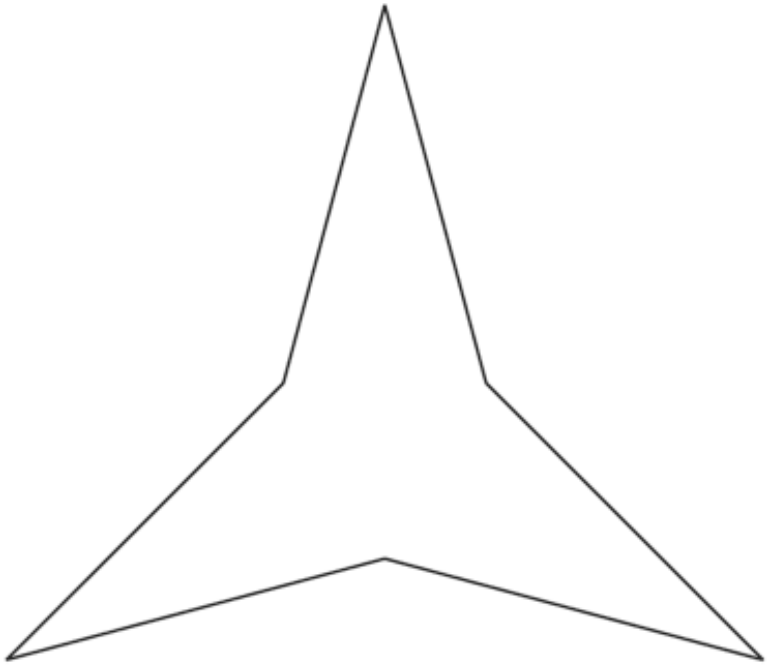
Aspetti clinici: nuovi scenari legati alla migrazione

HBV, HDV, HEV: ATTUALITA' NELLA DIAGNOSTICA E NELLA TERAPIA

XI Workshop Nazionale
Innovazione e Ricerca per la Pratica Clinica
TERAPIE INNOVATIVE DELLE EPATITI CRONICHE VIRALI E DELLE INFEZIONI VIRALI
Firenze, 11-12 Gennaio 2021
VIRTUAL EDITION

Prof. Carlo Torti
Università *Magna Graecia* di Catanzaro

The virus



The host

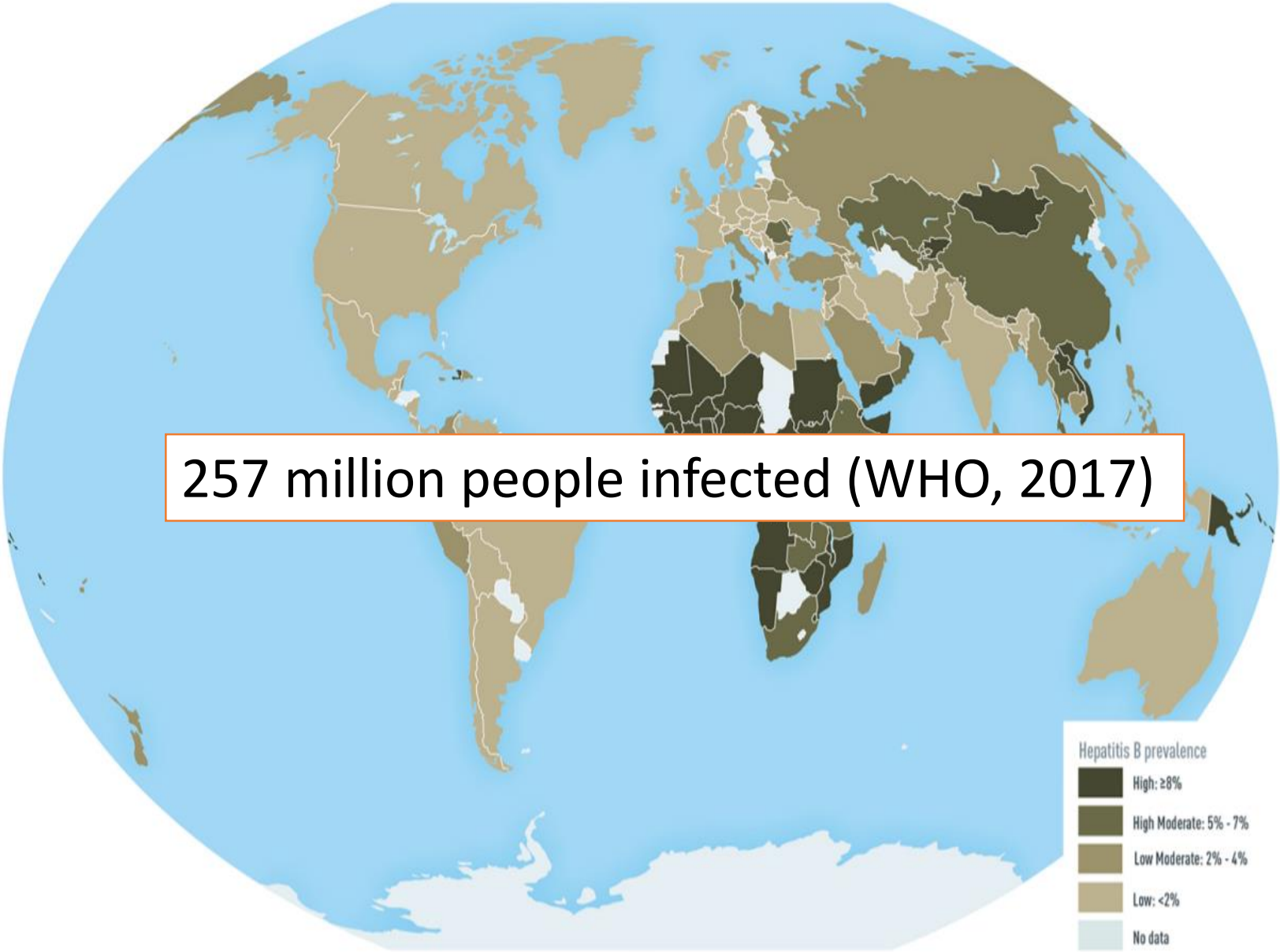
Socio-political, economical and medical contexts

Mass migration to Europe: an opportunity for elimination of hepatitis B virus?

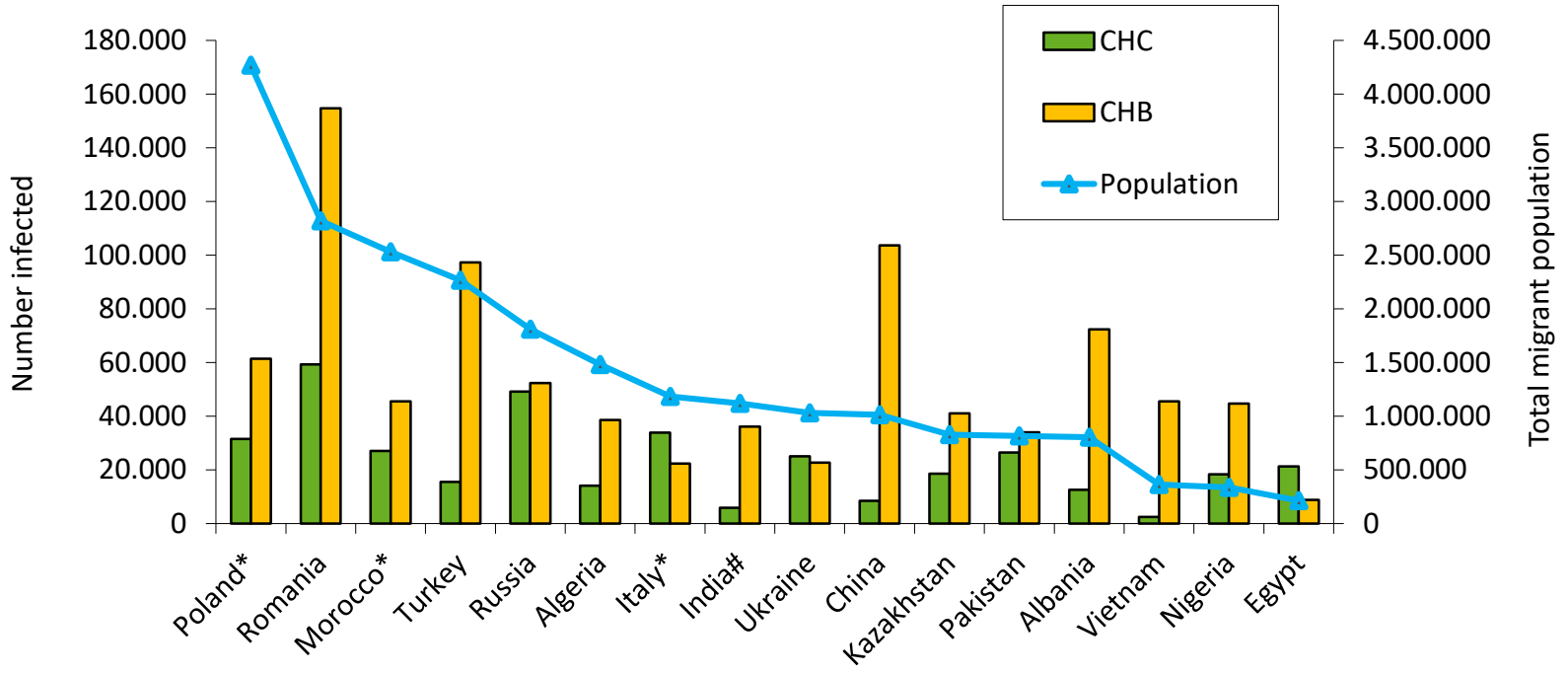
Marijn Thijssen, Philippe Lemey, Samad Amini-Bavil-Olyaee, Simon Dellicour, Seyed Moayed Alavian, Frank Tacke, Chris Verslype, Frederik Nevens, Mahmoud Reza Pourkarim

People from low-to-middle income countries have been migrating to western Europe on a large scale in recent years. Data indicate that the number of first-time asylum applications by non-EU members increased from 290 000 in 2011 to more than 1·3 million in 2015. During the peak period of migration, The Global Health Sector Strategy on Viral Hepatitis was adopted by WHO. Viral hepatitis, and particularly hepatitis B virus (HBV), is an important disease because of its high prevalence and associated mortality. In some cases, HBV can be carried by refugees arriving from regions of high and intermediate prevalence. Refugees with HBV might not show clinical symptoms and not be diagnosed in destination countries with a low prevalence, where screening is not regularly done. Although transmission to the host population is low, dedicated surveillance and tailored public health policies are required. It is important to note that some of the countries that receive many migrants do not have a universal HBV vaccination programme. In this Viewpoint, we argue that the current large-scale movement from regions with high or intermediate HBV prevalence should be taken as an opportunity to achieve viral hepatitis elimination targets, by establishing a well prepared infrastructure for HBV screening, vaccination, and treatment.

HBV hepatitis



Estimated number of CHB and CHC cases among migrants in the EU/EEA and size of the migrant population



*HBsAg endemicity <2%
#Anti-HCV endemicity <1%

Migrants comprise around 10% of the EU/EEA population, yet account for 25% of all chronic HBV cases

Source: ECDC. Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA. Stockholm: ECDC; 2016.

