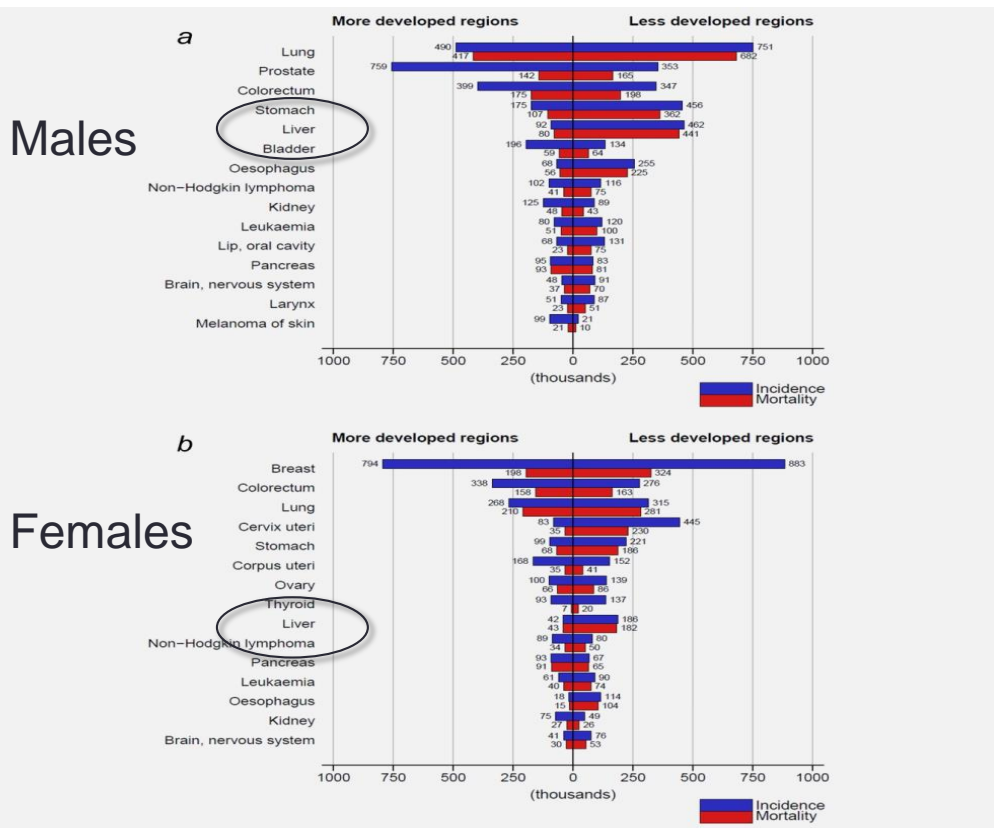


Hepatitis B Virus-Related Hepatocellular Carcinoma Presenting at an Advanced Stage: Is it Preventable?

