

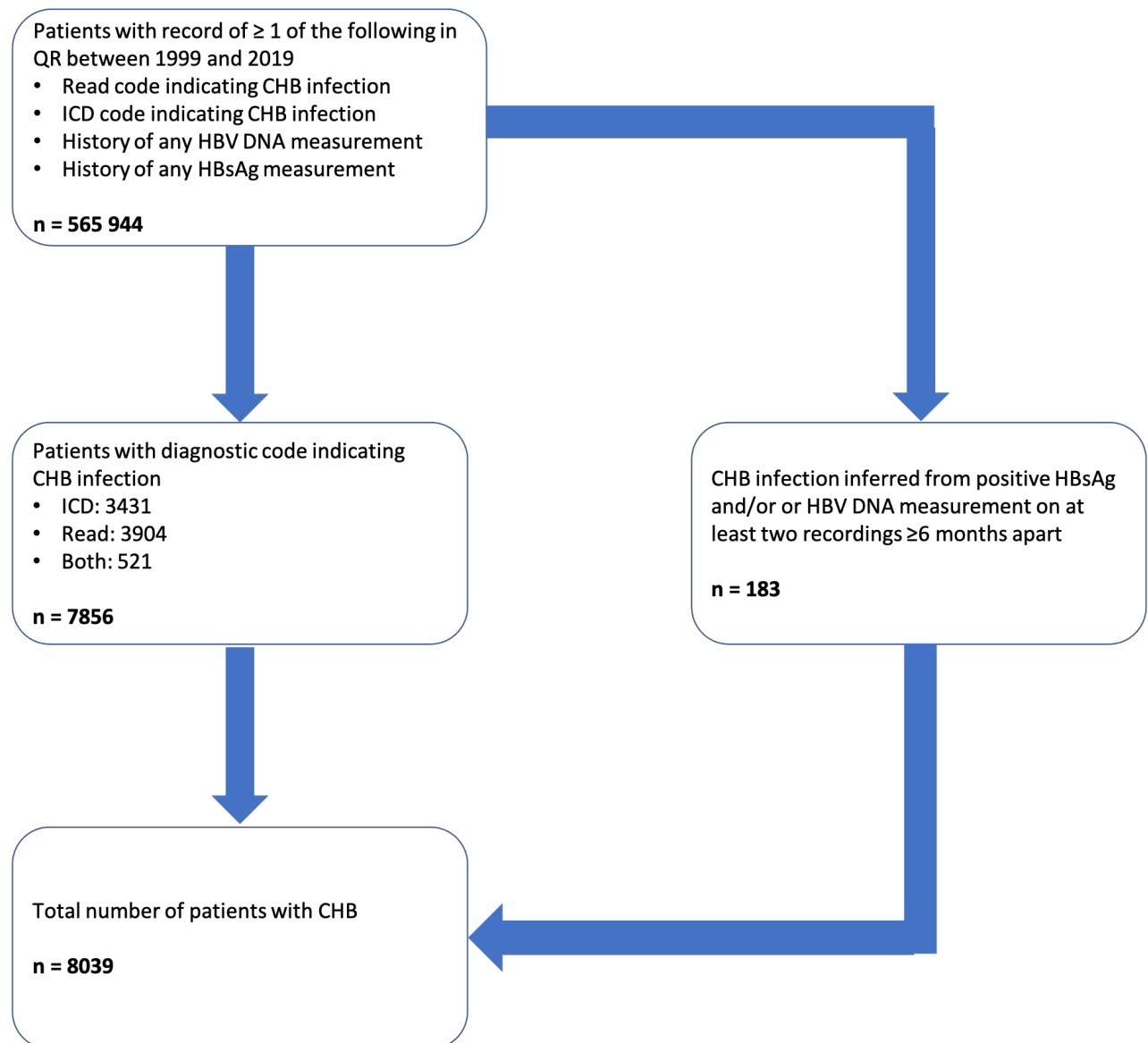
## **SUPPLEMENTARY MATERIAL**

**Analysis of primary care electronic health record data of people living with hepatitis B virus (HBV): infection and hepatocellular carcinoma (HCC) risk associated with socioeconomic deprivation**

