

new epidemiology of hepatitis delta

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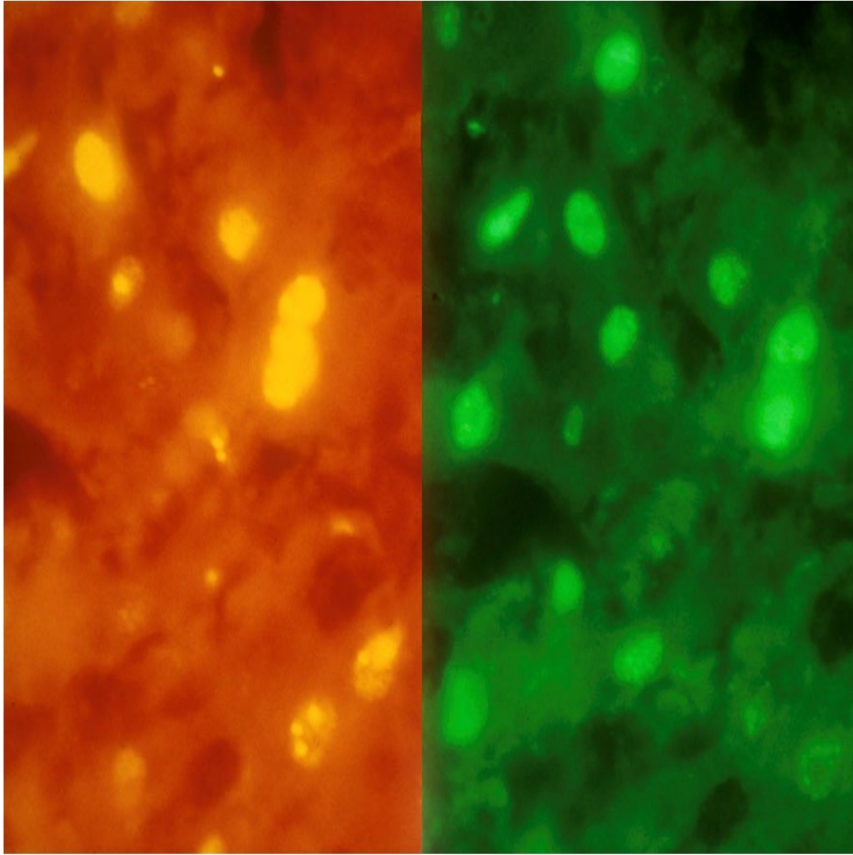




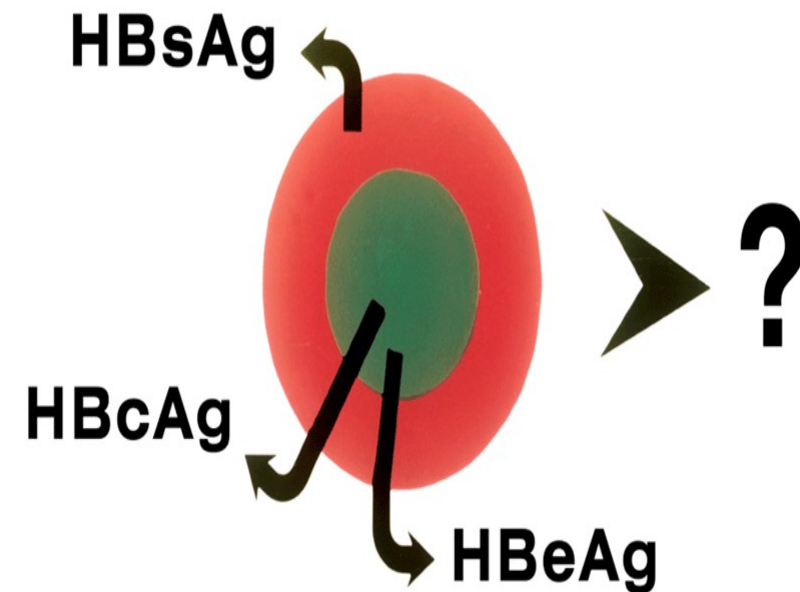
Speaker's name : George PAPATHEODORIDIS, Athens

☐ I do not have any potential conflict of interest

Discovered in 1977 among HBV patients with serious episodes of acute liver disease

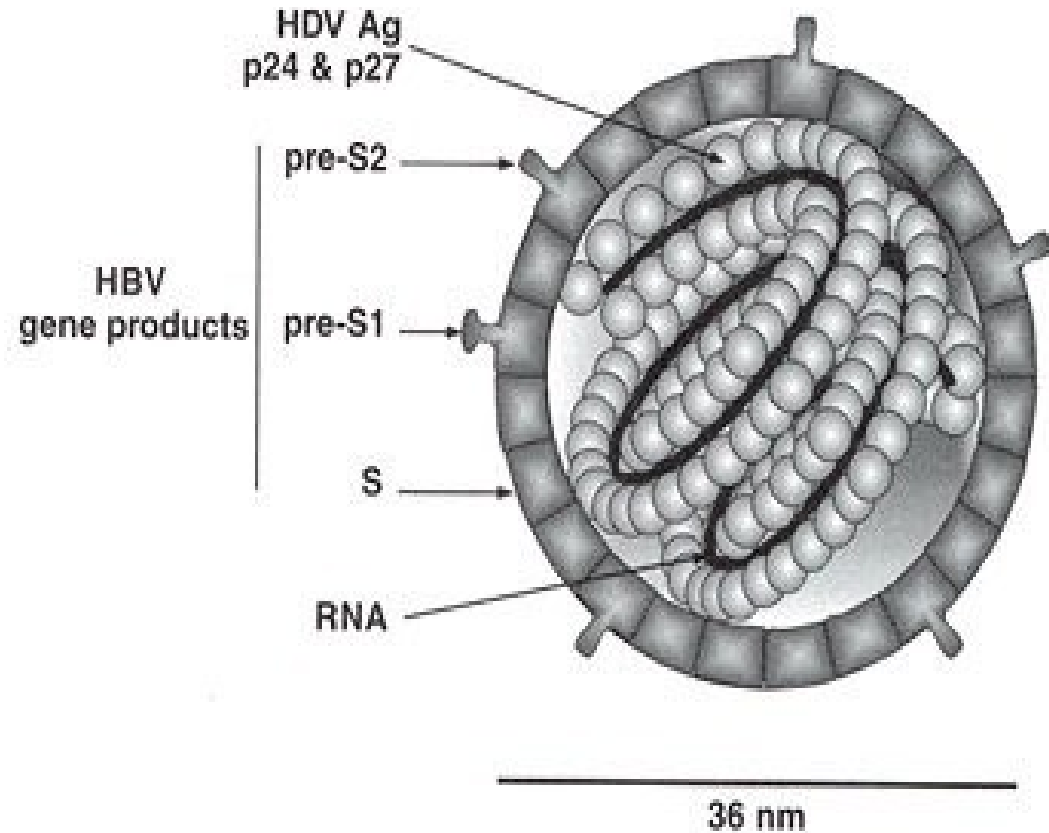


HEPATITIS B VIRUS



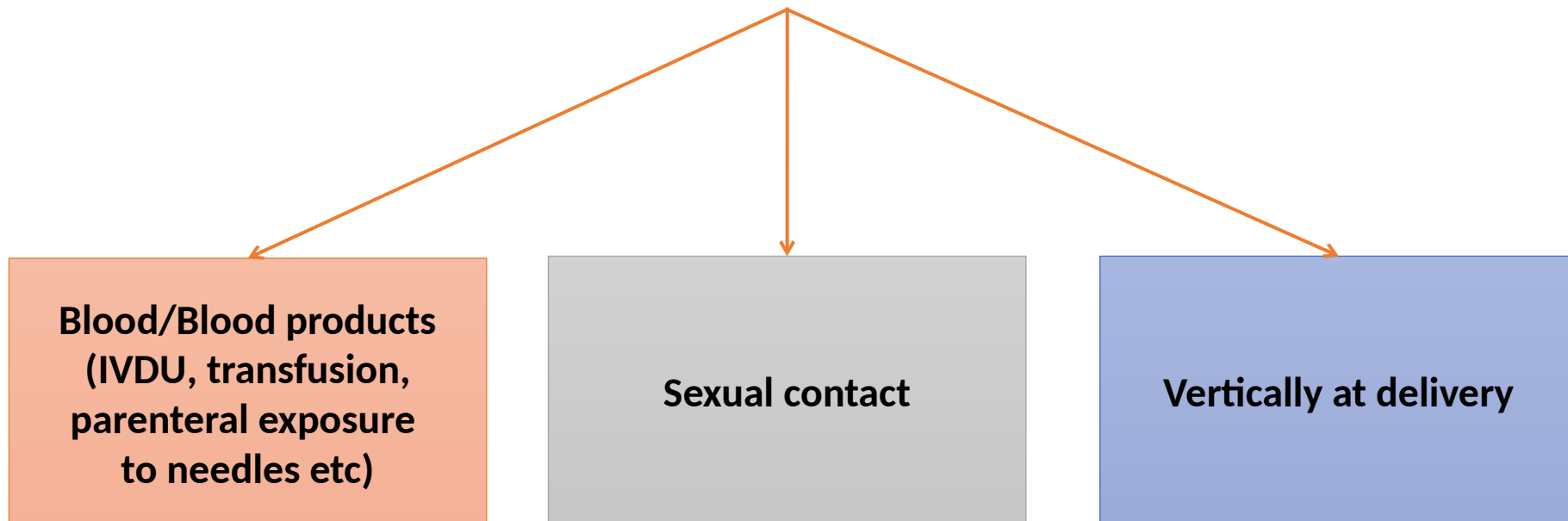
The smallest among mammalian viruses

35-37 nm diameter virus
featuring a **small single-stranded, circular RNA**
genome of 1672-1697
nucleotides



HDV transmission

- ◆ Parenteral transmission, like HBV
- ◆ Always with HBV



HDV infection

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graph TD; A[HDV infection] --> B[HDV + HBV coinfection]; A --> C[HDV superinfection];
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HDV + HBV coinfection

HDV + HBV acute infection

HDV superinfection

acute HDV infection on
chronic HBV infection

Rare (<10%) – Progression to chronicity - Common

Chronic hepatitis delta – a clinically important liver disease

- Chronic hepatitis delta is associated with:
 - Accelerated fibrosis progression
 - Increased risk of HCC and early decompensation

Rizzetto M. J Hepatol 2009; 50: 1043-50

Chronic hepatitis delta: heterogeneous course

- Chronic hepatitis delta is associated with:
 - Accelerated fibrosis progression
 - Increased risk of HCC and early decompensation