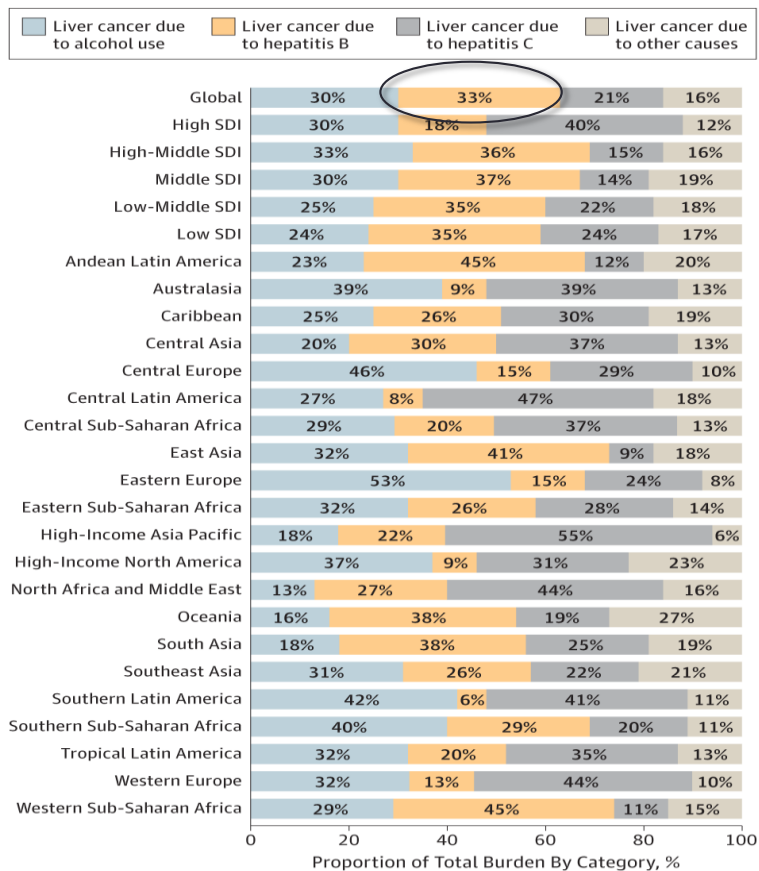
Dr Tom Mules NZSG ASM 2018

HCC



Ferlay et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015

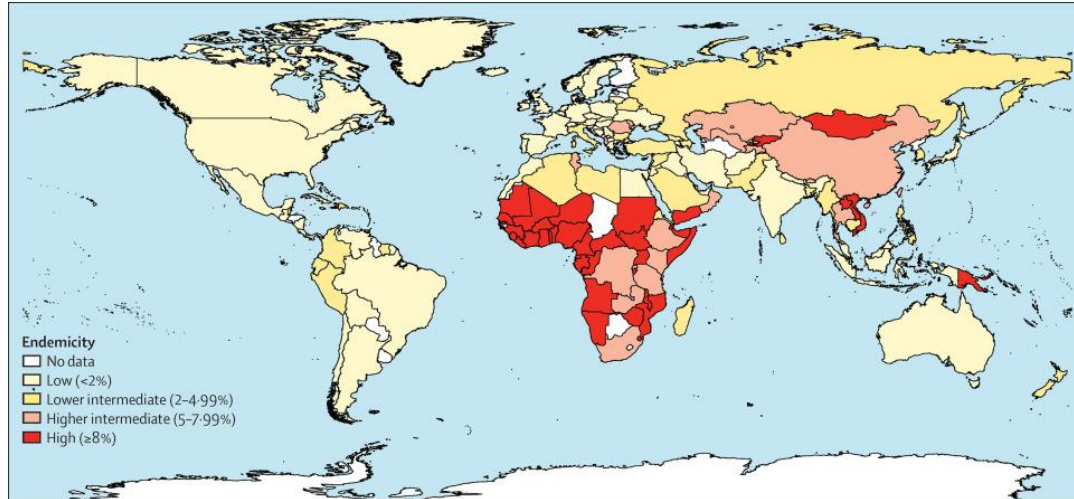
HBV-related HCC



Collaboration, 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

HBV in NZ

- Chronic HBV infection prevalence
 - 4.11% (4.04–4.18). 180,000 people



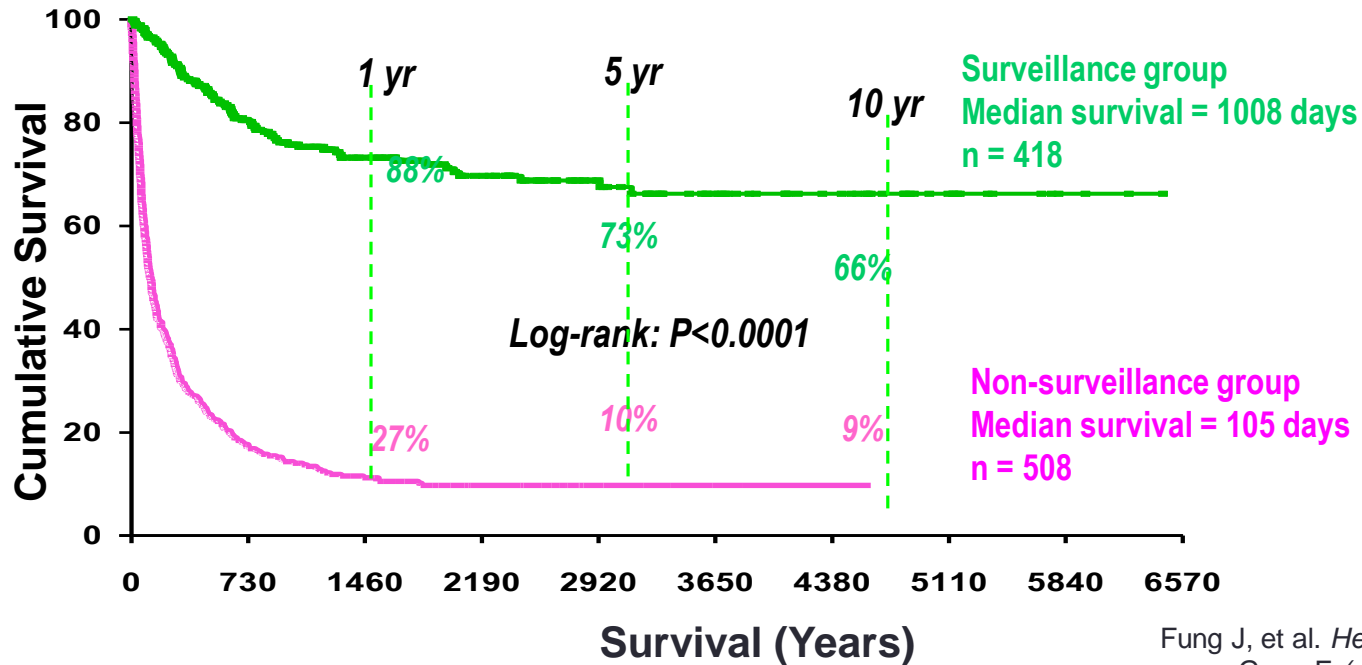
Schweitzer et al. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet 2015

