



IS HEPATITIS DELTA UNDERESTIMATED?

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Conflict of interest:

advisor/lecturer for, research grants from and principal investigator in clinical trials sponsored by Gilead Sciences;

principal investigator in clinical trials sponsored by Eiger BioPharmaceuticals.

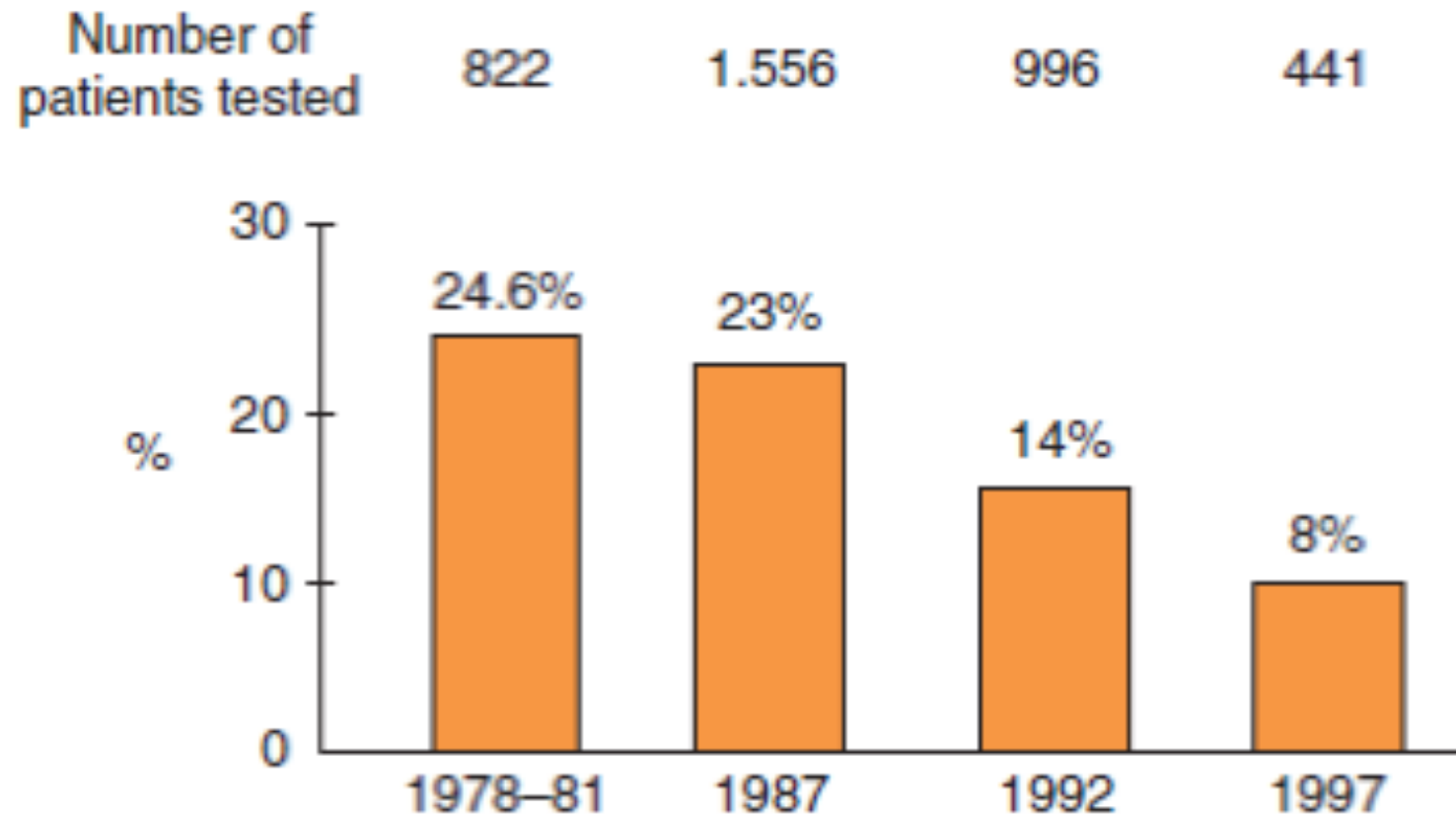
IS HEPATITIS DELTA UNDERESTIMATED?

- Is HDV prevalence underestimated?
- Is HDV related burden of disease underestimated?

