The Emerging Issue of Hepatitis Delta in Asia

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I disclose the following financial relationship(s) with a commercial interest:

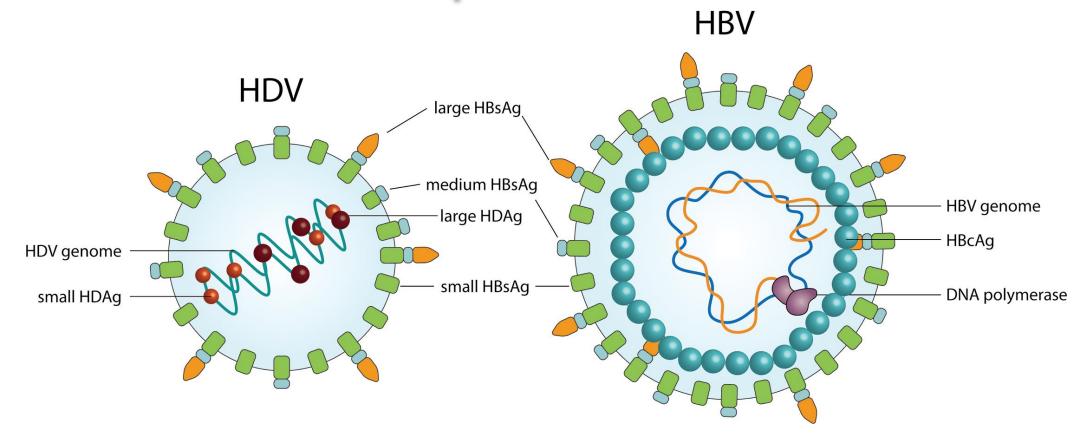
Research/Grant

Roche, MSD, Vir Biotechnology, Janssen

Outlines

- Prevalence and route of Hepatitis Delta infection
- Impact of HBV vaccination on Hepatitis Delta
- More recent evidence of Hepatitis Delta burden
- Take home message

HBV as a helper virus for HDV¹



- HDV considered as the most severe form of viral hepatitis in humans.
- As compared to mono-infection with HBV, HBV/HDV coinfection is associated with an accelerated course of fibrosis progression, earlier hepatic decompensation of cirrhosis, and an increased risk of HCC²

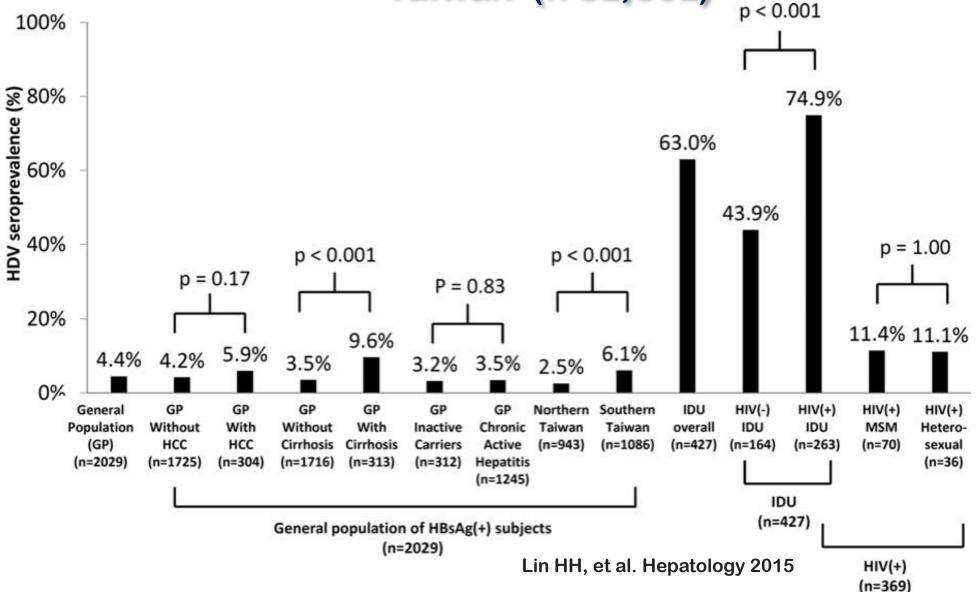
Pattern of Hepatitis Delta infection

- Co-infection:
 - infection with both HBV and HDV at the same time
 - Severe hepatitis, majority results in clearance of both virus, Anti-HDV +
- Superinfection:
 - Superinfection of HDV on top of CHB
 - Acute but frequently leads to persistent HDV, transient HBV suppression