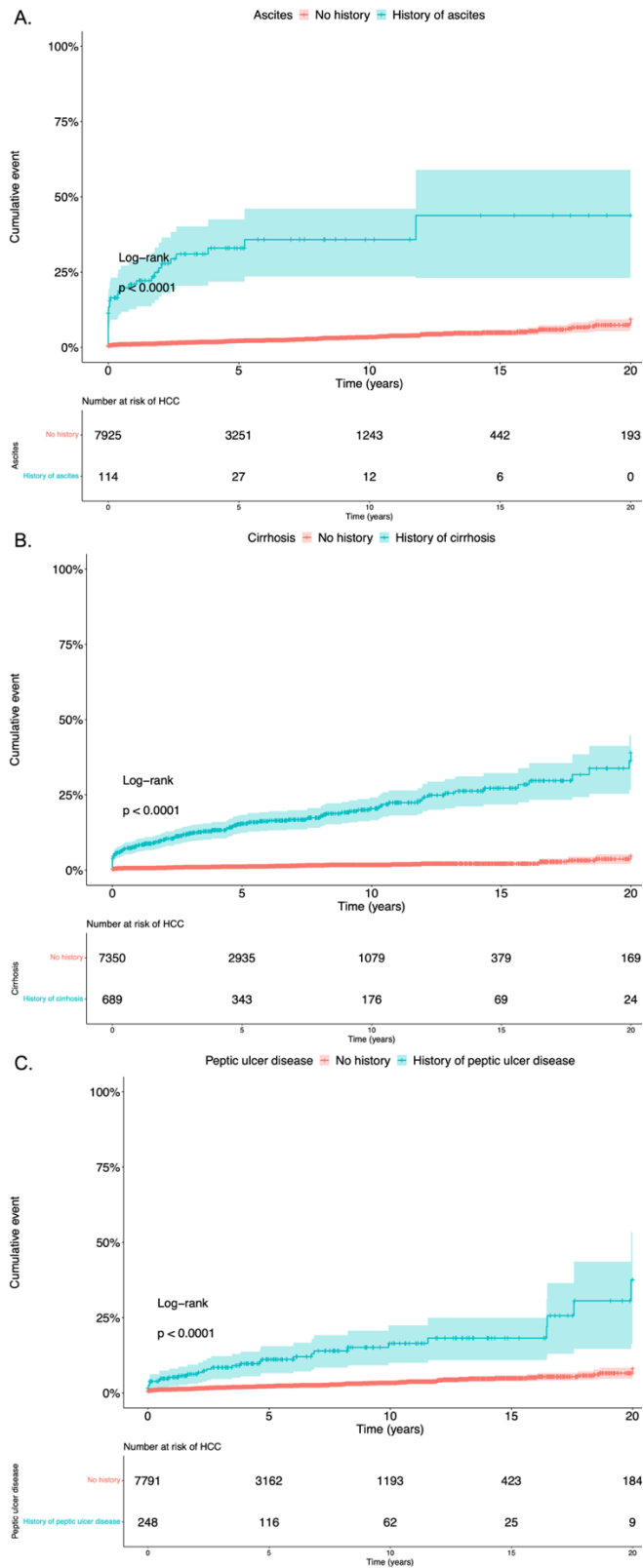
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## [I] Supplementary figures

**Supplementary Figure 1. Study flowchart depicting identification of adults from the QResearch (QR) primary care database eligible for inclusion an analysis of chronic hepatitis B (CHB) infection.** HBV DNA = hepatitis B virus DNA viral load; HBsAg = hepatitis B surface antigen; ICD = international classification of disease.



**Supplementary Figure 2. Kaplan Meier plots visualising the associations of ascites, cirrhosis and peptic ulcer disease to compare time to hepatocellular carcinoma development in those with and without each respective comorbidity. *P* value is that from log-rank test.**



## II Supplementary tables

**Supplementary Table 1. Systemised Nomenclature of Medicine primary care codes indicative of hepatocellular carcinoma used to capture cases of hepatocellular carcinoma (HCC) in adults with CHB from the QResearch database.**

<b>SNOMED ConceptID</b>	<b>SNOMED Fully Specified Name</b>
92644006	Carcinoma in situ of liver (disorder)
93870000	Malignant neoplasm of liver (disorder)
95214007	Primary malignant neoplasm of liver (disorder)
109841003	Liver cell carcinoma (disorder)
187767006	Malignant neoplasm of liver and intrahepatic bile ducts (disorder)
187769009	Primary carcinoma of liver (disorder)
271525004	Carcinoma in situ of liver and/or biliary system (disorder)
395099008	Cancer confirmed (situation)
620441000000107	Malignant neoplasm of liver and intrahepatic bile ducts NOS (disorder)

SNOMED, Systemised Nomenclature of Medicine.