HDV prevalence in the eighties

- **Anti-HDV prevalence:** wide variation among geographical regions
- **High endemicity:** low income countries in central Africa & S America
- **Intermediate endemicity:** Mediterranean area
(Italy: 25%, Turkey: 30% of HBsAg+ cases)
- **Low endemicity:** low HBV prevalence - N Europe & N America (IVDUs)
high HBV prevalence – Korea, Indonesia, Japan
(endemic HDV pockets)

Anti-HDV prevalence in CHB patients in Italy



Decreasing HDV prevalence in the nineties

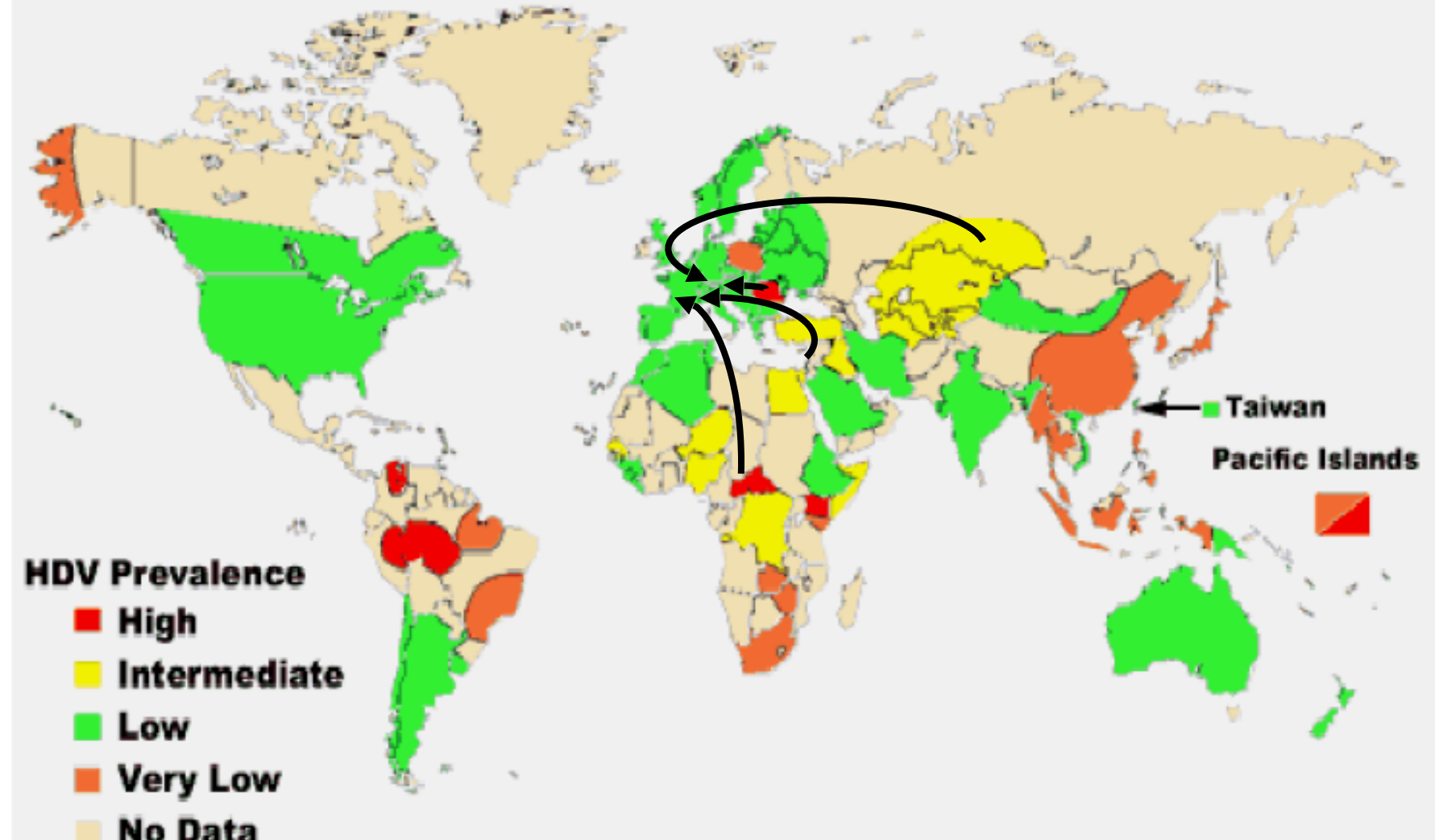
- Significant improvements in public health
- Modifications in sexual behaviors due to HIV
- Introduction of universal HBV vaccination at an early age
- Widespread availability of single use syringes