DOI 10.1186/s12879-017-2801-4

RESEARCH ARTICLE Open Access

Estimating the scale of chronic hepatitis B virus infection among migrants in EU/EEA countries

Amera A. Ahmad[1,2*], Abby M. Falla[1,4†], Erika Duffell[5], Teymur Noori[5], Angela Bechini[6], Ralf Reintjes[3] and Irene K. Veldhuijzen[4,7]

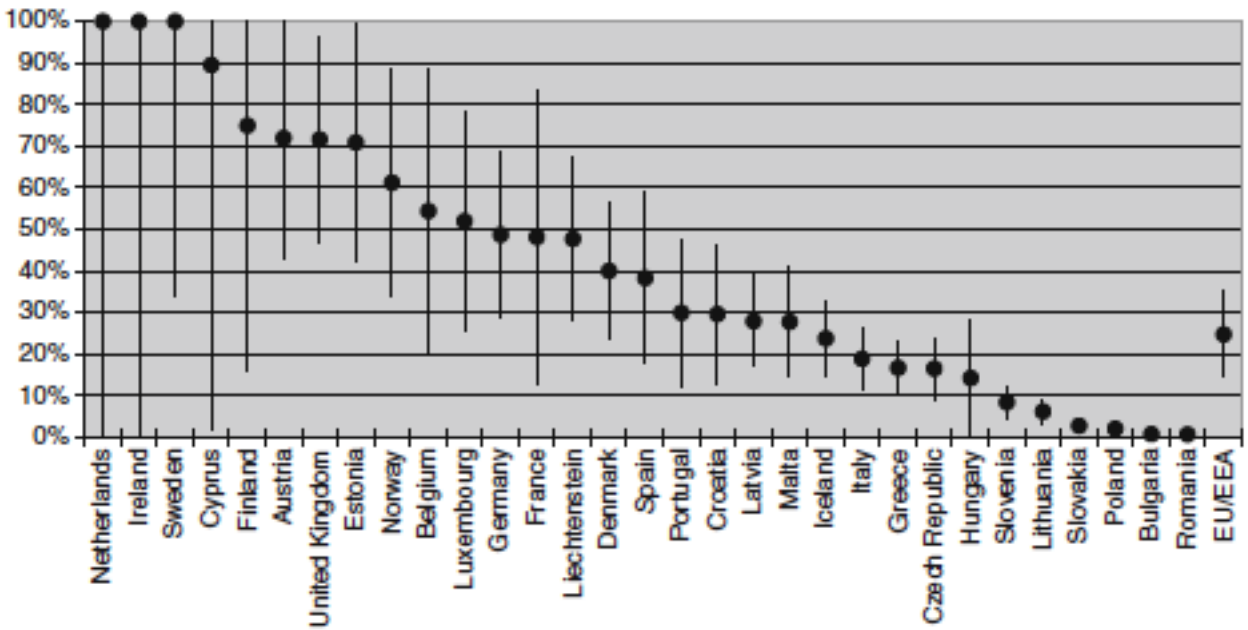


Fig. 3 Relative contribution of migrants to the total number of CHB cases per EU/EEA country

DOI 10.1186/s12879-017-2801-6

RESEARCH ARTICLE Open Access

Estimating the scale of chronic hepatitis B virus infection among migrants in EU/EEA countries

Amena A. Ahmad[1,2*], Abby M. Falla[1,4†], Erika Duffell[5], Teymur Noori[5], Angela Bechini[6], Ralf Reintjes[3] and Irene K. Veldhuijzen[4,7]

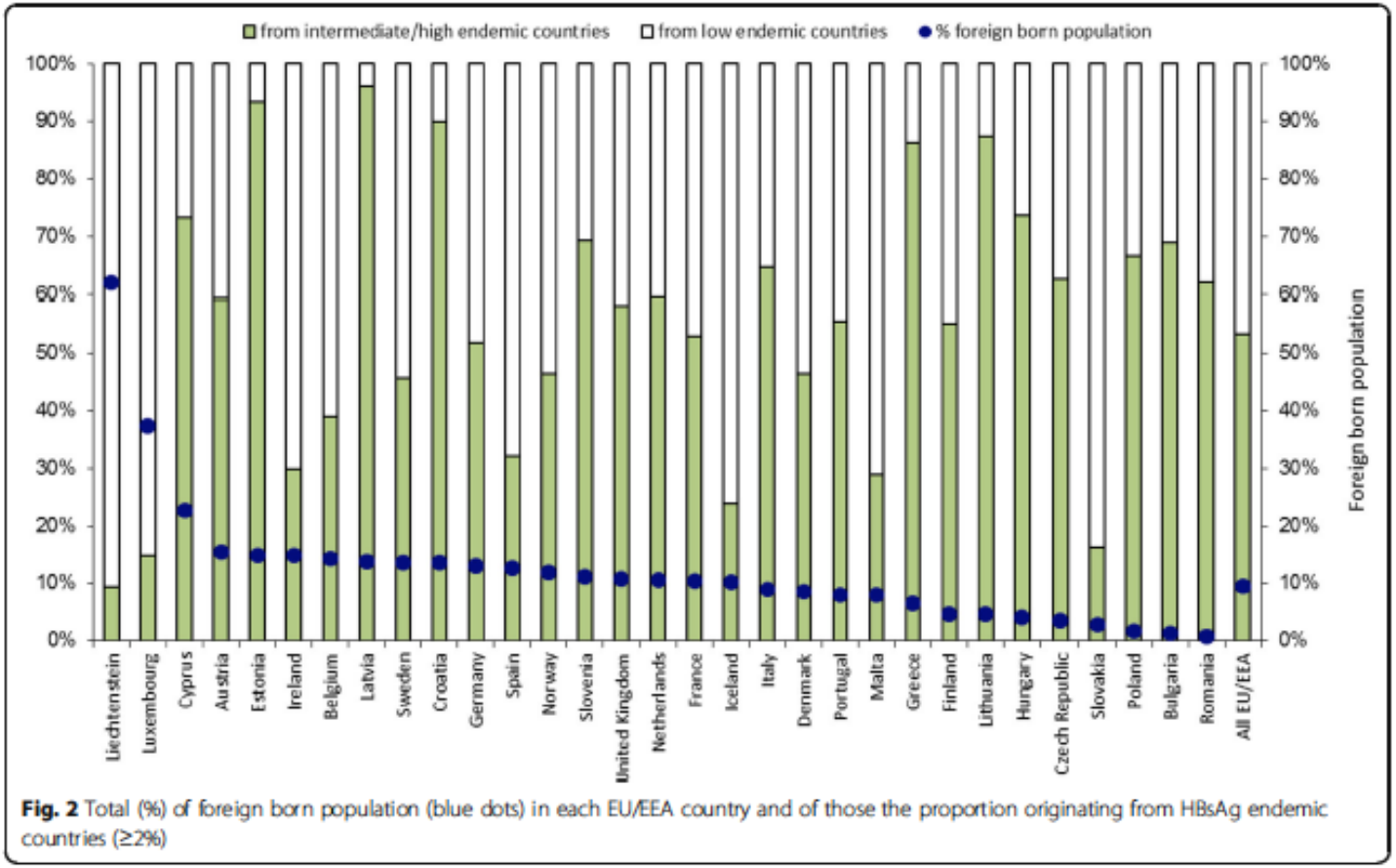
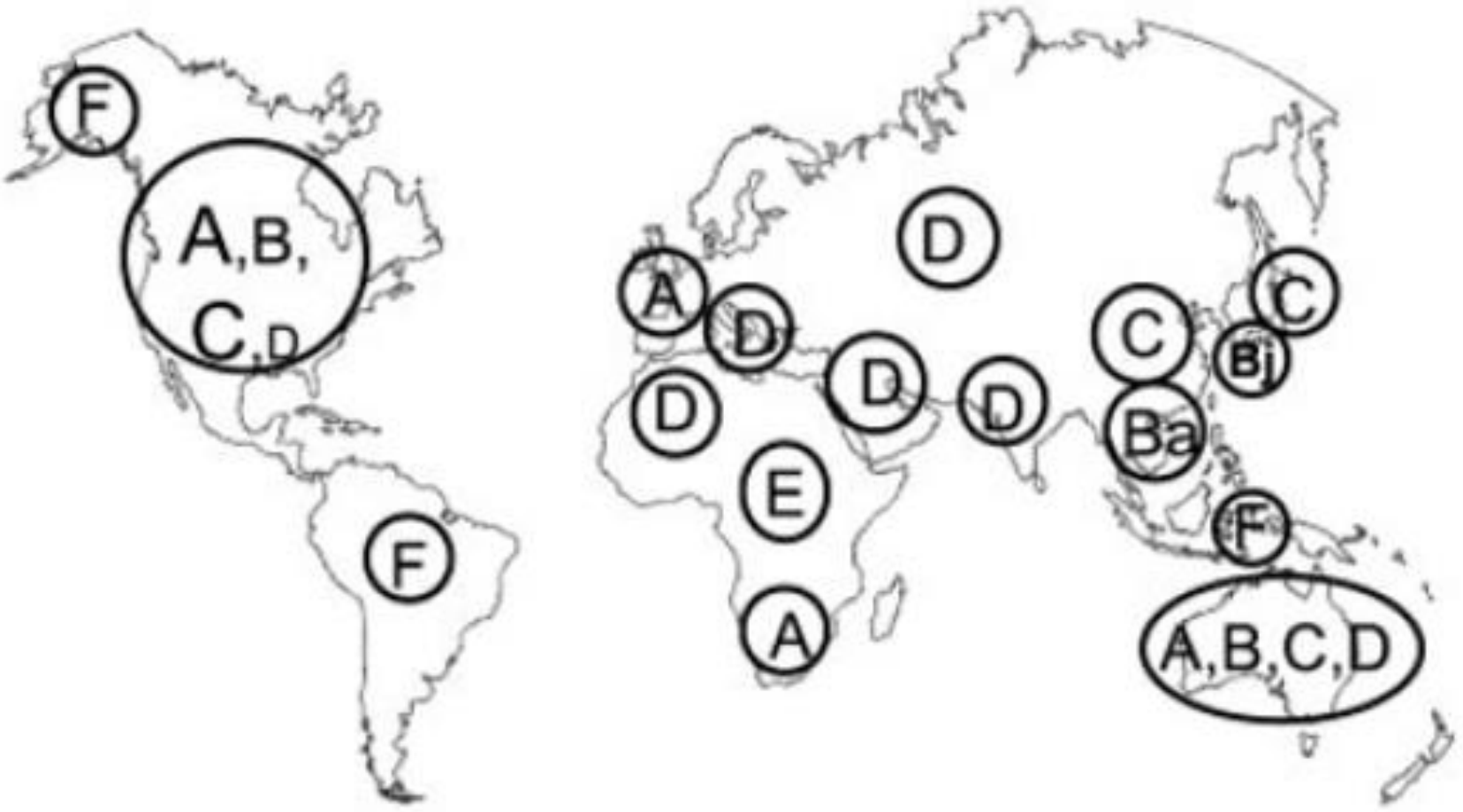


Fig. 2 Total (%) of foreign born population (blue dots) in each EU/EEA country and of those the proportion originating from HBsAg endemic countries (≥2%)

Distribution of HBV genotypes



Clinical significance of hepatitis B virus genotypes - UpToDate

Significance of HBV genotypes

	Genotype C	Genotype B
Prevalence of HBeAg	High	Low
Spontaneous HBeAg seroconversion	Late	Early
Histological activity	High	Low
Rate of progression to cirrhosis	High	Low
Risk of HCC	High	Low (Japan, China)
		Variable (Taiwan)
Frequency of PC variant (G1896A)	Low	High
Frequency of CP variant (A1762T, G1764A)	High	Low
Response to IFN	Low	High
		(Similar in 1 study on PEG-IFN)
Response to nucleotide(side) analogues		
On treatment	Similar	Similar

Clinical significance of hepatitis B virus genotypes - UpToDate

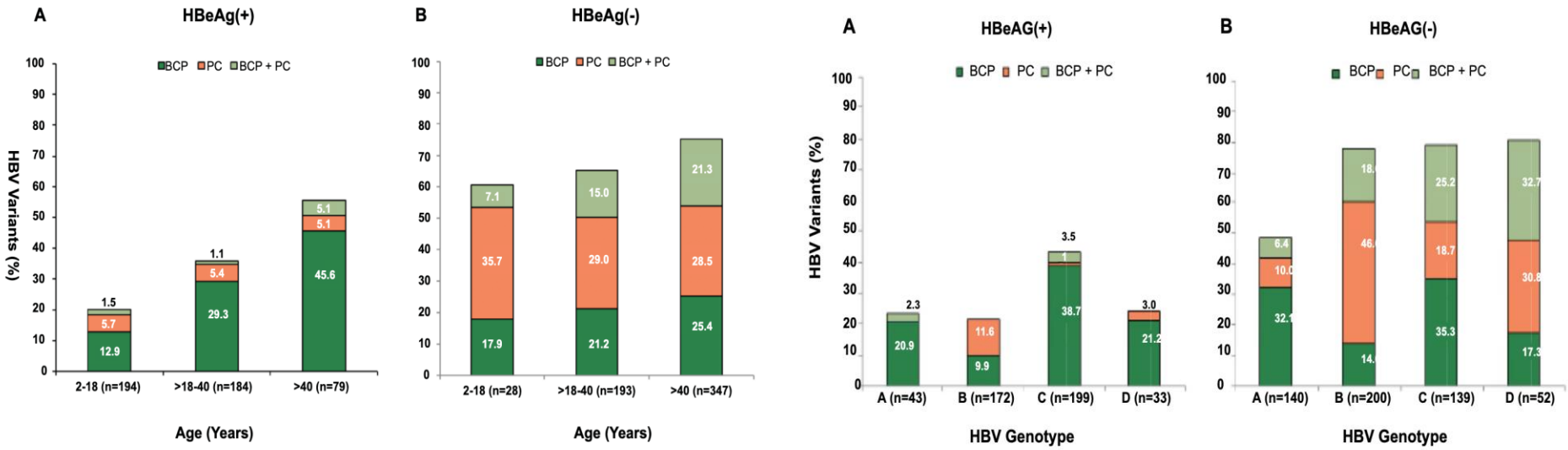
HEPATOLOGY

AASLD

ORIGINAL ARTICLE | Full Access

Precore and basal core promoter hepatitis B virus (HBV) variants are present from a young age and differ across HBV genotypes

