Sistema Socio Sanitario
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ASST GRANDE OSPEDALE
METROPOLITANO NIGUARDA
MILANO

Strategie terapeutiche attuali nel migrante con epatite virale

Strategie terapeutiche attuali nel migrante con epatite virale

- Epatite come causa di morte nei paesi a risorse limitate
- HBV nei migranti
  - Epidemiologia
  - Differenze nell'indicazione al trattamento
- HCV nei migranti
  - Prevalenza
  - Trattamento il ruolo del genotipo HCV

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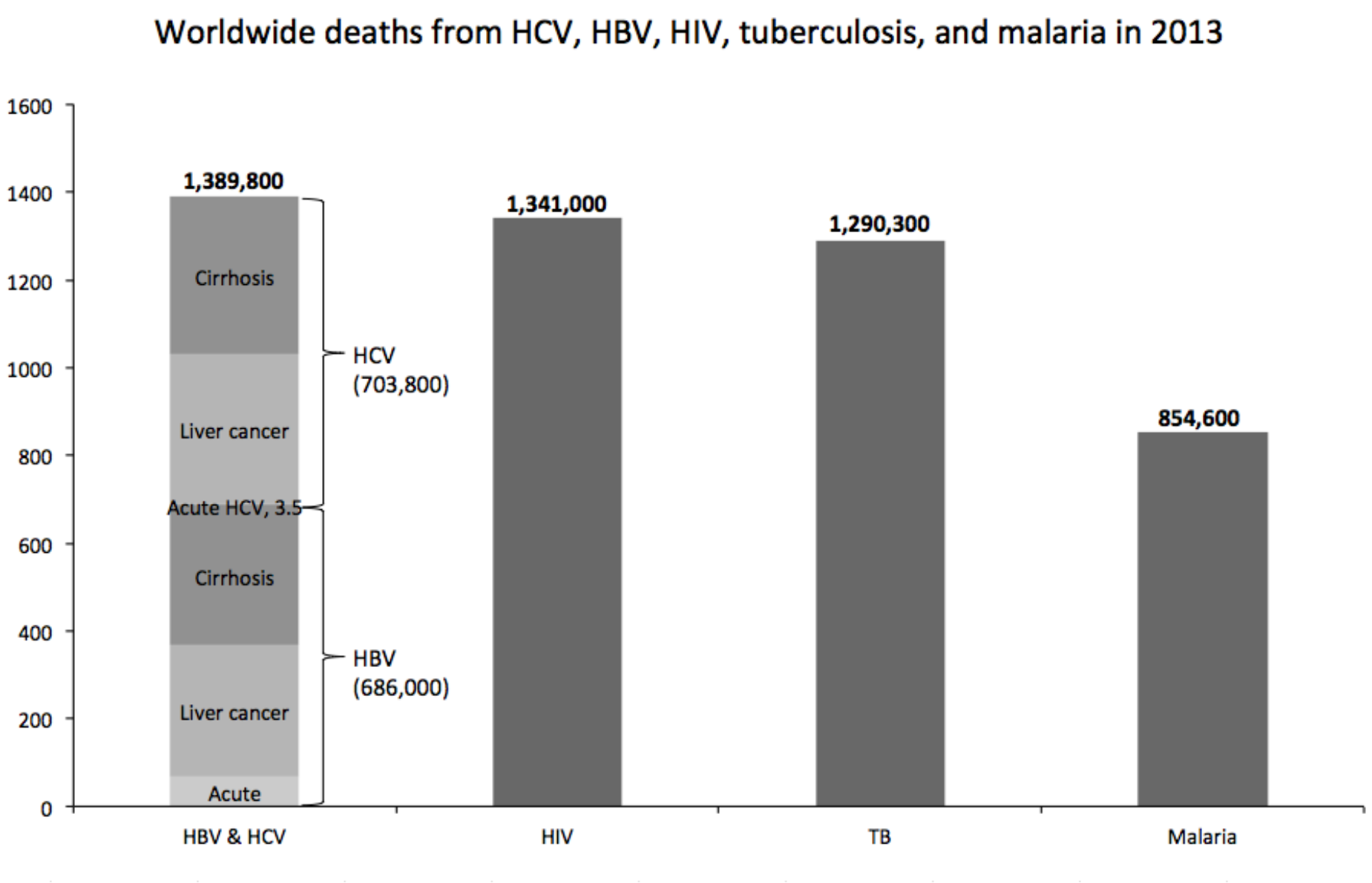
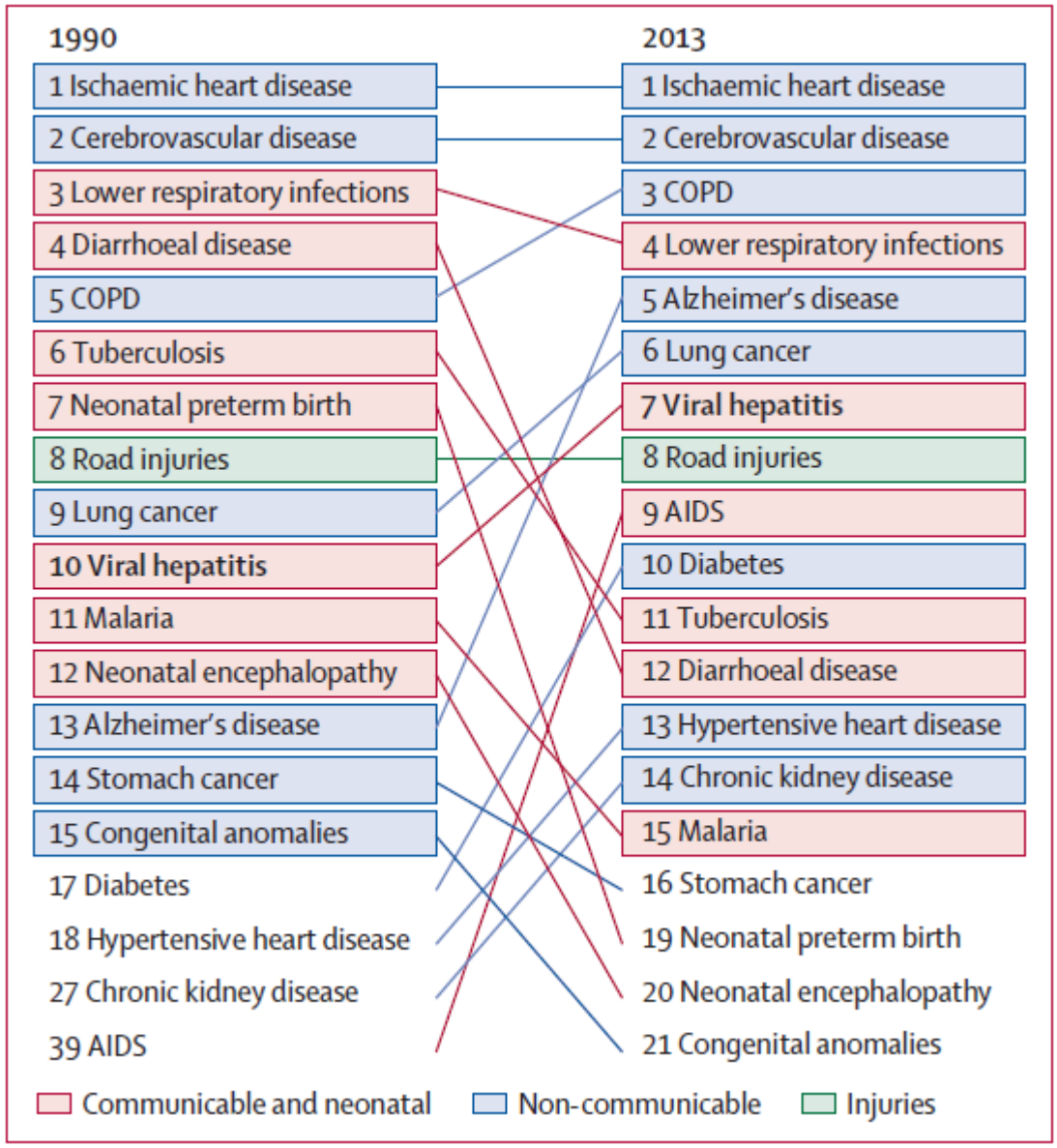