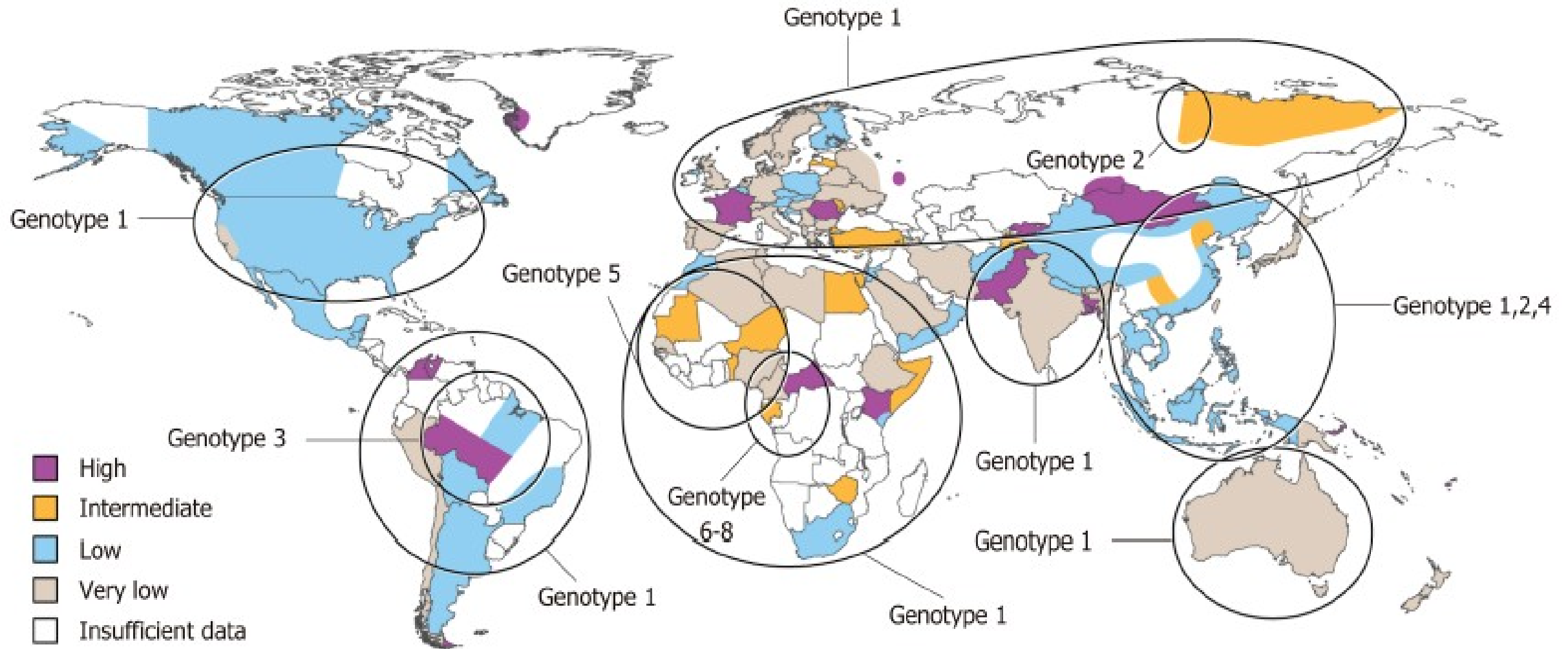
Rizzetto M. J Hepatol 2009; 50: 1043-50

- Asymptomatic HDV-HBV carriers may also exist

Rizzetto M. J Hepatol 2009; 50: 1043-50;

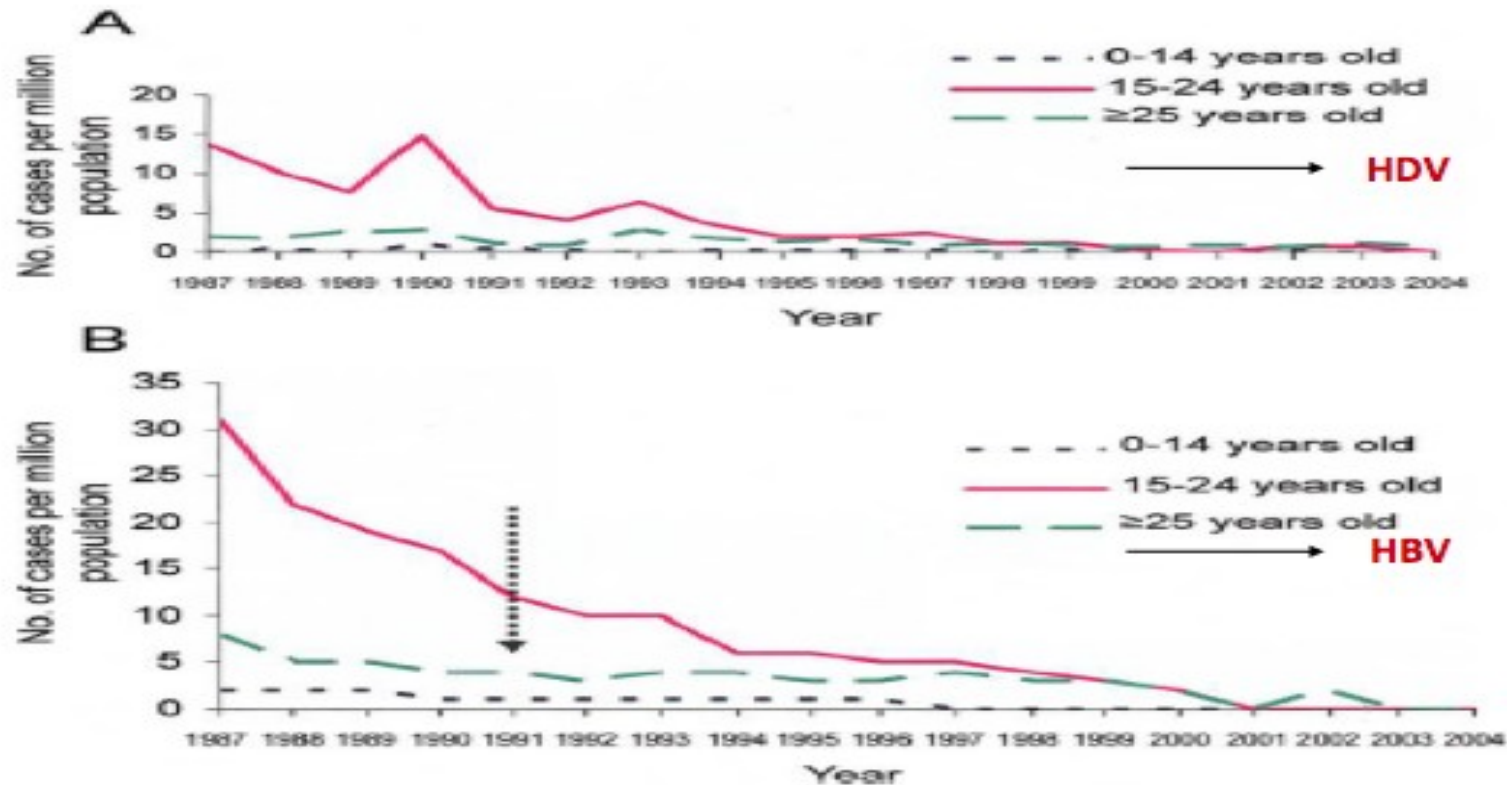
Hadziyannis SJ et al. Prog Clin Biol Res 1987; 234: 181-202.

Estimated prevalence of HBV infection with genotype distribution

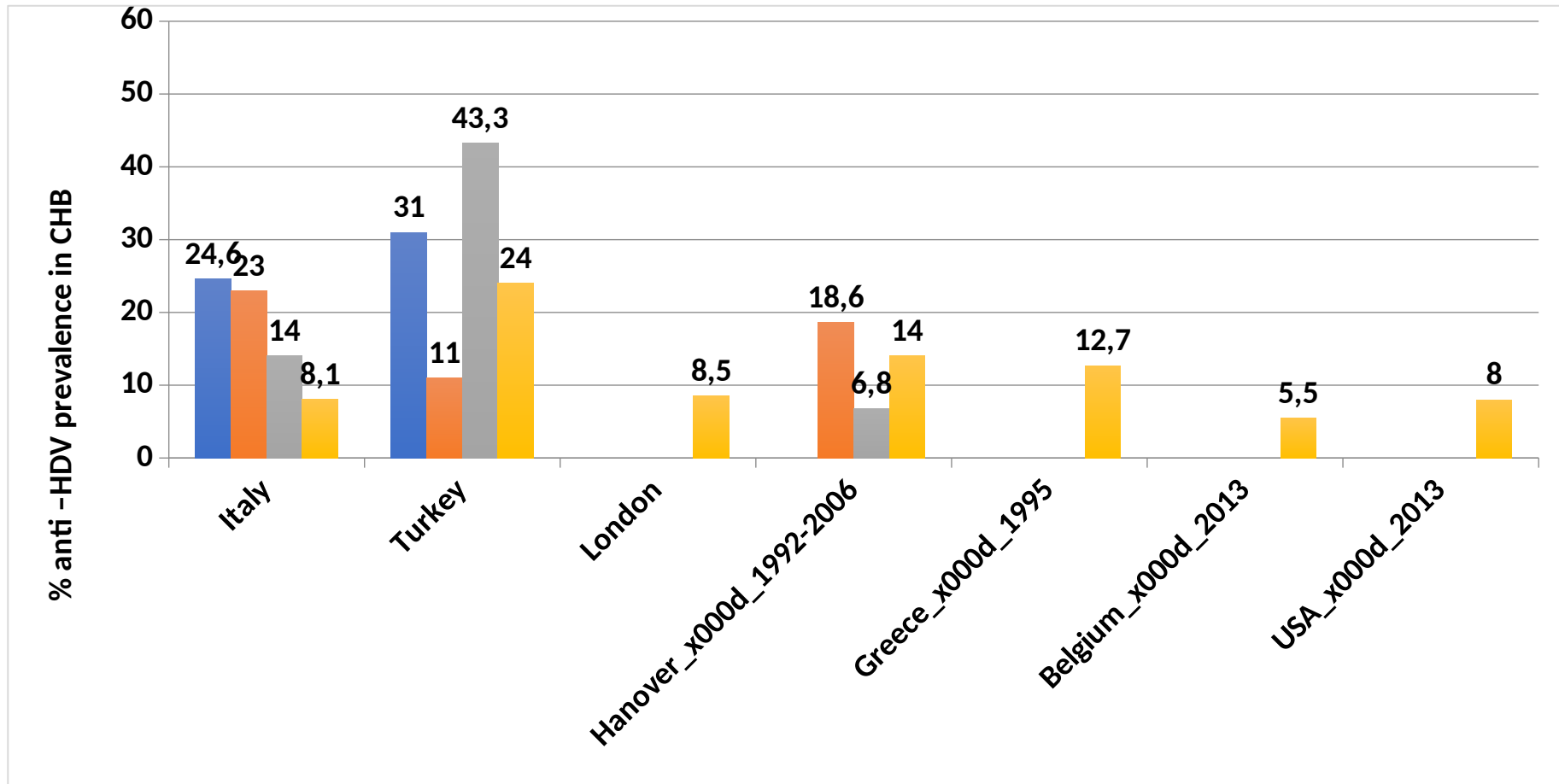


HDV prevalence

Decreasing anti-HDV prevalence due to HBV vaccination



Hepatitis D is still present...



Smedile et al, Am J Epidemiol 1983. Sagnelli et al, J Hepatol 1992.

