Significant gaps in the cascade of care contribute to poor liver cancer outcomes among people with hepatitis B: a longitudinal cohort study

Dina Moussa[*1,2,3], **Joan Ericka Flores**[2,3*], Marno Ryan[2], Thai Hong[2], Brett Knowles[2], Adrian Fox[2], Ashu Jhamb[2], Tom Sutherland[2], Stuart Roberts[4,5], William Kemp[4,5], Ammar Majeed[4], Marie Sinclair[3,6], Rohit Sawhney[4,7], Stephen Bloom[4,7], Amanda Nicoll[4,7], Zina Valaydon[3,8], Gauri Mishra[9], Sid Sood[10], Diana Lewis[10], Alex Thompson[2,3], Jessica Howell[1,2,3,4]

1. Burnet Institute; 2. St Vincent's Hospital; 3. University of Melbourne; 4. Monash University; 5. Alfred Health; 6. Austin Health; 7. Eastern Health; 8. Western Health; 9. Monash Health; 10. Northern Health

** Co-first author*

Disclosures

- None relevant to this study

Introduction

- Hepatitis B (HBV) is a major cause of hepatocellular carcinoma (HCC) in Australia, despite availability of effective, subsidised treatment that reduces HCC risk.

- The cascade of hepatitis B care and clinical outcomes among people presenting with HCC in Australia is not well characterised.

Aim: To describe the clinical characteristics, cascade of care and clinical outcomes among people with HBV-related HCC in Greater Melbourne, Victoria.

Methods

- Multicentre study
- All incident HCC cases from 1st January 2018 to 31st October 2022 across six tertiary health networks
- Clinical and demographic data obtained from EMR and MDT notes
- Followed up to October 31st 2023

Definitions

- Cirrhosis defined using elastography, radiologic features or liver biopsy

- Antiviral treatment eligibility (GESA Australian consensus statement 2021 criteria):
  - Individuals with cirrhosis
  - Individuals with persistently elevated ALT (>19IU/mL F; >30IU/mL M) and
    - eAg negative: HBV DNA >2000 IU/mL
    - eAg positive: HBV DNA >20 000 IU/mL

- Surveillance: at least 1 scan in the 12 months preceding HCC diagnosis

Outcomes

- Primary outcome: number (proportion) incident HBV-related HCC

- Secondary outcomes
  - Compare clinical characteristics between HBV-related HCC and non-HBV related HCC cases
  - Describe the cascade of care with number (proportion) HBV-HCC receiving guideline-based treatment and surveillance
  - Survival time (days) since HCC diagnosis and factors impacting