Global Burden of Disease report, Lancet 2014, 385: 117-171

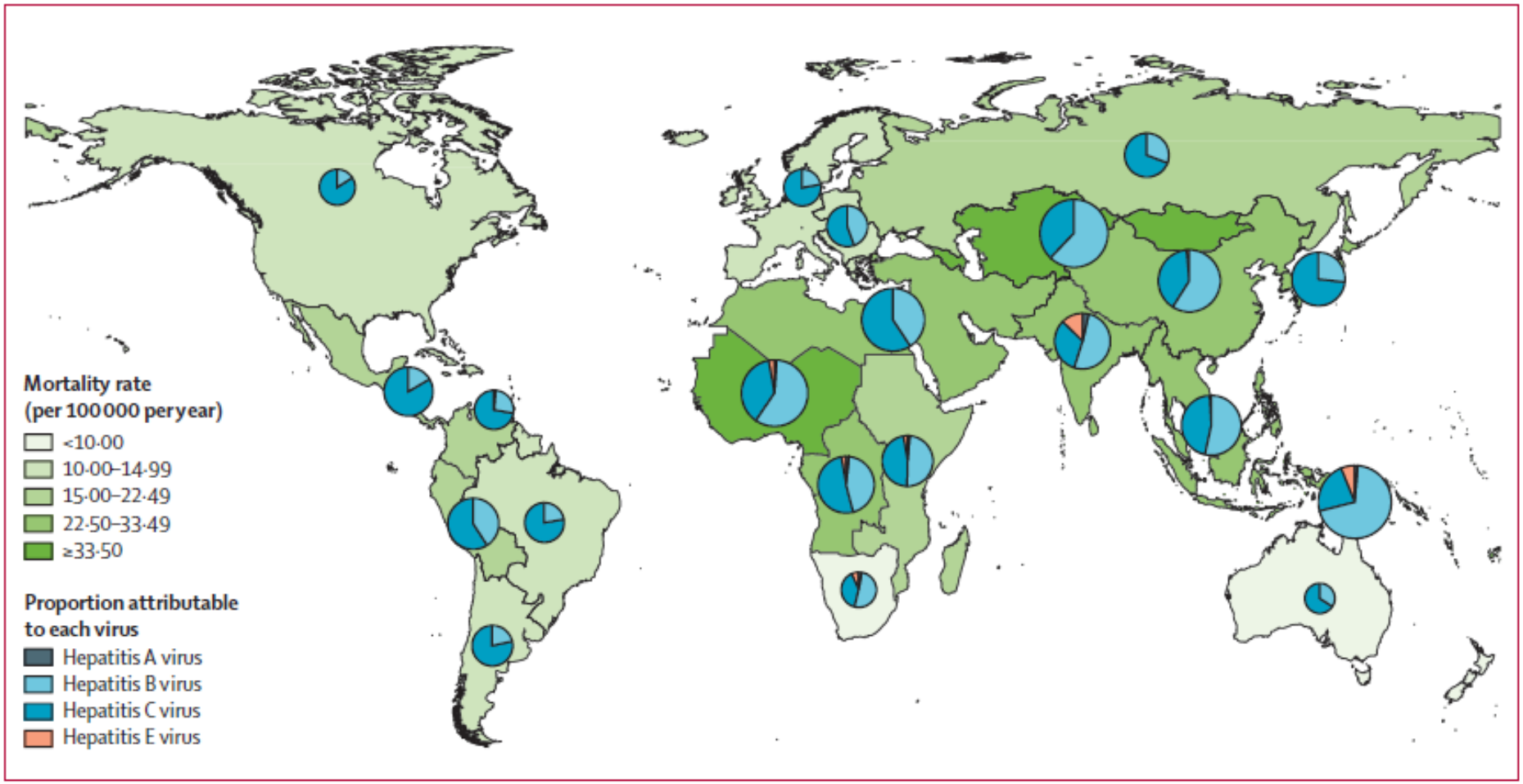
Leading causes of worldwide mortality and trends, 1990–2013