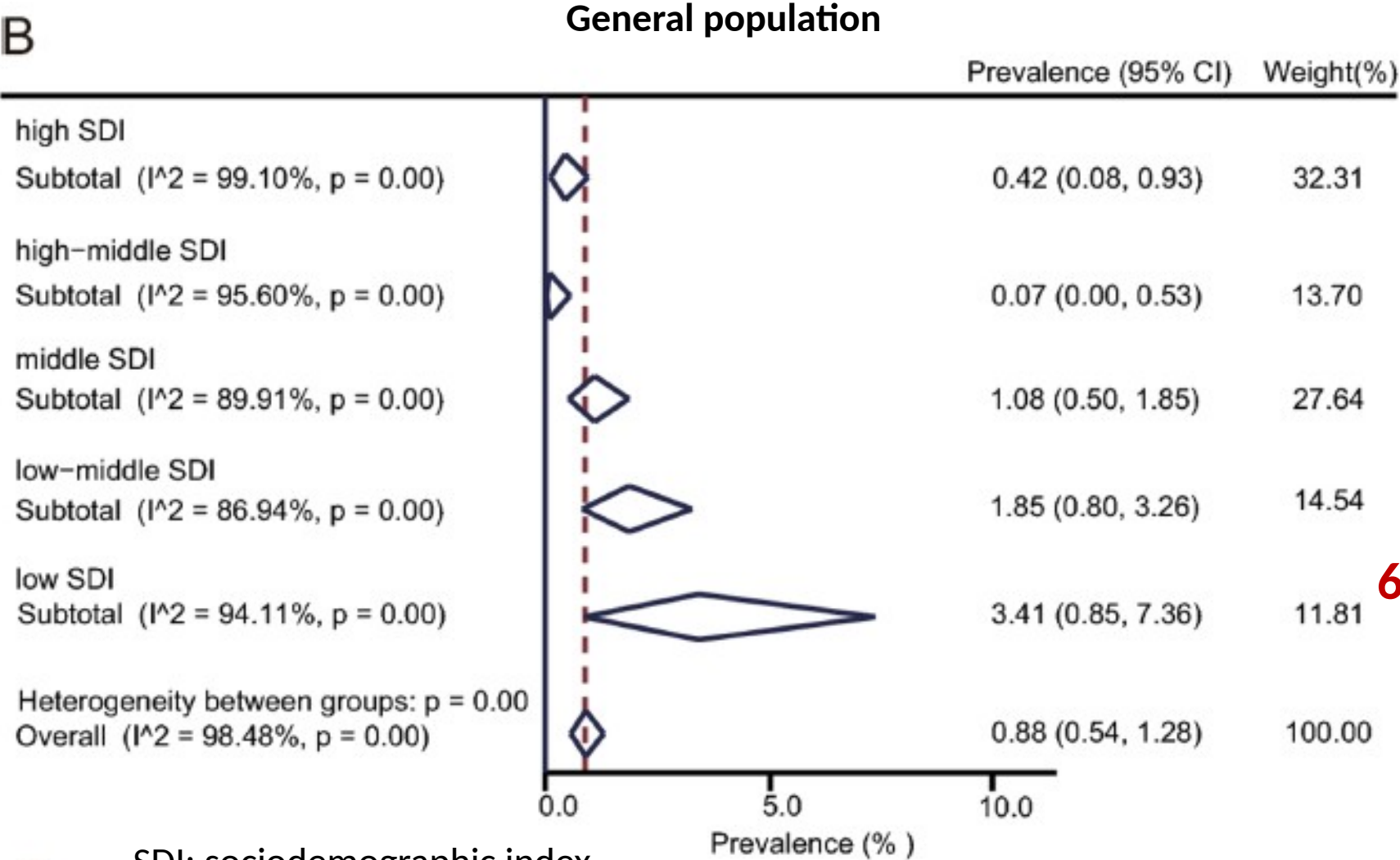
Sagnelli et al, J Hepatol 1997. Gaeta et al, Hepatology 2000. Degertekin, Turk J Gastroenterol 2006.

Cross et al, J Med Virol 2008. Wedemeyer et al, Hepatology 2007. Gaeta et al, Hepatology 2007.

Dalekos et al, EJGH 1995. Gish et al, J Gastroenterol Hepatol 2013. Ho, J Med Virol 2013.

Recent estimations on anti-HDV prevalence

Systematic review: 182 studies, 295 cohorts from 61 countries/regions, 40,127,988 individuals (0.54% of global population)