Perception of HDV prevalence in early 2000

- Complete HDV eradication was expected sooner rather than later

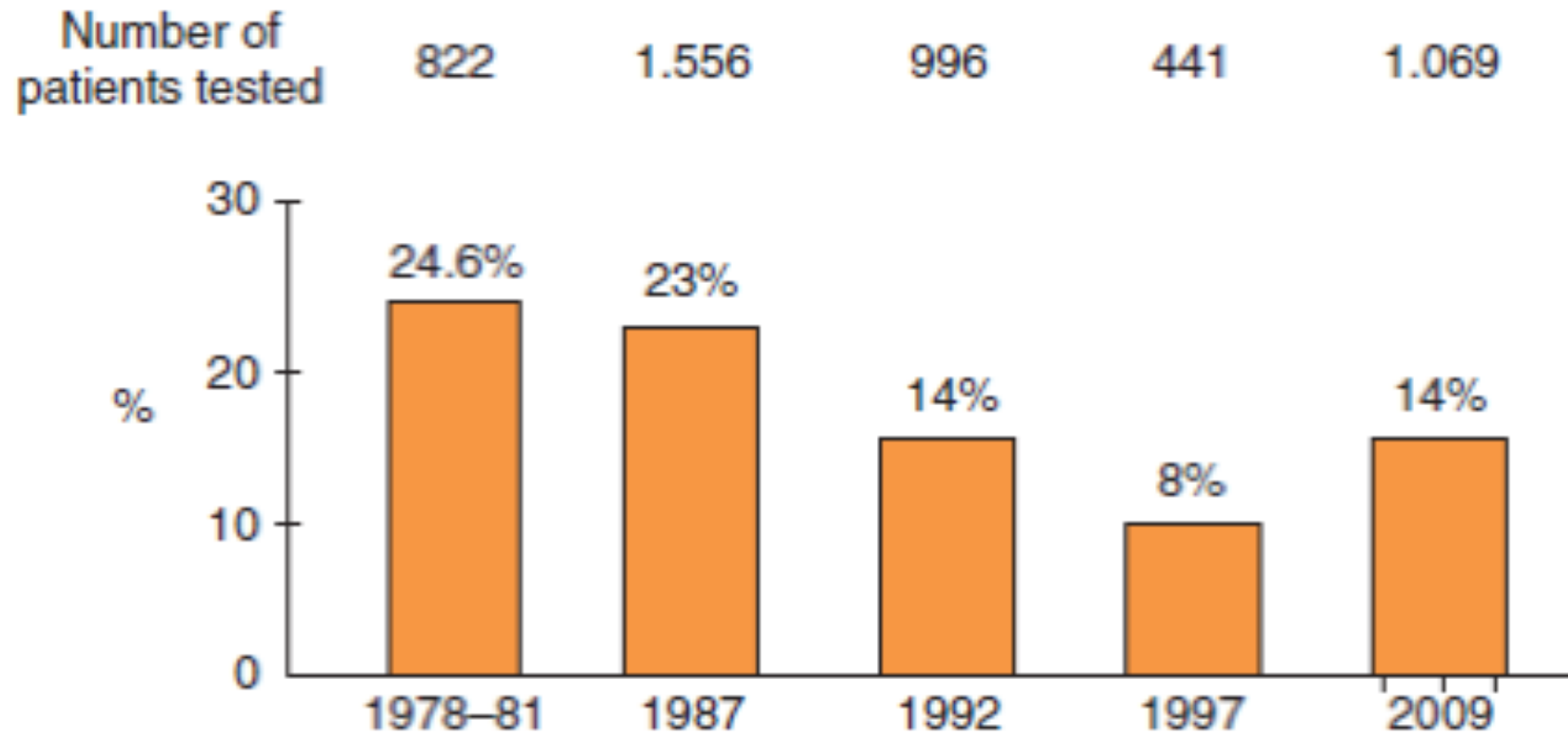
Worldwide distribution of HDV infection

Emerging HDV Epidemiology: Migration

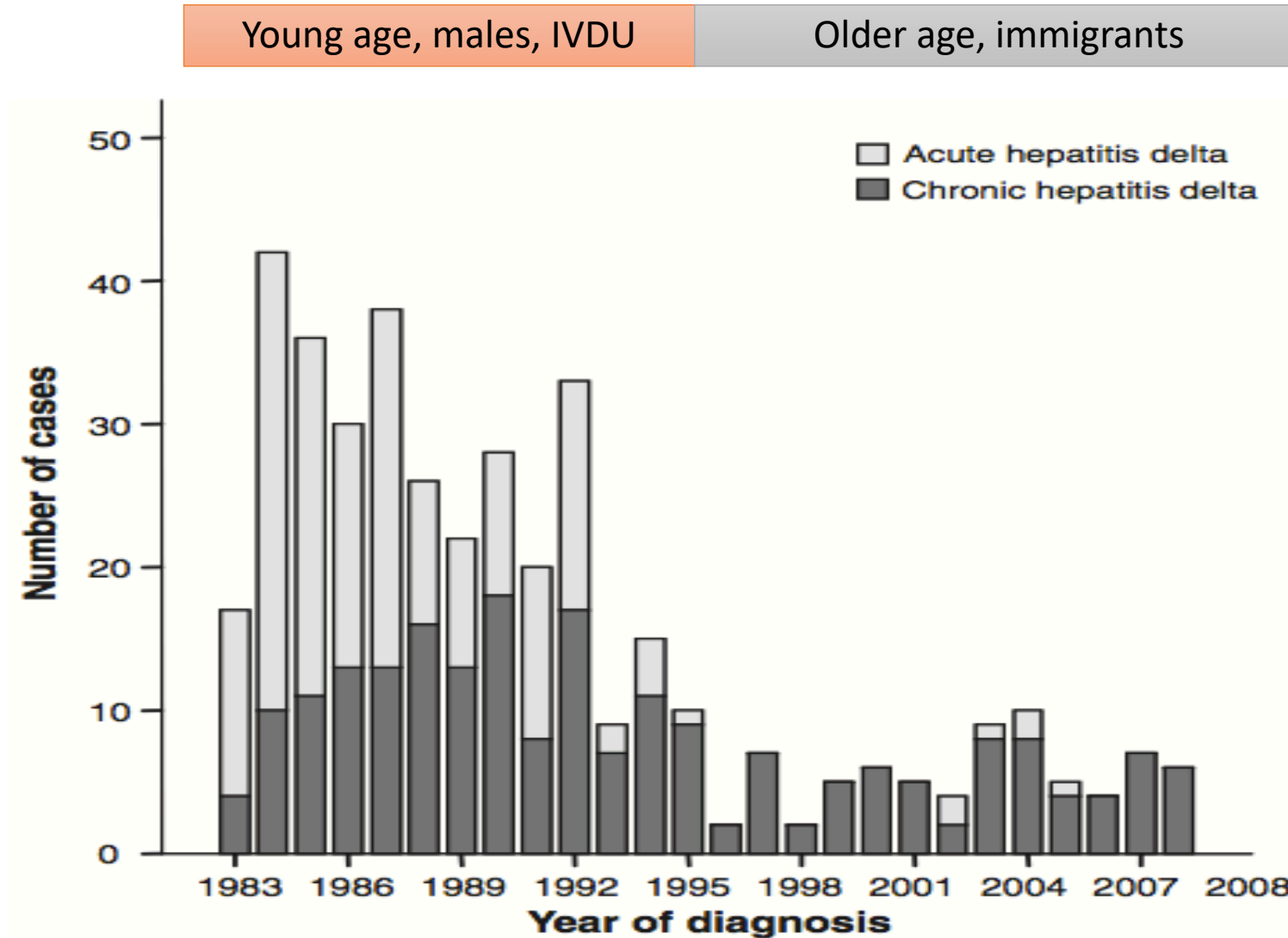