HBV-related HCC

- 10-25% lifetime risk of HCC
- Multiple risk factors
- Even without additional risk factors the risk of HCC is 100x higher than those not infected with HBV
- Treatment with nucleoside analogues more than halves the risk of HCC

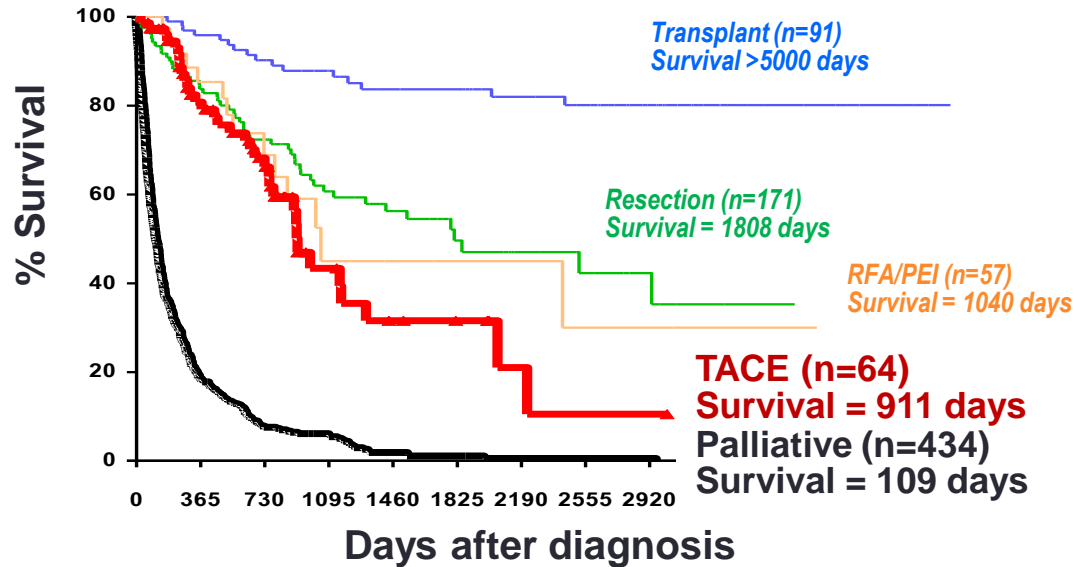
Papatheodoridis G et al. Incidence of hepatocellular carcinoma in chronic hepatitis B patients receiving nucleos(t)ide therapy: A systematic review. *Journal of Hepatology*, 2010

HCC surveillance improves survival in patients with HBV-related HCC



Treatment modality determines survival in HBV-related HCC

- 817 patients with HBV-HCC at NZLTU (2000-2010)



Hepatitis B Virus Related Hepatocellular Carcinoma Presenting at an Advanced Stage: Is it Preventable?

Mules T, Gane E, Lithgow O, Bartlett A, McCall J

Aim= To determine what factors contributed to patients presenting with late-stage/incurable HBV-related HCC

Method

- Retrospective review
- 2003 to 2017
- Inclusion criteria
 - HBsAg +ve
 - Advanced HCC at initial diagnosis
 - Treated with TAE, TACE, sorafenib or best practice supportive care
- Excluded
 - Prior diagnosis of HCC, non-resident status, diagnosis not made in NZ

Method

Patients were categorised according to potential reasons for late presentation. Four groups:

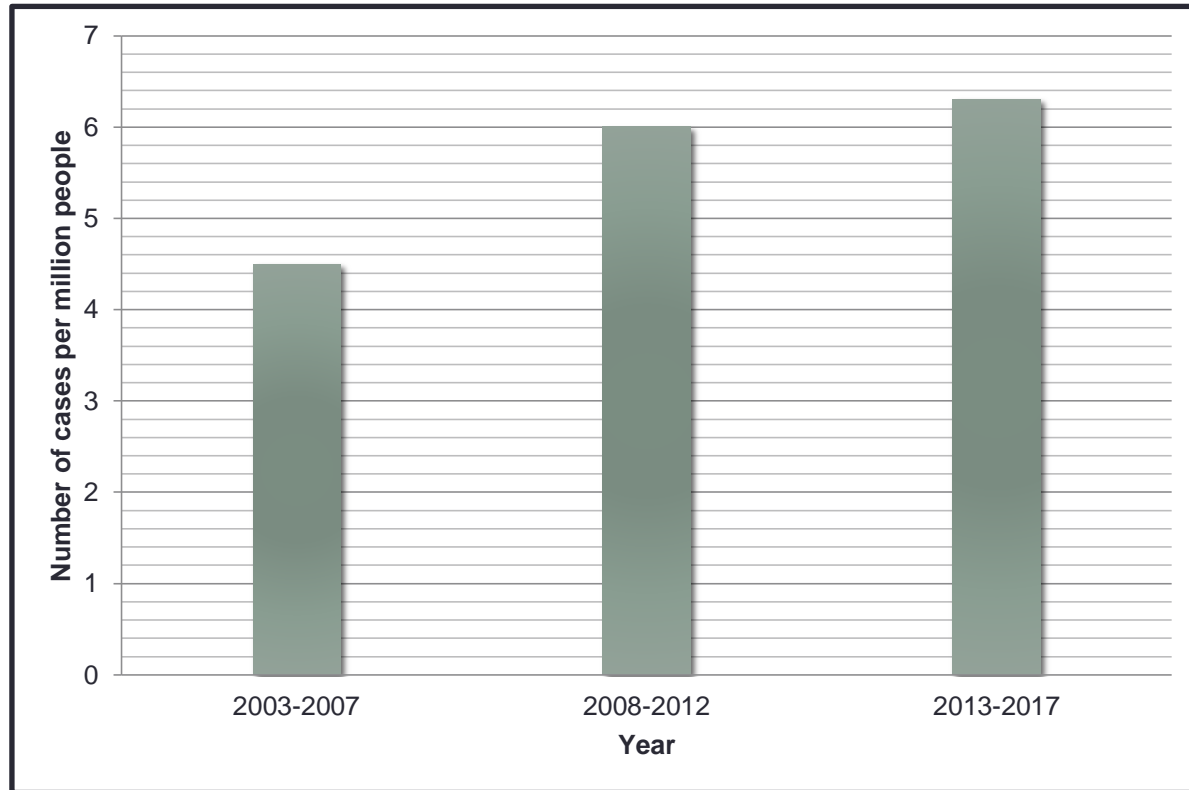
- A= No previous diagnosis of HBV infection
- B= Known HBV but not receiving HCC surveillance (defined as not having had a liver imaging or AFP for two or more years)
- C= Known HBV and receiving suboptimal HCC surveillance (defined as AFP without liver imaging in patients who are cirrhotic or have a positive FHx of HCC; or receiving surveillance outside the recommended time period)
- D= Known HBV diagnosis and receiving optimised HCC surveillance

Results

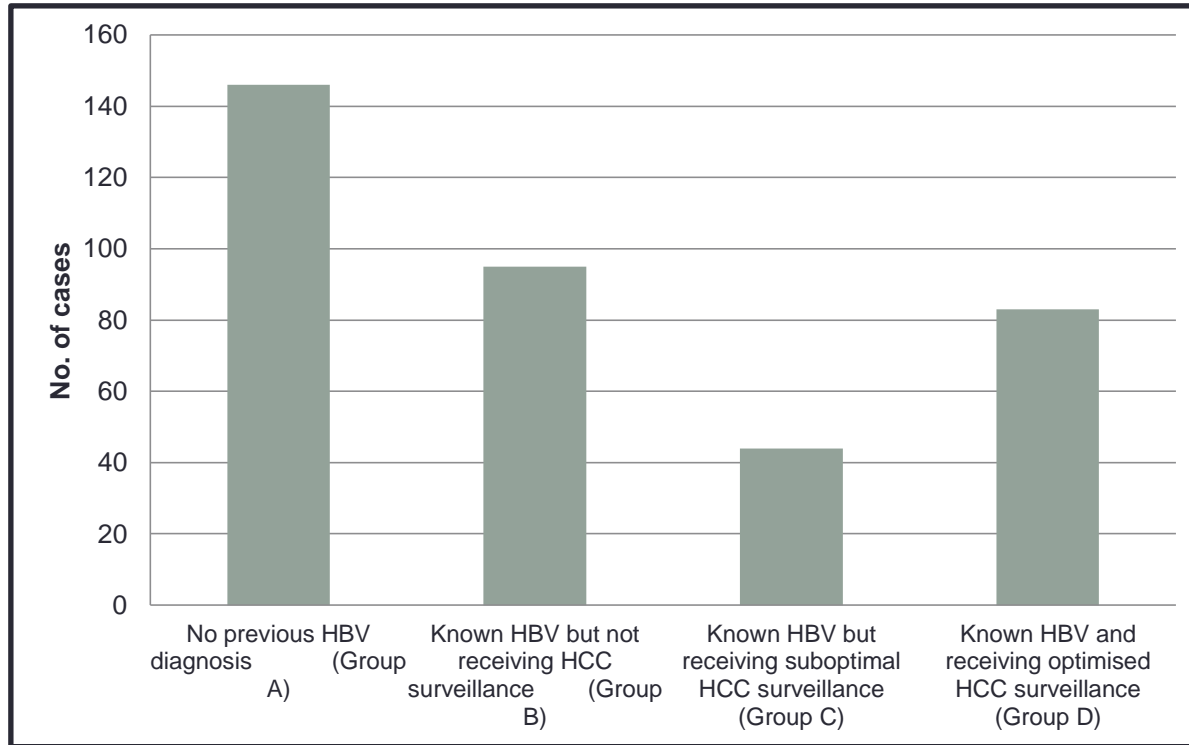
- 374 patients, 6 excluded= 368 patients
- 308 male
- Median age of death
 - 59 (range 24-88)
- Ethnicity