**Supplementary Table 2. Hepatocellular carcinoma cases stratified by source of diagnosis.**

<b>Source of HCC diagnosis</b>	<b>Number of cases</b>
ICD	20
NCR	22
SNOMED/Read	24
ICD and NCR	41
ICD and SNOMED/Read	15
NCR and SNOMED/Read	13
ICD and NCR and SNOMED/Read	75

HCC, hepatocellular carcinoma; ICD, international classification of disease; NCR, National Cancer Registry; SNOMED, Systemised Nomenclature of Medicine.

**Supplementary Table 3. Follow-up time in the QResearch dataset, stratified by source of chronic hepatitis B virus infection diagnosis.**

Source of CHB diagnosis	Follow-up time (years), mean (SD) or median (IQR)*	CHB diagnosis date precedes cohort exit date OR HCC diagnosis date, n	Cohort exit date precedes CHB diagnosis date, n	HCC diagnosis date precedes CHB diagnosis date, n	Cohort exit date equates to CHB diagnosis date, n	HCC diagnosis date equates to CHB diagnosis date, n
Total	5.12 (4.9)	7029	960	44	<5	5
ICD	7.0 (4.9)	2430	958	29	0	<5
ICD and laboratory test	7.1 (3.0)†	12	0	0	0	0
ICD and SNOMED/Read	8.8 (7.3)	516	0	<5	0	<5
Laboratory test	5.8 (2.5)	183	0	0	0	0
SNOMED/Read code	5.0 (5.6)	3831	≤5	11	<5	<5
SNOMED/Read code and laboratory test	8.7 (6.2)	57	0	0	0	0

SD, standard deviation; IQR, Interquartile range; CHB, chronic hepatitis b virus; HCC, hepatocellular carcinoma; ICD, International classification of disease; SNOMED, Systemised Nomenclature of Medicine.

\*Mean and SD or median and IQR calculated for patients for whom CHB diagnosis date precedes cohort exit date OR HCC diagnosis date

†Median and IQR presented

**Supplementary Table 4. Quintiles for natural log transformed alanine transaminase (ALT), natural log transformed aspartate transaminase (AST) and platelet count (Plt).**

ALT and AST were natural log transformed due to their skewed distributions.

First quintile – least deprived, to fifth quintile – most deprived.

Characteristic	Quintile				
	First	Second	Third	Fourth	Fifth
Log ALT					
N (%)	1429	1416	1400	1408	1376
Mean log ALT (SD)	2.69 (0.23)	3.12 (0.09)	3.45 (0.10)	3.85 (0.14)	4.79 (0.64)
Univariable HR (95% CI)	0.89 (0.50 to 1.60)	1.24 (0.73 to 2.11)	1.00 (ref)	1.19 (0.70 to 2.04)	2.17 (1.35 to 3.49)**
Log AST					
N (%)	1378	1415	1420	1409	1407
Mean log AST (SD)	2.89 (0.14)	3.18 (0.07)	3.39 (0.06)	3.67 (1.12)	4.55 (0.69)
Univariable HR (95% CI)	1.11 (0.66 to 1.88)	0.95 (0.55 to 1.65)	1.00 (ref)	1.16 (0.69 to 1.96)	1.96 (1.23 to 3.12)**
Plt					
N (%)	1410	1402	1393	1422	1402
Mean PL (SD)	4.80 (0.37)	5.21 (0.05)	5.37 (0.04)	5.52 (0.05)	5.76 (0.15)
Univariable HR (95% CI)	4.18 (2.50 to 7.00)**	1.18 (0.63 to 2.22)	1.00 (ref)	1.18 (0.63 to 2.21)	1.38 (0.75 to 2.54)

ALT, alanine aminotransferase; SD, standard deviation; HR, hazards ratio; CI, confidence intervals;

AST, aspartate aminotransferase; Plt, platelets.

