

Hospitalised Adults With Hepatitis Delta Virus Infection Have a Higher Risk of Disease Progression Than Those With Hepatitis B Virus Mono-infection in Italy

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Conclusions

- Among hospitalised patients in Italy, patients with hepatitis delta virus infection were more likely to progress towards greater liver disease severity than those with hepatitis B virus only
 - Noncirrhotic disease (NCD) → compensated cirrhosis (CC): hazard ratio (HR; 95% CI) = 1.451 (1.044, 2.016)
 - CC → decompensated cirrhosis (DC), liver transplant (LT), or death: HR (95% CI) = 3.502 (1.563, 7.843); 9.022 (2.114, 38.497); 1.697 (1.025, 2.808), respectively
 - DC → hepatocellular carcinoma (HCC) or LT: HR (95% CI) = 2.804 (1.158, 6.790); 4.975 (2.109, 11.736), respectively
 - HCC → LT: HR (95% CI) = 6.858 (2.594, 18.131)

Plain Language Summary

- In an inpatient setting, people living with hepatitis delta virus have a higher risk of progressing to greater liver disease severity than do patients living with hepatitis B virus only

Introduction

- Hepatitis delta virus (HDV), which requires hepatitis B virus (HBV) for its replication, causes a more severe form of viral hepatitis than HBV mono-infection (HBV only)¹
- HDV infection carries a greater risk of morbidity and mortality compared to HBV only²

Objective

- In this retrospective analysis, rates of disease progression were compared between patients with HDV infection and those with HBV only among hospitalised adults in Italy