Daryl T.Y. Lau ✉, Lilia Ganova-Raeva, Junyao Wang, Douglas Mogul, Raymond T. Chung, Mauricio Lisker-Melman, Kyong-Mi Chang, Obaid S. Shaikh ... See all authors



HEPATOLOGY AASLD

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Precore and basal core promoter hepatitis B virus (HBV) variants are present from a young age and differ across HBV genotypes

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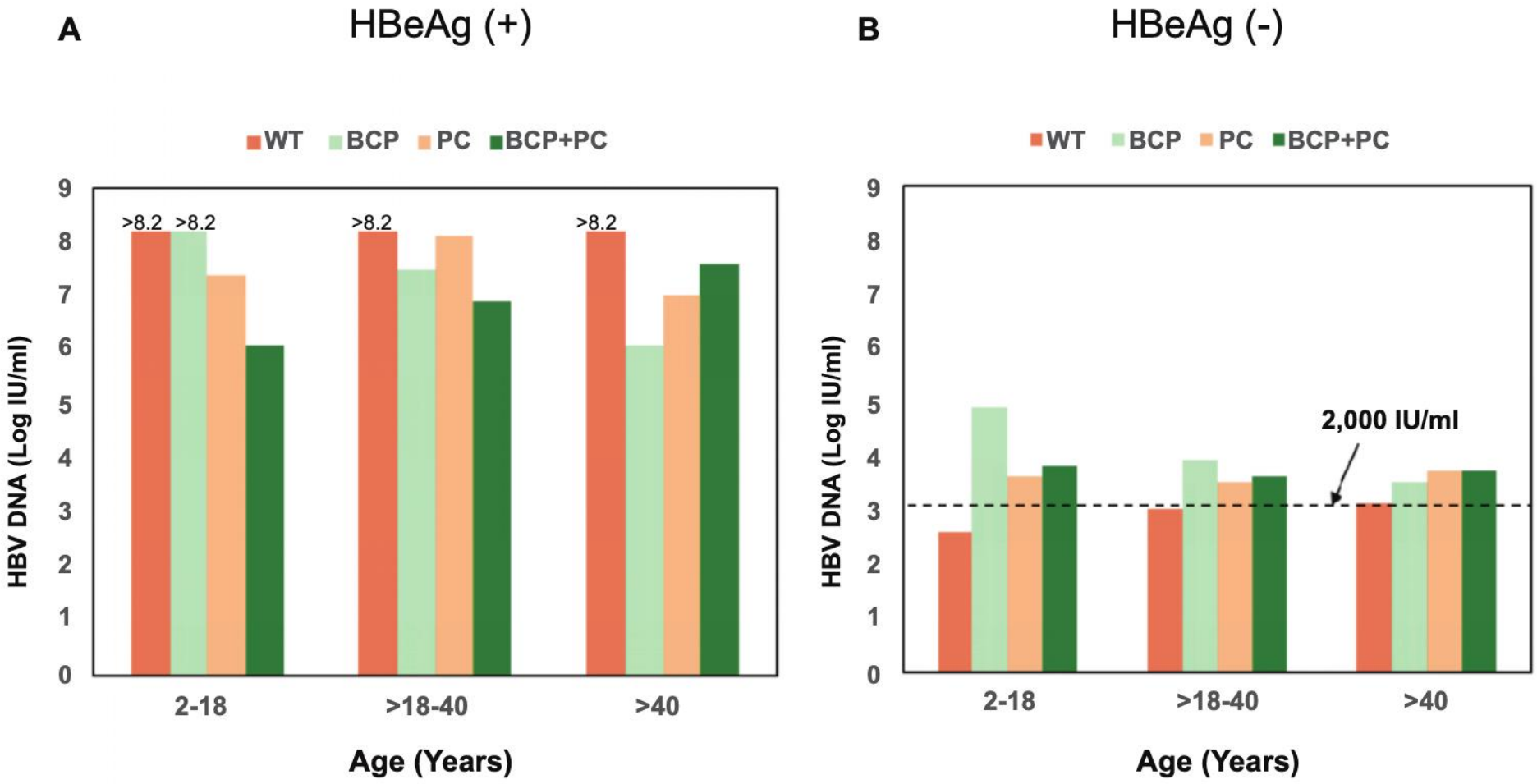


PLOS ONE

RESEARCH ARTICLE

High rates of chronic HBV genotype E infection in a group of migrants in Italy from West Africa: Virological characteristics associated with poor immune clearance

Vincenzo Malagnino[1☯], Romina Salpini[2☯], Gaetano Maffongelli[1], Arianna Battisti[2], Lavinia Fabeni[2], Lorenzo Piermatteo[2], Luna Colagrossi[2], Vanessa Fini[2], Alessandra Ricciardi[1], Cesare Sarrecchia[1], Carlo Federico Perno[2], Massimo Andreoni[1], Valentina Svicher[2‡], Loredana Sarmati[1‡]*

1 Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Rome, Italy,
2 Department of Experimental Medicine and Surgery, Tor Vergata University, Rome, Italy

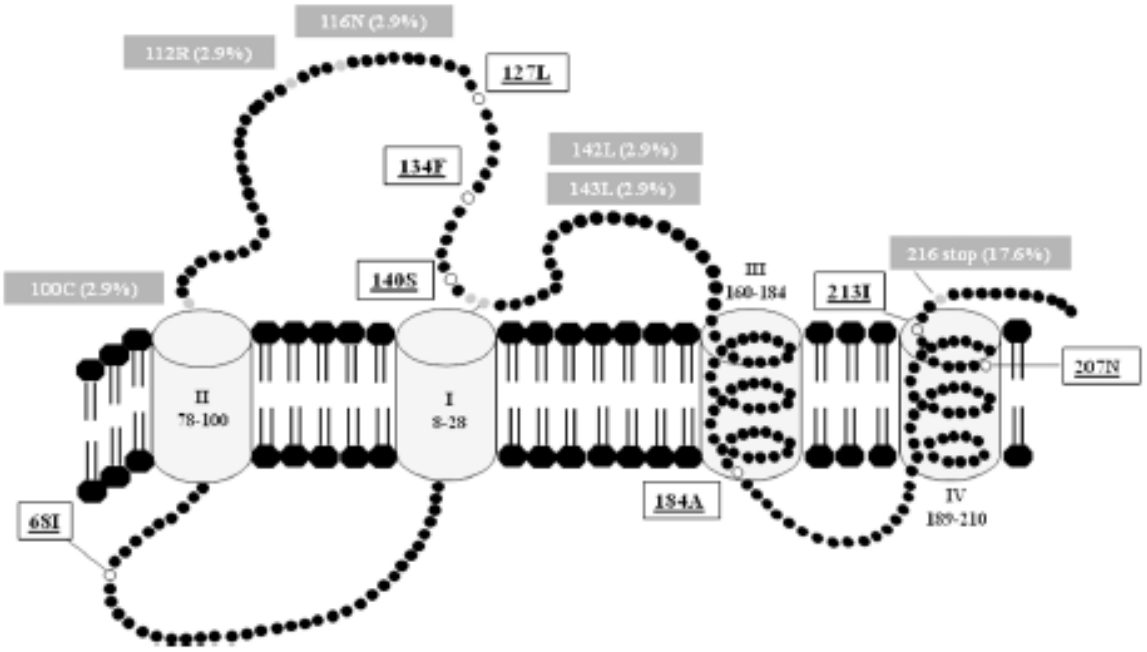
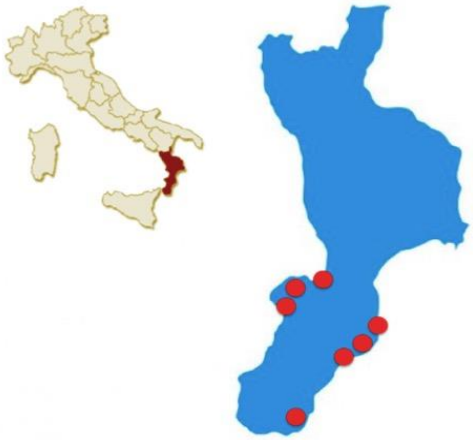


Fig 1. Putative structure of HBsAg reporting the immune-escape mutations and stop-codons (grey box) and HBsAg positions with wild-type amino acids different from genotype D (white box) observed in the group of 34 HBV genotype E infected patients.

https://doi.org/10.1371/journal.pone.0195045.g001

Outcome of HBV screening and vaccination in a cohort of migrant population in Southern Italy



Source population
n=330

First clinical check
in our clinic

Already screened
n=99

- HBsAg +, n=6
- Vaccinated, n=9
- Seronegative, n=64
- Natural immunization, n=11
- Seronegative OBI, n=9

Never tested
n=231

HBV testing
prescription

- Refused further testing, n=28
- HBsAg +, n=17
- Seronegative, n=140
- Natural immunization, n=29
- Seronegative OBI, n=17

Overall
- Refused further testing, n=28
- **HBsAg +, n=23**
- **Seronegative, n=204**
- Natural immunization, n=40
- Seronegative OBI, n=26
- Vaccinated, n=9

- **HBsAg +, n=23**

At 6 month follow-up
Still in care, n=17
Lost to follow-up, n=5

At 1 year follow-up
Still in care, n=10
Lost to follow-up, n=13

- **Seronegative, n=204**

At 6 month follow-up
Completed vaccination, n=116
Vaccination ongoing, n=36
Vaccination not started, n=35
Lost to follow-up, n=17

At 1 year follow-up
Completed vaccination, n=131
Vaccination ongoing, n=2
Vaccination not started, n=9
Lost to follow-up, n=62

Could resistant and escape variants of hepatitis B virus be a problem in the future?

Müge Özgüler & Murat Sayan

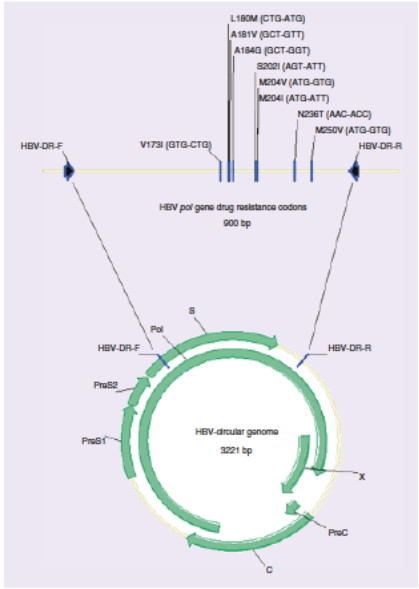


Table 4. Antiviral drug-associated potential vaccine-escape mutant related to treatment with nucleos(t)ide analogs

Mutation characteristic	Mutation pattern	Nucleos(t)ide analogs	Patient, n (%)
ADAPVEM	rtI169X/sF161L	ETV	1 (0.5)
	rtV173L/sE164D + rtM204V/sI195M	LAM, LdT	4 (1.8)
	rtA181T/sL172L	ADV	ND
	rtA181V/sL173F	ADV	1 (0.5)
	rtM204V/sI195M	LAM, LdT	14 (6.4)
	rtM204I/sW196L	LAM, LdT	19 (8.7)
		Total	39 (17.9)

ADAPVEM: Antiviral drug-associated potential vaccine-escape mutant; ADV: Adefovir; LAM: Lamivudine; LdT: Telbivudine.