- **Viral hepatitis** moved from 10th postion to 7th.
- **AIDS** moved from 39th position to 9th.

Stanaway et al., The Lancet 2016

Worldwide mortality attributable to viral hepatitis



Map of viral hepatitis-related, age-standardised mortality rate, by GBD region

Stanaway et al., The Lancet 2016

Prevalenza di HBV, HCV, HIV in 2861 immigrati*. Anni 2001-2009

Studio condotto in un'area a nord di Napoli

HBsAg pos ○ HBeAg pos ○ HBeAb pos	206 (7,6%) 12 (5,8%) 139 (67,5%)
Anti-HCV pos	84 (3,1%)
Anti-HIV pos	129 (5%)
Anti-HBc (anti-core isolato)	533 (19%)
Anti-HBs □ Naturali (HBsAb + HBcAb) □ Vaccinati	756 (28,2%) 659 (87,2%) 97 (12,8%)
TPHA	129 (4,8%)

* 85% from sub-saharian Africa

Stornaiuolo et al.Monotematica AISF 2011

Strategie terapeutiche attuali nel migrante con epatite virale

- Epatiti virali prima causa di morte per infezione nel mondo con maggioranza dei decessi nei paesi a risorse limitate
- Elevata prevalenza infezioni da HBV e HCV negli immigrati

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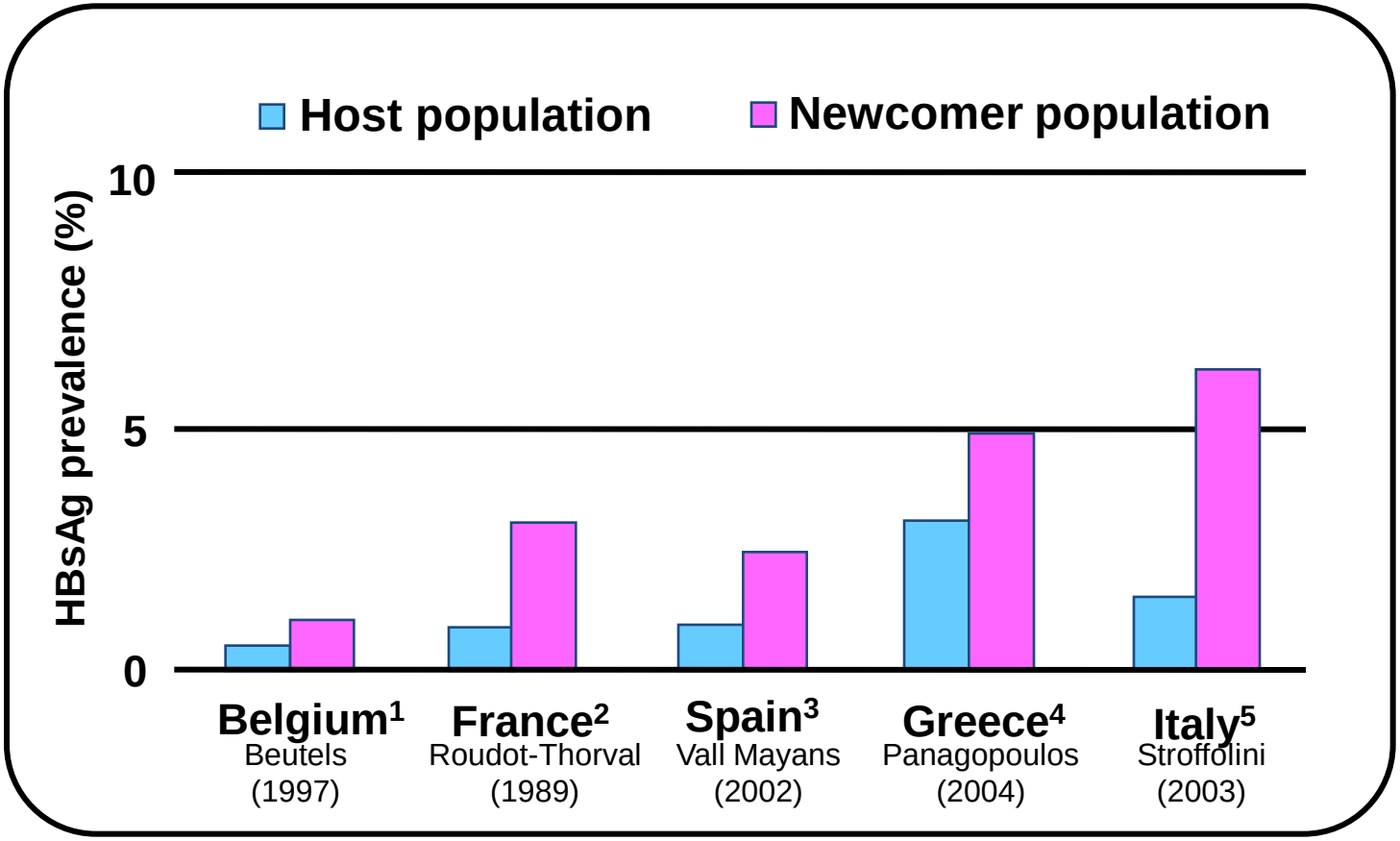
The Prevalence of Hepatitis B Surface Antigen (HBsAg) is Higher in Newcomer vs. Host Populations in Western Europe



