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Poster for you

Baseline Characteristics and Risk of Liver-Related Events in Hepatitis B and C Coinfection With and Without Hepatitis Delta Infection

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Conclusions

- Among people with hepatitis B virus/hepatitis C virus coinfection, those with hepatitis delta virus (HDV) infection had more advanced liver disease at baseline than those without HDV
- Over the approximately 2 years of follow-up, no increased risks of liver-related events associated with HDV infection were observed
- Additional follow-up time may be needed to further evaluate differences in risk between cohorts

Plain Language Summary

- At cohort entry, people with hepatitis B/hepatitis C/hepatitis delta virus had more evidence of advanced liver disease than people without hepatitis delta virus
- After excluding people who already had advanced liver disease before cohort entry, the risk of new occurrences of advanced liver disease over 2 years of available follow-up data was similar between people with and those without hepatitis delta virus

Introduction

- The prevalence of coinfection with hepatitis B and C viruses (HBV, HCV) ranges from 1% to 15% globally, and HBV/HCV coinfection is associated with an increased risk of liver-related events compared to monoinfection with either virus[1]
- Hepatitis delta virus (HDV) is an incomplete RNA virus that occurs only in the presence of HBV[2]
- Infection with HDV is associated with rapid progression to advanced liver disease, including compensated and decompensated cirrhosis (CC, DC) and hepatocellular carcinoma (HCC)[2]
- Some US-based population studies have reported high incidence of HCV infection among people with HDV[3-5]
- Limited research is available that describes the consequences of infection with HDV among those with HBV/HCV coinfection

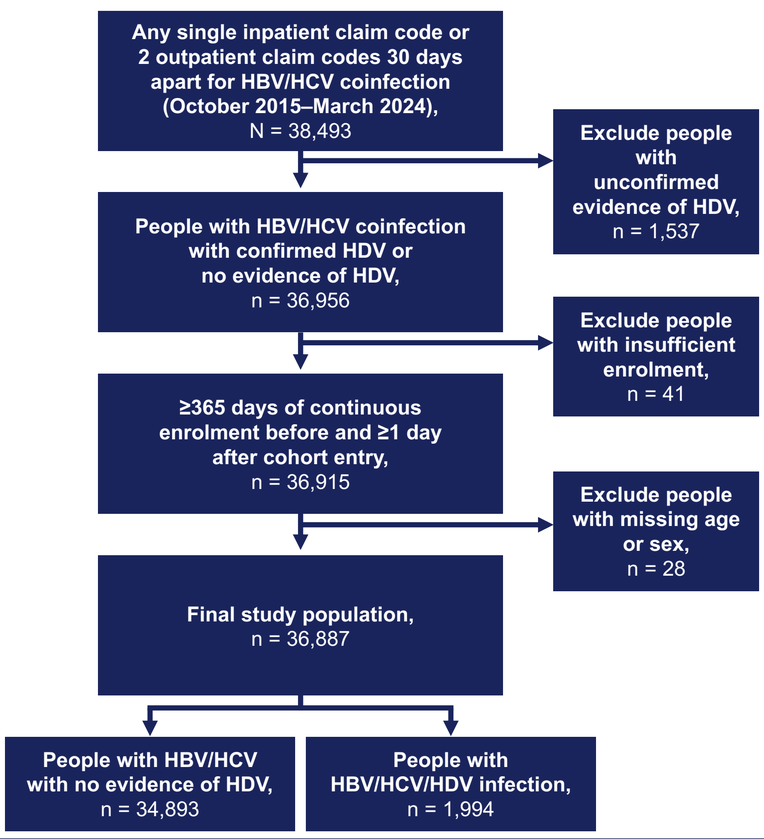
Objective

- To describe baseline characteristics and risk of liver-related events in people with HBV/HCV coinfection with and without HDV

Methods

- A retrospective cohort study was conducted using the HealthVerity Marketplace dataset from October 2015 to March 2024 that includes medical and pharmacy claims and electronic health records for more than 100 million people living in the US (**Figure 1**)
- Inclusion criteria
  - ≥18 years of age at cohort entry
  - Prior continuous insurance coverage of at least 365 days
  - ≥1 day of available follow-up
  - Either 1 inpatient or 2 outpatient *ICD-10-CM* codes, at least 30 days apart, for HBV, HCV, and HDV
- Exclusion criteria
  - Missing age or sex information
  - Evidence of cirrhosis, liver decompensation, or HCC in the year prior to cohort entry
  - History of liver transplant (LT)
  - Evidence of HIV coinfection at baseline

Figure 1 **CONSORT Diagram**



CONSORT, Consolidated Standards of Reporting Trials; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis delta virus.