**Overall
prevalence:
0.88%**

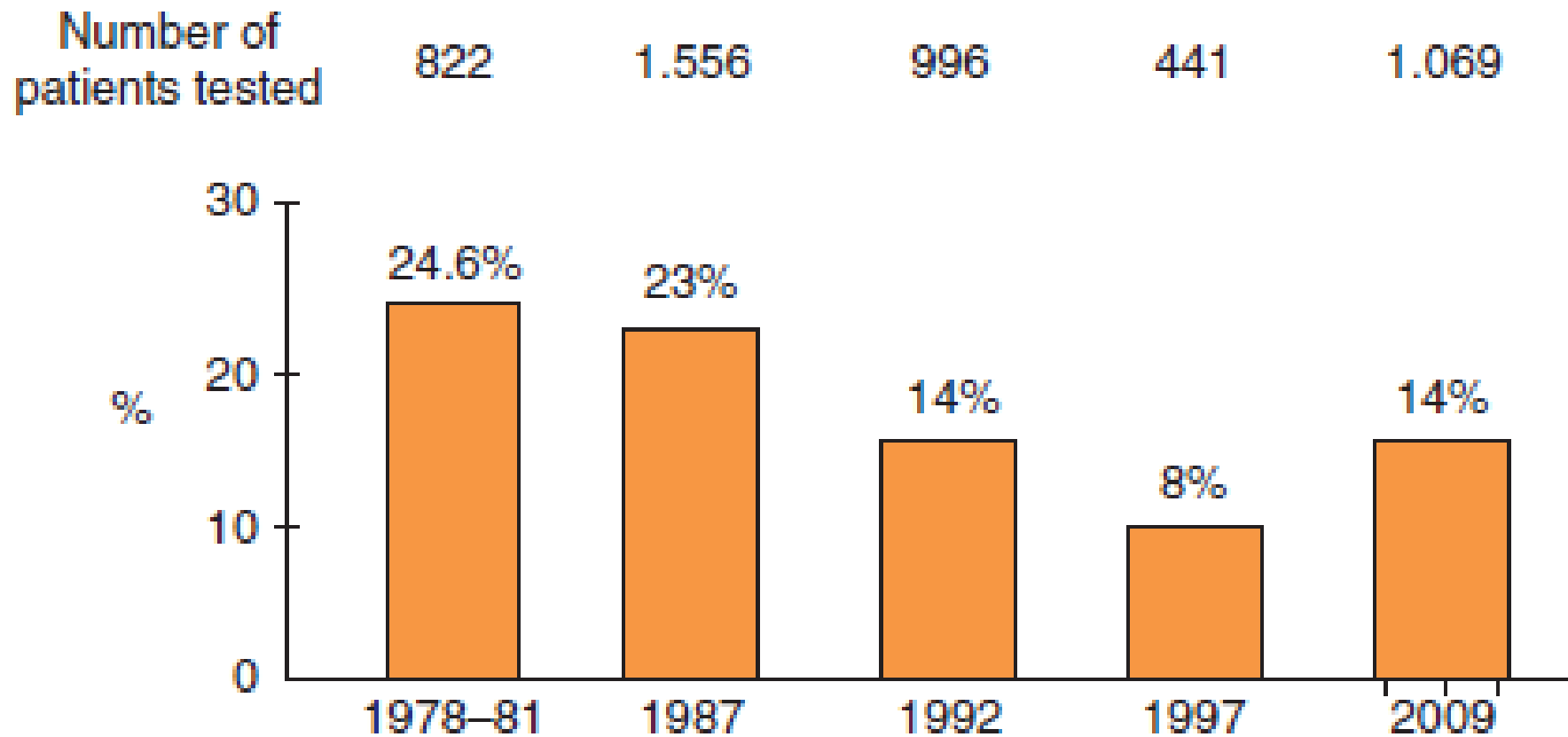
**Overall
prevalence:
0.80%**

**Global
burden:
60-70 millions**

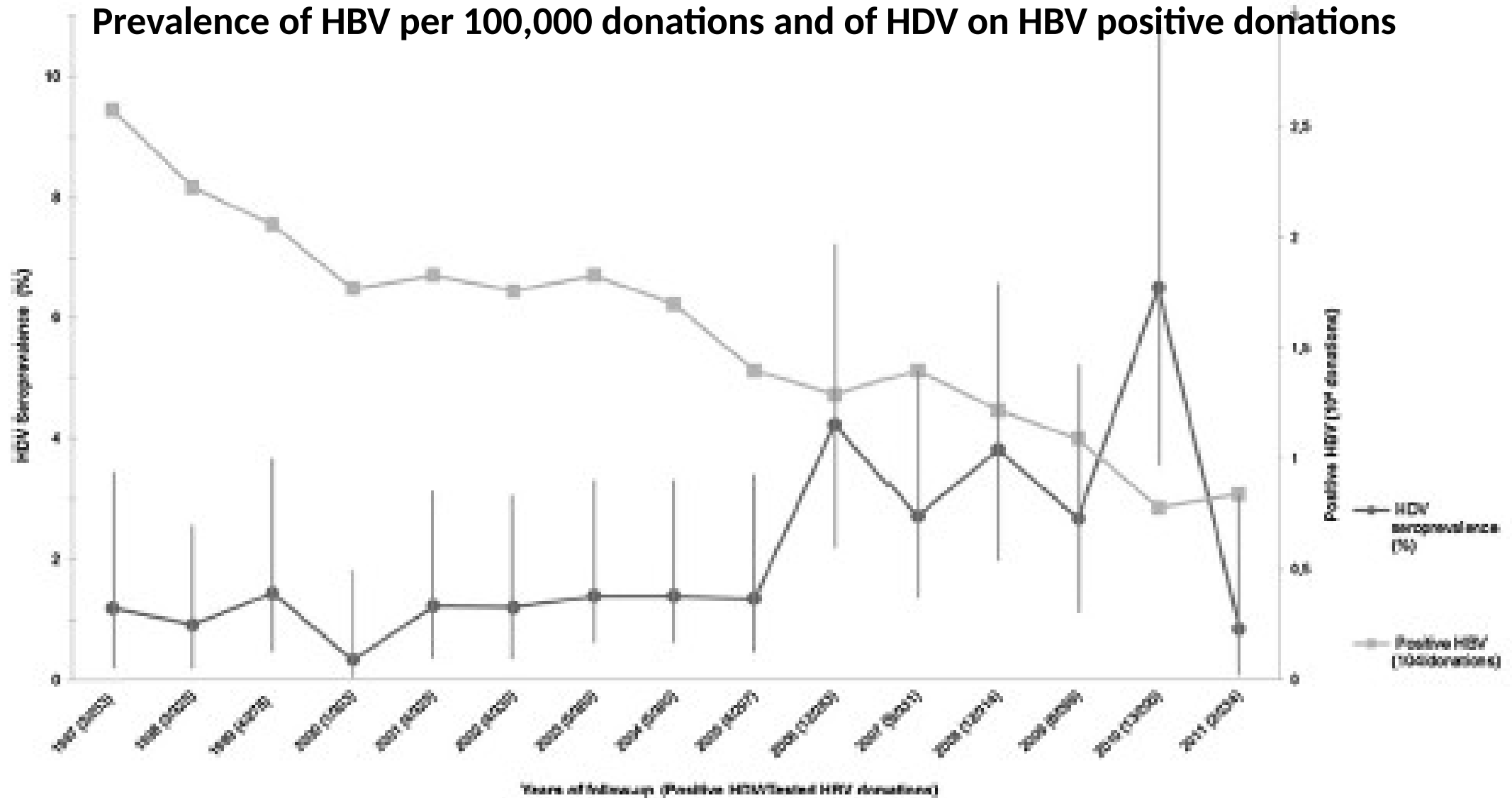
**Global
burden:
48-60 millions**

Miao Z et al.
J Infect Dis 2019

Anti-HDV prevalence in CHB patients in Italy

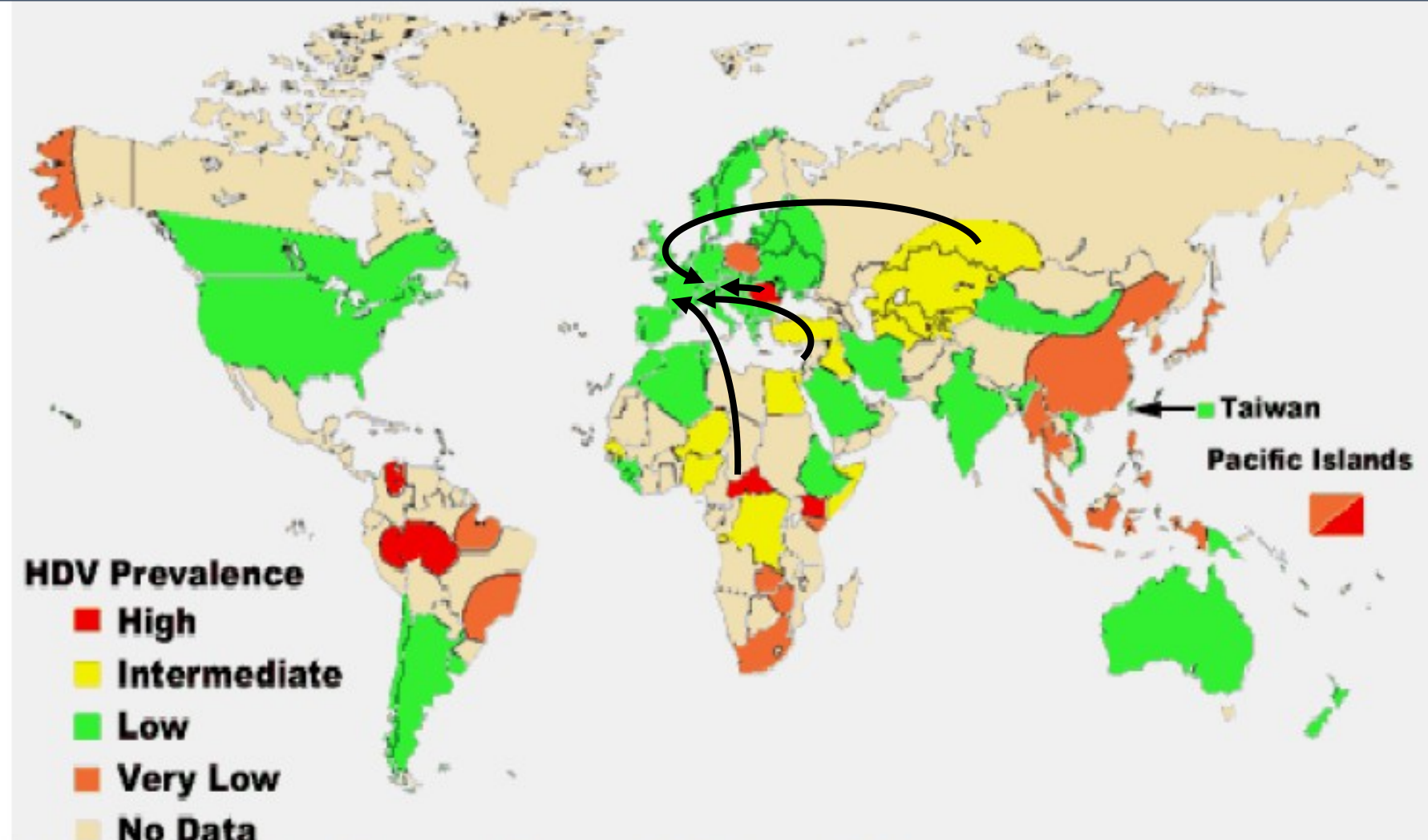


Increasing prevalence of HDV infection over 15 years (1997-2011) in France



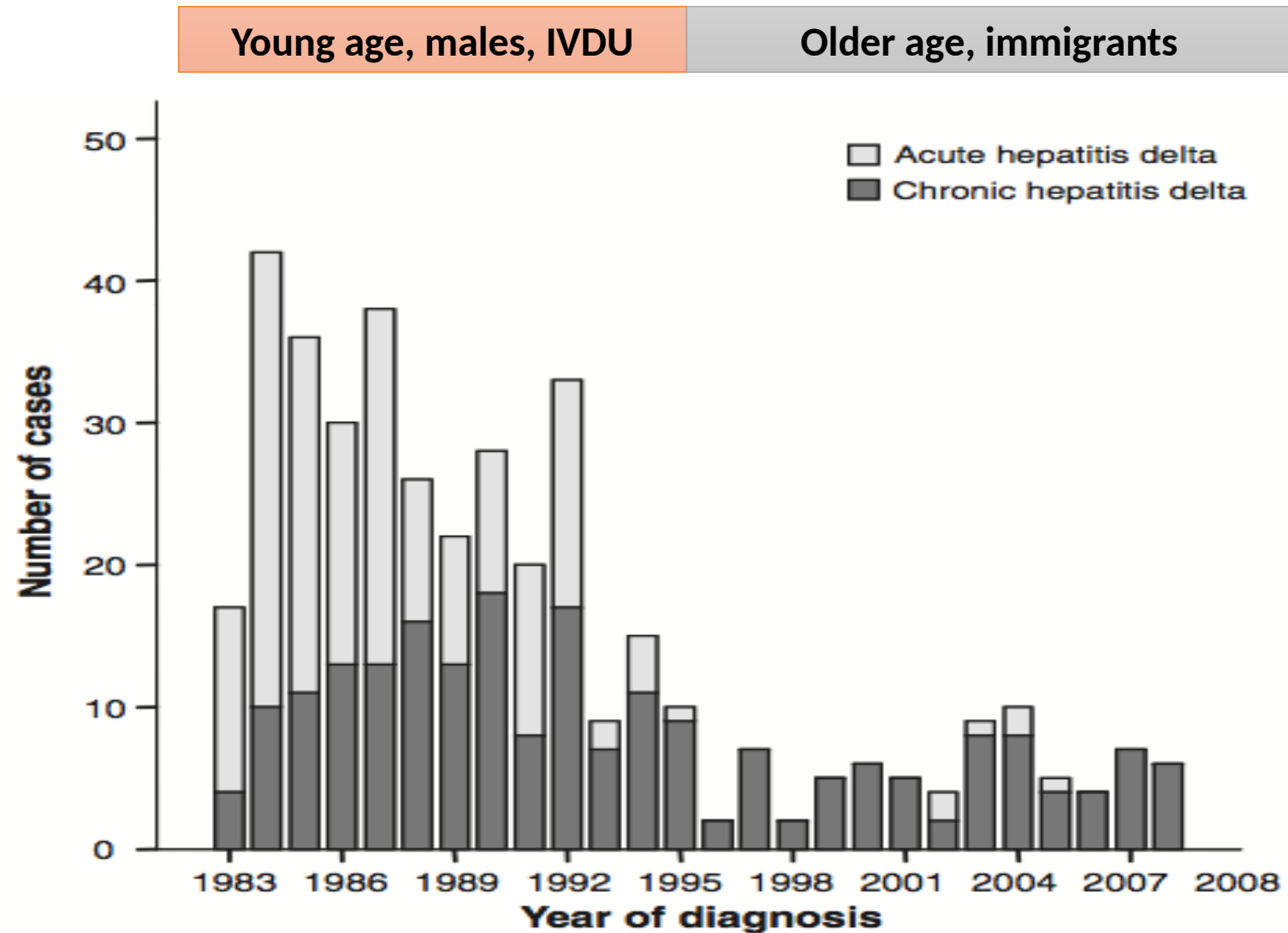
Worldwide distribution of HDV infection

Emerging HDV Epidemiology: Migration



From: Centers for Disease Control and Prevention (CDC), Atlanta, USA.⁶
http://www.cdc.gov/ncidod/diseases/hepatitis/slideset/hep_d/slide_6.htm

Changing epidemiology of HDV infection in Spain



Changes in epidemiology of chronic hepatitis delta: a report from Northern Spain

1215 patients diagnosed with CHB (1983-2012): **8.2% anti-HDV (+)**

- **Group A [1983-1997 (n=786)]: 9.4% anti-HDV**
 - risk factors: IVDU, blood transfusion, anti-HIV (+), ↑ ALT
- **Group B [1998-2012 (n=429)]: 6.1% anti-HDV**
 - risk factors: IVDU, **immigration, promiscuous sexual activity**, ↑ ALT

Etiology of chronic viral hepatitis in Romania

- Delta infection is the 3rd most common etiology of chronic viral hepatitis
- Occurs in ~50% of HBV infected patients

HDV infection in Turkey

- ▶ High prevalence among HBsAg+ patients
 - West: 16%, Southeast: 37%

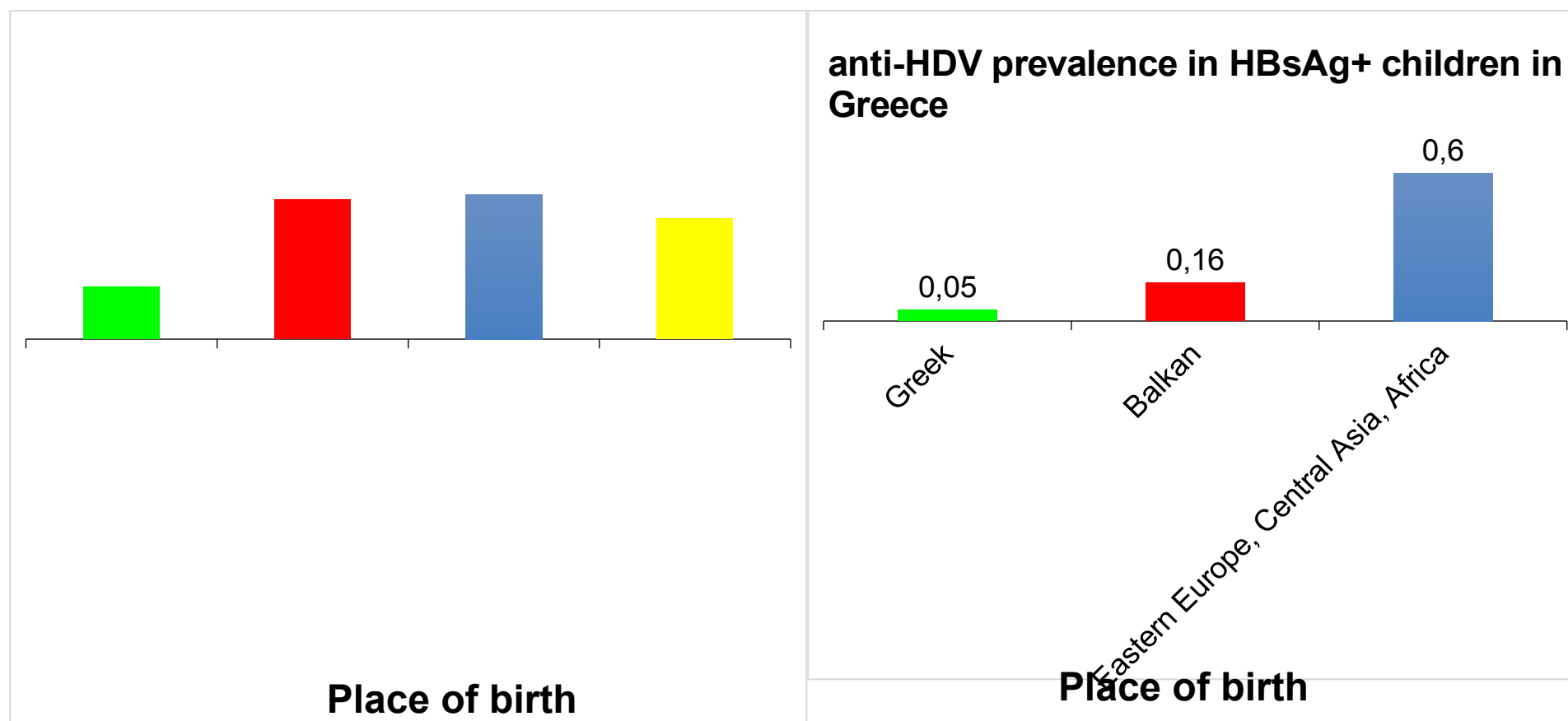
Toy et al. AASLD 2009

- ▶ Large retrospective study of anti-HDV prevalence in Turkey since 1980
- ▶ Anti-HDV prevalence decreasing over the last two decades

Degertekin H et al. Turk J Gastroenterol 2006; 17: 25-34.