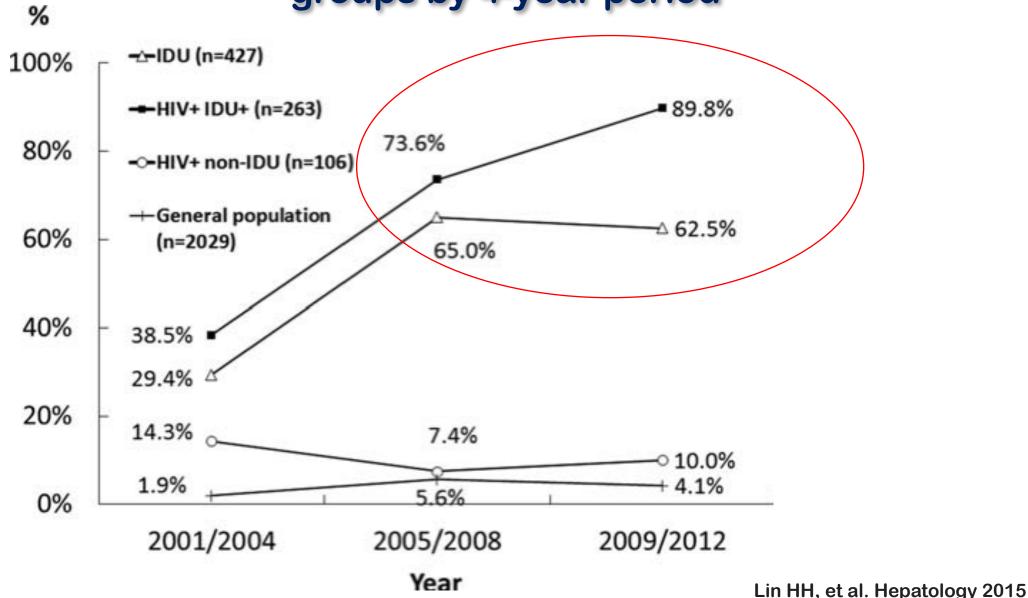
HDV is among neglected viral hepatitis

- HDV test is not widely available
- No highly effective treatment and no commercial interest
- Prevalence is not directly correlated with HBV burden in that community
- Transmission
 - Northern Europe and USA: mainly in IVDU
 - Mediterranean basin: inapparent parenteral, sexual, family members
 - Asia: IVDU, high risk sexual behavior (HRSB)
- Study in 2003, estimated 5% of HBV carriers or about 15 million¹

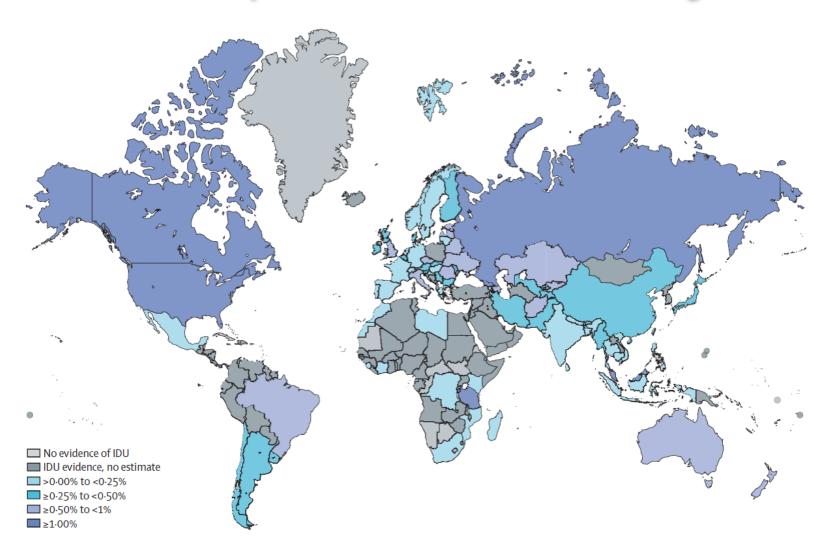
Seroprevalence of HDV infection among various groups in Taiwan (n 52,562)