\*  $P < 0.05$

\*\*  $P < 0.01$

**Supplementary Table 5. Missingness in CHB data in QResearch cohort of adults according to cohort characteristics.**

<b>Characteristic</b>	<b>Missingness, n (%)</b>
Age	0 (0%)
Sex	0 (0%)
Townsend Deprivation Quintile	22 (0.3%)
Ethnicity	1289 (16.0%)
Alcohol consumption	3527 (43.9%)
Cigarette consumption	2287 (28.5%)
BMI	3111 (38.7%)
ALT	3497 (43.5%)
AST	6370 (79.2%)
Plt	3217 (40.0%)
HBsAg	7964 (99.1%)
VL	7656 (95.2%)

BMI, body mass index; ALT, alanine transaminase; AST, aspartate transaminase; Plt, platelets; HBsAg, hepatitis B virus surface antigen; VL, hepatitis B DNA viral load.

**Supplementary Table 6. Details of main and sensitivity analyses performed to investigate risk factors for hepatocellular carcinoma in QResearch cohort of adults with chronic hepatitis B virus (CHB) infection.**

<b>Analysis</b>	<b>Main or sensitivity</b>	<b>Variables included</b>	<b>Corresponding table(s)/figure</b>
Cox proportional hazards model on imputed dataset	Main	Age, Alcohol consumption, Antidiabetic drug use, Antihypertensive use, Antiviral treatment, ARLD, Ascites, BMI, Cerebrovascular disease, CHF, Cigarette consumption, Cirrhosis, CKD, ESLD, Ethnicity, Hypertension, IHD, NAFLD, Non-HCC neoplasm; NSAID use, Peptic ulcer, Sex, Statin use, T2DM, Townsend deprivation quintile,	Figure 1, Supplementary table 8
Cox proportional hazards model on complete-case dataset	Sensitivity	Age, Alcohol consumption, Antidiabetic drug use, Antihypertensive use, Antiviral treatment, ARLD, Ascites, BMI, Cerebrovascular disease, CHF, Cigarette consumption, Cirrhosis, CKD, ESLD, Ethnicity, Hypertension, IHD, NAFLD, Non-HCC neoplasm; NSAID use, Peptic ulcer, Sex, Statin use, T2DM, Townsend deprivation quintile,	Supplementary table 10
Cox proportional hazards model on imputed	Sensitivity	Age, Alcohol consumption, Antidiabetic drug use,	Supplementary table 8



dataset whereby individuals with history of non-HCC neoplasm were excluded		Antihypertensive use, Antiviral treatment, ARLD, Ascites, BMI, Cerebrovascular disease, CHF, Cigarette consumption, Cirrhosis, CKD, ESLD, Ethnicity, Hypertension, IHD, NAFLD, NSAID use, Peptic ulcer, Sex, Statin use, T2DM, Townsend deprivation quintile,	
Cox proportional hazards model on imputed dataset with AST, ALT and Plt additionally added to model	Sensitivity	Age, Alcohol consumption, ALT, Antidiabetic drug use, Antihypertensive use, Antiviral treatment, ARLD, Ascites, AST, BMI, Cerebrovascular disease, CHF, Cigarette consumption, Cirrhosis, CKD, ESLD, Ethnicity, Hypertension, IHD, NAFLD, Non-HCC neoplasm; NSAID use, Peptic ulcer, Plt, Sex, Statin use, T2DM, Townsend deprivation quintile,	Supplementary table 8

BMI, body mass index; T2DM, type 2 diabetes mellitus; CHF, congestive heart failure; CKD, chronic kidney disease; IHD, ischaemic heart disease; ARLD, alcohol-related liver disease; ESLD, end-stage liver disease; NAFLD, non-alcoholic fatty liver disease; NSAID, non-steroidal anti-inflammatory drug; AST, aspartate transaminase; ALT, alanine transaminase; Plt, platelets.

**Supplementary Table 7. Tabulation of non-hepatocellular neoplasms in the CHB cohort, overall and stratified by hepatocellular carcinoma (HCC) status.**

Type of Non-HCC neoplasm, n (%)	Overall	Individuals not experiencing HCC	Individuals with HCC
Total	381 (4.7 %)	345 (4.4%)	36 (17.1%)
Bone, connective tissue, skin and breast	124 (1.5%)	115 (1.5%)	9 (4.3%)
Digestive organs and peritoneum	44 (0.5%)	31 (0.4%)	13 (6.2%)
Eye, brain, meninges and other parts of the CNS	<5	<5	<5
Genitourinary organs	91 (1.1%)	81 (1.0%)	10 (4.8%)
Lip, oral cavity and pharynx	16 (0.2%)	16 (0.2%)	<5
Lymphatic and haemopoietic tissue	81 (1.0%)	79 (1.0%)	<5
Respiratory tract and intrathoracic organs	13 (0.2%)	11 (0.1%)	<5
Thyroid gland and other endocrine gland structures	8 (0.1%)	8 (0.1%)	<5

HCC, hepatocellular carcinoma; CNS, central nervous system.