Prevalence and clinical course of hepatitis delta infection in Greece: A 13-year prospective study

Emanuel K. Manesis^{1,*}, Georgia Vourli², George Dalekos³, Themistoclis Vasiliadis⁴,
Nina Manolaki⁵, Athina Hounta⁶, Sotirios Koutsounas⁷, Irini Vafiadis⁸, Georgia Nikolopoulou⁹,
Gregory Giannoulis¹⁰, George Germanidis¹¹, George Papatheodoridis¹², Giota Touloumi²



Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers in studies published after 1995

Area/Country	No. of studies	Date of data collection	Subjects tested, n	HDV prevalence among HBsAg-positive carriers
Europe				
Italy	1	2008	1386	8.1%
UK (London)	1	2000-2006	962	8.5%
Spain	1	1998-2012	429	6.1%
Greece	1	1997-2010	2137	4.2%
France	1	1997-2011	4492	2.0%
Romania	1	2011	2761	23.1%

Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers in studies published after 1995

Area/Country	No. of studies	Date of data collection	Subjects tested, n	HDV prevalence among HBsAg-positive carriers
North and South America				
USA	1	1999-2013	2175	3.4%
Colombia	2	2011-5	58	32.8%
Equador	1	1998	47	31.9%
Peru	1	1996	82	39.0%
Venezuela	1	2002-4	54	11.1%
Brazil (Amazon	6	1996-2006	291	36.8%

Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers in studies published after 1995

Area/Country	No. of studies	Date of data collection	Subjects tested, n	HDV prevalence among HBsAg-positive carriers
Asia including Middle East				
China	27	1997-2016	17163	5.6%
Iran	13	2000-2010	4358	3.9%
Pakistan	3	2000-2009	21	28.8%
Turkey	12	1997-2003	4712	7.9% (West: 4.8%, South-East: 27.1%, Central: 12.1%)
Lebanon	1	2007	107	0.9%

Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers in studies published after 1995

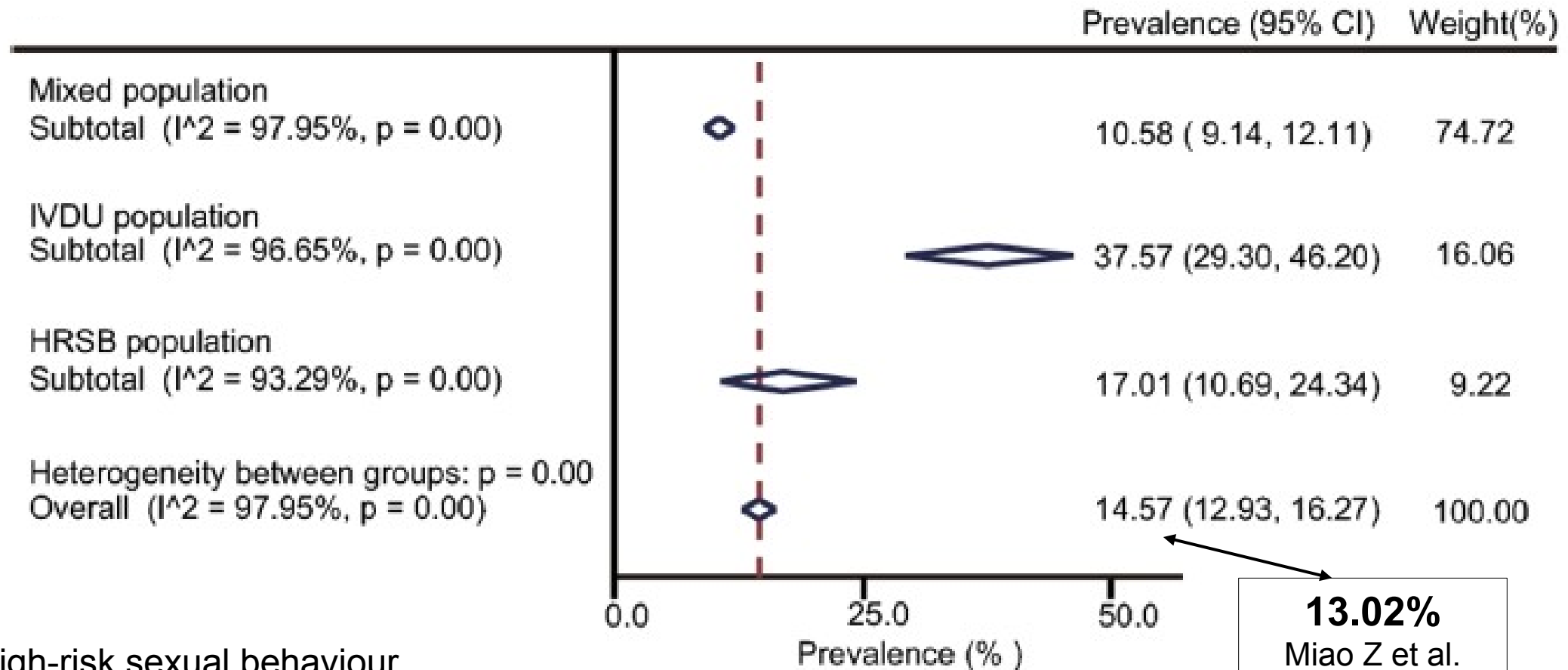
Area/Country	No. of studies	Date of data collection	Subjects tested, n	HDV prevalence among HBsAg-positive carriers
West & Central Africa				
Burkina Faso	2	2001 & 2015	217	3.2%
Benin	1	2011	44	11%
Gambia	2	2011	686	1.3%
Ghana	1	2015	107	8%
Mauritania	3	2008-2009	718	19%
Nigeria	1	2014	103	5%
Senegal	1	2003	175	3%
Cameroon	3	2007-2011	1903	13%

Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers in studies published after 1995

Area/Country	No. of studies	Date of data collection	Subjects tested, n	HDV prevalence among HBsAg-positive carriers
East & Southern Africa				
Mozambique	1	2007	146	0%
South Africa	2	2008	93	0%

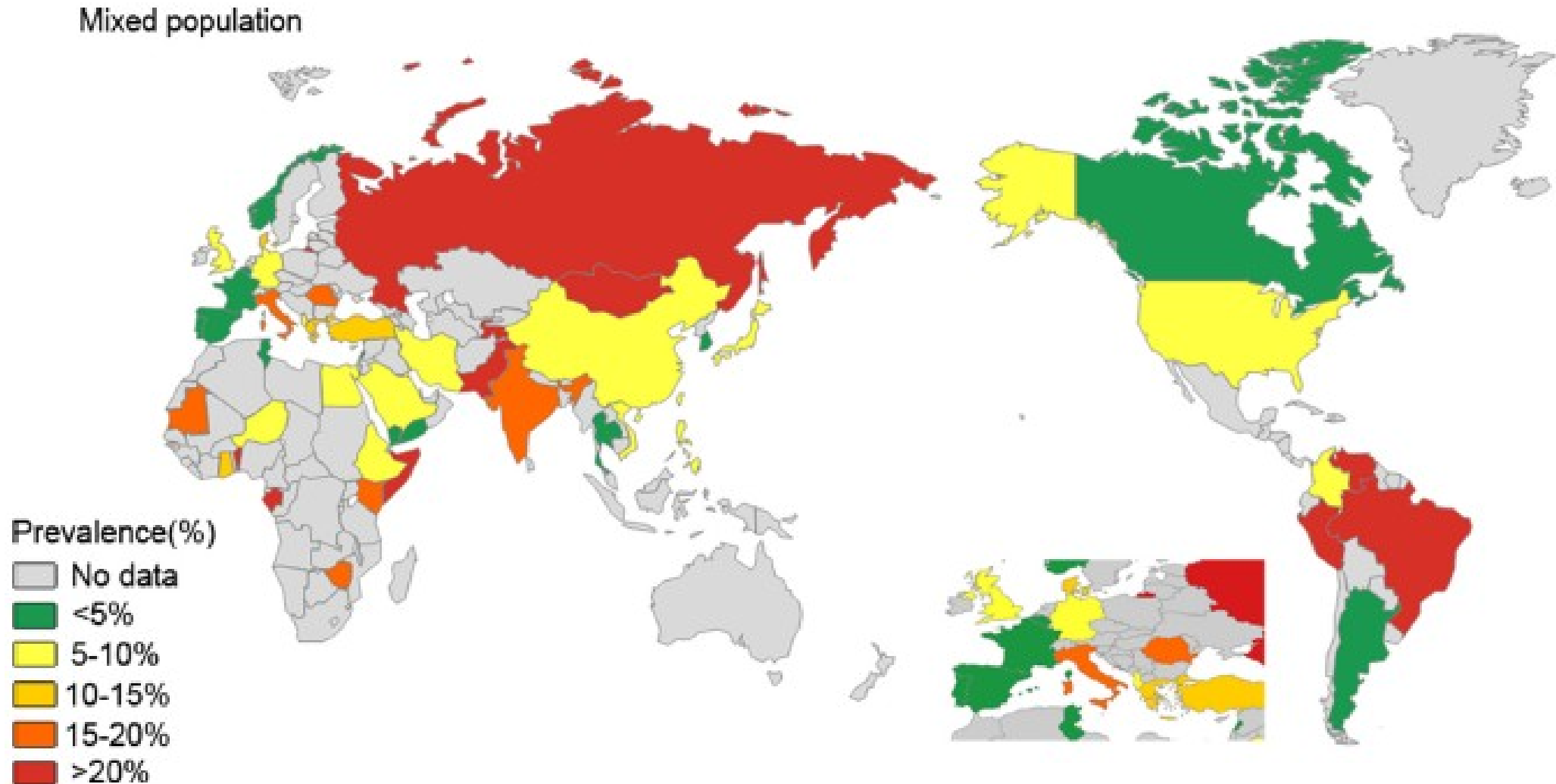
Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers: Systematic review

182 studies, 295 cohorts from 61 countries/regions, 40,127,988 individuals (0.54% of global population)



