

Supplementary Table 1. Prevalence of clinical conditions stratified by hepatitis delta virus status

Variable	Total patients with HDV laboratory testing N = 5,388	HDV N = 294	No HDV N = 5094	p-value¶
Clinical comorbidities				
Hypertension	1738 (32.3)	102 (34.7)	1636 (32.1)	0.36
Hyperlipidemia	1559 (28.9)	68 (23.1)	1491 (29.3)	0.02
Cardiovascular disease	2 (0.04)	0 (0)	2 (0.04)	0.73
Diabetes	921 (17.1)	48 (16.3)	873 (17.1)	0.72
Metabolic syndrome	53 (0.98)	3 (1.0)	50 (0.98)	0.95
Obesity	616 (11.4)	35 (11.9)	581 (11.4)	0.79
Chronic kidney disease	671 (12.5)	35 (11.9)	636 (12.5)	0.77
Autoimmune diagnoses				
General autoimmune disease	2 (0.04)	1 (0.3)	1 (0.02)	0.11
Systemic lupus erythematosus	27 (0.5)	0 (0.0)	27 (0.5)	0.40
Rheumatoid arthritis	3 (0.06)	1 (0.34)	2 (0.04)	0.16
Autoimmune thyroid disease	402 (7.5)	22 (7.5)	380 (7.5)	0.99
Autoimmune hepatitis	31 (0.6)	5 (1.7)	26 (0.5)	0.02
Sjögren's syndrome	25 (0.46)	0 (0)	25 (0.5)	0.40
Scleroderma	7 (0.1)	0 (0)	7 (0.1)	1.0
Primary biliary cholangitis	31 (0.58)	6 (2.0)	25 (0.49)	0.006
Primary sclerosing cholangitis	16 (0.3)	2 (0.68)	14 (0.27)	0.21
Malignancies				
Lung cancer	57 (1.1)	5 (1.7)	52 (1.0)	0.20
Prostate cancer	73 (1.4)	5 (1.7)	68 (1.3)	0.60
Breast cancer	79 (1.5)	5 (1.7)	74 (1.5)	0.62
Colon cancer	40 (0.7)	1 (0.3)	39 (0.8)	0.72
Bladder cancer	12 (0.2)	1 (0.3)	11 (0.2)	0.49
Hodgkin lymphoma	10 (0.2)	0 (0)	10 (0.2)	1.0
Non-Hodgkin lymphoma	79 (1.5)	6 (2.0)	73 (1.4)	0.40
Waldenström macroglobulinemia	3 (0.06)	0 (0)	3 (0.1)	1.0
Chronic lymphocytic leukemia	34 (0.63)	2 (0.68)	32 (0.63)	0.71
Thyroid cancer	39 (0.7)	6 (2.0)	33 (0.65)	0.006
Pancreatic cancer	22 (0.4)	0 (0)	22 (0.4)	0.63
Ovarian cancer	8 (0.2)	0 (0.0)	8 (0.2)	1.0

¶Two-sided t-tests were performed without adjustment for multiple comparisons

Statistically significant p-values (<0.05) are denoted in bold

Abbreviation: HDV, hepatitis delta virus.

Supplementary Table 2. Prevalence of liver-related disease and laboratory outcomes stratified by hepatitis delta virus status