Ethnicity	Number (%)
Māori	143 (39)
Pacific	125 (34)
- Tongan	53 (14)
- Samoan	40 (11)
- Cook Island	24 (7)
- Niuean	7 (2)
- Tokelauan	1 (0.3)
Asian	72 (20)
- Chinese	52 (14)
- SEA	16 (4)
- Taiwanese	1 (0.3)
- Japanese	1 (0.3)
- Filipino	1 (0.3)
- Indian	1 (0.3)
NZ European	20 (5)
Other European	4 (1)
Middle Eastern	2 (0.5)
African	2 (0.5)

Incidence



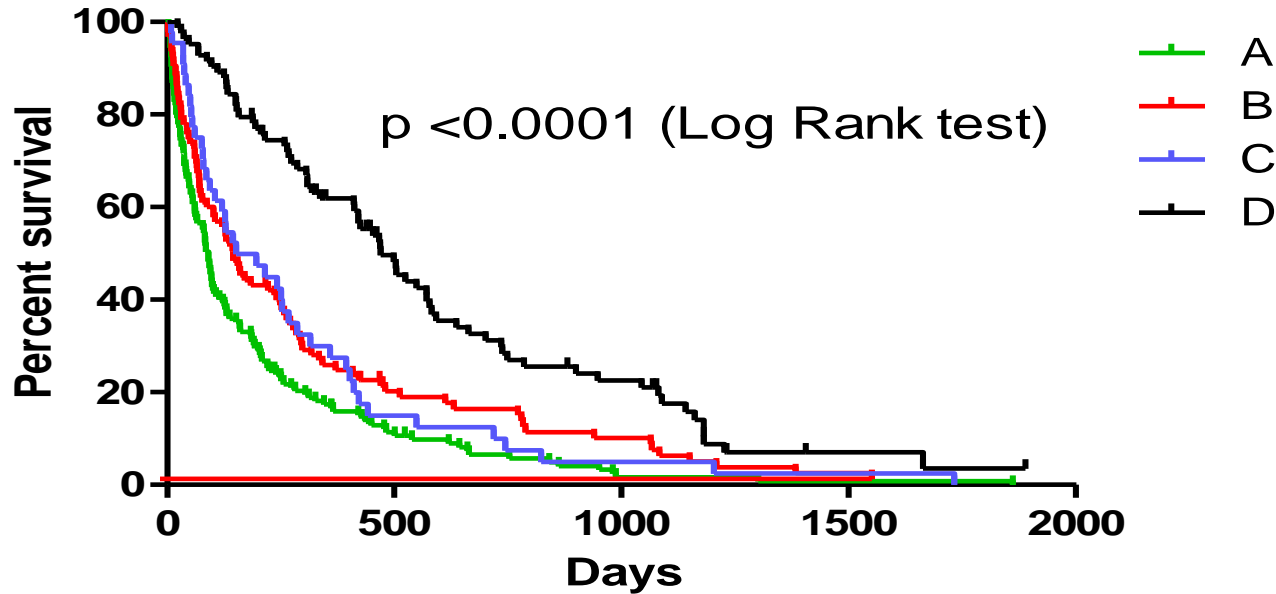
Factors associated with late diagnosis



Survival

	Overall	Group A	Group B	Group C	Group D
Median survival (days)	138	90	145	152	469