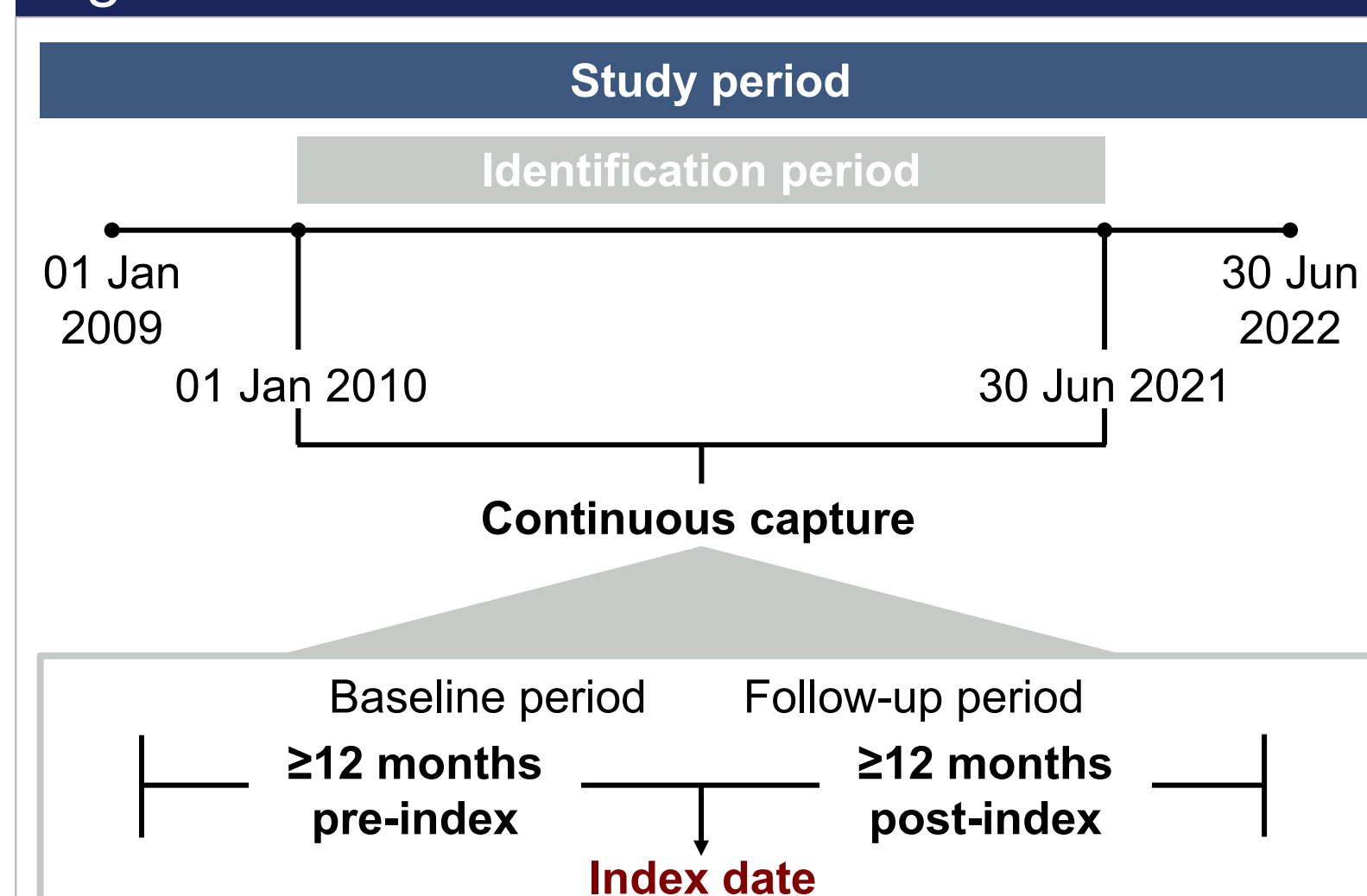
Methods

- In Italy, data from healthcare resources and services reimbursed by the National Health System are maintained in administrative databases from local health units covering approximately 12 million individuals
- **Study period:** Adult patients with ≥1 HBV or HDV hospitalisation discharge diagnosis (ICD-9-CM) between 1 Jan 2009 and 30 Jun 2022
- **Identification period**
 - HBV only cohort: HBV only diagnosis between 1 Jan 2010 and 30 Jun 2021
 - No diagnosis claim for HBV/HDV coinfection
 - ≥18 years of age as of the index date (date of first diagnosis)
 - ≥12 months of continuous capture before and after index diagnosis
 - HDV cohort: HDV infection diagnosis between 1 Jan 2010 and 30 Jun 2021
 - ≥18 years of age as of the index date