From: Centers for Disease Control and Prevention (CDC), Atlanta, USA.⁶
http://www.cdc.gov/ncidod/diseases/hepatitis/slideset/hep_d/slide_6.htm

Anti-HDV prevalence in CHB patients in Italy



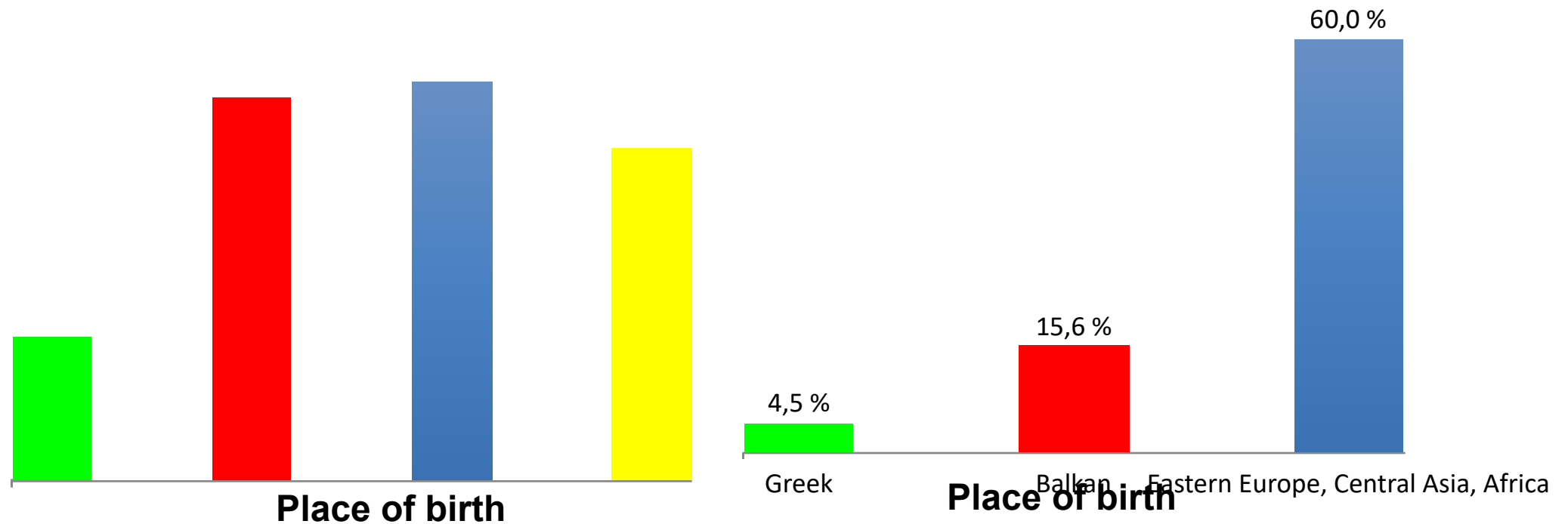
Changing epidemiology of HDV infection in Spain