Coppola *et al. Infectious Diseases of Poverty* (2017) 6:33
DOI 10.1186/s40249-016-0228-4

Infectious Diseases of Poverty

RESEARCH ARTICLE Open Access

Hepatitis B virus infection in undocumented immigrants and refugees in Southern Italy: demographic, virological, and clinical features

Nicola Coppola[1*], Loredana Alessio[1,2], Luciano Gualdieri[3], Mariantonietta Pisaturo[4,5], Caterina Sagnelli[6,7], Carmine Minichini[1], Giovanni Di Caprio[1,2], Mario Starace[1], Lorenzo Onorato[1,2], Giuseppe Signoriello[8], Margherita Macera[1], Italo Francesco Angelillo[9], Giuseppe Pasquale[1] and Evangelista Sagnelli[5]

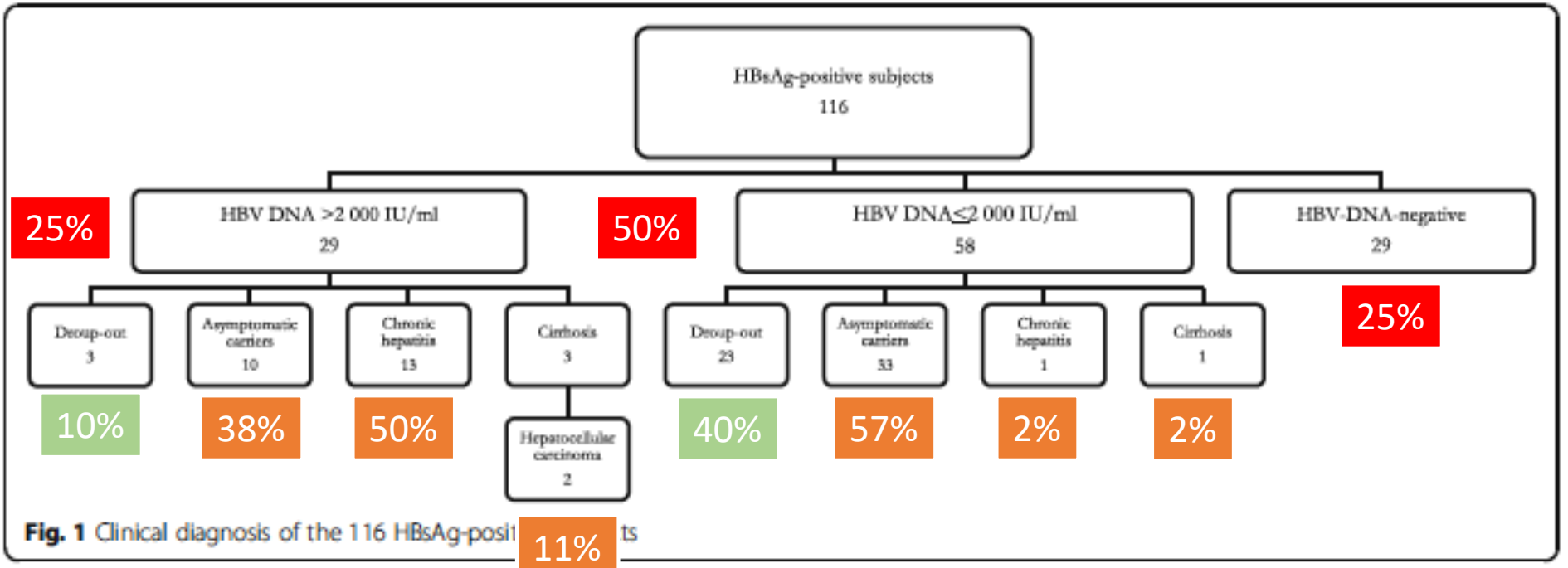


Fig. 1 Clinical diagnosis of the 116 HBsAg-posit ts

Comparison of clinical practice guidelines for the management of chronic hepatitis B: When to start, when to change, and when to stop

Hyung Joon Yim[1], Ji Hoon Kim[1], Jun Yong Park[2], Eileen L. Yoon[3], Hana Park[4], Jung Hyun Kwon[5], Dong Hyun Sinn[6], Sae Hwan Lee[7], Jeong-Hoon Lee[8], Hyun Woong Lee[2]

	KASL	AASLD	EASL	APASL
Immune tolerant CHB	1) Monitor patients with very high HBV DNA (≥10^7 IU/mL) and normal ALT (male <34 IU/mL, female <30 IU/mL)	1) Monitor patients with high HBV DNA (≥10^6 IU/mL) and normal ALT (male <35 IU/mL, female <25 IU/mL)	1) Monitor patients with high HBV DNA (≥10^7 IU/mL) and normal ALT (<40 IU/L) if there are no signs of chronic hepatitis	1) Monitor patients with high HBV DNA (e.g., >2×10^6–10^7 IU/mL) and normal ALT (<40 IU/L) if age <30 years
1) Monitor 2) Consider	2) Liver biopsy to determine treatment if there are risk factors (age ≥30–40 years, HBV DNA levels <10^7 IU/mL, noninvasive fibrosis tests suggesting significant hepatic fibrosis, or ALT is approaching the ULN)	2) Antiviral therapy is suggested in selected patients (age >40 years with normal ALT and elevated HBV DNA [1,000,000 IU/mL], liver biopsy showing significant necroinflammation or fibrosis)	2) Antiviral therapy may be indicated for patients >30 years of age, regardless of the severity of liver histological lesions Patients with a family history of HCC or cirrhosis and extrahepatic manifestations can be treated	2) Liver biopsy if indicated (age is >35 years or there is a family history of HCC or cirrhosis, noninvasive tests suggest evidence of significant fibrosis, persistently elevated ALT) Treat if ≥A2 or ≥F2

CLINICAL and MOLECULAR HEPATOLOGY

SCIENTIFIC REPORTS

Corrected: Author Correction

OPEN

Comparison between chronic hepatitis B patients with untreated immune-tolerant phase vs. those with virological response by antivirals

Received: 24 October 2018
Accepted: 14 January 2019
Published online: 21 February 2019

The cumulative risks of HCC were similar between the UIT and the VR groups (1.1% and 2.7% vs. 1.0% and 2.9% at 5- and 10-years, respectively; p = 0.704) (Fig. 1A).

In addition, **the cumulative risks of LRE development was also similar between the UIT and the VR groups** (3.0% and 4.6% vs. 2.6% and 6.1% at 5- and 10-years, respectively; p = 0.903) (Fig. 1B).

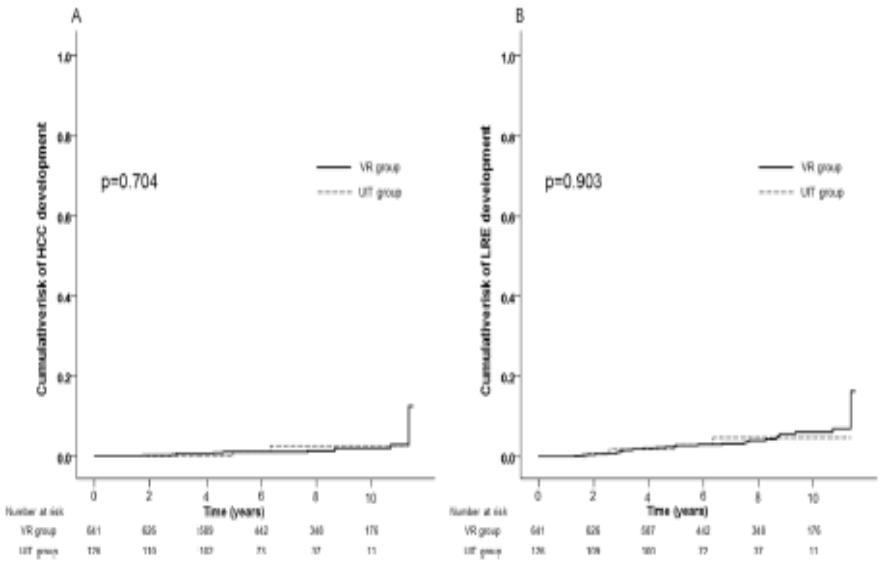


Figure 1. Cumulative risks of HCC (**A**) and LRE (**B**) development between the UIT and the VR groups.

Variables	UIT group	VR group	*P* value
Age, years	47.8 ± 11.2	47.2 ± 10.2	0.636
Male gender, %	49.6	53.6	0.527
Diabetes, %	4.8	4.8	1.000
Platelet count, $\times 10^3$/uL	198 ± 87	216 ± 67	0.070
ALT, U/mL	23.4 ± 7.8	23.0 ± 10.0	0.735
Total biltrubin, mg/dL	0.7 ± 0.3	0.8 ± 0.3	0.138
Prothrombin time, INR	0.6 ± 0.5	0.7 ± 0.4	0.211
Liver stiffness values, kPa	5.7 ± 2.4	5.9 ± 2.3	0.656

Table 3. Comparison of baseline characteristics between two groups after PS matching. Data are expressed as mean ± standard deviation, or %. Abbreviations: PS, propensity score; UIT, untreated immune-tolerant; VR, virological response; HBV, hepatitis B virus; ALT, alanine aminotransferase; INR. international normalized ratio.

Comparison between chronic hepatitis B patients with untreated immune-tolerant phase vs. those with virological response by antivirals. Lee HW et al. *Scientific Reports* **2019**,*9*:2508

However…

Even if the present study consistently showed overall similar cumulative risks for disease progression in the UIT group, recent opinions favoring routine NUCs in untreated IT-phase should be further verified with more robust evidence.

In addition, large-scale prospective studies on whether treated IT-phase patients are less likely to have disease progression than untreated IT-phase patients are still required.

Comparison between chronic hepatitis B patients with untreated immune-tolerant phase vs. those with virological response by antivirals. Lee HW et al. *Scientific Reports* **2019**,*9*:2508

Original research

Cost-effectiveness of antiviral treatment in adult patients with immune-tolerant phase chronic hepatitis B

Hye-Lin Kim,[1] Gi-Ae Kim,[2] Jae-A Park,[3] Hye-Rim Kang,[3] Eui-Kyung Lee,[3] Young-Suk Lim [4]

What are the new findings?

- Starting antiviral treatment with entecavir or tenofovir in the IT phase was cost-effective compared with delaying the treatment until the active hepatitis phase.
- From a societal perspective considering the cost for productivity loss by premature death, treatment in the IT phase was extremely cost-effective with negative values of the incremental cost-effectiveness ratio, suggesting that the treat-IT strategy incurs less costs than delaying the treatment.
- Cost-effectiveness was further improved with higher HCC risk and cheaper drug costs.

How might it impact on clinical practice in the foreseeable future?

- Starting antiviral therapy in IT phase may be cost-effective compared with delaying the treatment until the active hepatitis phase in CHB patients.
- With decreasing cost of entecavir and tenofovir in the forthcoming years, the cost-effectiveness of treatment in the IT phase could be further improved.

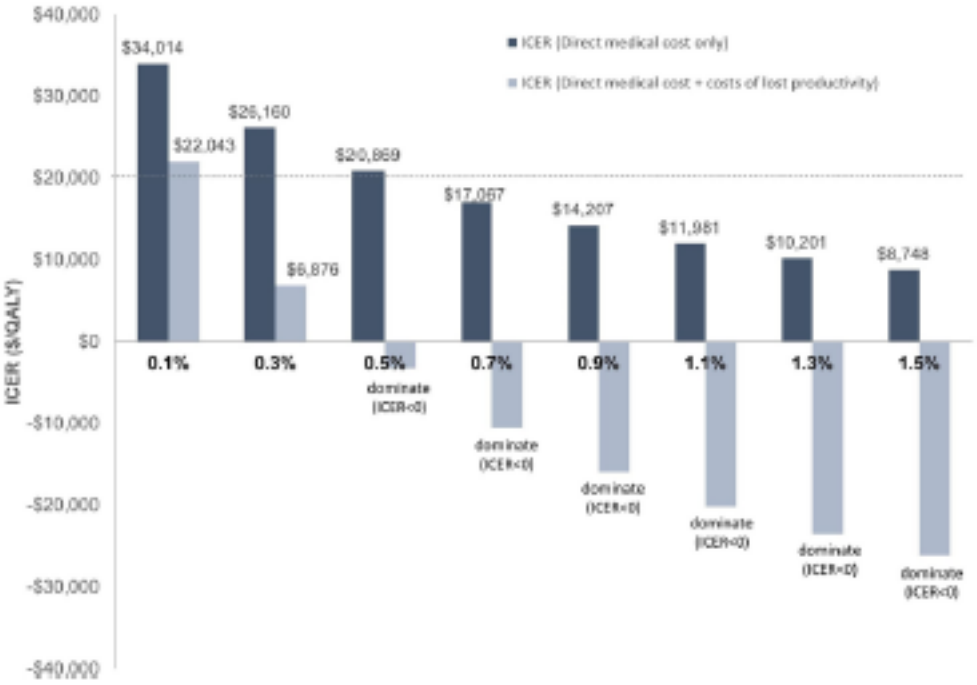


Figure 2 Incremental cost-effectiveness ratio (ICER) by annual rates of hepatocellular carcinoma incidence (HCC). Annual HCC incidence rates of untreated patients are presented. QALY, quality-adjusted life-year.