Trend of HDV seroprevalence among different HBsAg-positive groups by 4-year period



Estimated prevalence of IVDU by country

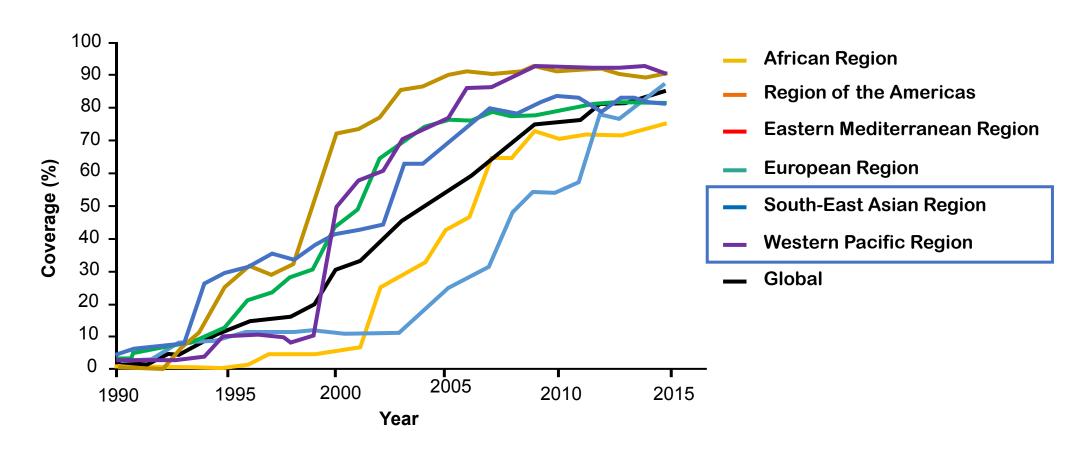


HDV Genotypes in IVDU in Taiwan: Decreasing Prevalence and Lack of Correlation with HBV Genotypes

- 144/368 HBsAg positive IVDU; positive anti-HDV (39%) as compare with 85-91% in 1986, 1988 studies
- Rate of anti-HDV reduction 4.7%/year (1986 to 1997), after HBV vaccination
- 31 HDV RNA positive

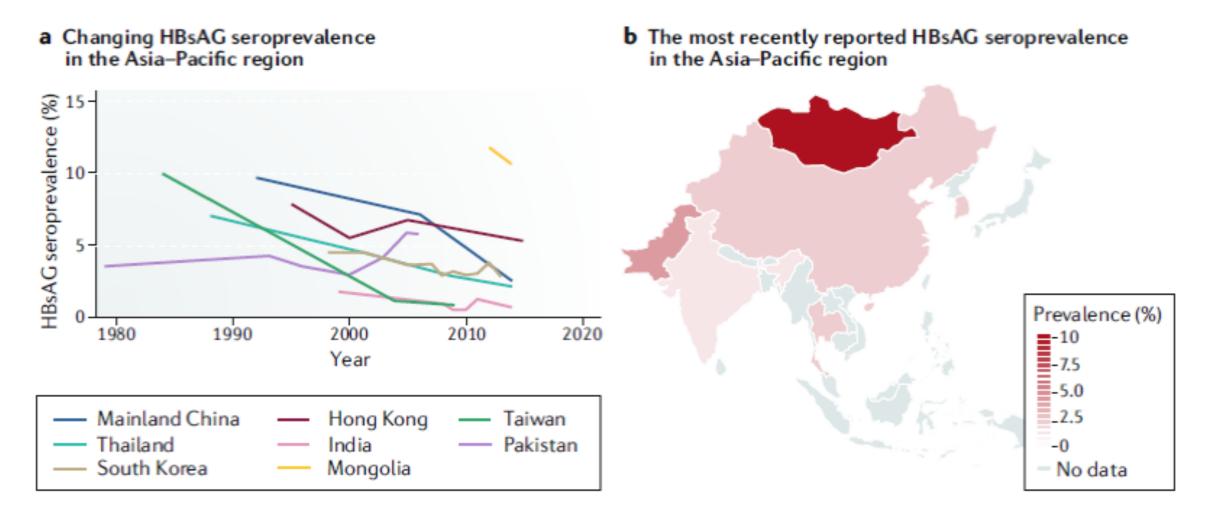
HBV genotype (no)	No. (%) of subjects infected with HDV			
	I	II	1+11	
B(23)	8(35)	13(57)	2(8)	
C(8)	3(37)	5(63)	0(0)	