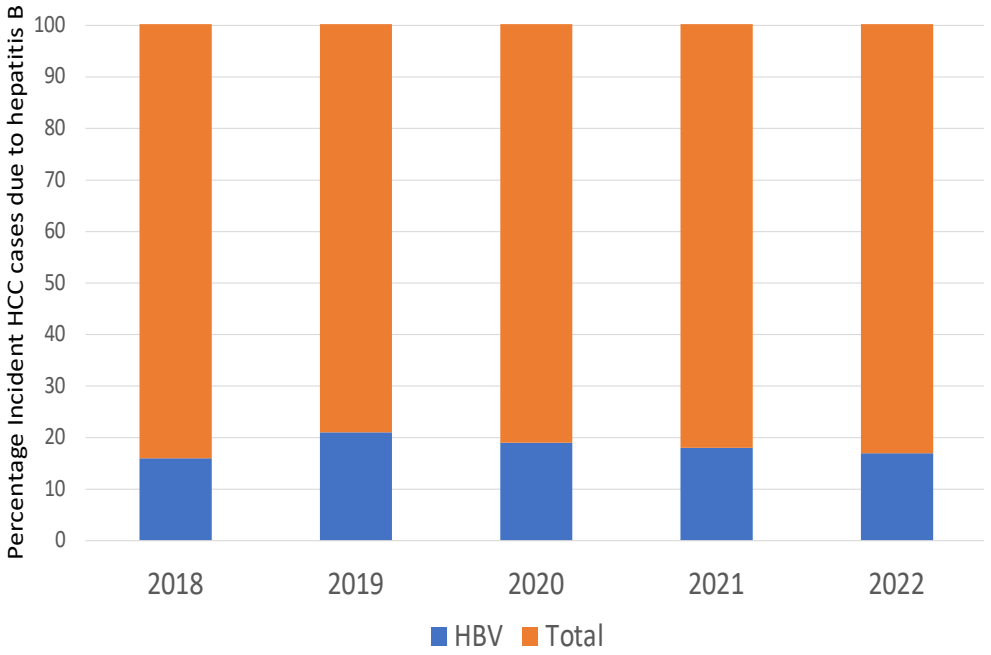
Results

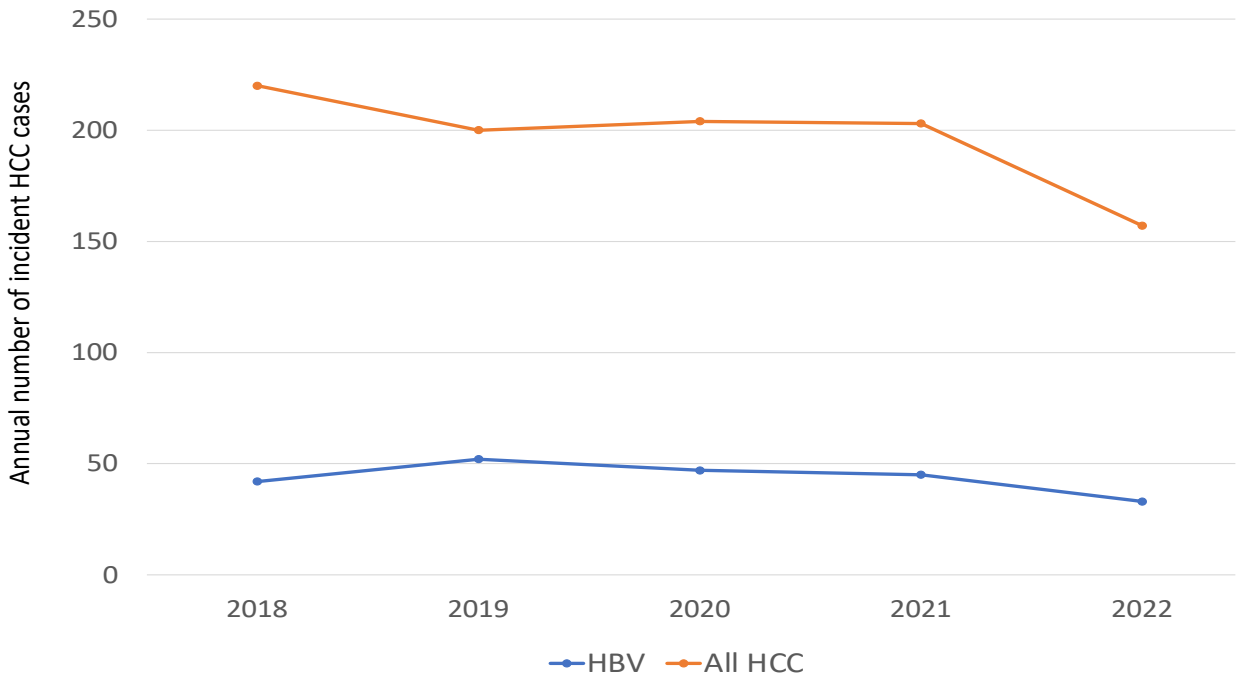
1203 incident HCC cases identified

- **219 (18%) were due to hepatitis B**

Over the years studied:

- Stable proportion of cases related to hepatitis B
- Decreasing trend of annual cases from 24% in 2019 to 15% in 2022





Clinical characteristics

	HBV (N=219)	No HBV (N=984)	Total (N=1203)	χ^2 p-value
Age category				<0.001
<=35 years	0	9 (1%)		
36-45 years	17 (8%)	12 (1%)		
46-55 years	38 (17%)	99 (11%)		
56-65 years	72 (33%)	320 (33%)		
66-75 years	61 (28%)	330 (34%)		
>75 year	31 (14%)	214 (22%)		
Male	195 (89%)	773 (79%)	968 (80%)	<0.001
Ethnic background (N=1193):				<0.001
African	9 (4%)	5 (1%)		
Asian	131 (60%)	101 (10%)		
ATSI	1 (1%)	13 (1%)		
Caucasian	76 (35%)	857 (88%)		
Non-English speaking	100 (47%)	101 (10%)	201 (17%)	<0.001