**Supplementary Table 8. Baseline characteristics of complete-case and imputed (by multiple imputation with chained equations) datasets used in Cox proportional hazards models.**

Characteristic	Complete-case dataset, n (%)	Imputed dataset, n (%)
N	3648	7029*
HCC cases, n (%)	68 (1.9%)	161 (2.3%)
Age group, n (%)		
18-25 years	292 (8.0)	659 (9.4)
26-35 years	1253 (34.3)	2500 (35.6)
36-45 years	1126 (30.9)	2108 (30.0)
46-55 years	593 (16.3)	1086 (15.5)
56-65 years	270 (7.4)	468 (6.7)
≥66 years	114 (3.1)	208 (3.0)
Sex, n (%)		
Male	2082 (57.1)	4186 (59.6)
Townsend Deprivation Quintile, n (%)		
First (least deprived)	174 (4.8)	419 (6.0)
Second	261 (7.2)	645 (9.2)
Third	523 (14.3)	1094 (15.6)
Fourth	924 (25.3)	1781 (25.3)
Fifth (most deprived)	1766 (48.4)	3090 (44.0)
Ethnicity, n (%)		
Black African	956 (26.2)	1772 (25.2)
Bangladeshi	213 (5.8)	322 (4.6)
Caribbean	58 (1.6)	112 (1.6)
Chinese	428 (11.7)	894 (12.7)
Indian	131 (3.6)	224 (3.2)
Other	441 (12.1)	863 (12.3)
Other Asian	194 (5.3)	397 (5.6)
Pakistani	241 (6.6)	420 (6.0)
White	986 (27.0)	2025 (28.8)
Cigarette consumption, n (%)		
Non-smoker	2484 (68.1)	4661 (66.3)
Ex-smoker	480 (13.2)	924 (13.1)

Characteristic	Complete-case dataset, n (%)	Imputed dataset, n (%)
Light smoker (1-9 cigarettes/day)	531 (14.6)	1110 (15.8)
Moderate to heavy smoker (≥10 cigarettes per day)	153 (4.2)	334 (4.8)
Alcohol consumption, n (%)		
Non-drinker	3013 (82.6)	5784 (82.3)
Trivial drinker (<1 unit per day)	371 (10.2)	737 (10.5)
Light drinker (1-2 units per day)	170 (4.7)	318 (4.5)
Moderate to heavy drinker (≥3 units per day)	94 (2.6)	190 (2.7)
BMI (kg/m <sup>2</sup> ), mean (SD)	26.14 (5.07)	26.05 (5.02)
BMI, n (%)		
Underweight (<18.5 kg/m <sup>2</sup> )	113 (3.1)	222 (3.2)
Normal weight (18.5-24.9 kg/m <sup>2</sup> )	1530 (41.9)	2948 (41.9)
Overweight (25.0-29.9 kg/m <sup>2</sup> )	1292 (35.4)	2527 (36.0)
Obese (≥30 kg/m <sup>2</sup> )	713 (19.5)	1332 (19.0)
Antiviral initiation, n (%)		
No initiation	3168 (86.8)	6092 (86.7)
Before CHB diagnosis	67 (1.8)	121 (1.7)
Within 1 year of CHB diagnosis	116 (3.2)	214 (3.0)
Within 1-2 years of CHB diagnosis	73 (2.0)	120 (1.7)
Within 2-3 years of CHB diagnosis	49 (1.3)	78 (1.1)
≥4 years after CHB diagnosis	175 (4.8)	404 (5.7)
Type 2 DM, n (%)	503 (13.8)	678 (9.6)