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

anti-HDV prevalence in HBsAg+ children in
Greece



2017 WHO Global Hepatitis Report

- Global and regional estimates on viral hepatitis in 2015
- HDV prevalence: still a subject of debate -
declared uncertain

Recent estimations on global HDV prevalence

	Chen, Gut 2019/2020	Miao, J Infect Dis/J Hep 2020	Stockdale, J Hep 2020
Studies included in meta-analysis	182	634	282
Publication period of studies included	01/01/1977 - 31/12/2016	01/01/1982 - 01/02/2019	01/01/1998 - 28/01/2019
Number of subjects included	40,127,988 general population subjects from 61 countries (one study from France: 39,911,011 subjects); 101,363 HBsAg+ cases from 51 countries	332,155 general population subjects from 48 countries 271,629 HBsAg+ cases from 83 countries	24,025,000 general population subjects from 50 countries; 120,293 HBsAg+ cases from 95 countries
Global HDV prevalence	0.98% (0-8%) in general population (1% in 1977-2016 & 2017-18), 14.6% in HBsAg+ cases (10% in 1977-2016 & 7% in 2017-18)	0.80% in general population, 13.0% in HBsAg+ cases; revised to 0.70% in general population & 13.0% in HBsAg+ cases	0.16% in general population, 4.5% in HBsAg+ cases of general population, 16.4% in HBsAg+ cases of Hepatology clinics
Estimated global HDV cases, n	Approximately 72 million	48-60 million, revised to 32-61 million	12 (8.7-18.7) million

Uncertainties of current HDV prevalence

- Denominator (general population or HBsAg+ cases)
- Uncertainty of denominator (HBsAg+ cases)
- Representative study samples used for HDV prevalence estimation

Recent estimations on global HDV prevalence

	Chen, Gut 2019/2020	Miao, J Infect Dis/J Hep 2020	Stockdale, J Hep 2020
Method of HDV diagnosis	Anti-HDV, HDAg, HDV RNA	Anti-HDV, HDAg, HDV RNA	Anti-HDV
Publication period of studies included	01/01/1977 - 31/12/2016	01/01/1982 - 01/02/2019	from community surveys, antenatal clinics, occupational settings, students, blood donors
Global HDV prevalence	0.98% (0-8%) in general population (1% in 1977-2016 & 2017-18), 14.6% in HBsAg+ cases (10% in 1977-2016 & 7% in 2017-18)	0.80% in general population, 13.0% in HBsAg+ cases; revised to 0.70% in general population & 13.0% in HBsAg+ cases	4.5% in HBsAg+ cases of general population, 16.4% in HBsAg+ cases of Hepatology clinics
Estimated global HDV cases, n	Approximately 72 million	48-60 million, revised to 32-61 million	12 (8.7-18.7) million
Method of estimation	7393 million global population x 0.98% = 72 million HDV+?	7487 million global population x 0.70% = 52 million HDV+? 250 million HBsAg+ cases x 13% = 32.5 million HDV+?	267 million HBsAg+ cases x 4.5% = 12 million HDV+?

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Chronic hepatitis D in anti-HDV+ patients

Not all anti-HDV+ cases have active HDV related liver injury

HDV RNA+ in anti-HDV+ patients:
58.5% (95% CI: 52.4% - 64.5%)