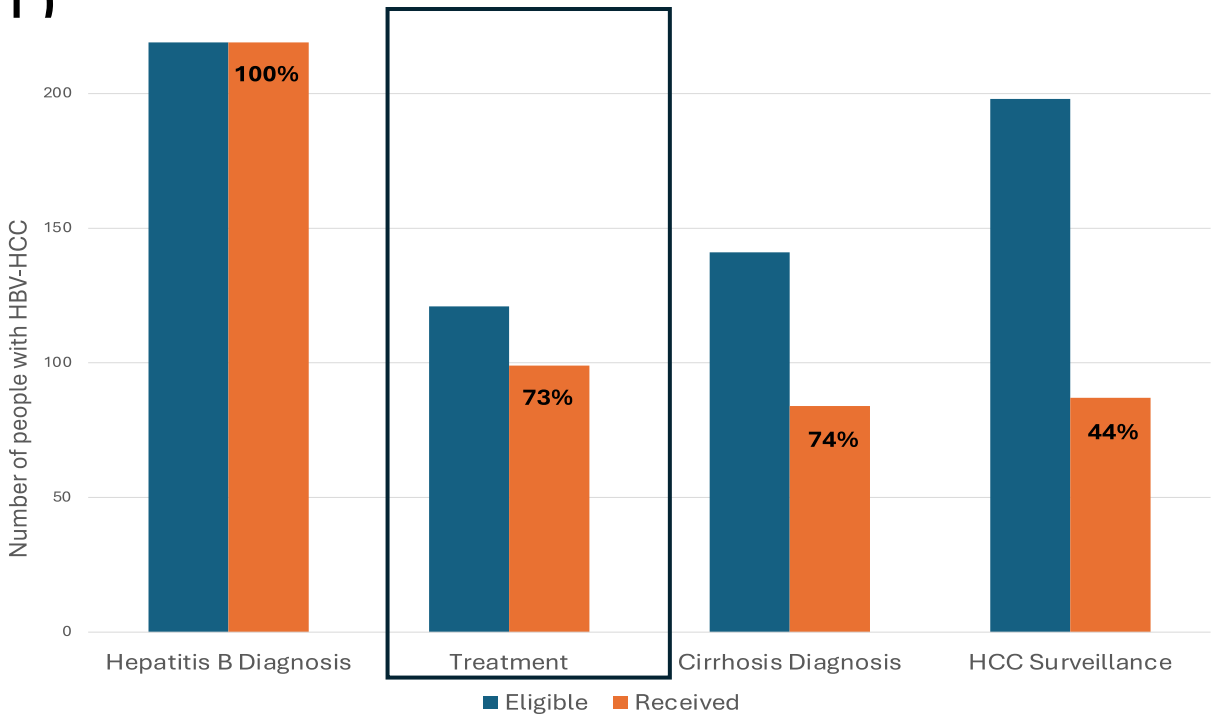
	HBV (N=219)	No HBV (N=984)	Total (N=1203)	χ^2 p-value
T2DM (N=1193)	61 (28%)	383 (39%)	444 (37%)	0.003
Obesity (N=1165)	13 (6%)	138 (15%)	151 (13%)	0.001
Mental health (N=1172)	16 (8%)	149 (16%)	165 (14%)	0.001
Smoking status (N=1166)				0.018
Current	33 (16%)	217 (23%)	250 (21%)	
Past	31 (15%)	168 (18%)	199 (17%)	
Non-smoker	148 (70%)	569 (60%)	717 (61%)	
Alcohol misuse (N=1183)				<0.001
Current	28 (13%)	300 (31%)	328 (28%)	
Past	22 (10%)	226 (23%)	248 (21%)	
None	162 (76%)	445 (46%)	607 (51%)	
Family history HCC	15 (7%)	12 (1%)	27 (2%)	<0.001
ECOG				0.004
0	148 (69%)	544 (57%)	692 (60%)	
1	48 (23%)	238 (25%)	286 (25%)	
2	12 (6%)	104 (11%)	116 (10%)	
3	5 (2%)	53 (6%)	58 (5%)	
4	0	10 (1%)	10 (1%)	