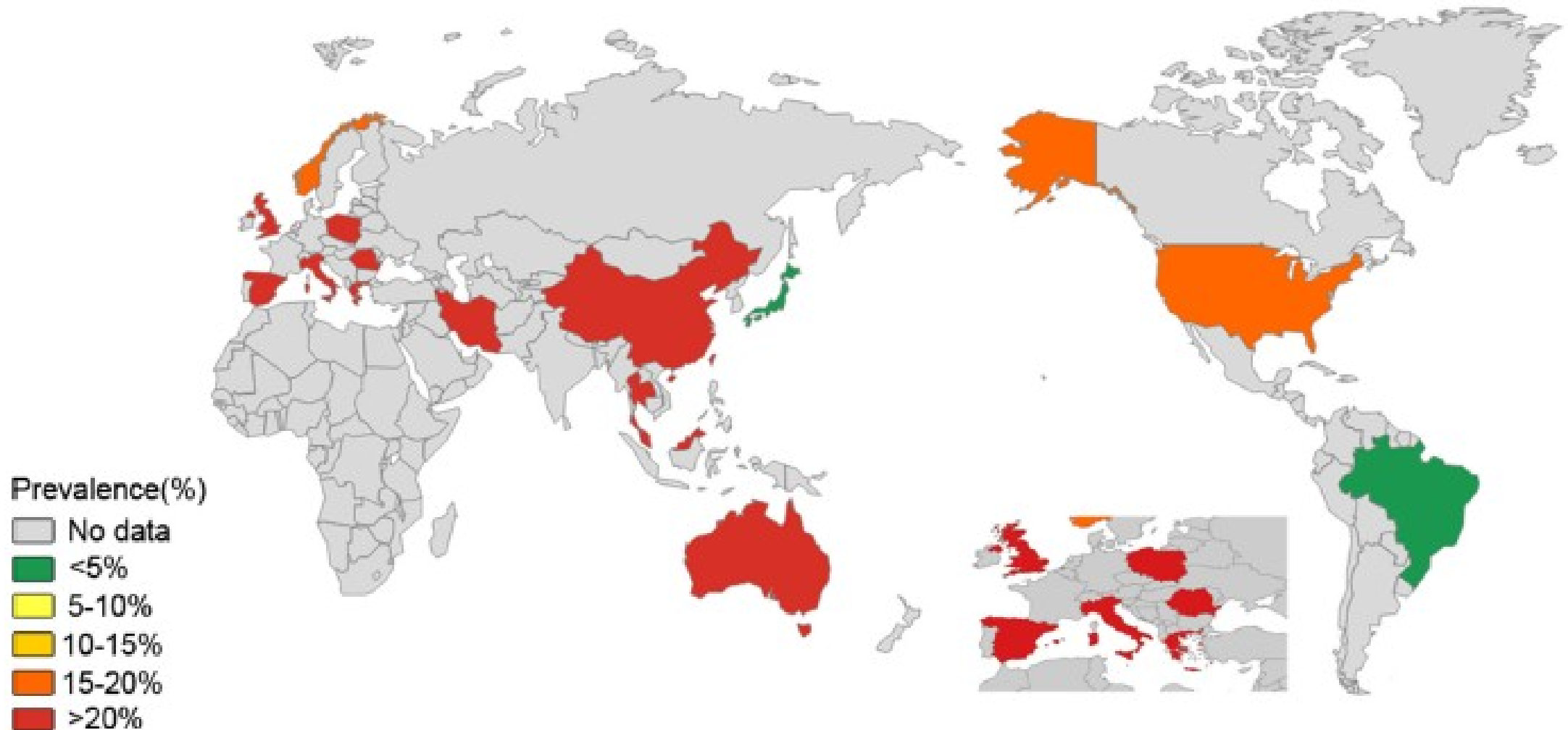
HRSB: high-risk sexual behaviour

Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers: Systematic review



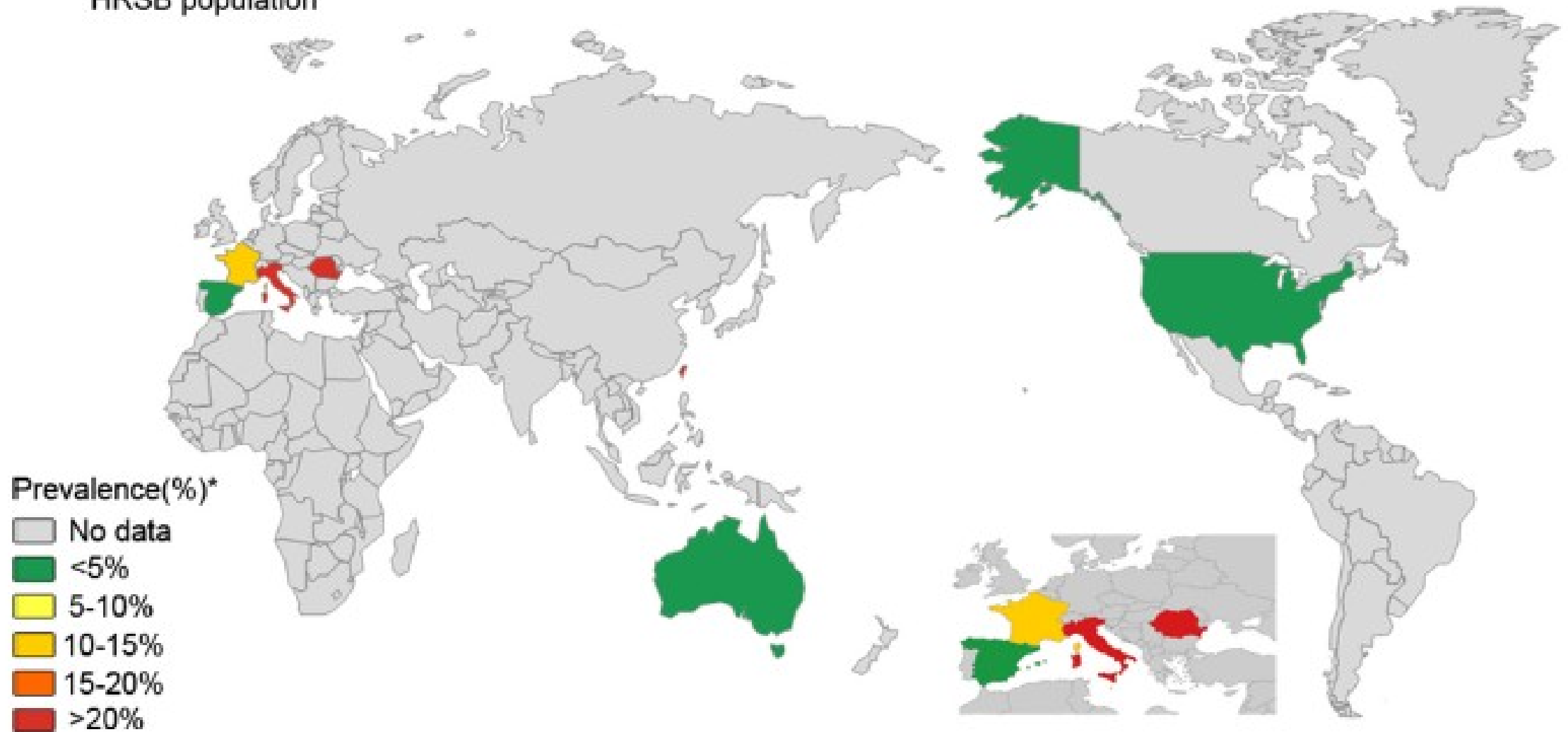
(HDV) among HBsAg-positive carriers: Systematic review

IVDU population



Seroprevalence of antibodies against hepatitis D virus (HDV) among HBsAg-positive carriers: Systematic review

HRSB population



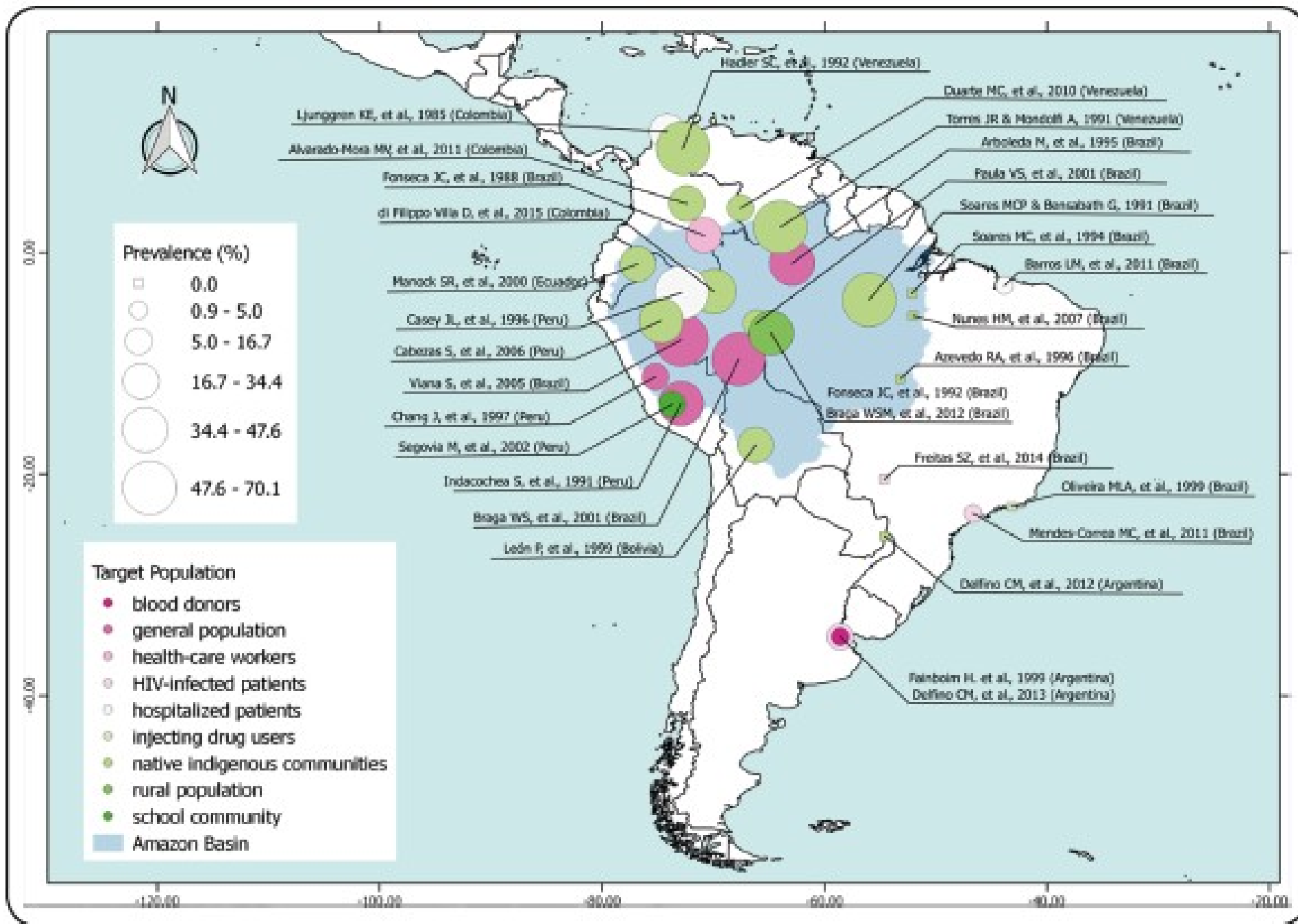
HRSB: high-risk sexual behaviour

Chen H-Y et al. Gut 2018, Sep 18

HDV prevalence

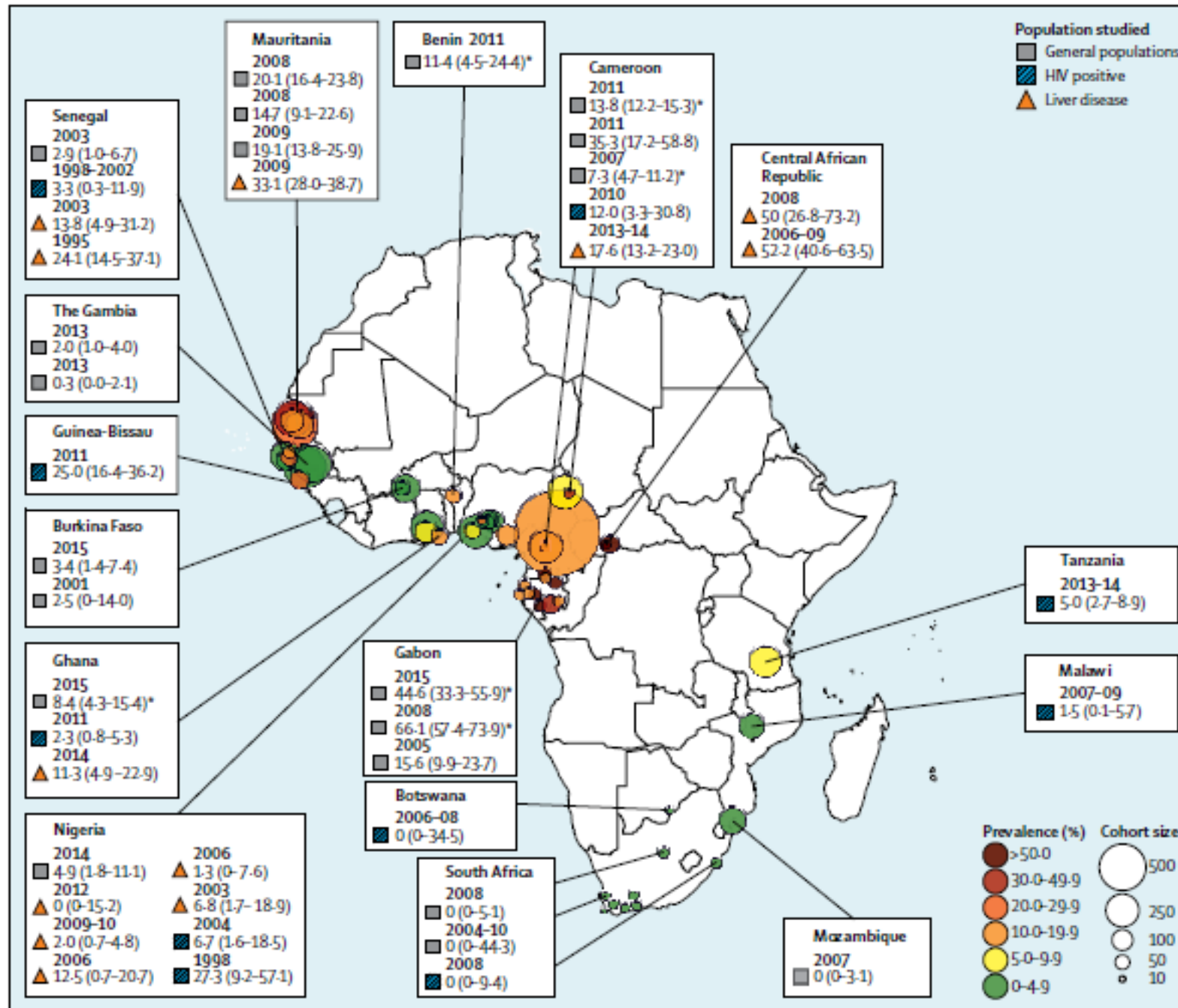
Representative Study Samples?