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

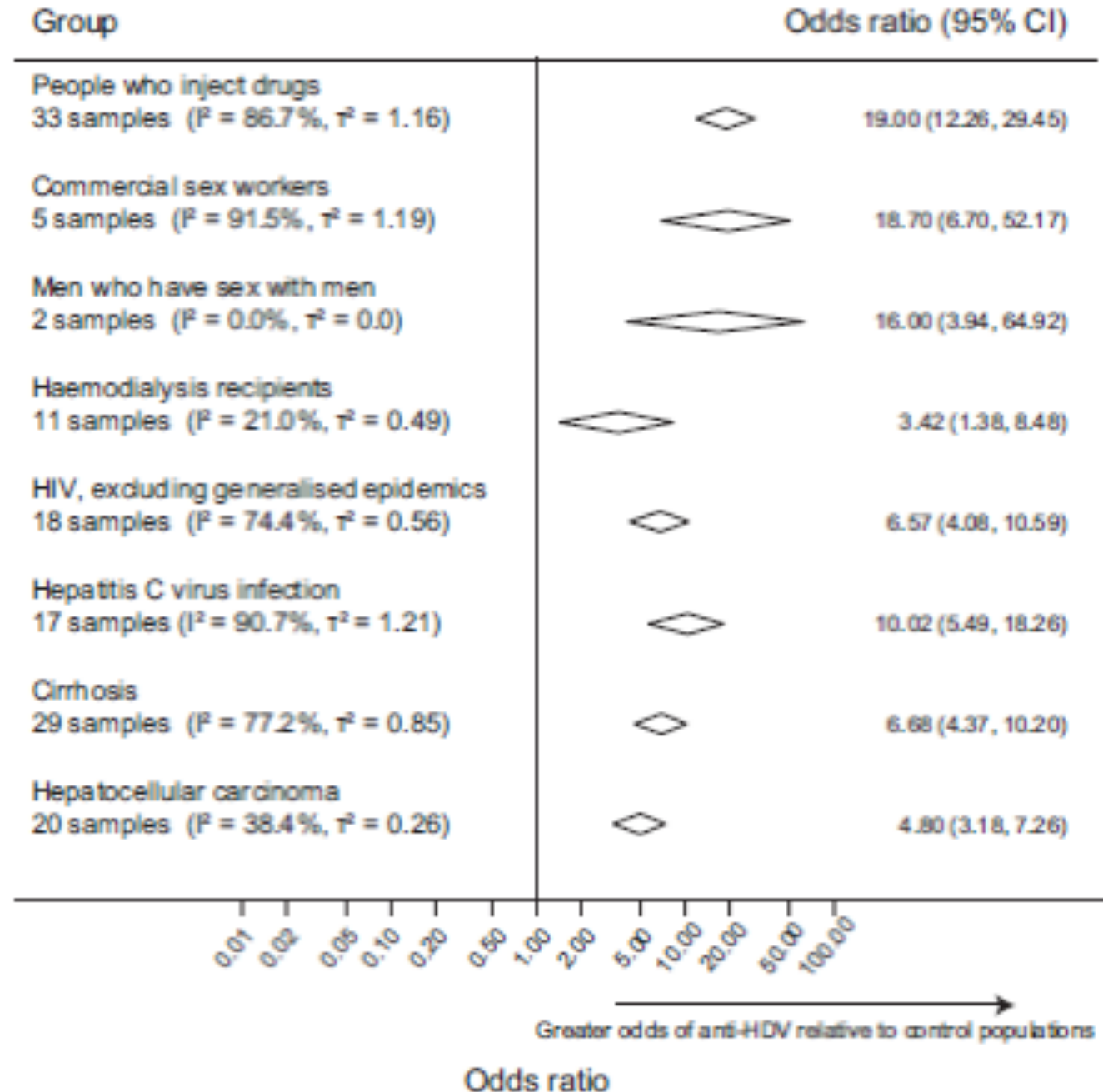
Rizzetto M. J Hepatol 2009; 50: 1043-50;