- A propensity score (PS) model was constructed using baseline demographics, clinical characteristics, and treatment history
- The PS model estimated hazard ratios (HRs) with 95% CIs comparing risk of advanced liver disease events (CC, DC, HCC, LT) among people with HBV/HCV infection with and without HDV
- A secondary analysis was conducted in patients who had CC at baseline, describing the risk of DC, HCC, or LT among those with vs without HDV

Results

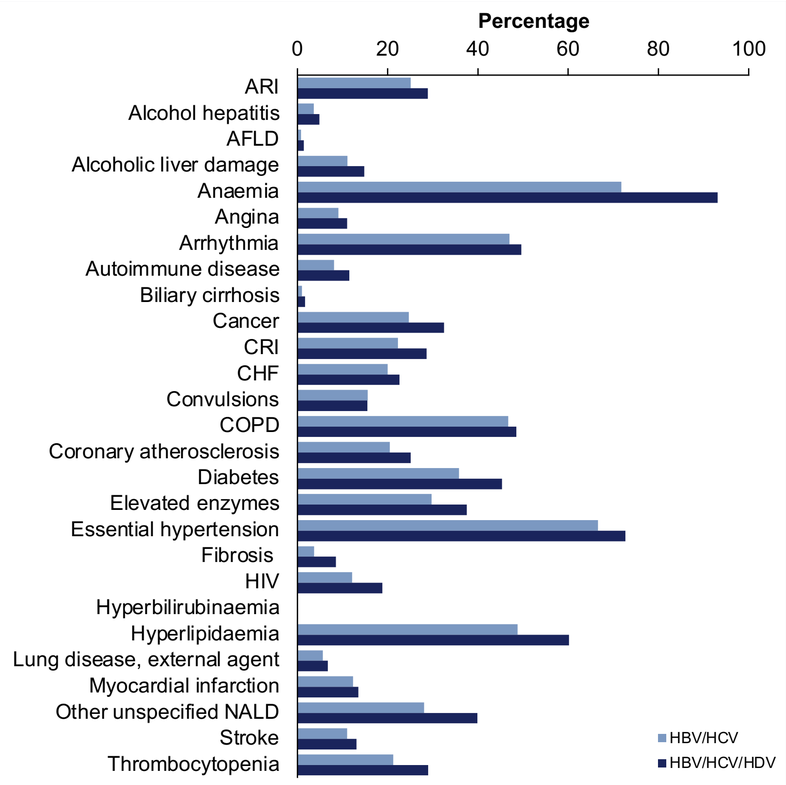
Table 1 **Demographics and Baseline Liver and Medication Characteristics[a]**

HBV/HCV Cohort	HBV/HCV (n = 34,893)	HBV/HCV/HDV (n = 1,994)
Demographics		
Male	21,054 (60.3)	1,261 (63.2)
Age group, years		
18 to <35	3,932 (11.3)	185 (9.3)
35 to <45	6,133 (17.6)	301 (15.1)
45 to <55	7,463 (21.4)	432 (21.7)
55 to <65	11,193 (32.1)	662 (33.2)
≥65	6,172 (17.7)	414 (20.8)
Baseline liver status		
CC	9,617 (27.6)	784 (39.3)
DC	7,139 (20.5)	575 (28.8)
HCC	1,574 (4.5)	170 (8.5)
Liver transplant	718 (2.1)	95 (4.8)
Portal hypertension	3,850 (11.0)	351 (17.6)
End-stage liver disease	3,700 (10.6)	340 (17.1)
Baseline medications		
DAAs	7,619 (21.8)	428 (21.5)
Interferon	23 (0.1)	14 (0.7)
NAs	6,377 (18.3)	728 (36.5)
ART	5,050 (14.5)	525 (26.3)
Antidiabetics	6,832 (19.6)	466 (23.4)

Values in table represent n (%) unless otherwise noted. All differences between "HBV/HCV" and "HBV/HCV/HDV" were significant at $P < .05$ except for age 45 to <55 ($P = .79$), age 55 to <65 ($P = .31$), and DAAs ($P = .72$).
[a]Values include the full cohort prior to applying exclusion criteria.
ART, antiretroviral therapy; CC, compensated cirrhosis; DAA, direct-acting antiviral; DC, decompensated cirrhosis, HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis delta virus; NA, nucleos(t)ide analogue.