Characteristic	Complete-case dataset, n (%)	Imputed dataset, n (%)
Congestive heart failure, n (%)	41 (1.1)	71 (1.0)
Hypertension, n (%)	754 (20.7)	1165 (16.6)
Chronic kidney disease, n (%)	175 (4.8)	271 (3.9)
Alcohol-related liver disease, n (%)	39 (1.1)	74 (1.1)
Ascites, n (%)	34 (0.9)	88 (1.3)
Autoimmune hepatitis, n (%)	3 (0.1)	9 (0.1)
Cerebrovascular disease, n (%)	181 (5.0)	290 (4.1)
Cirrhosis, n (%)	301 (8.3)	608 (8.6)
End-stage liver disease, n (%)	28 (0.8)	78 (1.1)
Ischaemic heart disease, n (%)	143 (3.9)	229 (3.3)
Non-alcoholic fatty liver disease, n (%)	248 (6.8)	393 (5.6)
Non-HCC neoplasm, n (%)	167 (4.6)	340 (4.8)
Peptic ulcer, n (%)	113 (3.1)	221 (3.1)
Antidiabetic drug use, n (%)	495 (13.6)	689 (9.8)
Antihypertensive use, n (%)	293 (8.0)	389 (5.5)
NSAID use, n (%)	331 (9.1)	446 (6.3)
Statin use, n (%)	342 (9.4)	443 (6.3)

CHB, chronic hepatitis B virus infection; ICD, International classification of disease; SNOMED, Systemised Nomenclature of Medicine; IQR, interquartile range; SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; HCC, hepatocellular carcinoma; NSAID, non-steroidal anti-inflammatory drug.

**Supplementary Table 9. Sensitivity analysis using Cox proportional hazards modelling and propensity scoring for antiviral therapy to interrogate the association of antiviral therapy with increased hazards of hepatocellular carcinoma observed in main results.** Two models to investigate how the association of antiviral therapy with HCC risk changed before and after the addition of the propensity score.

Characteristic	Propensity score not included, HR (95% CI)	Propensity score included, HR (95% CI)
Cigarette consumption, n (%)		
Non-smoker	1.00 (ref)	1.00 (ref)
Ex-smoker	1.1 (0.7 to 1.74)	1.04 (0.65 to 1.64)
Light smoker (1-9 cigarettes/day)	1.39 (0.94 to 2.05)	1.41 (0.96 to 2.09)
Moderate to heavy smoker ( $\geq 10$ cigarettes per day)	1.67 (0.89 to 3.14)	1.75 (0.92 to 3.34)
Alcohol consumption, n (%)		
Non-drinker	1.00 (ref)	1.00 (ref)
Trivial drinker ( $< 1$ unit per day)	1.3 (0.81 to 2.09)	1.3 (0.8 to 2.09)
Light drinker (1-2 units per day)	0.81 (0.33 to 1.98)	0.77 (0.31 to 1.9)
Moderate to heavy drinker ( $\geq 3$ units per day)	2.07 (1 to 4.28)*	1.83 (0.87 to 3.82)
Antiviral initiation, n (%)		
No initiation	1.00 (ref)	1.00 (ref)
Initiation during study	1.79 (1.27 to 2.52)***	1.05 (0.73 to 1.51)
Chronic kidney disease, n (%)	1.68 (1.03 to 2.72)*	1.23 (0.77 to 1.98)
Ascites, n (%)	5.69 (3.37 to 9.61)***	1.77 (1.02 to 3.06)*
Any cardiovascular disease <sup>†</sup>	2.15 (1.51 to 3.06)***	1.86 (1.32 to 2.63)***
Non-HCC neoplasm, n (%)	1.18 (0.72 to 1.92)	1.2 (0.74 to 1.95)
Peptic ulcer, n (%)	2.85 (1.86 to 4.38)***	1.86 (1.19 to 2.9)**
Antidiabetic drug use, n (%)	3.94 (2.07 to 7.53)***	1.94 (0.99 to 3.8)
Antihypertensive use, n (%)	0.68 (0.32 to 1.44)	0.55 (0.25 to 1.19)
NSAID use, n (%)	0.66 (0.34 to 1.29)	0.89 (0.46 to 1.75)
Statin use, n (%)	0.45 (0.22 to 0.92)*	0.49 (0.23 to 1.02)

HR, hazards ratio; CHB, chronic hepatitis B virus infection; CI, confidence interval;; NSAID, non-steroidal anti-x drug.

\*  $P < 0.05$

\*\*  $P < 0.01$

† Includes congestive heart failure, hypertension, cerebrovascular disease and ischaemic heart disease.