	HBV (N=219)	No HBV (N=984)	Total (N=1203)	χ^2 p-value
Cirrhosis	**141 (64%)**	**851 (86%)**	**992 (82%)**	**<0.001**
Portal hypertension	**69 (32%)**	**498 (51%)**	**567 (48%)**	**<0.001**
Child-Pugh Class **A** **B** **C**	 **169 (77%)** **32 (15%)** **18 (8%)**	 **634 (64%)** **266 (27%)** **84 (9%)**	 **803 (67%)** **298 (25%)** **102 (8%)**	**<0.001**
Enrolled in surveillance (N=1178)	**103 (48%)**	**388 (40%)**	**491 (42%)**	**0.029**
Mode of presentation (N=1193): **Surveillance** **Incidental** **Symptomatic**	 121 (56%) 24 (11%) 73 (33%)	 513 (53%) 148 (15%) 314 (32%)	 634 (53%) 24 (11%) 73 (33%)	0.284
BCLC stage **0** **A** **B** **C** **D**	 **29 (13%)** **97 (44%)** **26 (12%)** **38 (17%)** **29 (13%)**	 **104 (11%)** **339 (35%)** **188 (19%)** **150 (15%)** **199 (20%)**	 **133 (11%)** **436 (36%)** **214 (18%)** **188 (16%)** **228 (19%)**	**0.003**
BCLC early stage (0/ A)	**126 (58%)**	**443 (45%)**	**569 (47%**	**<0.001**
First treatment curative intent	**100 (46%)**	**324 (33%)**	**424 (35%)**	**<0.001**

Cascade of Care

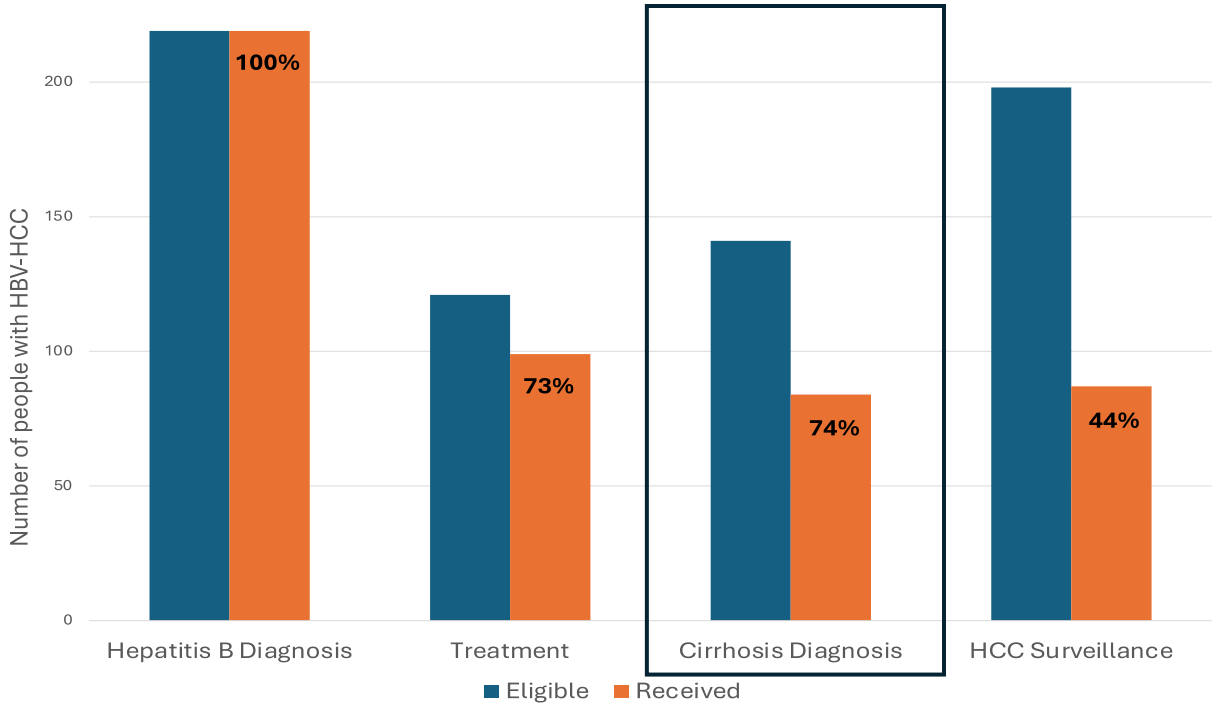
60% (121 of 203) were eligible for treatment at the time of HCC diagnosis, but **27% were not on treatment**

- Referral from primary care at time HCC diagnosis (adjOR 0.18, 95% CI 0.03-0.96, p=0.04)
- Admission to hospital at the time of HBV-HCC diagnosis (adjOR 0.09, 95% CI 0.02-0.34, p<0.001)