Use of the 3-dose HBV vaccine showed a dramatic increase at the beginning of the 21st century...

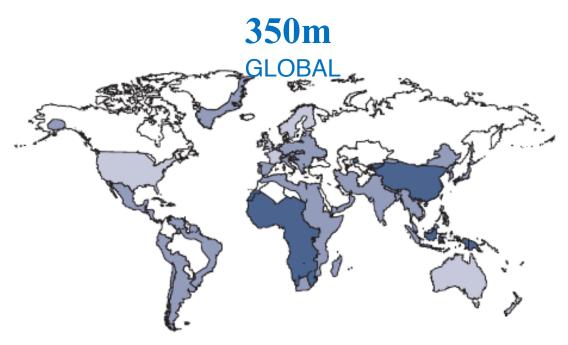


WHO. Global Hepatitis Report 2017. Available at: http://www.who.int/hepatitis/publications/global-hepatitis report2017/en/ (accessed February 2019)

HBV prevalence in the Asia–Pacific region



Hepatitis B status 2004 >>> 2015



World prevalence of hepatitis B carriers

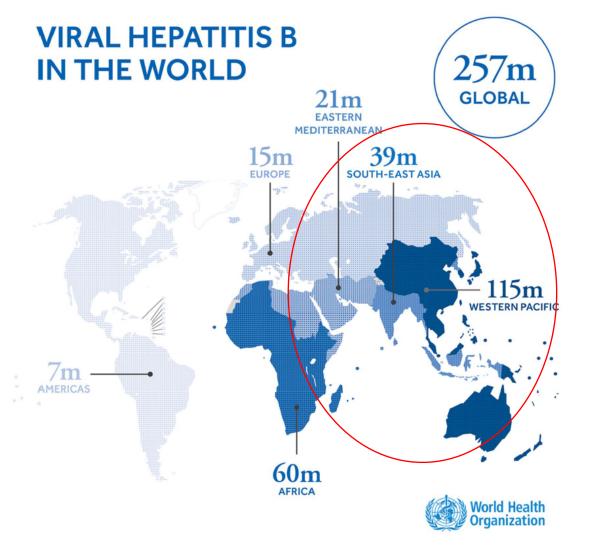
HBs Ag carriers prevalence

<2%

) <2**–**7%

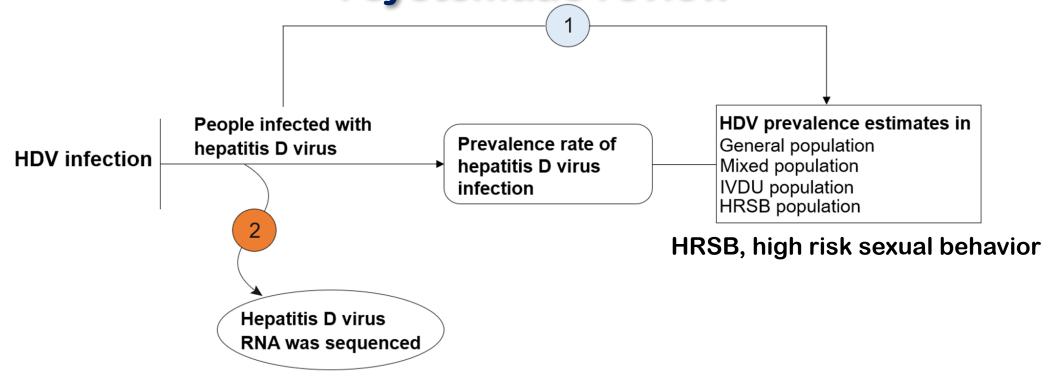
>8%

Poorly documented



D. Lavanchy. J Viral Hepatitis, 2004, 11, 97–107

Prevalence and burden of HDV in global population. : systematic review



Key topics

- 1 Prevalence of hepatitis D virus infection in the global population.
- 2 Global distribution of hepatitis D virus genotypes.