Kim H-L, *et al*. *Gut* 2020;**0**:1–11. doi:10.1136/gutjnl-2020-321309

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	KASL	AASLD	EASL	APASL
Pregnant women 1) Treat/switch 2) Prevention 3) Lactation	1) Initiate or switch to TDF if treatment is needed 2) For pregnant women with serum HBV DNA levels >200,000 IU/mL, TDF administration is recommended to prevent MTCT, beginning at 24–32 weeks of gestation and stopping 2–12 weeks after delivery	1) TDF is preferred 2) If HBV DNA >200,000 IU/mL at 28–32 weeks of gestation, antiviral therapy is recommended to reduce the risk of perinatal transmission	1) TDF should be continued, whereas ETV or other NAs should be switched to TDF 2) In all pregnant women with high HBV DNA levels (>200,000 IU/mL) or HBsAg levels >4 $\log_{10}$ IU/mL, antiviral prophylaxis with TDF should begin at 24–28 weeks of gestation and continue for up to 12 weeks after delivery	1) TDF is the drug of choice for mothers requiring antiviral treatment 2) For pregnant women with HBV DNA >6–7 $\log_{10}$ IU/mL, short-term maternal NA therapy with tenofovir or telbivudine is recommended beginning at 28–32 weeks of gestation

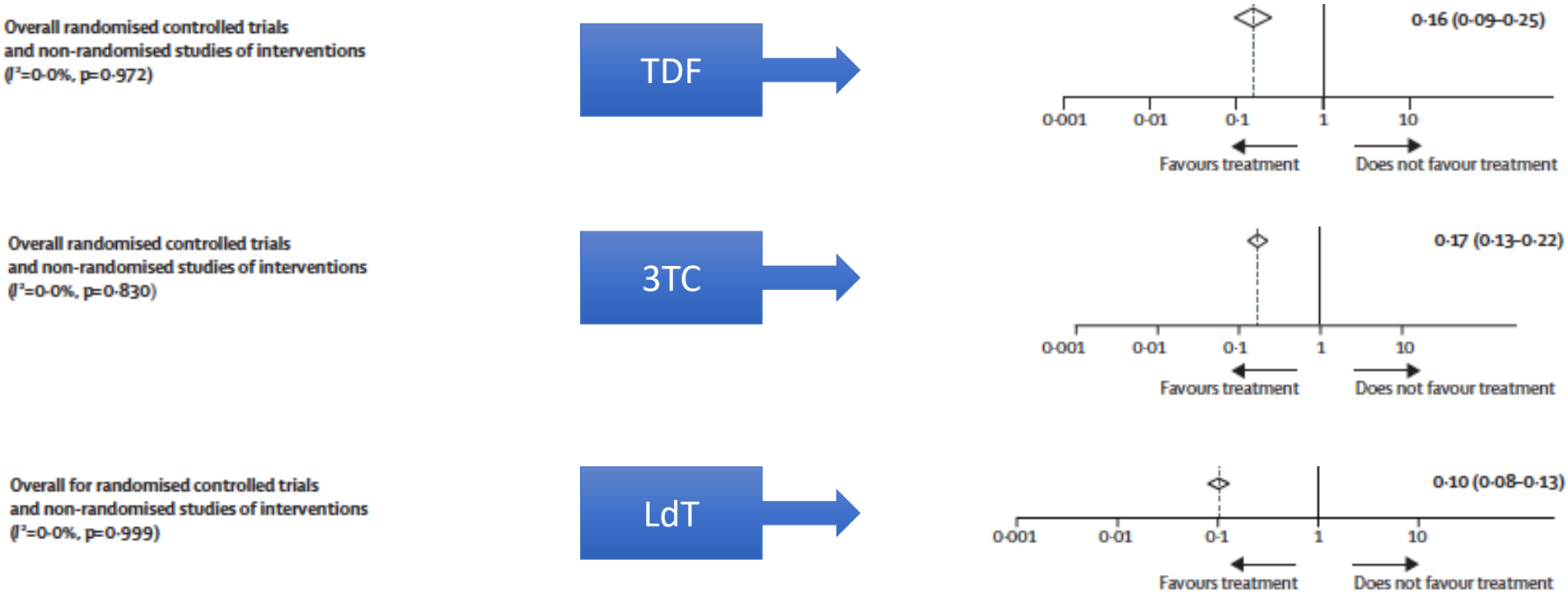
CLINICAL and MOLECULAR HEPATOLOGY

Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis

Anna L Funk, Ying Lu, Kyoko Yoshida, Tianshuo Zhao, Pauline Boucheron, Judith van Holten, Roger Chou, Marc Bulterys, Yusuke Shimakawa

Lancet Infect Dis 2020

Figure 2: Efficacy of peripartum antiviral prophylaxis from randomised controlled trials, and overall for randomsied controlled trials and non-randomised studies, using tenofovir disoproxil fumarate 300 mg (A), lamivudine 100–150 mg (B), and telbivudine 600 mg (C) in the prevention of MTCT



Tenofovir Alafenamide (TAF) for prevention of vertical HBV transmission in mothers with high viremia

- **Retrospective single-arm study**
  - HBeAg-positive mothers with HBV DNA > 200,000 IU/mL receiving 2nd/3rd trimester TAF for prevention of MTCT of HBV infection (N = 71)
  - Eligibility: Maternal age > 20 yrs, no HIV/HAV/HCV/HDV coinfection, no other antivirals, no hepatocellular carcinoma or cirrhosis, no fetal deformity at baseline
- **Primary endpoints:** Birth malformation, MTCT of HBV
- **Secondary endpoints:** Maternal delivery HBV DNA < 200,000 IU/mL, ALT flares, complications, 28-wk infant development
- At baseline, mean HBV DNA 7.78 IU/mL (SD ± 0.72), mean ALT 32.64 U/L (SD ± 68.86), mean serum creatine 52.88 umol/L (SD ± 9.49)
- Current analysis includes outcomes data from TAF initiation to postpartum Wk 28

Pan. AASLD 2020. Abstr 20. Ding. Aliment Pharmacol Ther. 2020;52:1377.

Maternal and infant outcomes following use of TAF for prevention of vertical HBV transmission

Primary Endpoints in Infants at Wks 20-28, n (%)	Infants (N = 73)
Congenital defects or malformations	0 (0)
HBsAg positive or detectable levels of HBV DNA (100 IU/mL)	0 (0)

- 61 of 71 (85.9%) mothers achieved serum HBV DNA < 200,000 IU/mL by delivery
- 11 of 71 (15.5%) mothers experienced postpartum ALT flares
  - Mean ALT peak level 140.2 U/mL (SD ± 81.3)
- No severe AEs observed in mothers nor infants and markers of infant development comparable to national standards

Pan. AASLD 2020. Abstr 20. Ding. Aliment Pharmacol Ther. 2020;52:1377.

TAF vs TDF for prevention of perinatal HBV transmission

- Multicenter, prospective, observational study of TAF or TDF from gestational Wks 24-35 to delivery in matched mothers aged 20-40 yrs with HBV DNA > 200,000 IU/mL (N = 232)
- **Primary outcome:** TAF well tolerated, with no discontinuations due to AEs
  - Nausea was most common AE in both TAF and TDF groups (19% and 20.7%); 9 (7.8%) and 10 (8.6%) of mothers in TAF group and TDF groups had abnormal ALT levels 6 mos postpartum

Variable	TAF (n = 116)			TDF (n = 116)		
	Delivery	Postpartum Month 3	Postpartum Month 6	Delivery	Postpartum Month 3	Postpartum Month 6
HBeAg positive, n (%)	107 (92.2)	107 (92.2)	107 (92.2)	107 (92.2)	107 (92.2)	107 (92.2)
Mean HBV DNA, $\log_{10}$ IU/mL (± SD)	3.5 (0.9)	7.7 (1.0)	7.8 (0.8)	3.4 (1.0)	7.7 (0.9)	7.8 (0.8)
HBV DNA < 2 x 10^5, n (%)	116 (100)	4 (3.4)	0 (0)	116 (100)	3 (2.6)	1 (0.9)
ALT > 40 U/L, n (%)	1 (0.9)	3 (2.6)	9 (7.8)	1 (0.9)	4 (3.4)	10 (8.6)
Creatine > 115 µmol/L, n/N (%)	0/114 (0)	0/115 (0)	0/113 (0)	0/116 (0)	0/115 (0)	0/114 (0)

- At 7-month visits, **no infants positive for HBsAg in either group (0% MTCT rate)**

Zang. AASLD 2020. Abstr 0160.

Chronic HBV infection in pregnant immigrants: a multicenter study of the Italian Society of Infectious and Tropical Diseases

Evangelista Sagnelli[1], Gloria Taliani[2], Francesco Castelli[3], Dario Bartolozzi[4], Bruno Cacopardo[5], Orlando Armignacco[6], Gaetano Scotto[7], Nicola Coppola[8], Tommaso Stroffolini[9], Caterina Sagnelli[10]

New Microbiologica, 39, 2, 114-118, 2016, ISSN 1121-7138

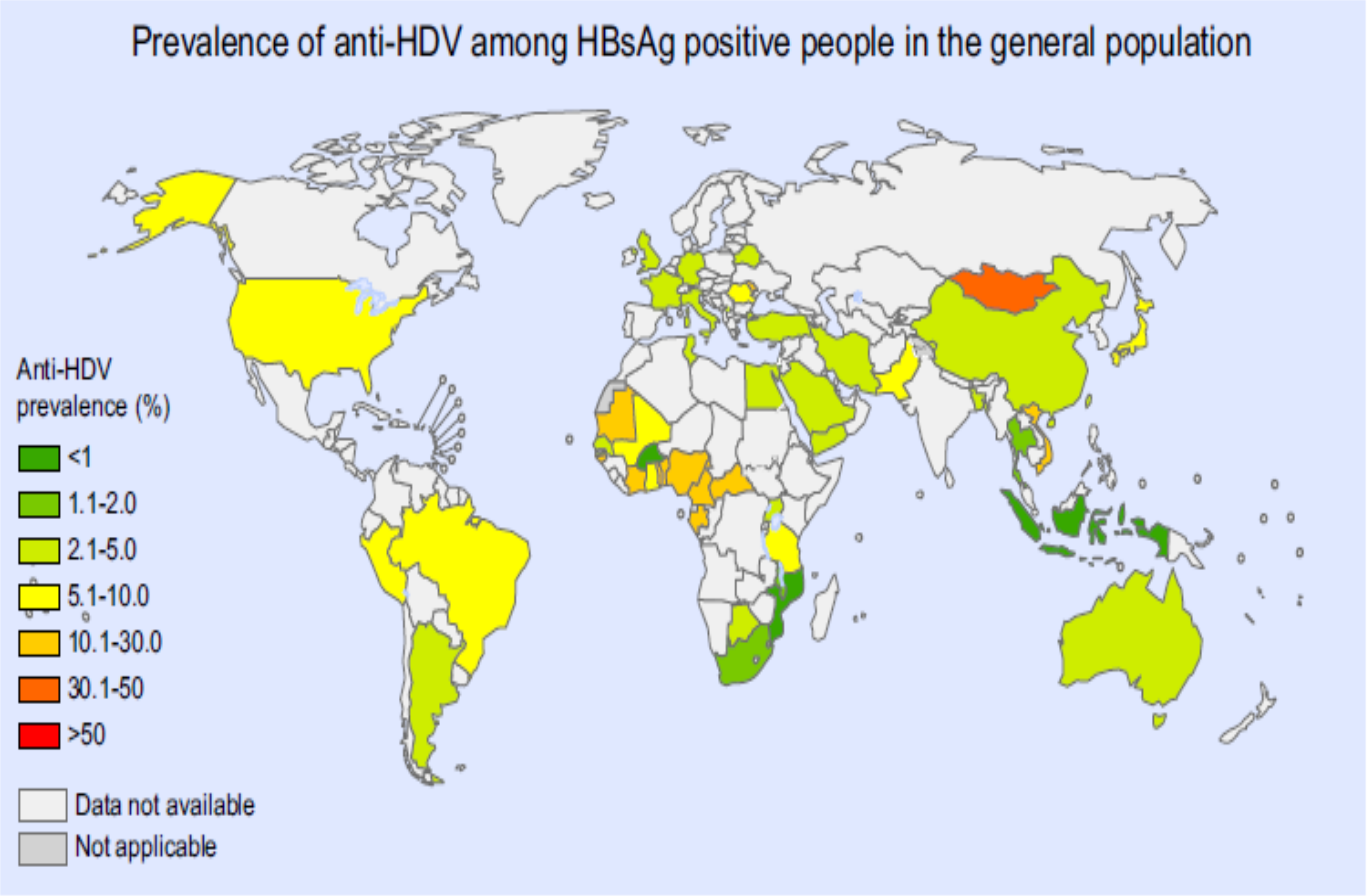
Table 1 - *Demographic and epidemiological characteristics of the 143 HBsAg-positive pregnant immigrants, and the data for the three largest subgroups.*