Cascade of Care

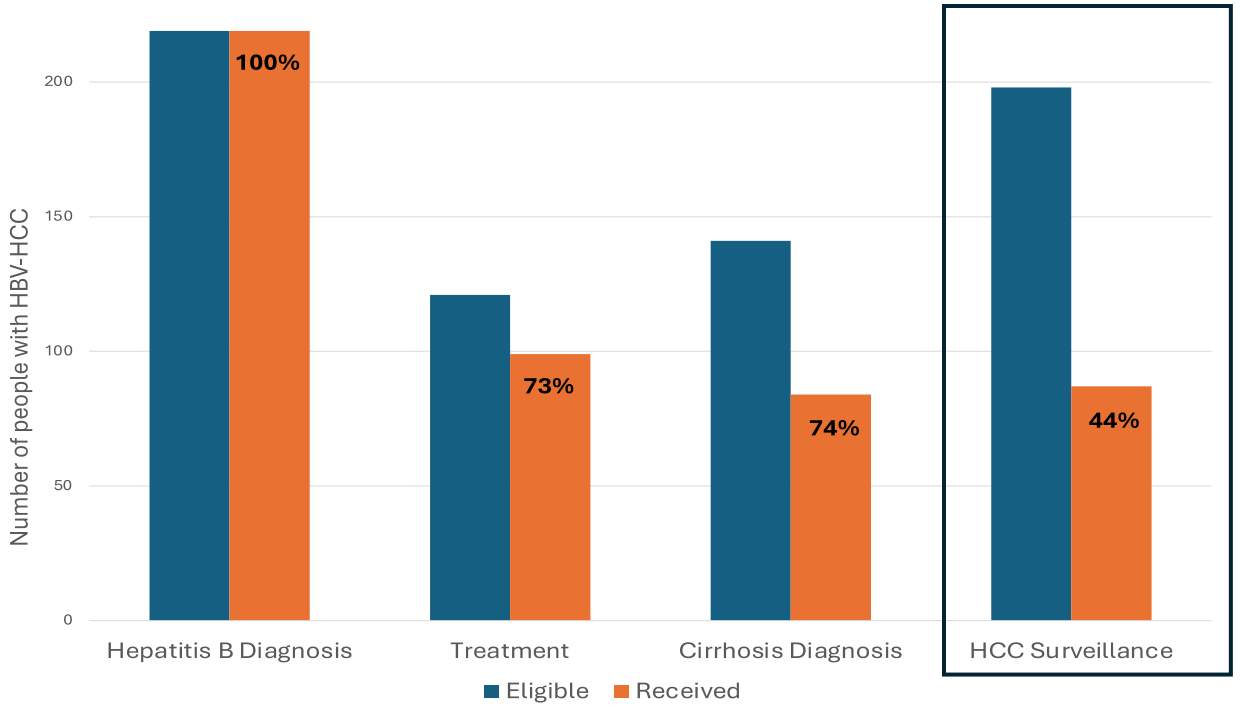
64% (149/219) had cirrhosis, but **26% were identified at the time of HCC diagnosis**