Global estimate HDV infection in general population/Asia

Location	Pop/thousands	Prevalence %(95% CI)	Estimates/thousand(95% CI
Asia			
Mongolia	2977	8.03 (5.26 to 12.08)	239 (157 to 360)
China	1 397 029	0.45 (0.15 to 0.89)	6287 (2096 to 12 434)
Iran	79360	0.11 (0.03 to 0.22)	87 (24 to 175)
Japan	127975	0.73 (0.04 to 2.15)	934 (51 to 2751)
Pakistan	189381	2.43 (1.63 to 3.62)	4602 (3087 to 6856)
Saudi Arabia	31 557	0.39 (0.06 to 0.95)	123 (19 to 300)
Thailand	68 658	0.00 (0.00 to 9.41)	0 (0 to 6461)
Turkey	78 2 7 1	0.03 (0.01 to 0.08)	23 (8 to 63)
Vietnam	93 572	0.24 (0.07 to 0.87)	225 (66 to 814)
Yemen	26916	0.14 (0.00 to 0.53)	38 (0 to 143)

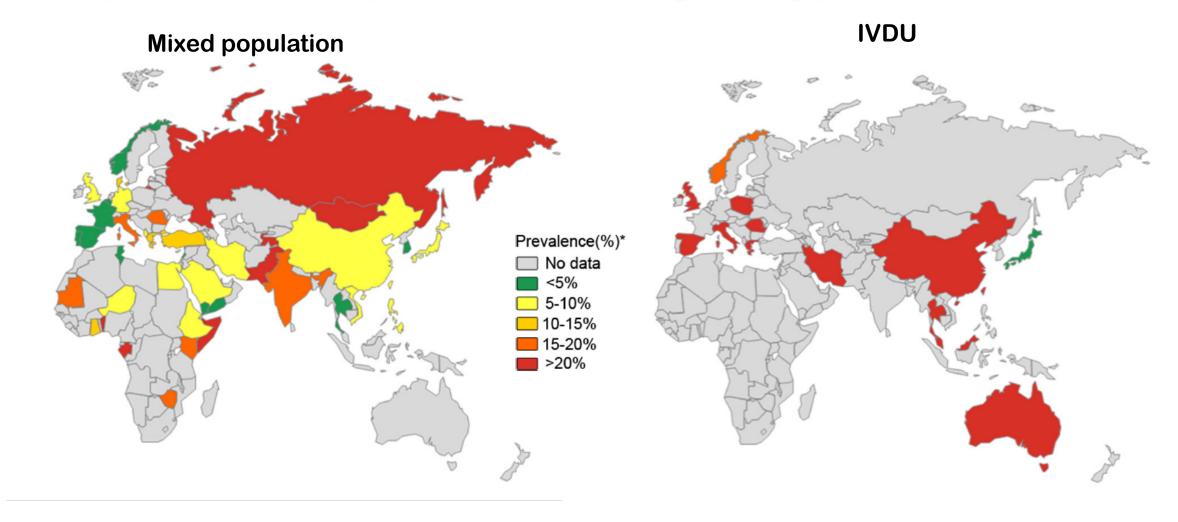
25.12 Million

Forest plot showing meta-analysis of HDV among selected HBsAg positive population