- 36,887 people with HBV/HCV coinfection met inclusion criteria; 1,994 (5.4%) had concurrent HDV infection (**Table 1**)
- Those with HDV were older, more likely to be male, had more claims for severe liver disease at baseline, and were more likely to have initiated treatment with HBV nucleos(t)ide analogues
- Approximately 21% of people with and without HDV had dispensing claims for direct-acting antiviral treatment

Figure 2 **Baseline Comorbidities and Conditions**



HBV/HCV Cohort	HBV/HCV (n = 34,893)	HBV/HCV/HDV (n = 1,994)
Additional conditions		
Mental illness	28,688 (82.2)	1,596 (80.0)
Substance abuse	25,636 (73.5)	1,326 (66.5)
Alcohol use	11,683 (33.5)	668 (33.5)
Overweight/obesity	10,705 (30.7)	656 (32.9)
Smoking	25,213 (72.3)	1,321 (66.2)

All values in table represent n (%). All differences between "HBV/HCV" and "HBV/HCV/HDV" were significant at $P < .05$, except for "Convulsions," "COPD," "Hyperbilirubinaemia," "Myocardial infarction," and "Alcohol use."
AFLD, alcoholic fatty liver disease; ARI, acute renal insufficiency; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRI, chronic renal insufficiency; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis delta virus; NALD, nonalcoholic liver disease.

- Liver-related comorbidities at baseline were significantly more common among those with HBV/HCV/HDV coinfection compared to those without HDV
- While the rate of obesity was greater among people with HBV/HCV/HDV, baseline alcohol use was similar in the 2 cohorts
- Rates of smoking, substance abuse, and mental health conditions were significantly lower among people with HDV (**Figure 2**; $P < .05$)

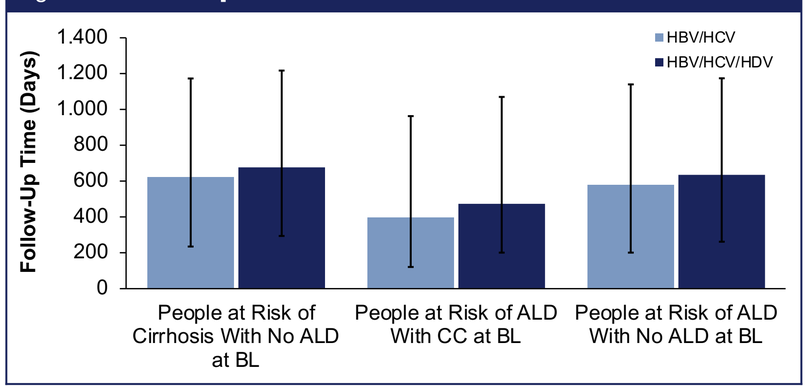
Table 2 **Risk of Developing Cirrhosis and ALD[a] in People With HBV/HCV/HDV vs HBV/HCV**

Analysis	Cohort	Persons, n	Events, n	PY	PS-Weighted HR (95% CI)
Risk of cirrhosis among people with no evidence of ALD at BL[b]	HBV/HCV	22,913	3,075	48,852	1.00[c]
	HBV/HCV/HDV	1,050	152	2,350	1.03 (0.87, 1.21)
Risk of ALD among people with CC at BL[d]	HBV/HCV	2,818	915	4,750	1.00[c]
	HBV/HCV/HDV	185	61	353	0.96 (0.74, 1.25)
Risk of ALD among people with no evidence of ALD at BL[e]	HBV/HCV	22,913	4,398	46,563	1.00[c]
	HBV/HCV/HDV	1,050	206	2,245	0.97 (0.84, 1.11)