	Total	*Eastern Europe*	*East Asia*	*Sub-Saharan Africa*
HBsAg positive, N.	*143	53	35	48
Age, years, M±SD	31±12.1	32.2±17.8	30.8±6	29.9±4.6
At their first pregnancy, N. (%)	80 (55.9)	36 (67.9) A	22 (62.9) C	15 (31.3) B D
Living in Italy for years, M±SD	5.0±4.1	5.4±3.9 E	7.3±5.3 F G	4.4±3.1 H
HBsAg positivity before pregnancy:				
known, N. (%)	61 (43.3)	19 (35.8) I	20 (60.6) J	20 (41.7)
unknown, N. (%)	80 (56.7)	34 (64.2)	13 (40.6)	28 (58.3)
missing, N.	2	0	2	0
HBsAg positivity before pregnancy, known for years, M±SD	6.0±5.6	5.9±6.7 K M	8.8±5.8 L	2.4±2.3 N
HBsAg positivity known before pregnancy, pregnancy:				
with chronic hepatitis B, N. (%)	20 (32.8)	8 (42.1)	4 (20)	6 (30)
asymptomatic carriers, N. (%)	41 (67.2)	11 (57.9)	16 (80)	14 (70)

*Only 5 pregnant immigrants were from Northern Africa and 2 from South America; consequently these subcontinents are not included in this table. A vs B: p=0.003; C vs D: p=0.003; E vs F: p=0.0001; G vs H: p=0.0001; I vs J: p=0.02; K vs L: p=0.04; M vs N: p=0.0001.

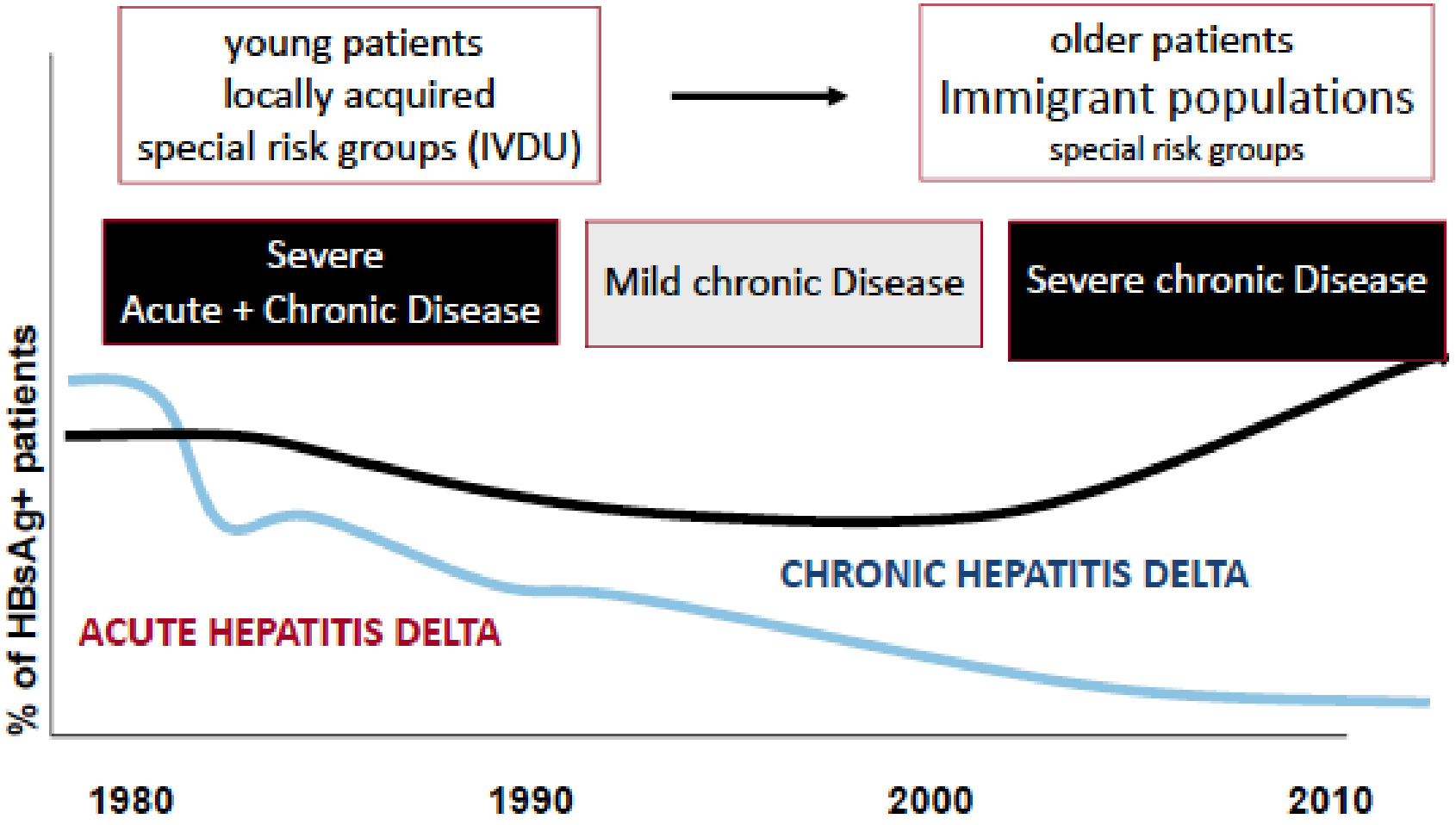
HDV Ab determined in 33% and positive in 10% patients tested

HDV hepatitis

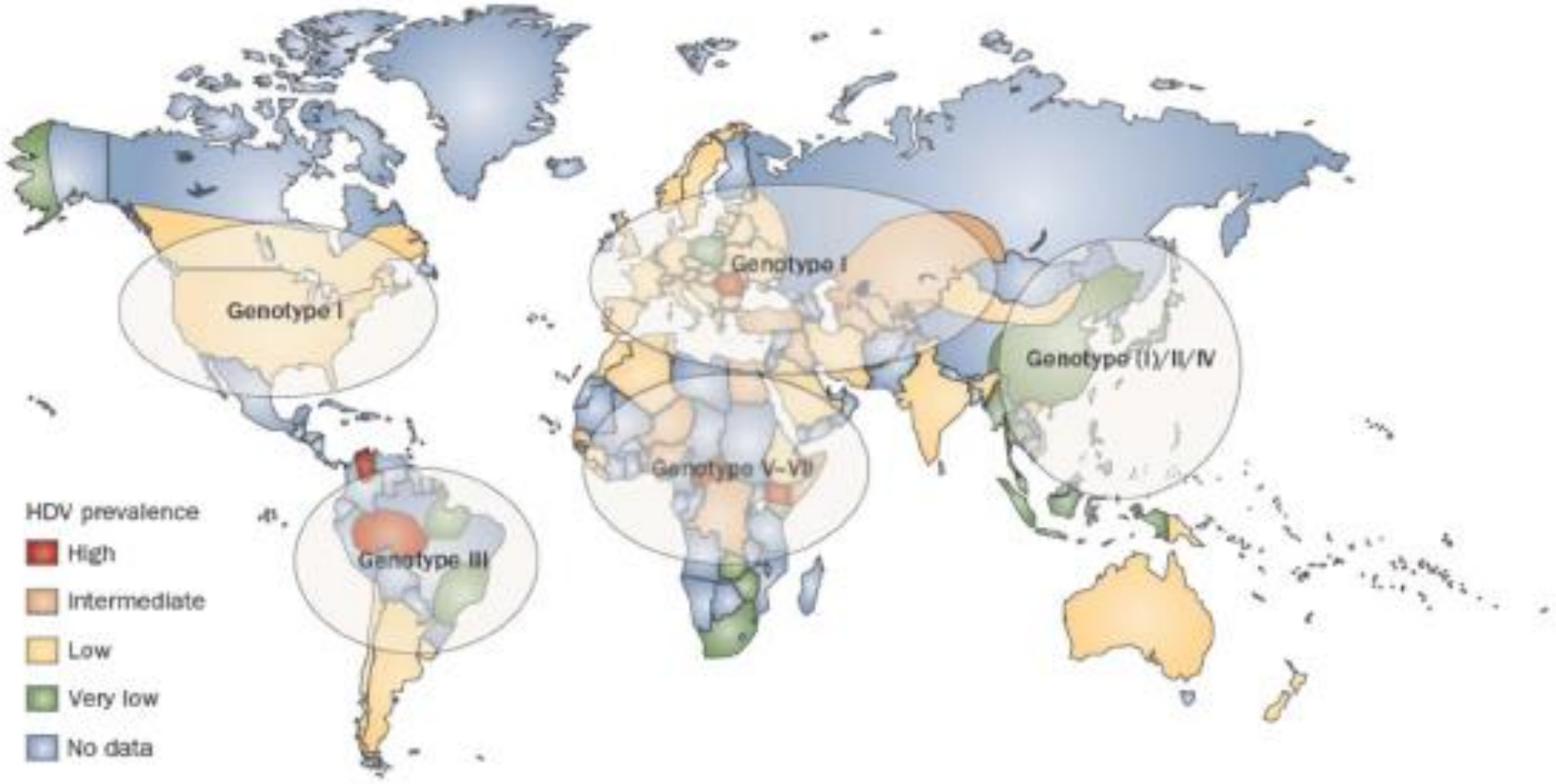


- HDV infection is common among HBsAg-positive people worldwide.
- Among HBsAg-positive people, estimated HDV prevalence is 4.5%, which translates into an estimated prevalence of 0.16% in the total population. This represents an estimated **12 million people** with serological evidence of HDV infection globally.
- HDV prevalence is higher in people who inject drugs, who have HCV or HIV, in haemodialysis recipients, men who have sex with men and commercial sex workers.
- Among HBsAg-positive people, Mongolia had the highest national anti-HDV prevalence (36.9%); prevalence rates >10% were also estimated for the Republic of Moldova and countries in Western and Middle Africa.
- HDV causes an estimated 18% of cirrhosis and 20% of HCC associated with hepatitis B