 - ≥12 months of continuous capture before and after index diagnosis
 - Incident patients were defined as patients without any diagnosis (ICD-9-CM) for HDV (HDV cohort) or HBV (HBV cohort) before the date of inclusion in the study

Analysis

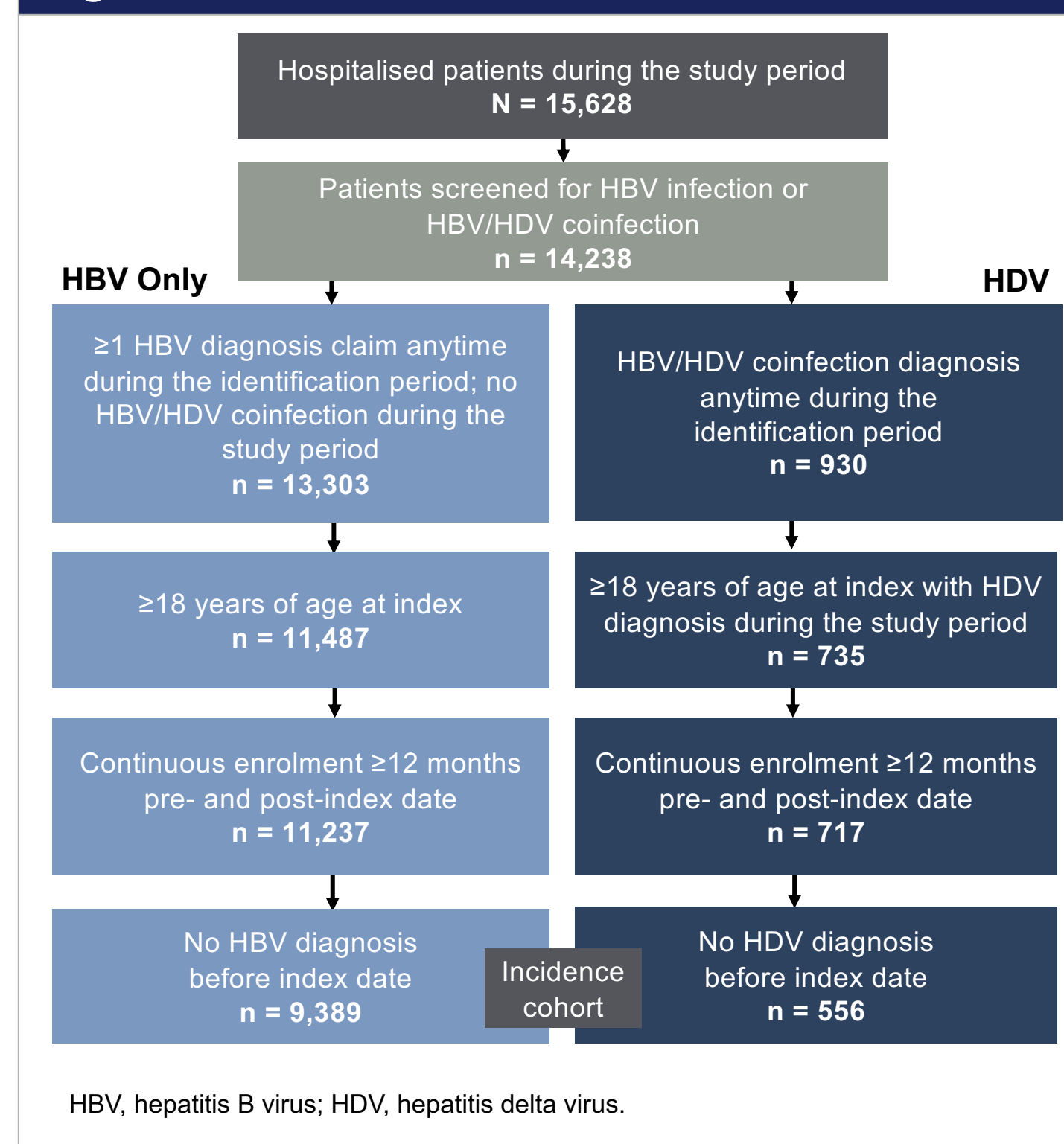
- Propensity scores were generated for patients with HBV only and HDV infection based on baseline demographics and clinical characteristics assessed 12 months prior to the index date
- Inverse probability of treatment weighting, based on propensity scores, was used to adjust for measured confounders between patients in the HBV only and HDV groups
- Cox proportional hazard regression was performed to compare the risk of disease progression from any of the disease states to a higher severity disease state, including liver transplant (LT) or death between cohorts