Survival for each group



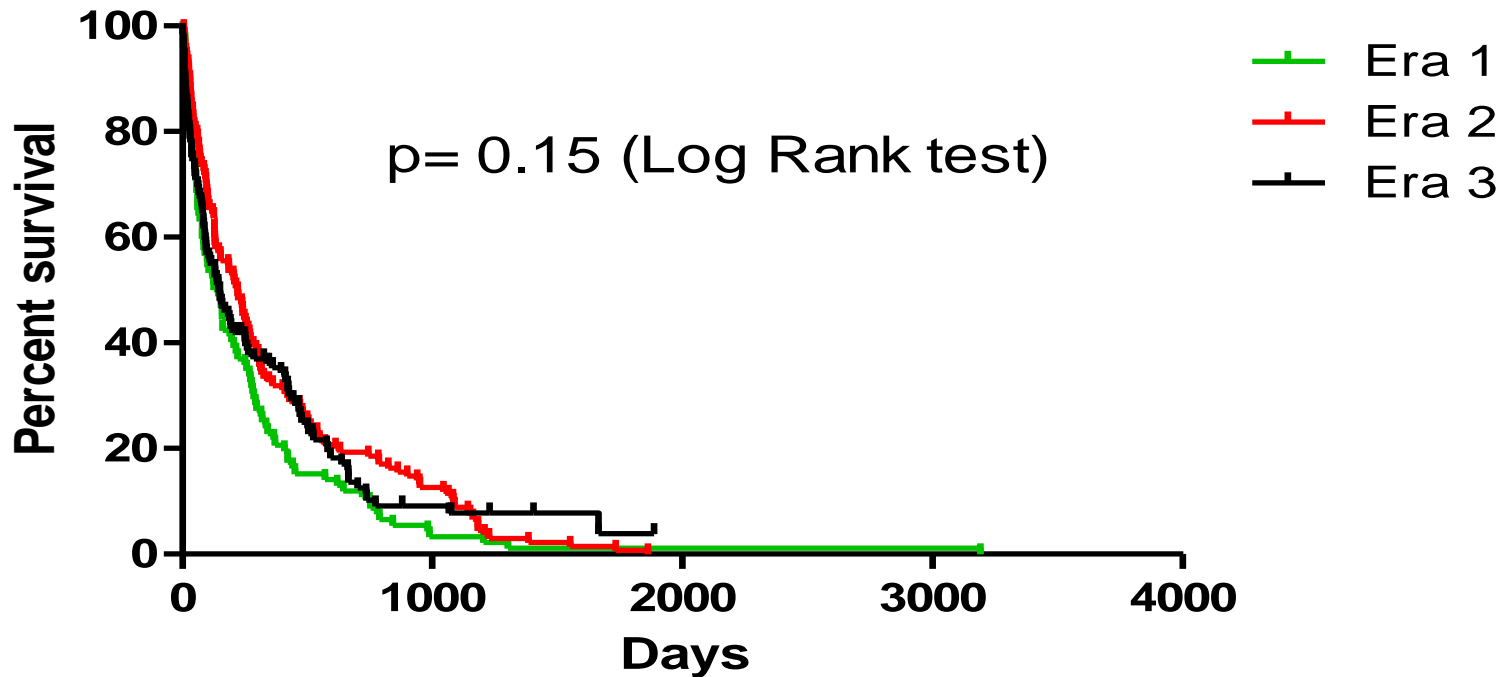
A= No previous HBV diagnosis

B= Known HBV but not receiving HCC surveillance

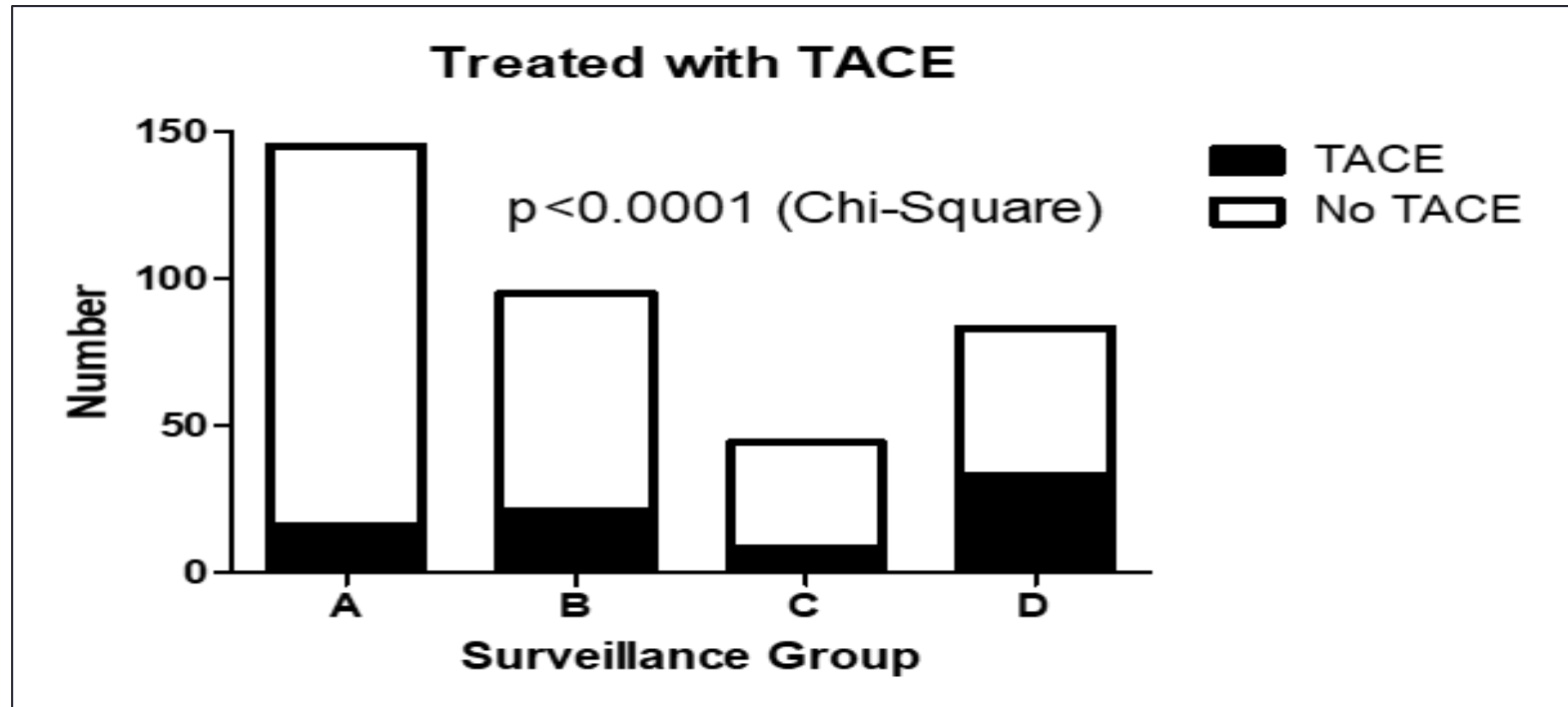
C= Known HBV and receiving suboptimal HCC surveillance

D= Known HBV and receiving optimised HCC surveillance

Survival for each five-year period



Proportion of patients receiving TACE



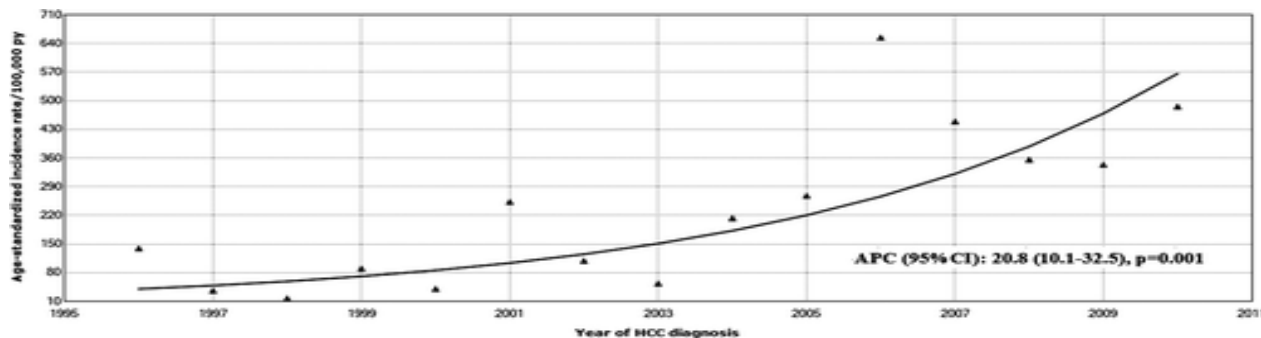
Contributing to inequality in NZ

- 85% male
- Median age of death= 59
- Ethnicity
- Survival 138 days

Ethnicity	Number (%)