HDV: evolution of clinical presentation



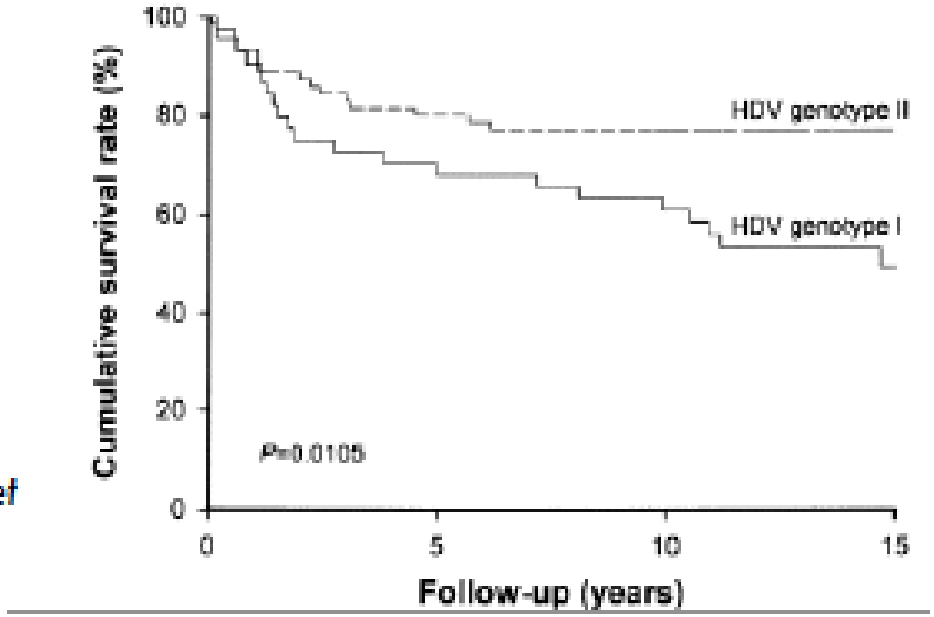
Distribution of HDV genotypes



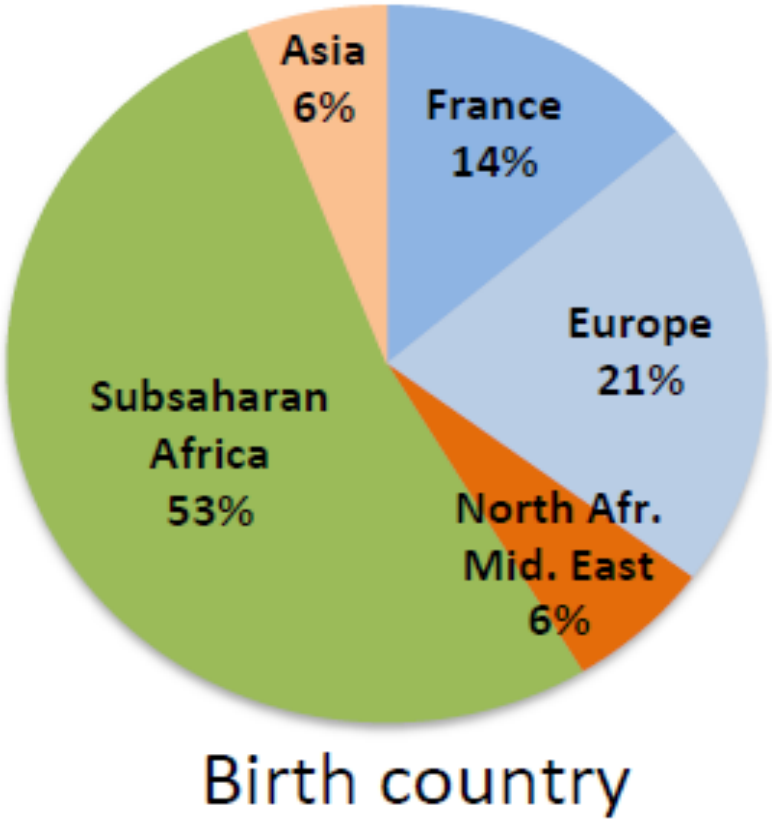
Significance of HDV genotypes (natural history)

- G1 HDV in acute hepatitis
  - A risk of fulminant failure
- G1 HDV in chronic hepatitis
  - Rapid progression to cirrhosis
  - Risk of HCC is as many as 3 times higher
  - Mortality is as many as 2 times higher

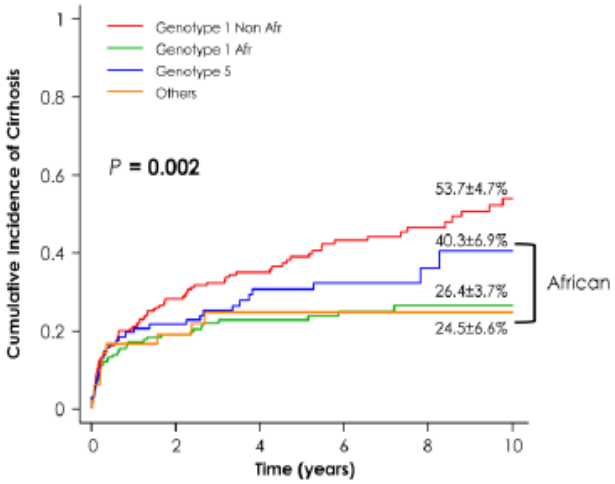
Fattovich G et al. Gut 2000; 46:420 2. Wu Lancet 1995; 3. Su et al. Gastroenterol 2006; 4. Wu Curr Top Micobiol Immunol 2006



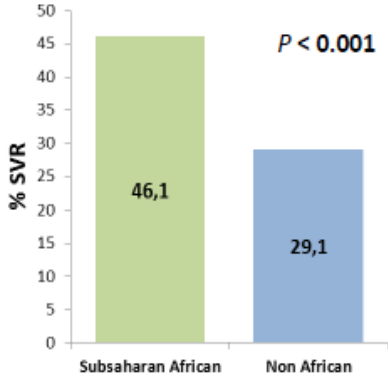
Significance of HDV genotypes (Tx response)



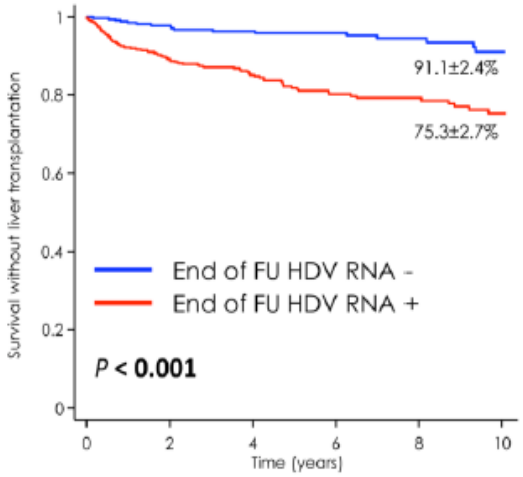
Cirrhosis incidence →



Treatment response →



Survival →



Roulot D. et al., Origin, HDV genotype and persistent viremia determine outcome and treatment response in patients with chronic hepatitis Delta, *Journal of Hepatology* (2020), doi: https://doi.org/10.1016/j.jhep.2020.06.038.

ORIGINAL ARTICLE

JVH WILEY

Migratory flow and hepatitis delta infection in Italy: A new challenge at the beginning of the third millennium

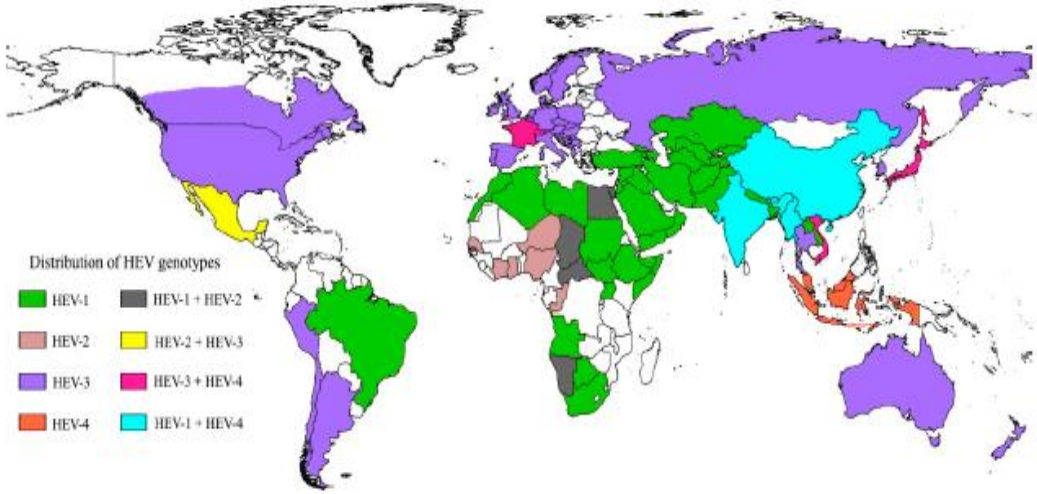
Tommaso Stroffolini[1] | Alessia Ciancio[2] | Caterina Furlan[1] | Maria Vinci[3] | Rosanna Fontana[4] | Maurizio Russello[5] | Guido Colloredo[6] | Filomena Morisco[7] | Nicola Coppola[8,9] | Sergio Babudieri[10] | Luigina Ferrigno[11] | Caterina Sagnelli[9] | Evangelista Sagnelli[9]

Characteristic	Anti-delta+ %	Anti-delta- %	Crude OR	95% CI	Adjusted[a] OR	95% CI
Age						
≤49 y	39.7	24.9	1.00		1.00	
>49 y	60.3	75.1	0.50	(0.31-0.81)	0.67	(0.33-1.35)
Sex						
Female	50.0	36.2	1.00		1.00	
Male	50.0	63.8	0.57	(0.35-0.91)	0.63	(0.37-1.07)
Country of birth						
Italy	52.6	85.5	1.00		1.00	
Abroad	47.4	14.6	5.30	(3.24-8.66)	6.02	(3.06-11.84)
Presence of cirrhosis						
No	46.2	84.1	1.00		1.00	
Yes	53.9	15.9	6.18	(3.79-10.07)	9.66	(5.39-17.30)

Bold values indicate statistically significant results.

[a]Each variable is adjusted for the confounding effect of all other listed variables.

HEV hepatitis

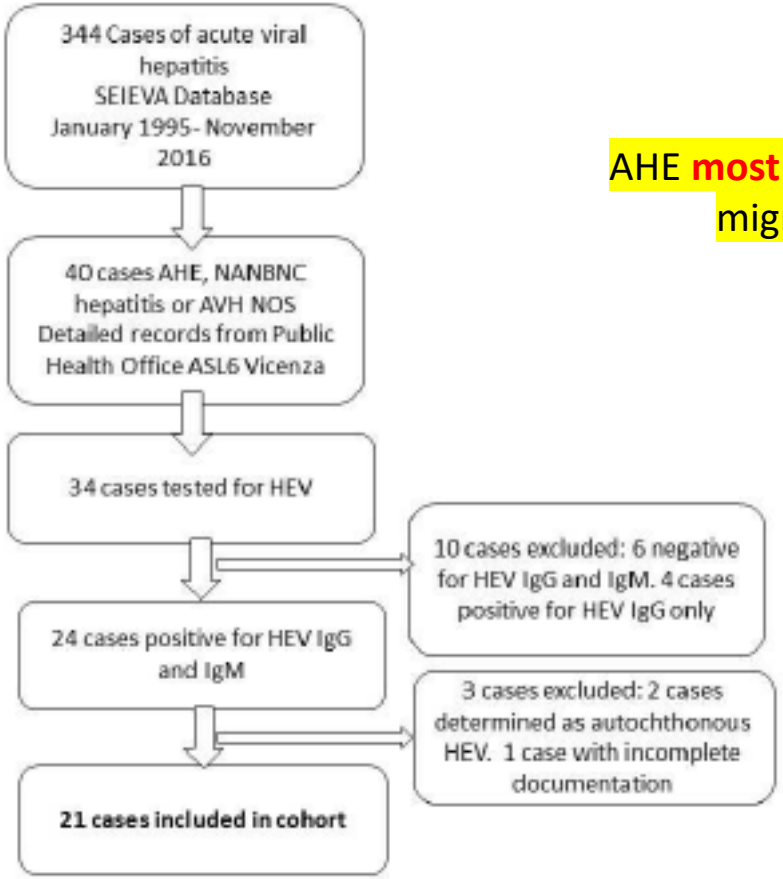


"Handbook on Selected Topics in Tropical Diseases" a cura di Roberto Cauda, Vita e Pensiero Editore, settembre **2020**

Acute hepatitis E virus infection in a migrant population in North East Italy: A retrospective analysis

Lucia Bradanini, Daniel Youkee, Paolo Fabris, Luisa Romanò, Enrico Brunetti, Maria Teresa Giordani

Flowchart of Case Inclusion



AHE **most common cause of AVH** in the migrant population (**42,5%**)