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

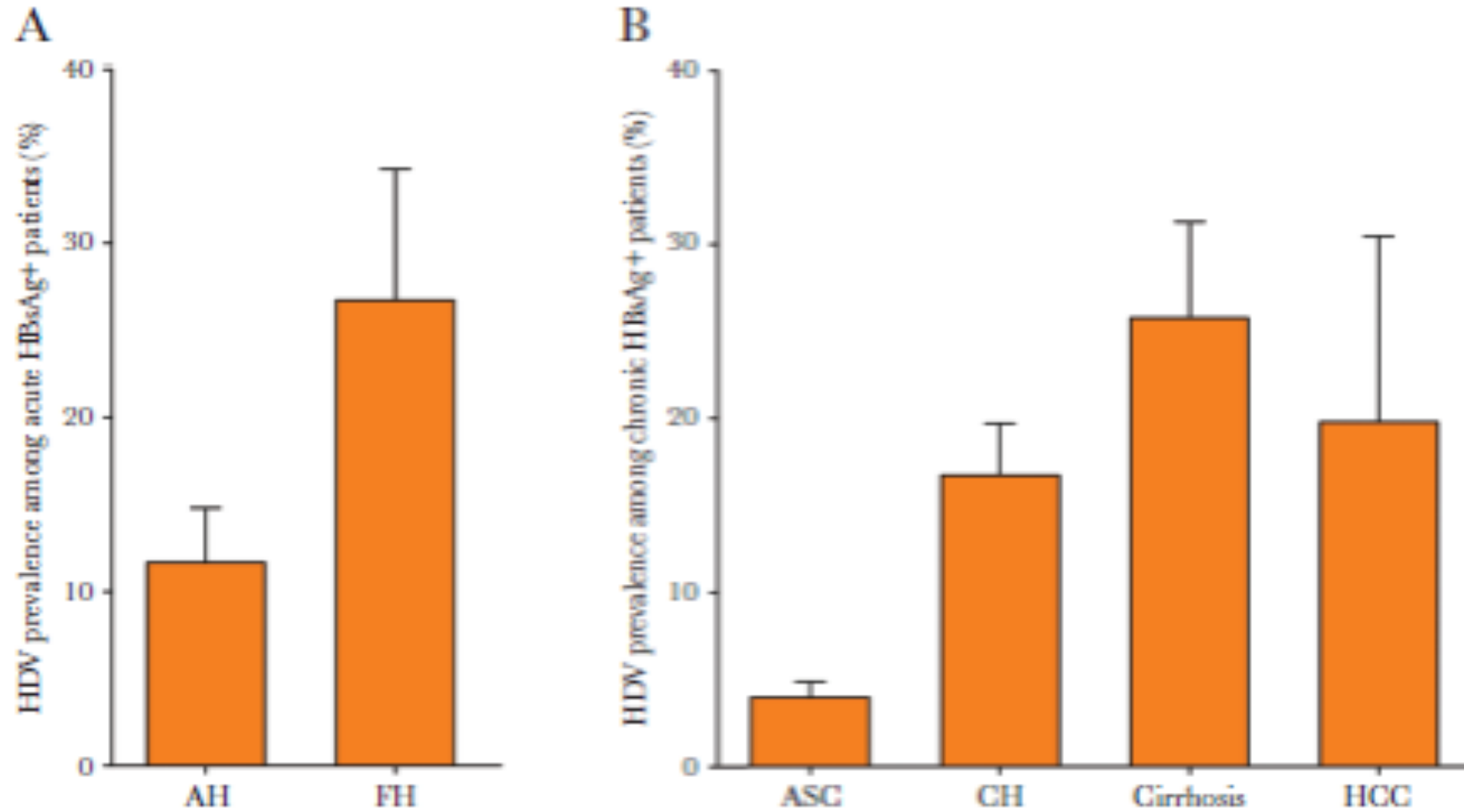
HDV prevalence

in specific subgroups
relative to HBsAg+ cases of
general population in the
same region

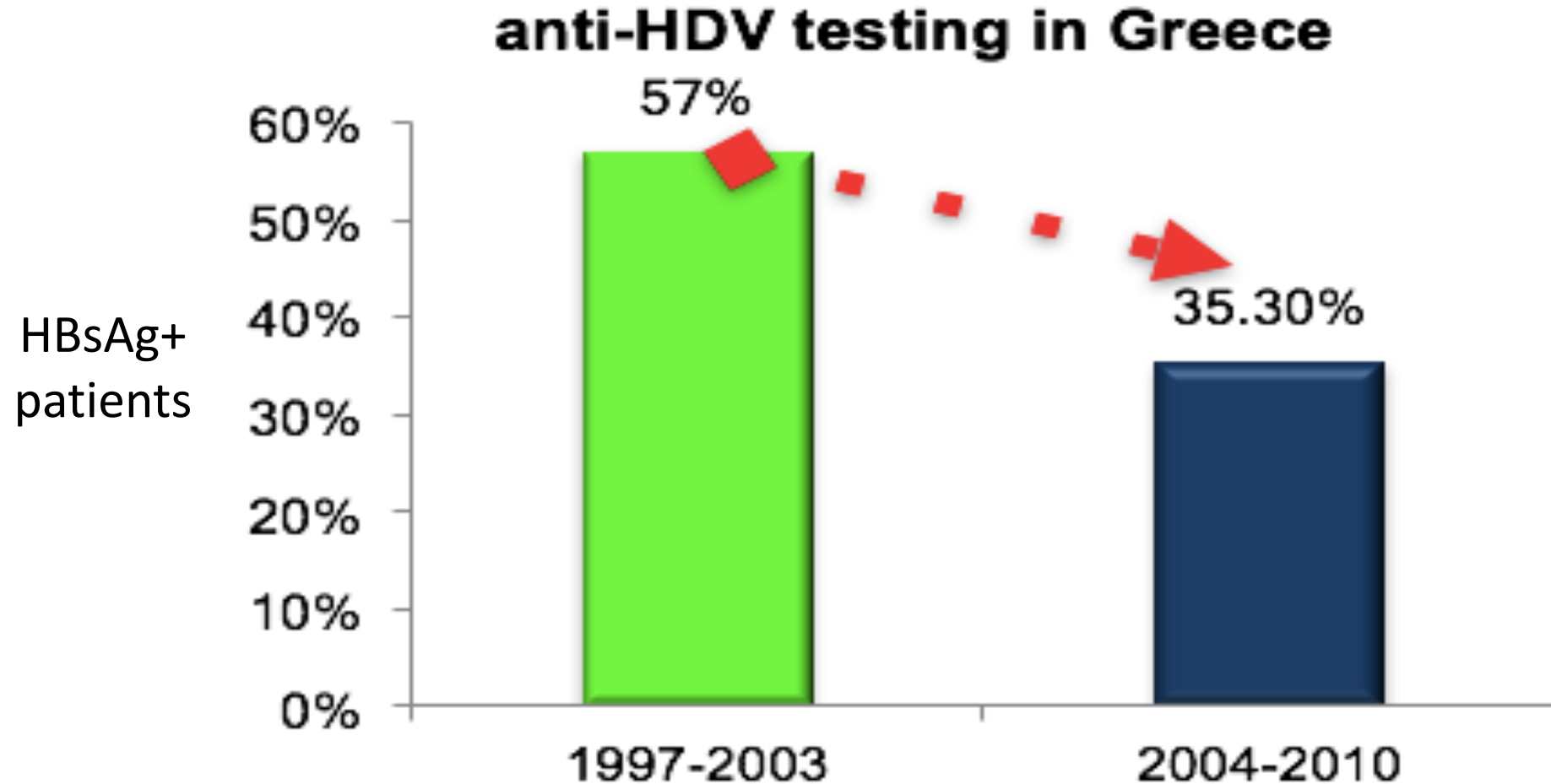
- HBsAg+ cirrhosis: 18%
- HBsAg+ HCC: 20%