		Prevalence (95% CI)	Weight(%)
Mixed population Subtotal (I^2 = 97.95%, p = 0.00)	\ \	10.58 (9.14, 12.11)	74.72
IVDU population Subtotal (I^2 = 96.65%, p = 0.00)		37.57 (29.30, 46.20)	16.06
HRSB population Subtotal (I^2 = 93.29%, p = 0.00)	-	17.01 (10.69, 24.34)	9.22
Heterogeneity between groups: p = 0.00 Overall (I^2 = 97.95%, p = 0.00)	\	14.57 (12.93, 16.27)	100.00
	0.0 25.0 Prevalence (%)	50.0	

Chen HY, et al. Gut 2019;68:512-521

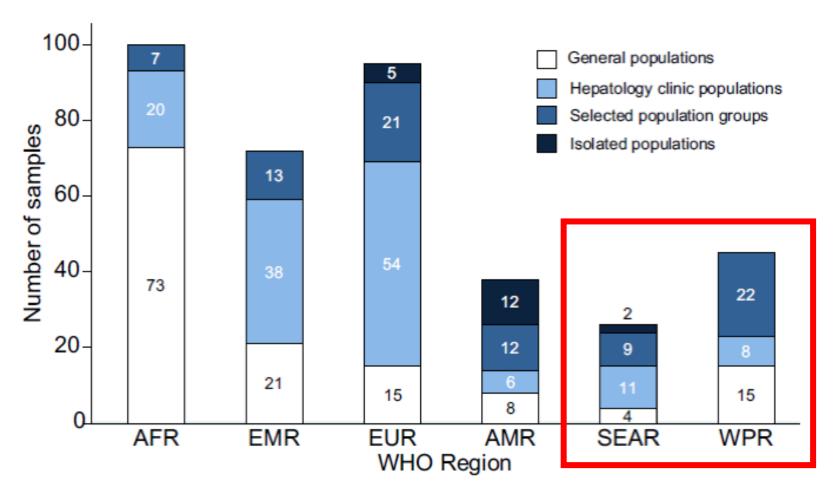
Seroprevalence of Hepatitis D virus among HBsAg-positive populations



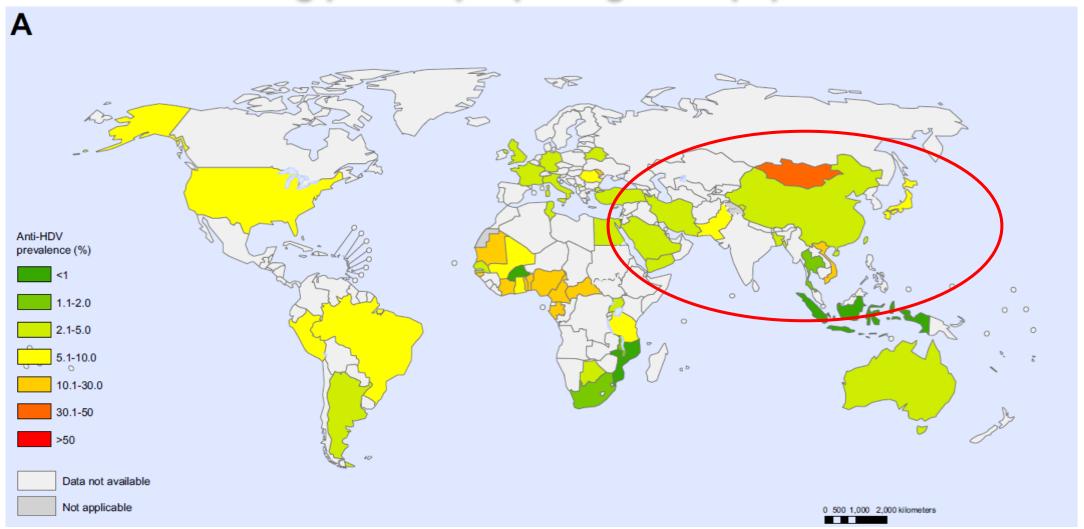
global burden 60-70 million

Chen HY, et al. Gut 2019;68:512-521

Systematic review and meta-analysis included samples by population category and WHO region