	Total patients with HDV laboratory testing N = 5,388	HDV N = 294	No HDV N = 5,093	p-value¶
Liver-related disease outcomes				
Hepatic fibrosis	366 (6.8%)	27 (9.2%)	339 (6.7%)	0.09
Cirrhosis	983 (18.2%)	117 (39.8%)	866 (17.0%)	<0.0001
Jaundice	253 (4.7%)	17 (5.8%)	236 (4.6%)	0.37
Ascites	539 (10.0%)	76 (25.9%)	463 (9.1%)	<0.0001
Esophageal varices	314 (5.8%)	48 (16.3%)	266 (5.2%)	<0.0001
Gastric varices	75 (1.4%)	9 (3.1%)	66 (1.3%)	0.01
HE	118 (2.2%)	15 (5.1%)	103 (2.0%)	0.0005
Spontaneous bacterial peritonitis	77 (1.5%)	9 (3.1%)	68 (1.4%)	0.02
Hepatorenal syndrome	72 (1.3%)	8 (2.7%)	64 (1.3%)	0.03
Portal hypertension	402 (7.5%)	60 (20.4%)	342 (6.7%)	<0.0001
PVT	130 (2.5%)	15 (5.1%)	115 (2.3%)	0.002
Fatty liver	1,048 (19.5%)	51 (17.4%)	997 (19.6%)	0.35
Liver failure	407 (7.6%)	48 (16.3%)	359 (7.1%)	<0.0001
HCC	487 (9.0%)	52 (17.7%)	435 (8.5%)	<0.0001
Liver transplant	251 (4.7%)	39 (13.3%)	212 (4.2%)	<0.0001
Liver transplant complications	149 (2.8%)	23 (7.8%)	126 (2.5%)	<0.0001
Liver-related laboratory outcomes				
Peak ALT (median, IQR)	50 (30, 120)	88 (39.5, 221.5)	48 (29, 116)	<0.0001
Peak AST (median, IQR)	40 (27, 101)	69 (32, 199)	39 (27, 94)	<0.0001
Peak total bilirubin (median, IQR)	0.9 (0.6, 1.5)	1.2 (0.8, 2.7)	0.9 (0.6, 1.5)	<0.0001
Peak international normalized ratio (median, IQR)	1.1 (1.0, 1.4)	1.1 (1.0, 1.4)	1.1 (1.0, 1.4)	0.53
Peak alkaline phosphatase (median, IQR)	94 (71, 146)	111 (79, 195)	93 (71, 143)	<0.0001
Peak gamma glutamyl transferase (median, IQR)	33 (19, 85)	66 (27, 195)	32 (19, 79)	<0.0001
Peak alpha fetoprotein (median, IQR)	3.1 (2.0, 6.1)	3.9 (2.1, 18.3)	3.1 (2.0, 6.0)	0.07
Minimum platelets (median, IQR)	170 (113, 213)	127 (64, 189)	172 (117, 214)	<0.0001
Minimum hemoglobin (median, IQR)	14.7 (13.6, 15.8)	14.8 (13.7, 15.9)	14.7 (13.6, 15.8)	0.28
Minimum albumin (median, IQR)	4.6 (4.3, 4.8)	4.5 (4.1, 4.8)	4.6 (4.3, 4.8)	0.12
FIB-4 index* (median, IQR)	1.6 (0.9, 4.5)	3.2 (1.2, 11.3)	1.51 (0.91, 4.13)	<0.0001
FIB-4 index* (mean, SD)	13.3 (86.5)	20.0 (52.6)	12.9 (88.1)	<0.0001

¶Two-sided t-tests were performed without adjustment for multiple comparisons

*Based on maximum ALT, maximum AST, minimum platelets, and age at cohort entry

Statistically significant p-values (<0.05) are denoted in bold

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; HCC, hepatocellular carcinoma; HDV, hepatitis delta virus; HE, hepatic encephalopathy; IQR, interquartile range; PVT, portal vein thrombosis; SD, standard deviation.

Supplementary Table 3. Sensitivity analysis for associations with liver-related outcomes in patients with laboratory evidence of hepatitis B and hepatitis delta virus (N=1,466)