Māori	143 (39)
Pacific	125 (34)
- Tongan	53 (14)
- Samoan	40 (11)
- Cook Island	24 (7)
- Niuean	7 (2)
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Rising incidence

- Follows trends in South Australia

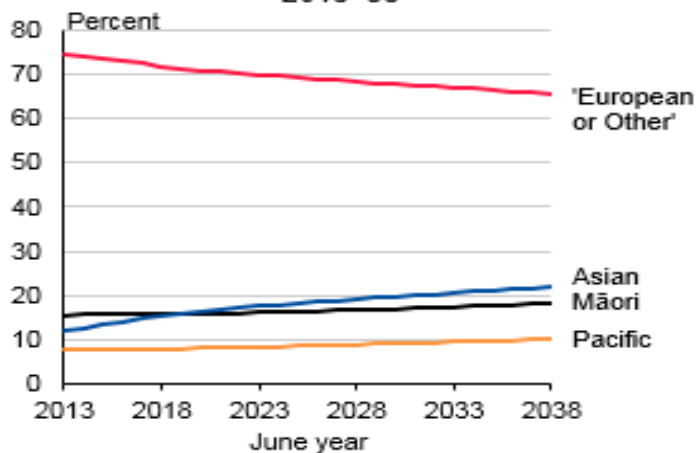


- Factors contributing to rising incidence
 - Aging of pre-immunisation population
 - Increasing levels of migration from regions with endemic HBV infection

Chinnaratha MA et al. Rising incidence of hepatitis B-related hepatocellular carcinoma in South Australia: 1996-2010. Intern Med J. 2016.