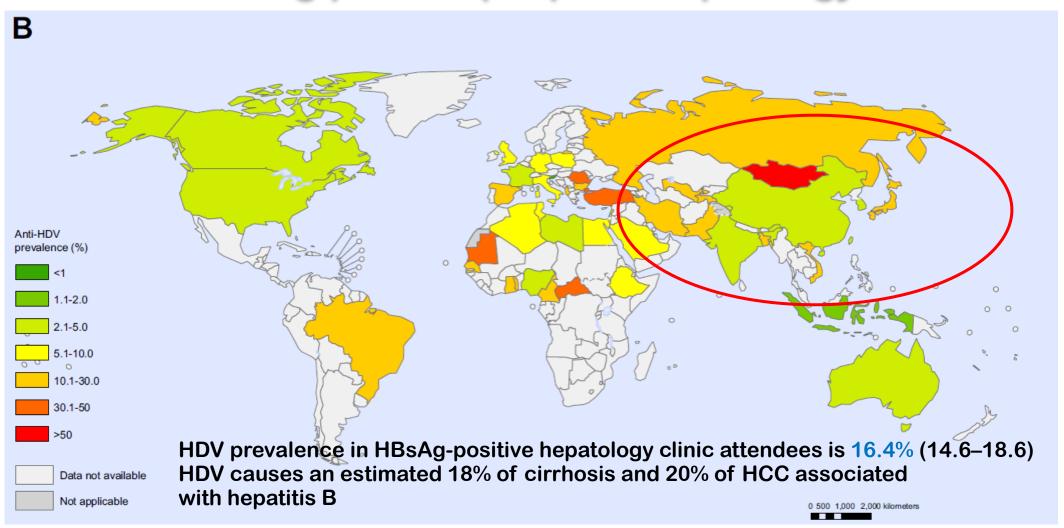


Country-level estimates of anti-HDV prevalence among HBsAg-positive people in general population

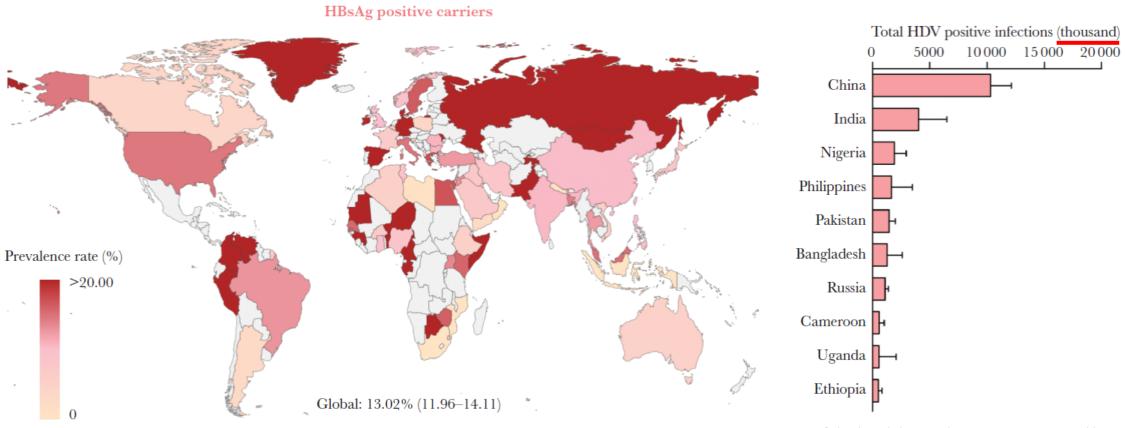


Among HBsAg-positive people, estimated HDV prevalence is 4.5% (95% CI 3.6–5.7)

Country-level estimates of anti-HDV prevalence among HBsAg-positive people in hepatology clinic



Global prevalence of HDV in HBsAg-positive carriers



Global burden 48-60 Million

Miao Z, et al. JID 2020 (May)

Take Home Message

- Burden of HDV is underestimated, especially in Asia
- HDV prevalence differs depending on routes of infection and local culture, unlikely from difference HBV or HDV genotypes
- Decreased prevalence of therapeutic injection, IVDU and implementation of HBV vaccine are among key factors of decreasing HDV prevalence
- HDV in Asia is high in Pakistan and Mongolia
- High HDV burden in Asia due to high HBV carriers

Thank you for attention