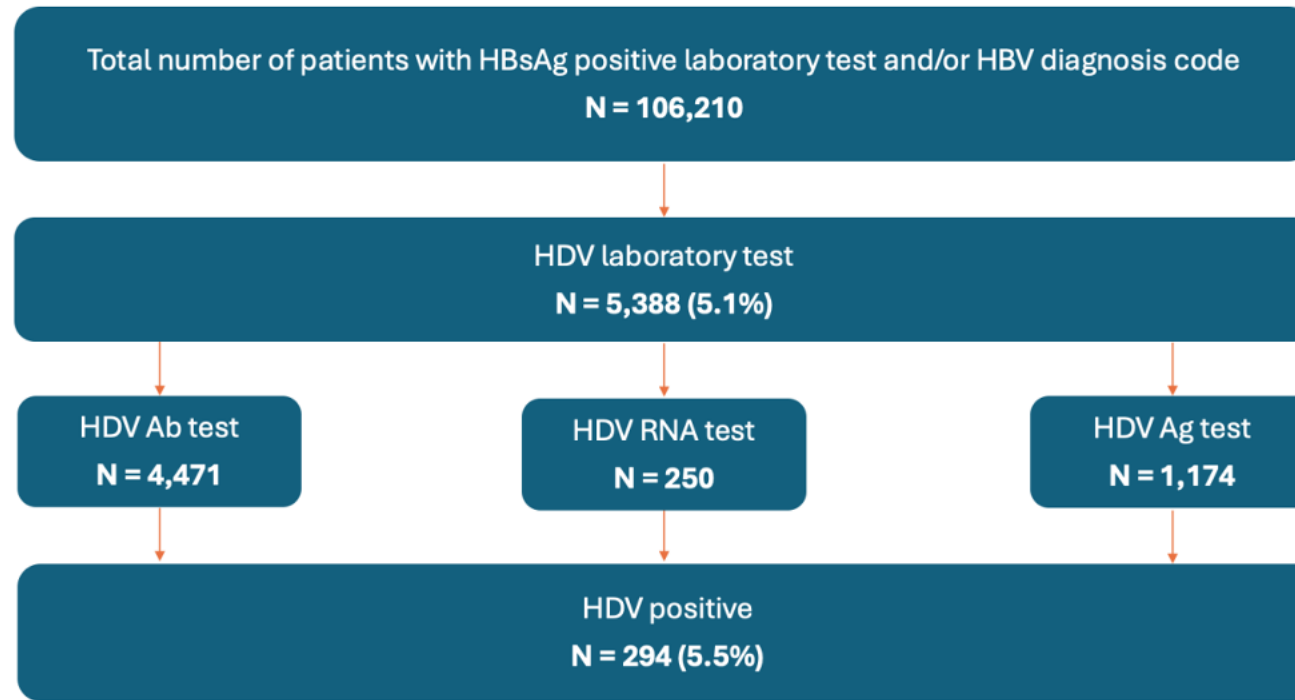
	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)
Hepatic fibrosis	1.05 (0.49, 2.27)	0.98 (0.45, 2.13)
Cirrhosis	1.48 (0.72, 3.05)	1.24 (0.60, 2.55)
HCC	1.02 (0.37, 2.80)	0.87 (0.31, 2.42)
Liver failure	2.28 (1.08, 4.80)	1.87 (0.88, 3.98)
Liver transplantation	2.72 (1.29, 5.78)	2.08 (0.97, 4.43)
Liver transplantation complications	0.97 (0.43, 2.20)	1.01 (0.42, 2.42)

*Adjusted for age, sex, race, and liver-related comorbidities (i.e., fatty liver and hepatitis C virus)