Under- / Over- estimation?



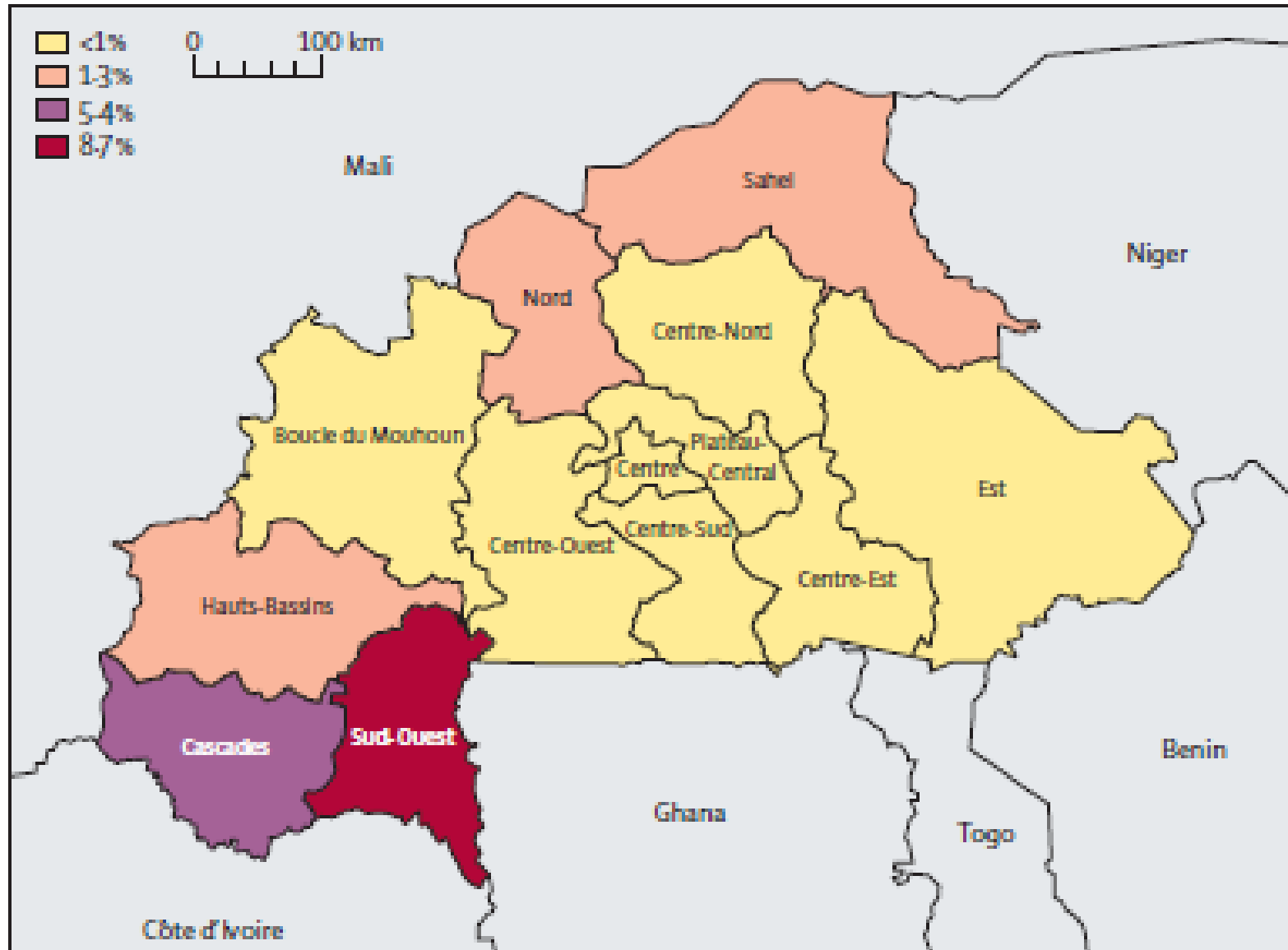
HDV seroprevalence in HBsAg+ patients in Sub-Saharan Africa

Systematic review
30 studies, 1995-2016



Stockdale AJ et al.
Lancet Glob Health
2017; 5: e992-e1003.

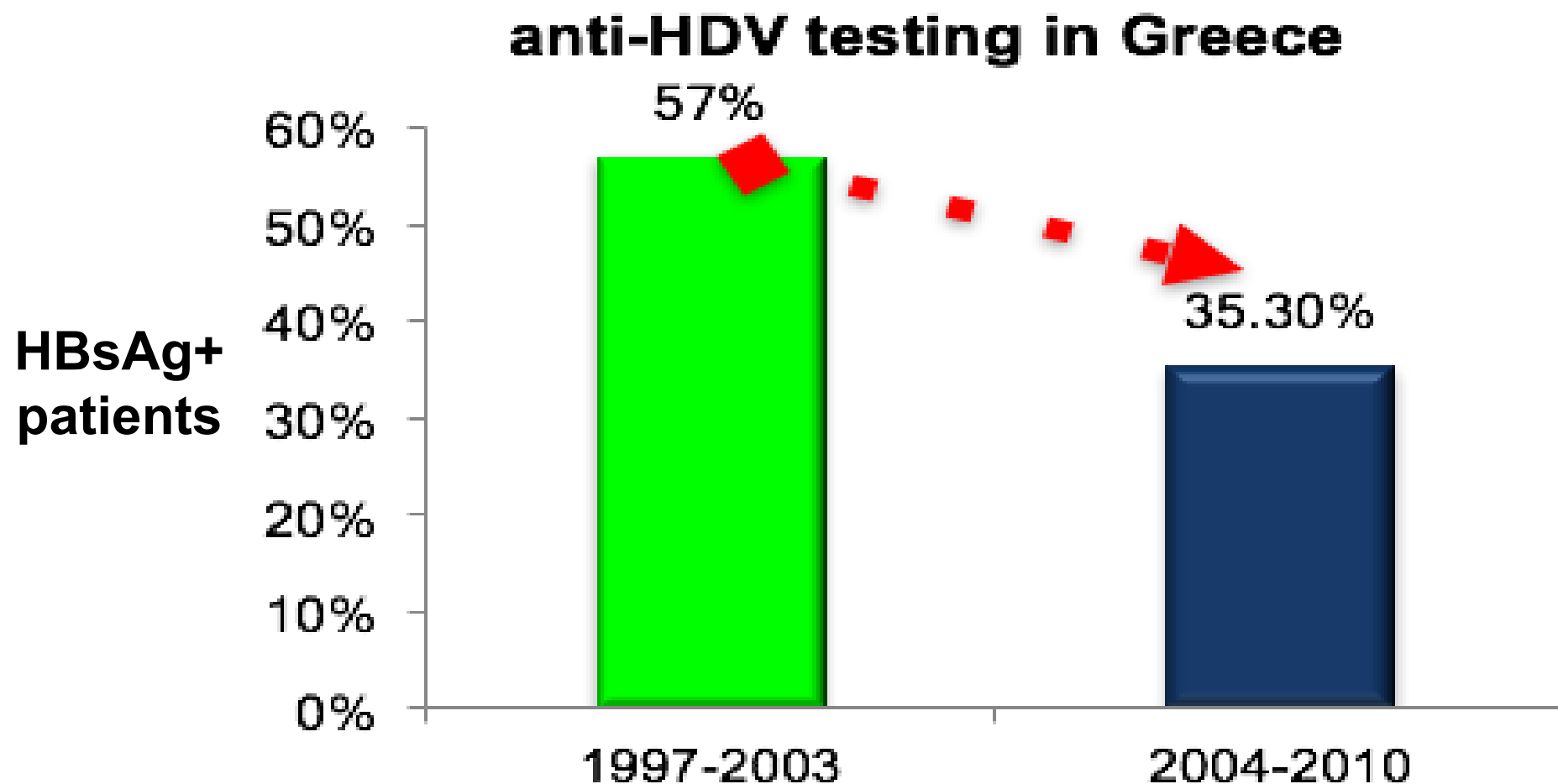
Anti-HDV prevalence in HBsAg+ patients in Burgina



Tuillon E et al. Lancet Global Health 2018; 6: e33.

HDV burden Underestimation

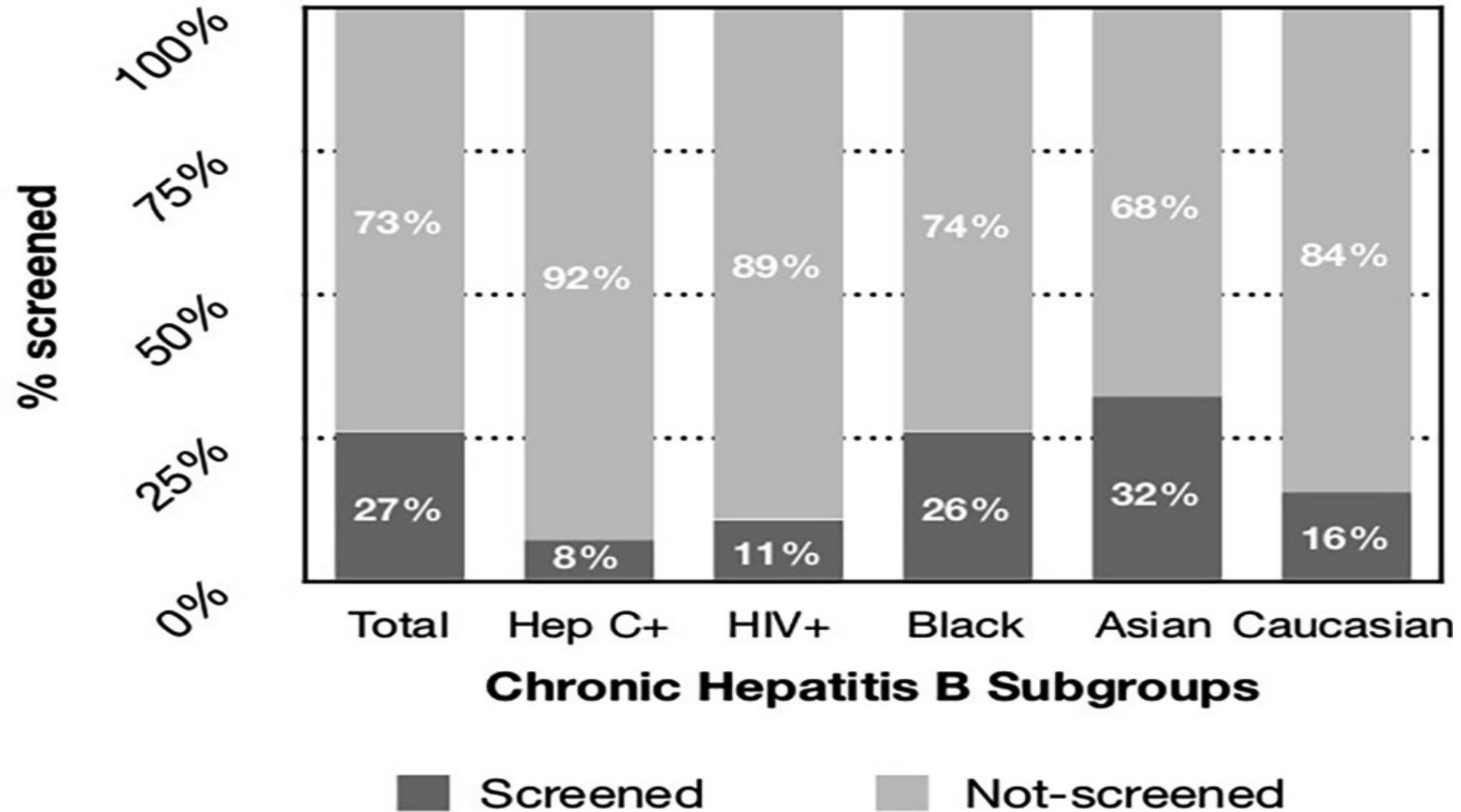
To find hepatitis D, you have to remember it