Figure 1 Patient Identification



Results

Figure 2 Patient Attrition Flow Chart



- Among 15,628 hospitalised patients, 14,238 were screened for HBV only and HDV infection
- Of 9,945 patients included, 9,389 were in the HBV only cohort and 556 were in the HDV cohort

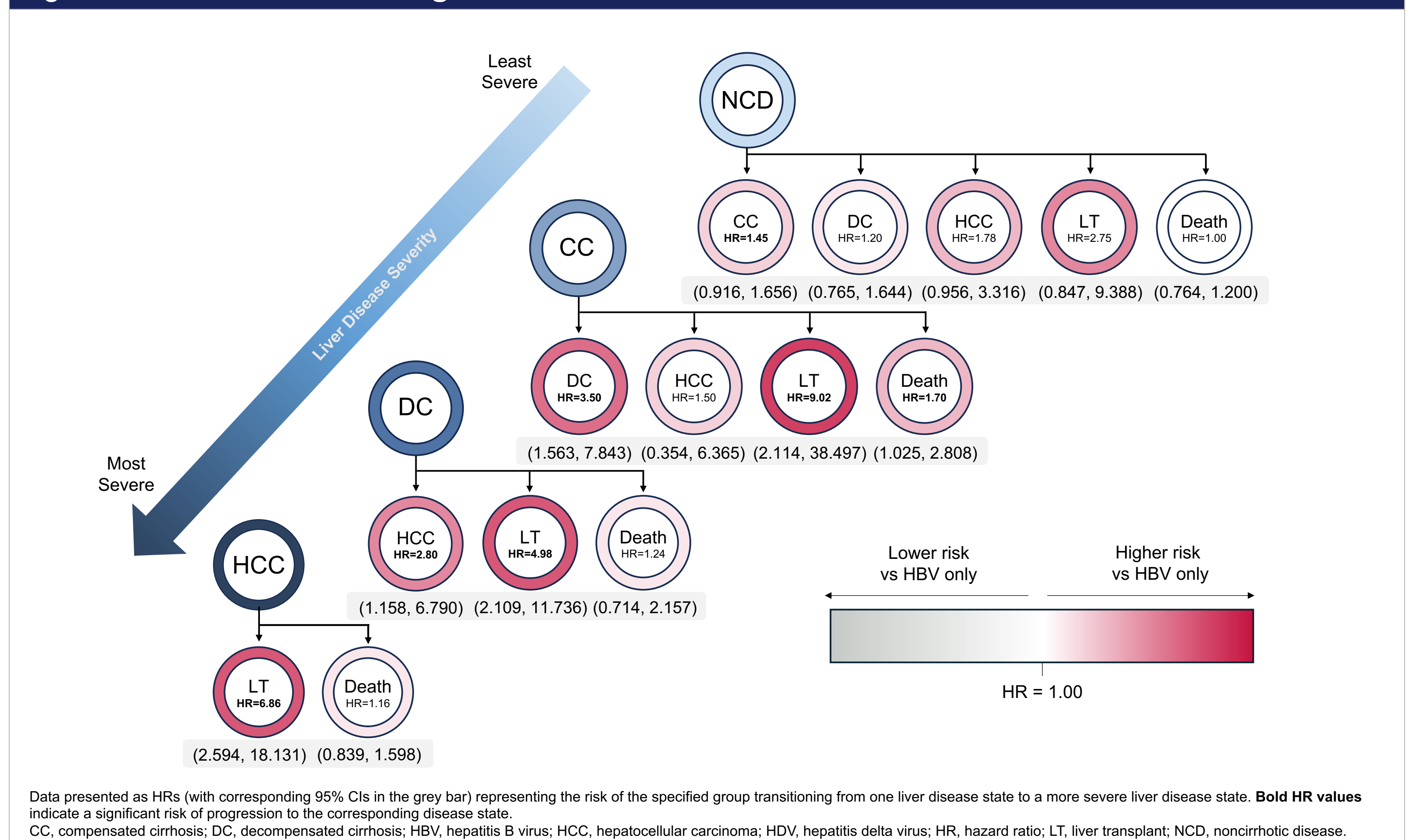
Table 1 Patient Characteristics

Baseline Variables	Before IPTW			After IPTW		
	HBV Only n = 9,389	HDV n = 556	P-Value	HBV Only n = 9,946	HDV n = 9,873	P-Value
Age, y, mean (SD)	56.8 (16.5)	55.8 (15.6)	.157	56.7 (16.4)	56.5 (16.3)	.763
Sex, male, n (%)	5,970 (63.6)	367 (66.0)	.248	6,339 (63.7)	6,449 (65.3)	.020
CCI, mean (SD)	1.2 (1.7)	1.3 (1.9)	.090	1.2 (1.7)	1.2 (1.8)	.856
Comorbidity profile, n (%)						
No cirrhosis	7,555 (80.5)	389 (70.0)	<.001	7,983 (80.3)	7,080 (71.7)	<.001
CC	1,081 (11.5)	109 (19.6)	<.001	1,158 (11.6)	1,900 (19.2)	<.001
DC	753 (8.0)	58 (10.4)	.043	805 (8.1)	893 (9.0)	.017
HCC	373 (4.0)	42 (7.6)	<.001	401 (4.0)	678 (6.9)	<.001
LT	72 (0.8)	27 (4.9)	<.001	78 (0.8)	591 (6.0)	<.001
STIs	48 (0.5)	<4 (NC)	NC	51 (0.5)	54 (0.5)	.740
Hypertension	3,948 (42.0)	247 (44.4)	.270	4,197 (42.2)	4,205 (42.6)	.576
History of smoking	21 (0.2)	<4 (NC)	NC	23 (0.2)	33 (0.3)	.172
HCV	672 (7.2)	160 (28.8)	<.001	833 (8.4)	860 (8.7)	.398
HIV	185 (2.0)	26 (4.7)	<.001	213 (2.1)	275 (2.8)	.003
Mental health disorder	1,472 (15.7)	91 (16.4)	.664	1,564 (15.7)	1,634 (16.6)	.114
Obesity	182 (1.9)	8 (1.4)	.403	190 (1.9)	165 (1.7)	.204
Substance abuse	140 (1.5)	11 (2.0)	.361	151 (1.5)	232 (2.3)	<.001
AA/AUD	294 (3.1)	23 (4.1)	.190	318 (3.2)	535 (5.4)	<.001
NASH	268 (2.9)	14 (2.5)	.642	282 (2.8)	222 (2.2)	.009

Data are reported as n (%) unless otherwise noted. **Bold P-values** indicate statistical significance. AAD, alcohol abuse and dependence; AUD, alcohol use disorder; CC, compensated cirrhosis; CCI, Charlson Comorbidity Index; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis delta virus; HIV, human immunodeficiency virus; IPTW, inverse probability of treatment weighting; LT, liver transplant; NC, not calculated; NASH, nonalcoholic steatohepatitis; STI, sexually transmitted infection; y, years.

- Patients were similar in age and Charlson Comorbidity Index severity between the HBV only and HDV groups

Figure 3 Risk of Transitioning From One Disease State to Another



Data presented as HRs (with corresponding 95% CIs in the grey bar) representing the risk of the specified group transitioning from one liver disease state to a more severe liver disease state. **Bold HR values** indicate a significant risk of progression to the corresponding disease state. CC, compensated cirrhosis; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HDV, hepatitis delta virus; HR, hazard ratio; LT, liver transplant; NCD, noncirrhotic disease.

- Compared to patients with HBV only, those with HDV were more likely to progress from NCD to CC; CC to DC, LT, or death; DC to HCC or LT; and HCC to LT

Limitations

- The limitations of any retrospective claims study apply. Diagnoses made via ICD-9-CM codes are subject to miscoding and can lead to misclassification bias, and time of diagnosis may not correspond to the time of infection
- There is a lack of approved assays, and screening practices to determine HDV and HBV status are suboptimal; thus, it is possible that the actual number of people with an HDV and/or HBV infection may be underestimated in this study
- Competing risk was not taken into account