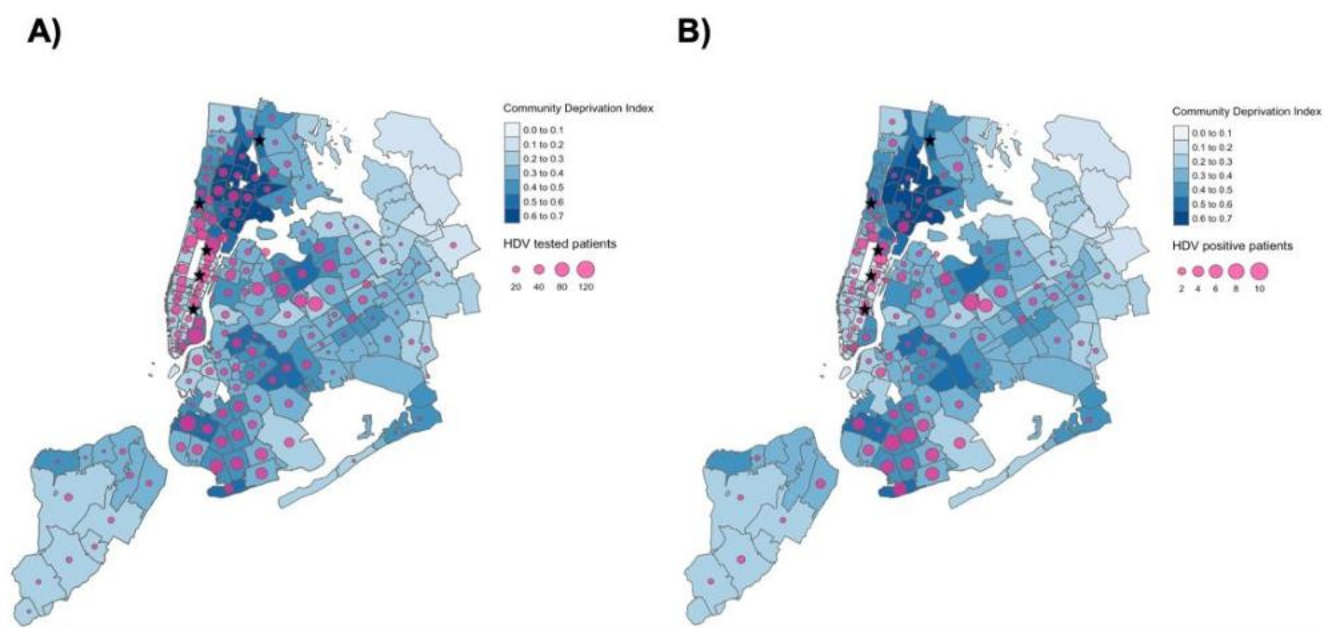
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Abbreviations: CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio.

Supplementary Figure 1.

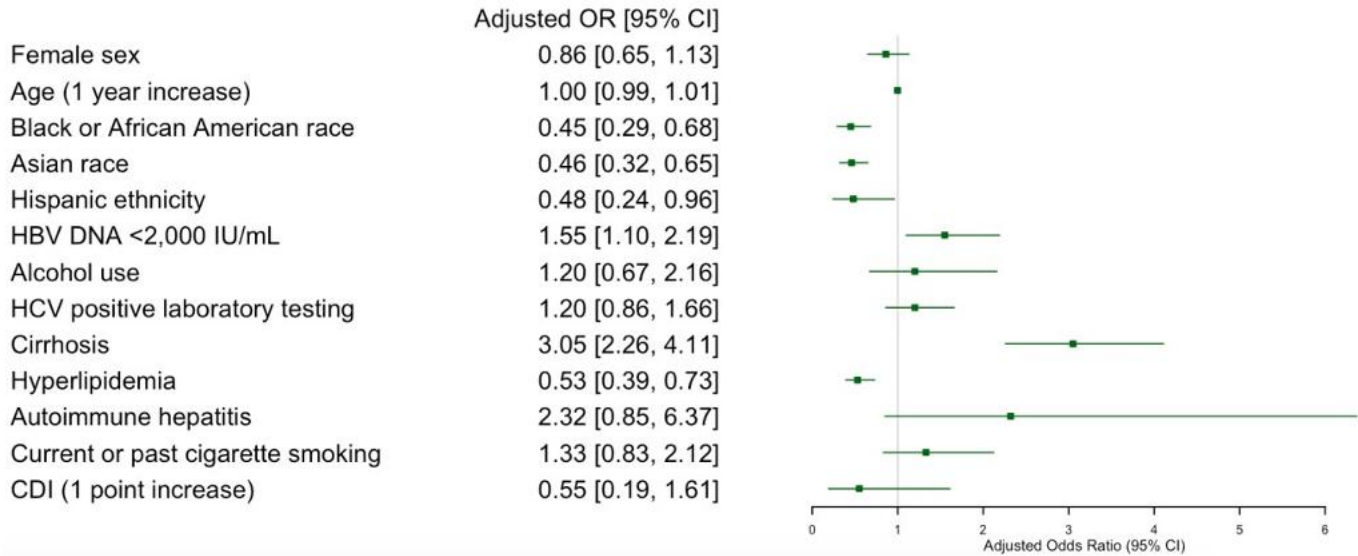


Supplementary Figure 2.



Supplementary Figure 3.

Forest Plot of Adjusted Odds Ratios



Supplementary Figure 4.