**Supplementary Table 10. Cox proportional hazards complete-case model conducted on adults with hepatitis B virus infection for whom data was complete in the original QResearch dataset (n = 3648, HCC cases = 68).**

Characteristic	Univariable HR (95% CI)	Multivariable HR (95% CI)	Multivariable HR (95% CI) †
Age group, n (%)			
18-25 years	0.85 (0.19 to 3.88)	1.7 (0.35 to 8.26)	1.98 (0.4 to 9.91)
26-35 years	1.00 (ref)	1.00 (ref)	1.00 (ref)
36-45 years	1.59 (0.72 to 3.51)	1.44 (0.61 to 3.37)	1.46 (0.61 to 3.48)
46-55 years	3.14 (1.43 to 6.85)**	2.4 (0.99 to 5.82)	1.91 (0.75 to 4.85)
56-65 years	6.84 (3.13 to 14.97)**	3.24 (1.23 to 8.53)**	3.89 (1.43 to 10.61)**
≥66 years	5.47 (1.98 to 15.14)**	2.41 (0.7 to 8.37)	1.7 (0.37 to 7.73)
Sex, n (%)			
Female	1.00 (ref)	1.00 (ref)	1.00 (ref)
Male	5.50 (2.63 to 11.50)**	3.35 (1.42 to 7.88)**	3.49 (1.35 to 8.99)**
Townsend Deprivation Quintile, n (%)			
First (least deprived)	3.12 (0.95 to 10.24)	3.6 (1 to 12.99)	3.95 (0.9 to 17.35)
Second	1.91 (0.55 to 6.61)	2.47 (0.63 to 9.74)	1.32 (0.27 to 6.54)
Third	1.00 (ref)	1.00 (ref)	1.00 (ref)
Fourth	1.74 (0.63 to 4.79)	1.69 (0.57 to 5.02)	1.78 (0.55 to 5.74)
Fifth (most deprived)	2.18 (0.86 to 5.56)	2.34 (0.84 to 6.53)	2.75 (0.92 to 8.16)
Ethnicity, n (%)			
White	1.00 (ref)	1.00 (ref)	1.00 (ref)
Black African	1.14 (0.58 to 2.24)	2.37 (0.96 to 5.81)	2.95 (1.13 to 7.73)*
Bangladeshi	2.16 (0.92 to 5.05)	1.77 (0.63 to 4.96)	1.88 (0.64 to 5.55)
Caribbean	1.91 (0.44 to 8.32)	3.32 (0.59 to 18.6)	8.31 (1.59 to 43.59)*
Chinese	0.68 (0.25 to 1.85)	1.3 (0.42 to 4.02)	2 (0.6 to 6.6)
Indian	2.52 (0.92 to 6.88)	5.19 (1.57 to 17.09)**	7.23 (1.98 to 26.49)*
Other	1.14 (0.49 to 2.66)	2.18 (0.8 to 5.92)	1.41 (0.43 to 4.67)
Other Asian	0.6 (0.14 to 2.63)	1.41 (0.28 to 7.03)	1.49 (0.28 to 8.1)
Pakistani	0.86 (0.29 to 2.57)	1.87 (0.53 to 6.61)	1.82 (0.48 to 6.84)
Cigarette consumption, n (%)			
Non-smoker	1.00 (ref)	1.00 (ref)	1.00 (ref)
Ex-smoker	1.57 (0.77 to 3.17)	1.1 (0.51 to 2.39)	1.56 (0.68 to 3.56)
Light smoker (1-9 cigarettes/day)	2.91 (1.68 to 5.06)**	2.29 (1.15 to 4.57)*	3.28 (1.54 to 6.97)**
Moderate to heavy smoker (≥10 cigarettes per day)	1.96 (0.70 to 5.53)	2.92 (0.92 to 9.29)	3.52 (1.06 to 11.67)*
Alcohol consumption, n (%)			
Non-drinker	1.00 (ref)	1.00 (ref)	1.00 (ref)
Trivial drinker (<1 unit per day)	1.17 (0.56 to 2.45)	1.79 (0.79 to 4.02)	1.48 (0.59 to 3.71)
Light drinker (1-2 units per day)	0.66 (0.16 to 2.71)	0.45 (0.1 to 2.13)	0.6 (0.13 to 2.78)