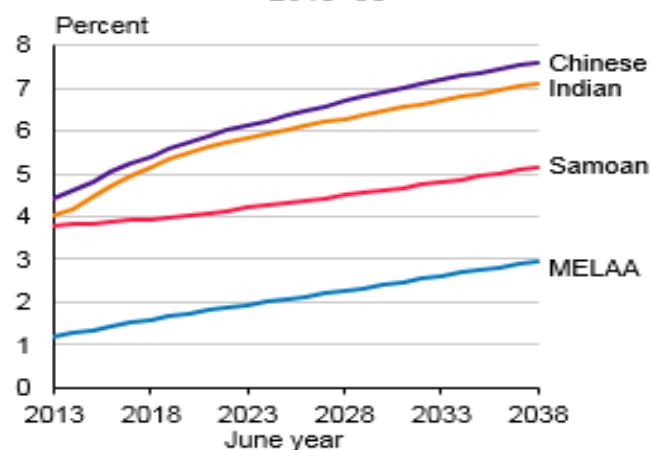
Projected ethnic make-up of NZ in 2038

Ethnic share of New Zealand population
Median projection
2013–38



Source: Stats NZ

Ethnic share of New Zealand population
Median projection
2013–38



Note: MELAA – Middle Eastern/Latin American/African
Source: Stats NZ

- **Hepatitis B Virus Related Hepatocellular Carcinoma Presenting at an Advanced Stage:
Is it Preventable?**

HBV screening

- 40% of patients had no previous HBV diagnosis. These patients had the worst survival (85 days)
- Hepatitis B Screening in New Zealand
 - 1999-2002, targeted high risk ethnic groups
 - >10,000 cases diagnosed
- >80,000 cases of undiagnosed HBV infection remain

Robinson T, et al. The New Zealand Hepatitis B Screening Programme: screening coverage and prevalence of chronic hepatitis B infection. NZMJ. March 2005.

Improving HCC surveillance uptake

- 26% of patients had known HBV but were not receiving any HCC surveillance
 - Lack of awareness of long-term HCC risk
 - Poor access to health care
 - Stigma associated with HBV
- Community-based organisations
 - Hepatitis Foundation

Optimal HCC surveillance

- 23% of patients were receiving optimised surveillance
 - Lack sensitivity
 - Improves survival
 - Reduces HCC mortality by 37% by diagnosing at an earlier stage
 - This study has shown that advanced HCC detected by surveillance has a significantly longer survival than non-surveillance detected (484 days vs. 115 days)- more TACE

Expanding HCC surveillance in NZ

- APASL/AASLD Guidelines

Table 3 Groups where HCC surveillance is recommended

	HCC risk (per year)
Cirrhotic hepatitis patients	
HBV	3–5%
HCV	2–7%
NASH	2–4%
Genetic hemochromatosis	Unknown, but probably >1.5%
Primary biliary cirrhosis	2–3%
Alpha 1 antitrypsin (AIAT) deficiency	Unknown, but probably >1.5%
Autoimmune hepatitis	
Other etiologies	Unknown
Chronic HBV carriers	
Noncirrhotic (HBsAg positive)	
Asian females >50 years	0.3–0.6%
Asian males >40 years	0.4–0.6%
Africans aged >20 years	NA
History of HCC in the family	NA

Omata M, et al. Asia–Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update
Hepatol Int (2017)

Conclusions

- HBV infection is endemic in New Zealand
- HBV-related HCC incidence is increasing
- Almost half of all cases of HBV-related HCC are diagnosed late when curative intervention is no longer possible
- This study has identified factors contributing to patients presenting with advanced HBV-related HCC
- It has highlighted the need for:
 - improved rates of HBV diagnosis
 - better follow-up of those infected
 - and the importance of optimal HCC surveillance
- HBV-related HCC disproportionately affects minority ethnic groups, and with an increasing incidence, provides a potential target to reduce health inequality in New Zealand

**Many thanks to Amanda Cooper,
Susan Hay and Prof Chris Cunningham
(The Hepatitis Foundation of NZ)**

Thank you

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