A PS model was constructed using BL demographics, clinical characteristics, and medication dispensing claims, and was used to estimate HRs with 95% CIs comparing risk of ALD events. [a]ALD includes CC, DC, HCC, and LT. [b]In the fully adjusted MV model, the following covariates were significant: age, sex, PWID, antidiabetic Tx, acute renal insufficiency, alcohol use, alcoholic hepatitis, alcoholic liver damage, anaemia, autoimmune disease, cancer, CHF, elevated enzymes, essential hypertension, hyperlipidaemia, MASLD, portal hypertension, smoking, substance abuse, and thrombocytopenia. [c]No HDV. [d]In the fully adjusted MV model, the following covariates were significant: antidiabetic Tx, HCV Tx, NA Tx, alcoholic liver damage, anaemia, CRI, ESLD, hyperlipidaemia, portal hypertension, and thrombocytopenia. [e]In the fully adjusted MV model, the following covariates were significant: age, sex, HCV Tx, NA Tx, AFLD, alcoholic hepatitis, alcoholic liver damage, autoimmune disease, CHF, diabetes, elevated enzymes, ESLD, hyperlipidaemia, MASLD, overweight/obesity, portal hypertension, substance abuse, and thrombocytopenia.
AFLD, alcoholic fatty liver disease; ALD, advanced liver disease; BL, baseline; CC, compensated cirrhosis; CHF, congestive heart failure; CRI, chronic renal insufficiency; DC, decompensated cirrhosis; ESLD, end-stage liver disease; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis delta virus; HR, hazard ratio; LT, liver transplant; MASLD, metabolic dysfunction-associated steatotic liver disease; MV, multivariate; NA, nucleos(t)ide analogue; PS, propensity score; PWID, people who inject drugs; PY, person-years; Tx, treatment.

- After applying exclusion criteria (baseline evidence of advanced liver disease or HIV) and PS weighting, there was no difference in the risk of CC (HR, 1.03; 95% CI, 0.87–1.21) or advanced liver disease (HR, 0.97; 95% CI, 0.84–1.11)
- Similarly, there was no difference with vs without HDV in the risk of DC, HCC, or LT among those with CC at baseline (**Table 2**)

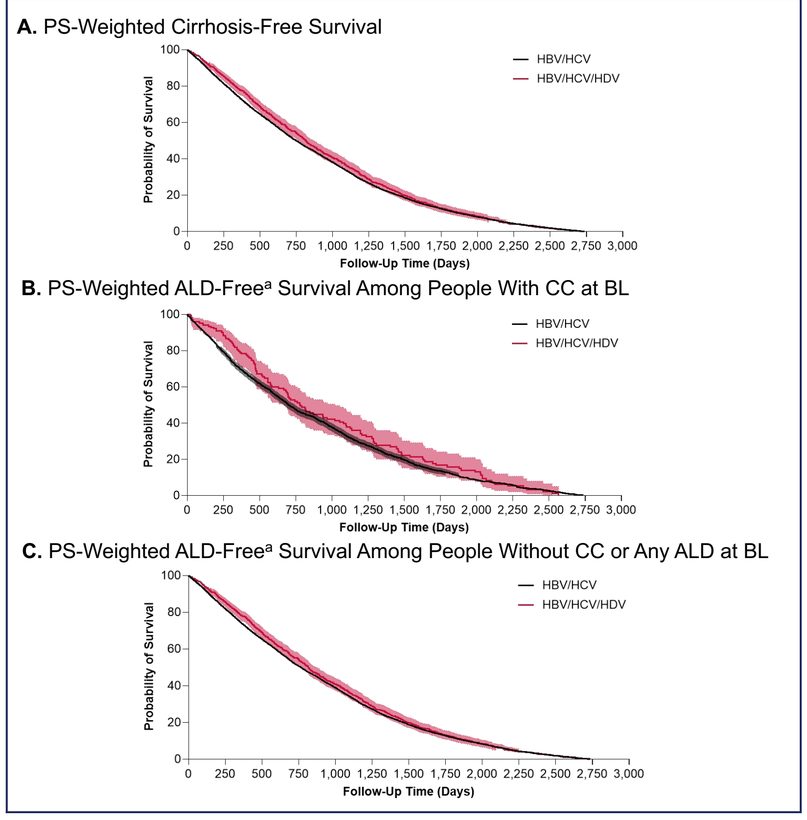
Figure 3 **Follow-Up Time**



Bars denote median (95% CI) follow-up time in days. ALD includes CC, DC, HCC, and LT.
ALD, advanced liver disease; BL, baseline; CC, compensated cirrhosis; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis delta virus; LT, liver transplant.

- The median follow-up times were similar across cohorts but were limited (**Figure 3**)

Figure 4 **PS-Weighted Survival Curves Among People With HBV/HCV/HDV vs HBV/HCV**



[a]ALD includes CC, DC, HCC, and LT.
ALD, advanced liver disease; BL, baseline; CC, compensated cirrhosis; DC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis delta virus; LT, liver transplant; PS, propensity score.

- After PS weighting, no difference was observed in the likelihood of people with HBV/HCV with HDV developing cirrhosis or advanced liver disease compared to those without HDV (**Figure 4**)

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