Moderate to heavy drinker (≥3 units per day)	1.25 (0.31 to 5.14)	0.46 (0.09 to 2.3)	1.15 (0.22 to 5.93)
BMI, n (%)			
Underweight (<18.5 kg/m <sup>2</sup> )	0.42 (0.06 to 3.11)	0.95 (0.12 to 7.78)	1.74 (0.21 to 14.22)
Normal weight (18.5-24.9 kg/m <sup>2</sup> )	1.00 (ref)	1.00 (ref)	1.00 (ref)
Overweight (25.0-29.9 kg/m <sup>2</sup> )	0.92 (0.55 to 1.55)	1 (0.57 to 1.77)	1.17 (0.62 to 2.18)
Obese (≥30 kg/m <sup>2</sup> )	0.54 (0.26 to 1.15)	0.68 (0.29 to 1.63)	0.9 (0.36 to 2.25)
Antiviral initiation, n (%)			
No initiation	1.00 (ref)	1.00 (ref)	1.00 (ref)
Before CHB diagnosis	3.29 (1.01 to 10.68)*	1.78 (0.45 to 6.97)	2.87 (0.71 to 11.65)
Within 1 year of CHB diagnosis	5.11 (2.45 to 10.66)**	2.32 (1 to 5.38)	1.84 (0.74 to 4.59)
Within 1-2 years of CHB diagnosis	4.04 (1.57 to 10.39)**	1.46 (0.5 to 4.26)	1.51 (0.51 to 4.44)
Within 2-3 years of CHB diagnosis	6.03 (2.36 to 15.37)**	2.36 (0.82 to 6.81)	2.26 (0.7 to 7.35)
≥4 years after CHB diagnosis	1.95 (0.90 to 4.23)	0.92 (0.4 to 2.1)	0.67 (0.24 to 1.87)
Type 2 DM, n (%)	3.26 (1.96 to 5.42)**	2.5 (0.75 to 8.34)	1.74 (0.42 to 7.32)
Congestive heart failure, n (%)	1.06 (0.15 to 7.70)	0.22 (0.03 to 1.92)	0.19 (0.02 to 1.82)
Hypertension, n (%)	2.29 (1.41 to 3.73)	1.05 (0.56 to 1.96)	1.11 (0.56 to 2.21)
Chronic kidney disease, n (%)	5.48 (3.14 to 9.53)**	3.32 (1.65 to 6.70)**	3.11 (1.43 to 6.79)**
Alcohol-related liver disease, n (%)	5.79 (2.50 to 13.42)**	1.51 (0.49 to 4.64)	1.18 (0.37 to 3.72)
Ascites, n (%)	18.11 (8.63 to 37.99)**	1.81 (0.69 to 4.74)	1.51 (0.55 to 4.17)
Cerebrovascular disease, n (%)	2.35 (1.16 to 4.76)*	1.08 (0.37 to 3.20)**	1.48 (0.46 to 4.72)
Cirrhosis, n (%)	17.12 (10.37 to 28.25)**	8.79 (4.85 to 15.93)**	11.54 (5.95 to 22.39)**
End-stage liver disease, n (%)	9.28 (3.71 to 23.20)**	1.52 (0.46 to 5.09)	1.73 (0.46 to 6.51)
Ischaemic heart disease, n (%)	1.76 (0.75 to 4.10)	0.37 (0.1 to 1.4)	0.31 (0.07 to 1.33)
Non-alcoholic fatty liver disease, n (%)	0.60 (0.19 to 1.91)	0.56 (0.16 to 1.93)	0.63 (0.18 to 2.2)
Non-HCC neoplasm, n (%)	2.49 (1.19 to 5.22)*	1.23 (0.5 to 3.03)	--
Peptic ulcer, n (%)	4.21 (2.18 to 8.13)**	2.20 (1.03 to 4.70)*	3.07 (1.35 to 7)**
Antidiabetic drug use, n (%)	3.02 (1.82 to 4.99)**	1.43 (0.37 to 5.56)	1.47 (0.31 to 6.95)
Antihypertensive use, n (%)	2.56 (1.42 to 4.62)**	0.6 (0.2 to 1.78)	0.62 (0.18 to 2.17)
NSAID use, n (%)	1.98 (1.08 to 3.64)*	0.81 (0.32 to 2.09)	0.88 (0.31 to 2.53)
Statin use, n (%)	1.81 (0.97 to 3.38)	0.67 (0.25 to 1.81)	0.93 (0.29 to 2.98)

HR, hazard ratio; CHB, chronic hepatitis B virus infection; ICD, International classification of disease; SNOMED, Systemised Nomenclature of Medicine; SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; HCC, hepatocellular carcinoma; NSAID, non-steroidal anti-inflammatory drug.

\*  $P < 0.05$ , \*\*  $P < 0.01$

† Patients with history of any non-hepatocellular carcinoma neoplasm excluded