the Gap • Add liver health screen and HCC risk assessment in the First Nations Australian preventive health assessment • Create MBS item for “healthy liver check” general practitioner assessment • Change policy to enable reflex viral hepatitis testing through Medicare*
5 years	<ul style="list-style-type: none"> • Fund transient elastography via MBS item for First Nations Australians* • Increase the number of ACCHS health workers trained in chronic liver disease prevention, diagnosis and management, including liver cancer surveillance • Train and employ a First Nations liver disease peer workforce • Create an MBS item number for telehealth case conferencing for general practitioners with specialist services, including attendance at specialist HCC multidisciplinary meetings* • Fund nurse-led one-stop shop models of chronic liver disease and HCC care provided on Country for First Nations Australians
10 years	<p>Achieve targets for HCC cascade of care*:</p> <ul style="list-style-type: none"> • > 90% of First Nations Australians have had a healthy liver check • > 90% of First Nations Australians know their hepatitis B and C status • > 80% of First Nations Australians know their cirrhosis status • > 70% of First Nations Australians who are eligible are enrolled in HCC surveillance • > 60% of HCC in First Nations Australians is diagnosed at the early stage

MBS = Medicare Benefits Schedule; ACCHS = Aboriginal Community Controlled Health Service. * Would benefit all Australians, although should be prioritised for First Nations Australians. ◆

4 Strategic action plan to reduce hepatocellular carcinoma (HCC) in First Nations Australians

	Community	Increase Indigenous community engagement and co-designed health promotion
	Policy	Create an enabling First Nations Australian health policy environment
	ACCHO	Expand First Nations Australian co-designed and led liver health services
	Prevention	Increase investment in chronic liver disease prevention and early diagnosis
	Diagnosis and linkage to care	Fund diagnosis of liver cirrhosis and facilitate rapid linkage to specialist care
	Surveillance	Increase access to timely HCC surveillance
	HCC services	Provide streamlined pathways to specialist HCC services and treatment
	Research	Support key research priorities to address gaps in knowledge

ACCHO = Aboriginal Community Controlled Health Organisations. ◆

Fund early detection of cirrhosis and facilitate rapid linkage to specialist care

There are major disparities in access and funding for the tools used for cirrhosis diagnosis across Australia. Transient elastography is the non-invasive international standard for diagnosis of cirrhosis;²² however, it remains unfunded by Medicare and there are no national access programs. Increased access to transient elastography is vital for all Australians; however, specific investment in portable transient elastography outreach services

provided through ACCHOs is paramount for timely diagnosis of cirrhosis for First Nations Australians, particularly in regional and remote areas.

The fibrosis-4 index and the aspartate aminotransferase to platelet ratio index are calculated using the results from routine blood tests and have a high negative predictive value for cirrhosis.²² Although not specifically validated in First Nations Australians, they provide a means of triaging those most in need of transient elastography and specialist

assessment.²² Investment in health worker education programs to increase routine use of these simple tests in primary care should be prioritised. Other accurate but commercial blood test algorithms, such as Hepascore or Enhanced Liver Fibrosis test (Siemens Healthcare),²² would increase access to cirrhosis diagnosis in remote Australia, but remain unfunded through Medicare.

For those with cirrhosis, rapid linkage to specialist liver care improves survival. Investment in models of care that increase access is vital, such as nurse-led care, telehealth hub-and-spoke models of care, and specialist outreach services.^{5,16,18}

Increase access to timely HCC surveillance

HCC surveillance using six-monthly liver ultrasounds is cost-effective for improving early detection and survival in HCC.^{4,23,24} Uptake of HCC surveillance is low in First Nations Australians due to lack of awareness and access barriers, although uptake is high when offered on Country.¹⁶ Investment in novel models of HCC surveillance for remote Australia is urgently needed; for example, pilot outreach models of care delivered in partnership with the Royal Flying Doctors Service, greater training of local health workers in liver ultrasound, and exploration of new technologies, such as small portable ultrasounds.⁵

HCC risk scores using blood biomarkers could be a game changer to improve access to HCC surveillance in remote Australia. For example, the commercial GAAD score (gender, age, alfa-fetoprotein, des-carboxyprothrombin; Roche Diagnostics) has a high negative predictive value for HCC.²⁵ Evaluation of accuracy and acceptability of HCC risk prediction scores for HCC surveillance in First Nations Australians should be prioritised, with fast-tracked Medicare reimbursement if effective.

Finally, streamlined systems of HCC surveillance and recall that rapidly link communities to confirmatory imaging and multidisciplinary HCC care are essential. Peer navigators have been effectively used for other cancers in First Nations Australians.²⁶

Provide streamlined pathways to specialist HCC services

HCC diagnosis and treatment access present a so-called tyranny of distance for First Nations Australians, with distances from specialist care and radiology services contributing to shorter survival times in First Nations Australians in remote communities.¹³ Liver transplantation provides excellent outcomes for people with early-stage HCC and impaired liver function,¹¹ however, First Nations Australians are under-represented in liver transplant recipients.²⁷ Greater virtual access to specialist hospital HCC multidisciplinary team meetings should be promoted to local health workers to improve two-way communication and training, enabling greater advocacy for First Nations Australians.

Most treatments for HCC are provided through tertiary hospitals, associated with significant cost, time off work for travel and disconnection from community

for First Nations Australians. Outreach interventional radiology services for HCC through local hospital networks may improve access for First Nations people in remote areas. Systemic therapies offer First Nations Australians options for care on Country through community delivered treatments. Greater training of local health workers in recognising and managing potential complications will improve treatment outcomes. Greater efforts to offer First Nations Australians participation in HCC clinical trials are needed; teletrial initiatives have expanded trial access for people in remote settings.²⁸

There is also a critical need for co-designed palliative care services for First Nations Australians with HCC,²⁹ supported by peers to promote uptake and improve coverage of culturally safe end-of-life care.

Support key research priorities

In Australia, most disease surveillance reports describe unspecified primary liver cancer.¹ Accurate coding of liver cancer subtypes in Australian cancer data registries is paramount to track the effect of public health interventions on HCC incidence and mortality and should be prioritised. Understanding the barriers and enablers to uptake of HCC surveillance in First Nations people and reasons for late presentation and low treatment uptake are paramount to co-design effective HCC surveillance and treatment programs that meet the needs of First Nations Australians.

Research priorities must be set and co-led by First Nations Australians.³⁰ Greater understanding of biological and epidemiological drivers of HCC; optimal HCC surveillance, diagnostic and treatment modalities; and effective, culturally safe health system solutions to improve HCC outcomes for First Nations Australians are urgently needed.

Funding for First Nations Australian-led research should sustainably support meaningful community engagement and research capacity building.³⁰ Importantly, it cannot be assumed that a model of care working in one community will translate effectively to another.³¹ Ongoing assessment should be embedded within HCC programs to ensure they are meeting the needs of First Nations Australians.

Conclusion

Although HCC prevalence and mortality remain unacceptably high in First Nations Australians, data from successful programs co-led by First Nations Australians provide new hope for achieving greater parity in HCC outcomes. Now is the time to act in partnership with First Nations Australians to close the gap in liver disease outcomes and reduce preventable deaths from HCC.

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