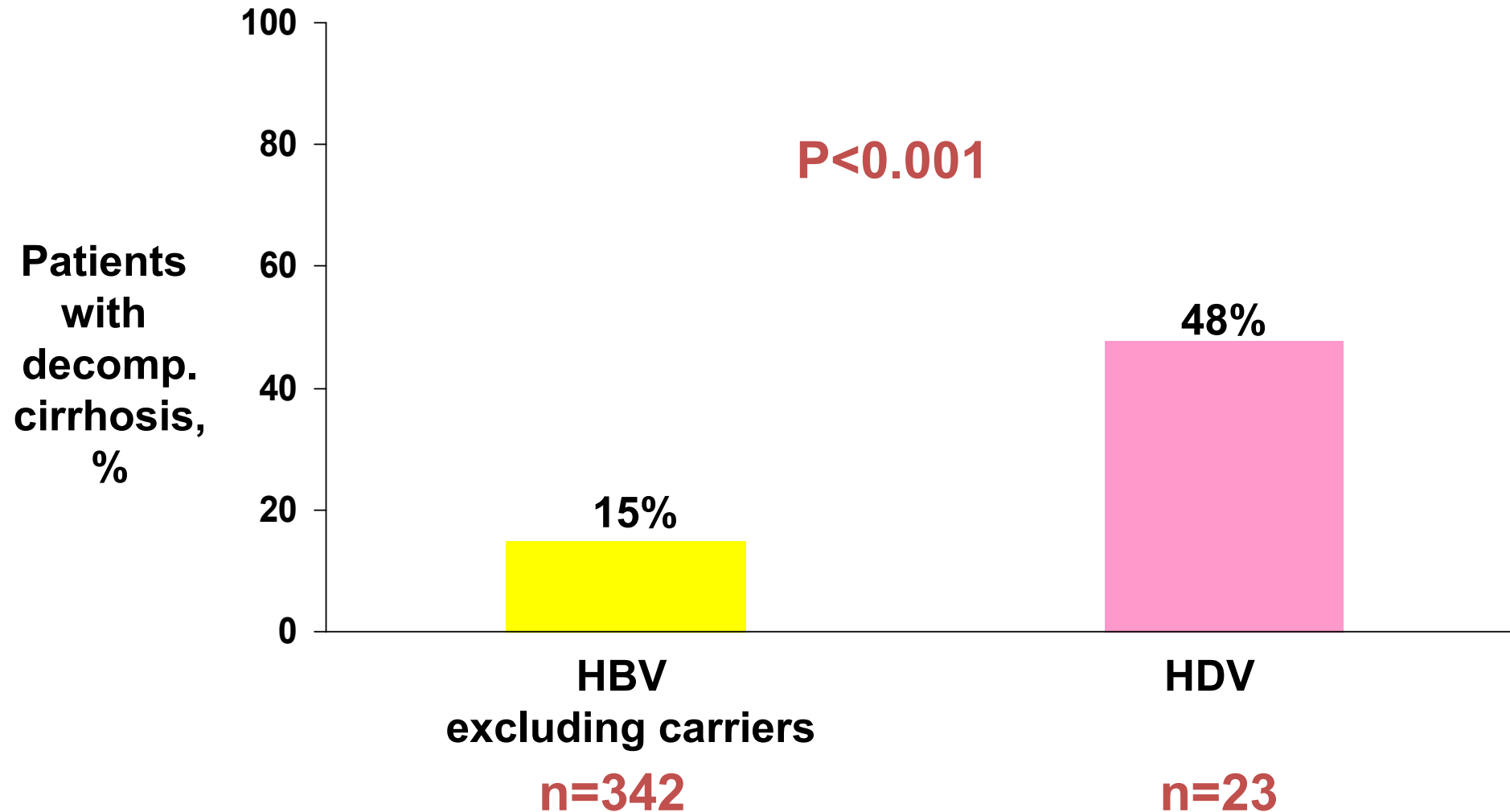
HDV screening in HBsAg+ patients

- 339 HBsAg+ patients
- Seen at a tertiary academic institution (*Department of Internal Medicine, Section of Hepatology, Rush University Medical Center, Chicago IL, USA*)
- January 1, 2014, and January 1, 2019

Hepatitis D Screening Rates Among Patients with Chronic HBV



Proportion of patients with decompensated cirrhosis among cases with chronic HBV ± HDV infection at Hippokration hospital, Athens, Greece (2002-2006)



HDV infection in Turkey

- ▶ Large retrospective study of anti-HDV prevalence in Turkey since 1980
 - 3% of 1416 patients with acute viral hepatitis
 - 8% of 766 patients with acute hepatitis B
 - 5% of 6613 inactive HBsAg carriers
 - 20% of 5961 patients with CHB
 - 32.5% of 1264 patients with liver cirrhosis
 - 23% of 748 patients with HCC

New epidemiology of hepatitis delta - Conclusions

- HDV infection: global health problem - increased liver related and overall mortality
- Global HDV - prevalence: under/over estimated? - burden: underestimated
- HDV: still endemic in many developing countries
- Immigrants from high prevalence countries, Illicit drug users, people with high-risk sexual behaviours and HIV co-infected: high-risk groups in the Western world
- Genuine decrease in HDV prevalence in developed countries in 1990's -
no further decline and perhaps a slight increase in the last decade due to migration from endemic countries
- Need for universal HBV vaccination –Need for universal HDV screening in HBV+ patients



HDV

Extreme infectivity in the HBsAg setting:
transmitted to HBsAg+ chimps with 100 000 000 000
dilutions of a HBV/HDV serum

Dissemination depends on HBsAg prevalence and
poor sociohygienic conditions

Ubiquitous , found everywhere it was tested

Prevalent in developing and poor areas of the world,
in rural more than urban areas

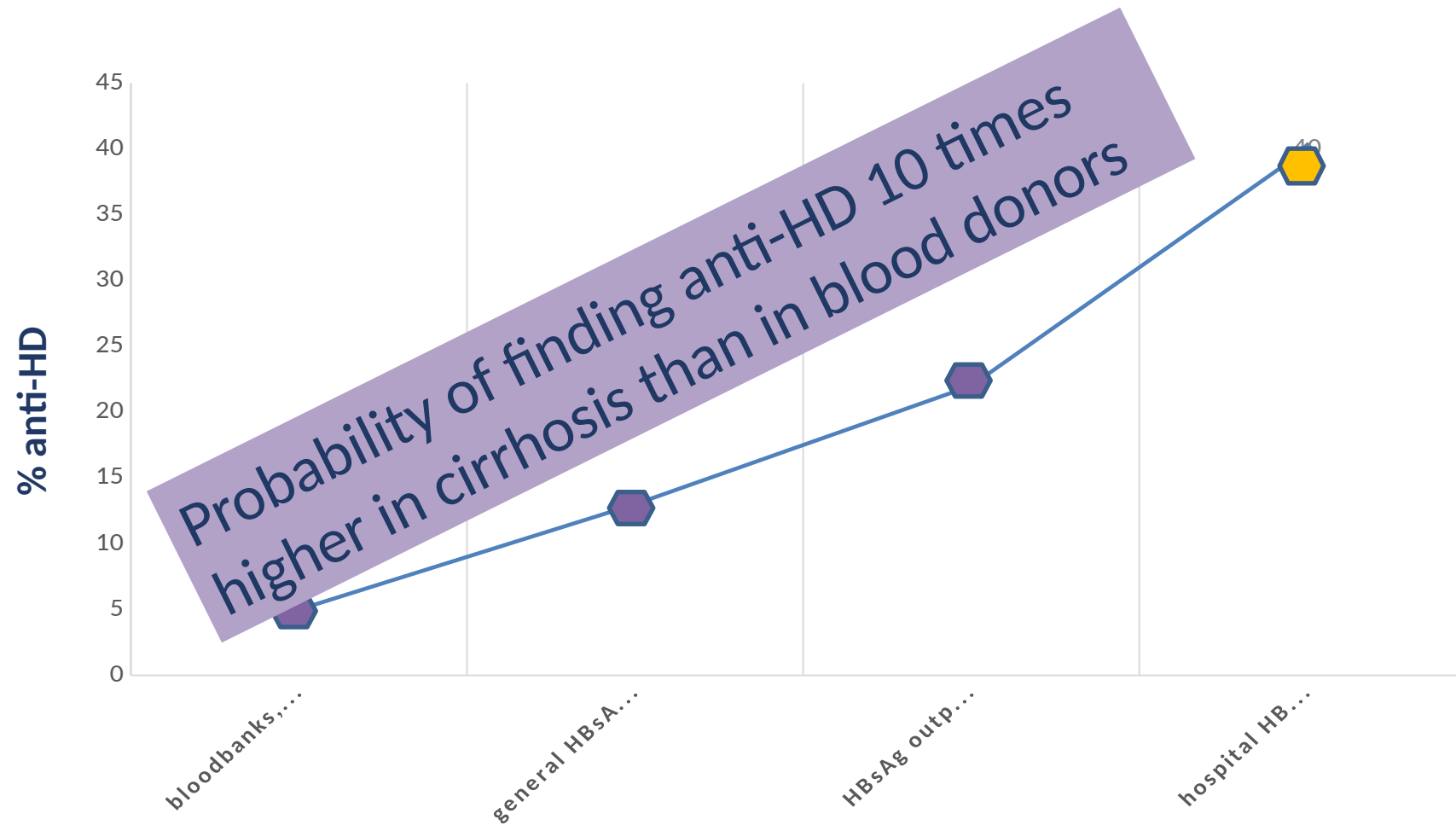
HDV results in the development of liver cirrhosis in approximately 70% of cases within 5 to 10 years of infection ,with a three fold higher risk of liver cirrhosis in HDV/HBsAg co-infected than in HBV mono-infected

Fattovich G et al Gut. 2000; 46: 420-26.

Thus anti-HD increases in parallel with severity of the liver disease and therefore the probability of finding the antibody throughout the spectrum of HBsAg liver disorders is lowest in asymptomatic/ minor forms and highest in cirrhosis

Rizzetto M,Ciancio A 2012;32:211-9

Endemic HDV areas: prevalence of anti-HD in HBsAg carriers recruited at different sites



PREVALENCE OF ANTI-HD IN DIFFERENT HBsAG CATEGORIES: ASYMPTOMATIC BLOOD DONORS VS CIRRHOTICS

	<u>Italy,1983</u> ¹	<u>Iran ,2014</u> ²	<u>Uzbekistan</u> ³
<u>Blood donors</u>	5 %	2 %	8 %
<u>Cirrhotics</u>	51 %	65,9 %	> 80 %

1 Smedile A, Lavarini C, Farci P,et al .Am J Epidemiol. 1983 ;117:223-9.

2 Keshvari M, Alavian SM, Aghaee B et al Transfus Med. 2014 ;24:411-7.

3 E.Musabaev, personal communication

Prevalence of anti-HD in Africa , 2019

Marocco, Algeria,Mali, Burkina-Faso, Sudan,
Gambia,,Benin ,Botswana,
Mozambique , South Africa:
*patients collected at blood banks,
pregnancy clinics, in the general
population, in outpatients clinics*

Tunisia,Libya.Egypt,Mauretania
,Senegal,Nigeria,CentraAf.Rep,
Ethiopia,Somalia :
*patients with chronic HBsAg liver
disease*

Cameroon and Gabon;
general population