Cascade of Care

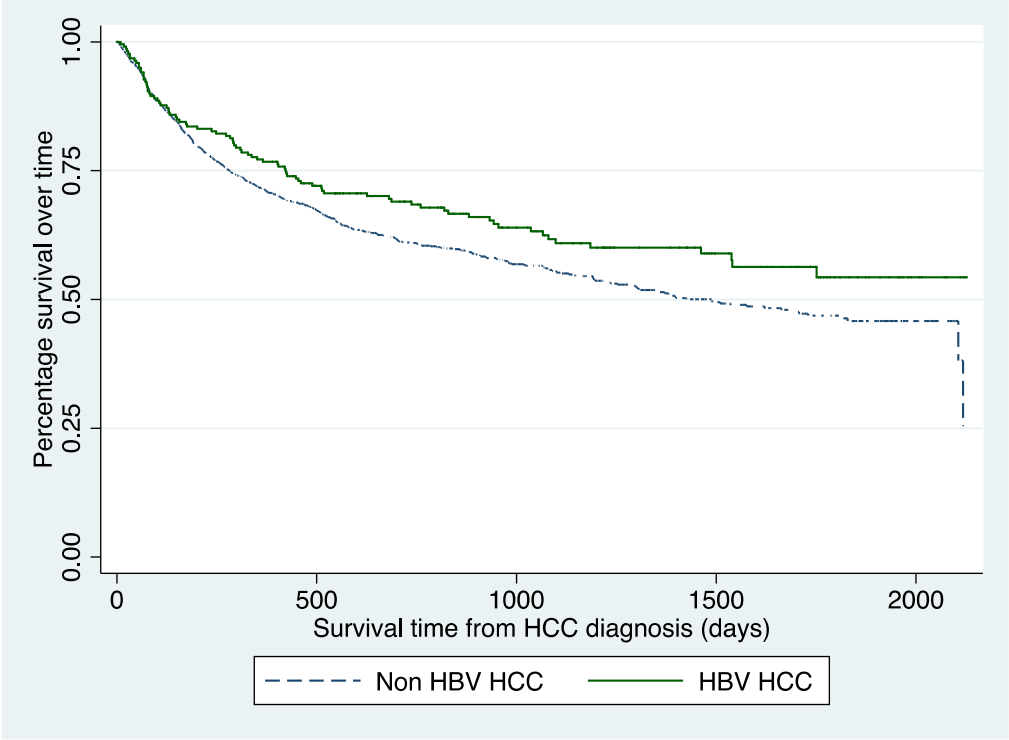
92% (201/219) were eligible for HCC surveillance, but **only 46% (92/201) were enrolled in HCC surveillance** at time of HCC diagnosis

- 78% of those in specialist hepatology care were enrolled in HCC surveillance, compared to 22% of those not enrolled in non-specialist and primary care (p<0.001)