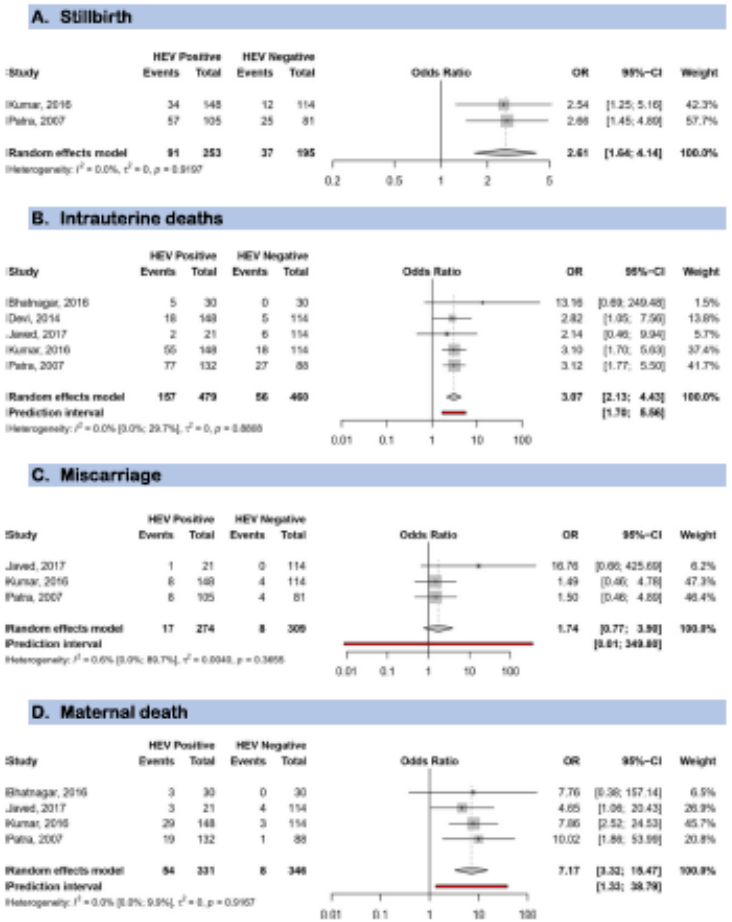
Our **secondary case**, where transmission of HEV occurred in Italy, **highlights the need for patient education on hygiene procedures and the need for increased surveillance** of patient contacts to detect secondary cases.

https://doi.org/10.1186/s12884-020-03116-2

RESEARCH ARTICLE Open Access

Burden of hepatitis E virus infection in pregnancy and maternofoetal outcomes: a systematic review and meta-analysis

Jean Joel Bigna[1*], Abdou Fatawou Modiyinji[2,3], Jobert Richie Nansseu[4,5], Marie A. Amougou[2,6], Moise Nola[3], Sébastien Kenmoe[2], Elvis Temfack[7] and Richard Njouom[2]



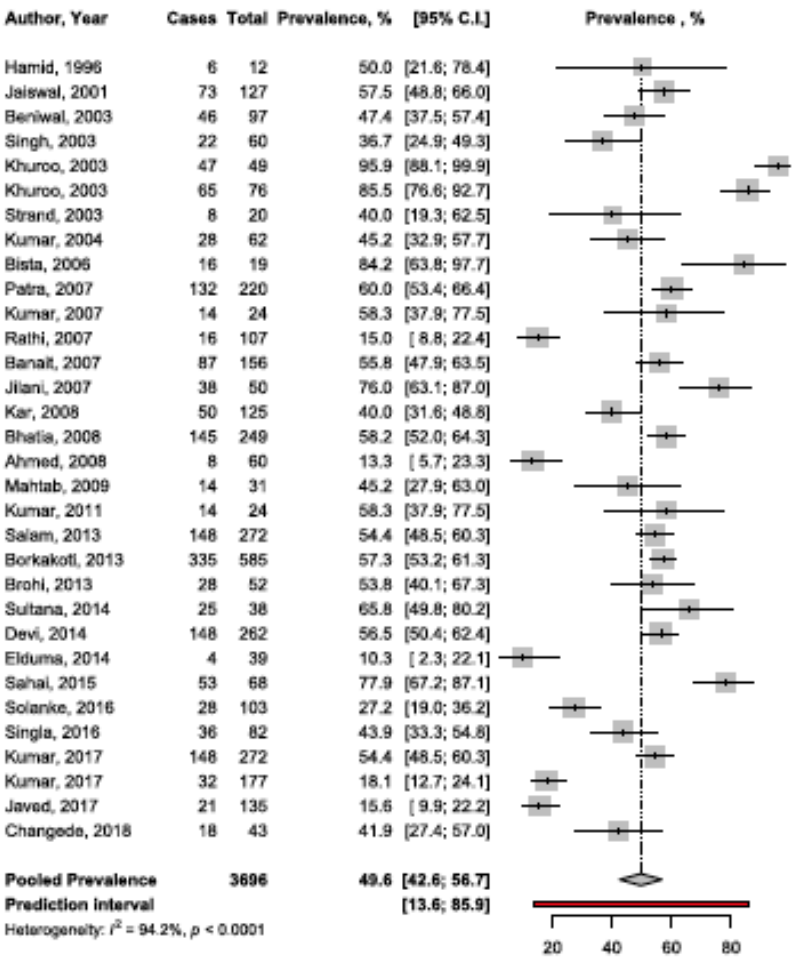
ig. 5 Forest plot of the risk of foetal and maternal mortality associated with HEV infection during pregnancy. **a** Stillbirth. **b** Intrauterine deaths. **c** liscarriage. **d** Maternal death

https://doi.org/10.1186/s12884-020-03116-2 BMC Pregnancy and Childbirth

RESEARCH ARTICLE Open Access

Burden of hepatitis E virus infection in pregnancy and maternofoetal outcomes: a systematic review and meta-analysis

Jean Joel Bigna[1*], Abdou Fatawou Modiyinji[2,3], Jobert Richie Nansseu[4,5], Marie A. Amougou[2,6], Moise Nola[3], Sébastien Kenmoe[2], Elvis Temfack[7] and Richard Njouom[2]



Forest plot of the meta-analysis of IgM seroprevalence of HEV infection among symptomatic pregnant women

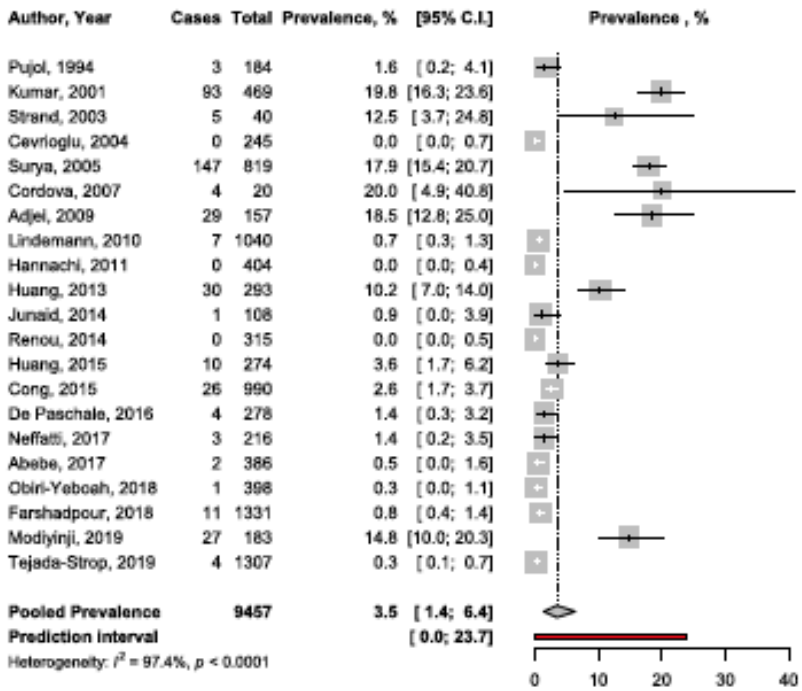


Fig. 2 Forest plot of the meta-analysis of IgM seroprevalence of HEV infection among asymptomatic pregnant women

Epidemiology and Infection

cambridge.org/hyg

Hepatitis E virus and blood transfusion safety

Hao Bi[1], Ru Yang[2], Chunchen Wu[1] and Jianbo Xia[1]

[1]Department of Laboratory Medicine, Maternal and Child Health Hospital of Hubei Province, Wuhan 430070, China and [2]Department of Blood Transfusion Research, Wuhan Blood Centre, Wuhan 430030, China

Review

Cite this article: Bi H, Yang R, Wu C, Xia J (2020). Hepatitis E virus and blood transfusion safety. *Epidemiology and Infection* **148**, e158, 1–9. https://doi.org/10.1017/S0950268820001429

Received: 8 February 2020
Revised: 22 May 2020
Accepted: 14 June 2020

Key words:
Blood donors; blood safety; HEV; transfusion; TT-HEV

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Abstract

While the majority of worldwide hepatitis E viral (HEV) infections that occur in people are from contaminated water or food sources, there has also been a steadily rising number of reported cases of transfusion-transmitted HEV (TT-HEV) in blood donation recipients. For most, HEV infection is acute, self-limiting and asymptomatic. However, patients that are immunocompromised, especially transplant patients, are at much higher risk for developing chronic infections, which can progress to cirrhosis and liver failure, along with overall increased mortality. Because of the rising trend of HEV serological prevalence among the global population, and the fact that TT-HEV infection can cause serious clinical consequences among those patients most at need for blood donation, the need for screening for TT-HEV has been gaining in prominence as an important public health concern for both developing and developed countries. In the review, we summarise evidence for and notable cases of TT-HEV infections, the various aspects of HEV screening protocols and recent trends in the implementation of TT-HEV broad-based blood screening programmes.

Le linee guida italiane

Linea guida
I CONTROLLI ALLA FRONTIERA

Condizioni di salute-malattia prese in esame:

Malattie infettive e diffusive:

- tubercolosi
- malaria
- HIV
- HBV/HCV
- infezioni sessualmente trasmissibili
- parassitosi intestinali

Malattie non infettive:

- diabete
- anemie
- ipertensione
- carcinoma cervice uterina

- gravidanza
- vaccinazioni

Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA

Schistosomiasis

- Offer serological screening and treatment (for those found to be positive) to all migrants from countries of high endemicity in sub-Saharan Africa, and focal areas of transmission in Asia, South America and North Africa

New! Coming soon

Strongyloidiasis

- Offer serological screening and treatment (for those found to be positive) for strongyloidiasis to all migrants from countries of high endemicity in Asia, Africa, Middle East, Oceania and Latin America

Latent TB
Active TB
HIV
HBV
HCV
Strongyloides
Schistosoma
VPDs

HDV??
HEV??

VPD

- Offer vaccination against measles/mumps/rubella (MMR) to all migrant children and adolescents without immunisation records as a priority.
- Offer vaccination to all migrant adults without immunisation records with either 1 dose of MMR or in accordance with the MMR immunisation schedule of the host country.
- Offer vaccination against DtaP-IPV-Hib to all migrant children and adolescents without immunisation records as a priority.
- Offer vaccination to all adult migrants without immunisation records according to the immunisation schedule of the host country. When this is not possible, adult migrants should be given a primary series of diphtheria, tetanus, and polio vaccine

Post-transplant liver graft schistosomiasis in a migrant from Sub-Saharan Africa

Paola Carrai [1], Lorenzo Zammarchi [2 3], Luca Emanuele Pollina [4], Luca Giordani [5], Valentina Mangano [5], Riccardo Iapoce [6], Francesca Rinaldi [2], Alessandro Bartoloni [2 3], Franco Filipponi [1], Paolo De Simone [1], Fabrizio Bruschi [5 7]

We report a case of post-transplant liver graft infection with *Schistosoma* spp in a migrant from Sub-Saharan Africa transplanted for HBV-related cirrhosis with pre-transplant undiagnosed schistosomiasis. The emergence of tropical diseases in non-endemic areas warrant screening protocols for donors and recipients with exposure in endemic areas.

Case Reports › Transpl Infect Dis. 2018 Oct;20(5):e12950. doi: 10.1111/tid.12950. Epub 2018 Jul 13.

Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA

Manifestation	HEV testing	Level of evidence
Acute	Recommended: All patients with symptoms consistent with acute hepatitis irrespective of travel history	A1
Acute	Recommended: Travellers with hepatitis returning from areas endemic for HEV gt1 or 2	A1
Acute	Recommended: Patients presenting with drug-induced liver injury	A1
Acute	Recommended: Patients with unexplained flares of chronic liver disease	C2
Chronic	Recommended: All immunosuppressed patients with unexplained abnormal LFTs	A1
Extrahepatic	Recommended: Patients presenting with neuralgic amyotrophy irrespective of LFT results	B1
Extrahepatic	Recommended: Patients presenting with Guillain-Barré syndrome irrespective of LFT results	B1
Extrahepatic	Suggested: Patients with encephalitis/myelitis	C2
SoHO	Recommended: Patients with abnormal LFTs after receiving blood products	A1
SoHO	Recommended: blood donor services screen blood donors for HEV by NAT, informed by local risk assessment and cost-effectiveness studies	A1

LFT: liver function test
NAT: nucleic acid amplification test
SoHO: substances of human origin

Recommendations and suggestions for HEV testing in clinical patients according to the European Association for the Study of the Liver

Grazie per l'attenzione...