HDV prevalence in specific HBsAg+ subgroups



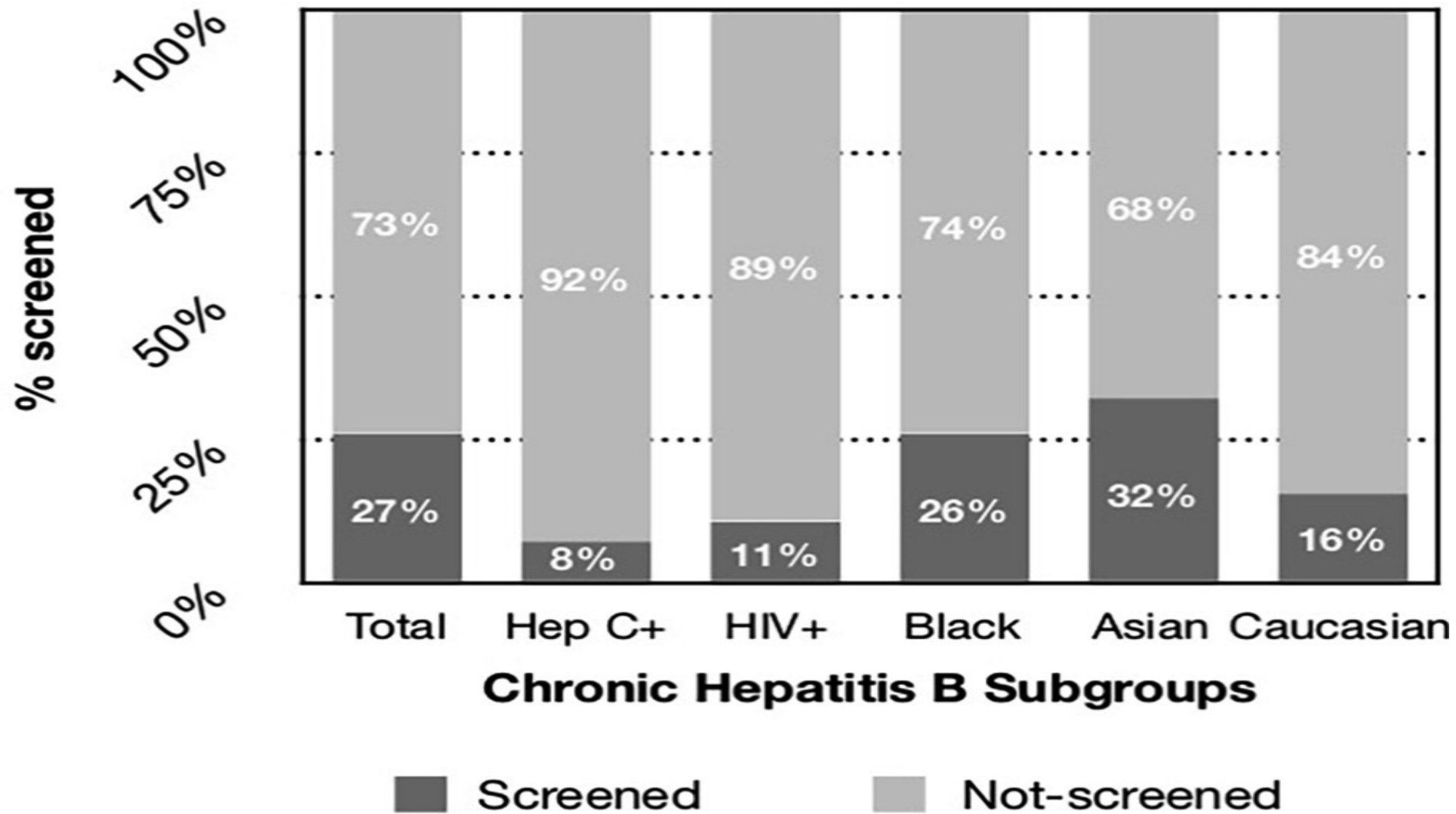
To find hepatitis D, you have to remember it



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



Is hepatitis D underestimated? - Conclusions

Global anti-HDV prevalence

- Currently uncertain, may range between 12-32 million
- May be under/over estimated depending on the accepted prevalence rate
- 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

Is hepatitis D underestimated? - Conclusions

Global HDV burden

➤ Underestimated

- Underdiagnosis of CHD – low HDV screening rates in HBsAg+ cases
- CHD: higher risk of cirrhosis and HCC compared to HBV monoinfected patients
- Need for universal HDV screening for HBV+ patients, particularly those with advanced liver disease



Thank

you