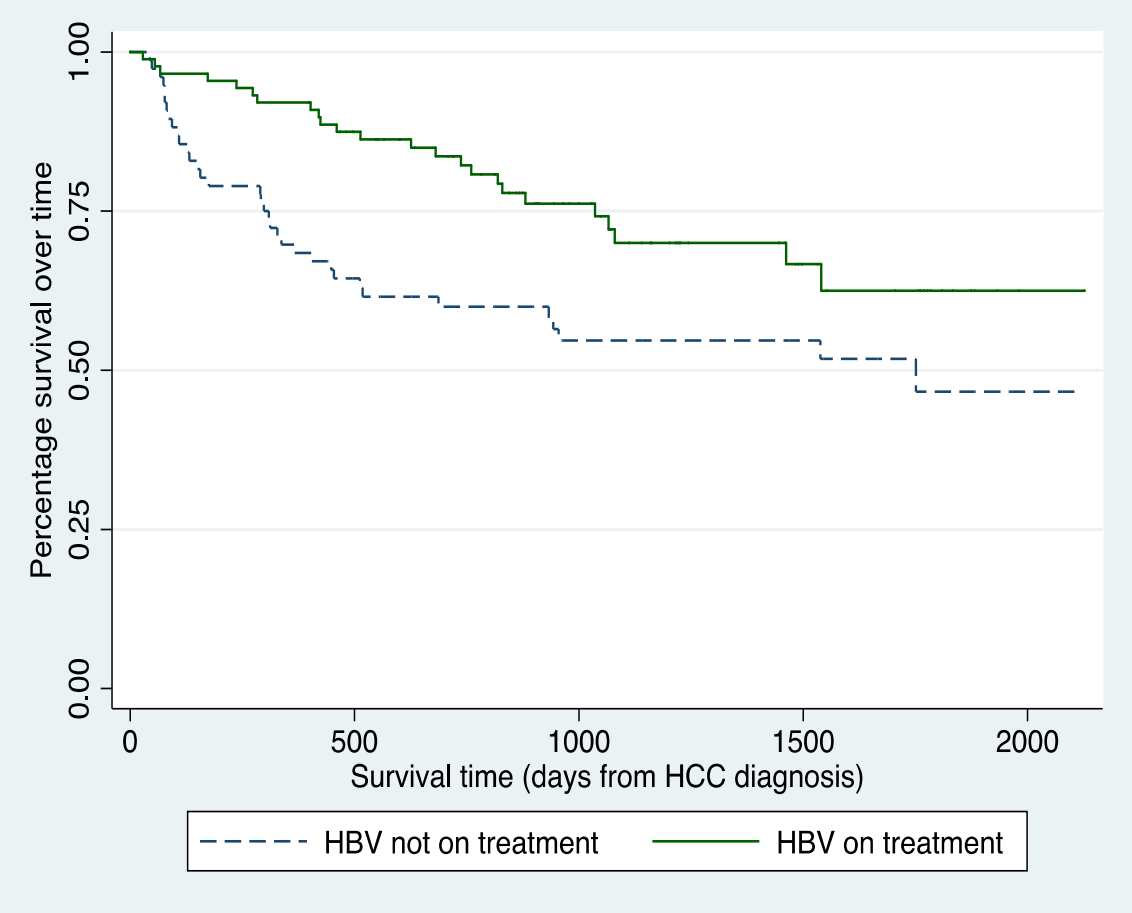


Overall Survival

Median survival from time of HCC diagnosis was longer among individuals with HBV-HCC (1540 days compared to 979 days; p<0.001)



Overall Survival in HBV-HCC



P<0.001

Factors associated with survival in HBV-HCC

	Crude HR	P-value	Adjusted HR	P-value
Antiviral therapy	**0.43 (0.27-0.69)**	**<0.001**	1.27 (0.59-2.71)	0.539
Liver specialist referral to MDT	**0.37 (0.24-0.58)**	**<0.001**	0.66 (0.37-1.19)	0.164
Age category				
36-45 years	Ref			
46-55 years	1.10 (0.44-2.73)	0.833		
56-65 years	0.96 (0.42-2.19)	0.919		
66-75 years	0.93 (0.39-2.18)	0.872		
>75 year	1.42 (0.58-3.49)	0.443		
Ethnic background				
Caucasian	Ref			
African	0.49 (0.12-2.04)	0.327		
Asian	0.66 (0.42-1.02)	0.063		
ATSI	4.13 (0.56-30.62)	0.166		
Non-English speaking background	0.90 (0.58-1.38)	0.624		

	Crude HR	P-value	Adjusted HR	P-value
ECOG	**2.26 (1.81-2.83)**	**<0.001**	**1.53 (1.14-2.05)**	**0.004**
T2DM	0.98 (0.61-1.59)	0.949		
Obesity	1.17 (0.51-2.68)	0.717		
Mental health	1.36 (0.66-2.82)	0.408		
Smoking status	0.68 (0.35-1.32)	0.256		
Alcohol misuse	**2.53 (1.46-4.39)**	**0.001**	**2.30 (1.29-4.10)**	**0.005**
IVDU	0.71 (0.17-2.90)	0.635		
Family history HCC	0.43 (0.14-1.36)	0.149		
Cirrhosis	1.48 (0.93-2.37)	0.164		
Portal hypertension	1.88 (1.21-2.94)	0.005		
Child-Pugh Class	**2.75(2.09-3.63)**	**<0.001**	1.35 (0.91-2.00)	0.131
Enrolled in surveillance	**0.48 (0.31-0.75)**	**0.001**	1.10 (0.57-2.14)	0.775
BCLC stage	**2.68 (2.22-3.24)**	**<0.001**	**2.21 (1.70-2.88)**	**<0.001**

Conclusion

- HBV-related HCC cases are reducing in these health networks in Greater Melbourne, Victoria

- Over 25% of people with HBV-related HCC were not receiving guideline-based care

- Overall survival for people with HBV related HCC is good, particularly for those on HBV treatment

Key Actions and Takeaways

- Key Action 1: While HBV-related HCC appears to be declining in Victoria, major gaps in care that must be addressed to reduce incidence and mortality.

- Key Action 2: Timely HBV treatment, fibrosis assessment and enrolment in HCC surveillance are critical steps in the cascade of HBV care that increase the likelihood of HCC diagnosis at an early, curable stage.

- Key Action 3: Greater investment in non-specialist health-worker education and training in HBV care, coupled with a national registry approach to HCC surveillance are urgently needed.

Acknowledgements

- PhD Supervisors: A/Prof Jessica Howell, Prof Alex Thompson, A/Prof Marno Ryan, Dr Zina Valaydon, Dr Thai Hong

- Multi-site PIs: Prof Stuart Roberts, Dr Marie Sinclair, Prof Amanda Nicolls, Dr Gauri Mishra, Dr Diana Lewis, A/Prof Sid Sood, Dr Zina Valaydon, Dr James Haridy

- Liver nurses and support staff: Tara Bunting, John Gough, Jessica Gonzalez, Virginia Bird, Anne Dowling, Katherine Bateman, Paul O'Neill, Carol McRae, Yolanda Ebanks, Jean Whittle