1. Beutels et al. *Eur J Epidemiol* 1997;13:275-80;
2. Roudot-Thoraval et al. *Gastroenterol Clin Biol* 1989;13:353-6;
3. Vall Mayans et al. *Enfern Infecc Microbiol Clin* 2002;20:154-6;
4. Panagopoulos et al. *J Matern Fetal Neonatal Med* 2004;16:106-10;
5. Stroffolini T, et al. *Vaccine* 2003;7:1246-9

Prevalence of HBV infection in immigrants born outside Italy

Author	Region	N. of patients	Mean Age	% of females	HBsAg +	Anti-HBc +	Anti-HCV+	Anti-HIV +
Tafuni (1)	Puglia	529	23.9	16.4	8.3	45.6	4.5	1.5
Majori (2)	Veneto	182	31.9	22.5	9.3	48.3	2.0	
Fabris (3)	Veneto	47			6.4			
Palumbo (4)	Puglia	890			10.7			
Zermiani (5)	Veneto	345 FSWs	24.3	100	3.10		0.9	4.6
Bonura (6)	Sicilia	310 pregnant women	29.0	100	4.2			
Stroffolini (7)	Italy	597 pregnant women		100	5.9			

1. S.Tafuri; BMC Infect Dis. 2010; 10: 213
2. S. Maiori; J Travel Med. 2008 ;15:323-7.
3. P. Fabris; J Clin Gastroenterol. 2008 May-Jun;42(5):527-32
4. East Mediterr Health J. 2008 Jul-Aug;14(4):784-90.
5. M. Zermiani; The Open AIDS Journal, 2012, 6, 60-64
6. F. Bonura Vaccine. 2005 May 9;23(25):3243-6.
7. T. Stroffolini, **Vaccine**. 2003 Mar 7;21(11-12):1246-9.

Point-of-Care Screening, Prevalence, and Risk Factors for Hepatitis B Infection Among 3,728 Mainly Undocumented Migrants From Non-EU Countries in Northern Italy

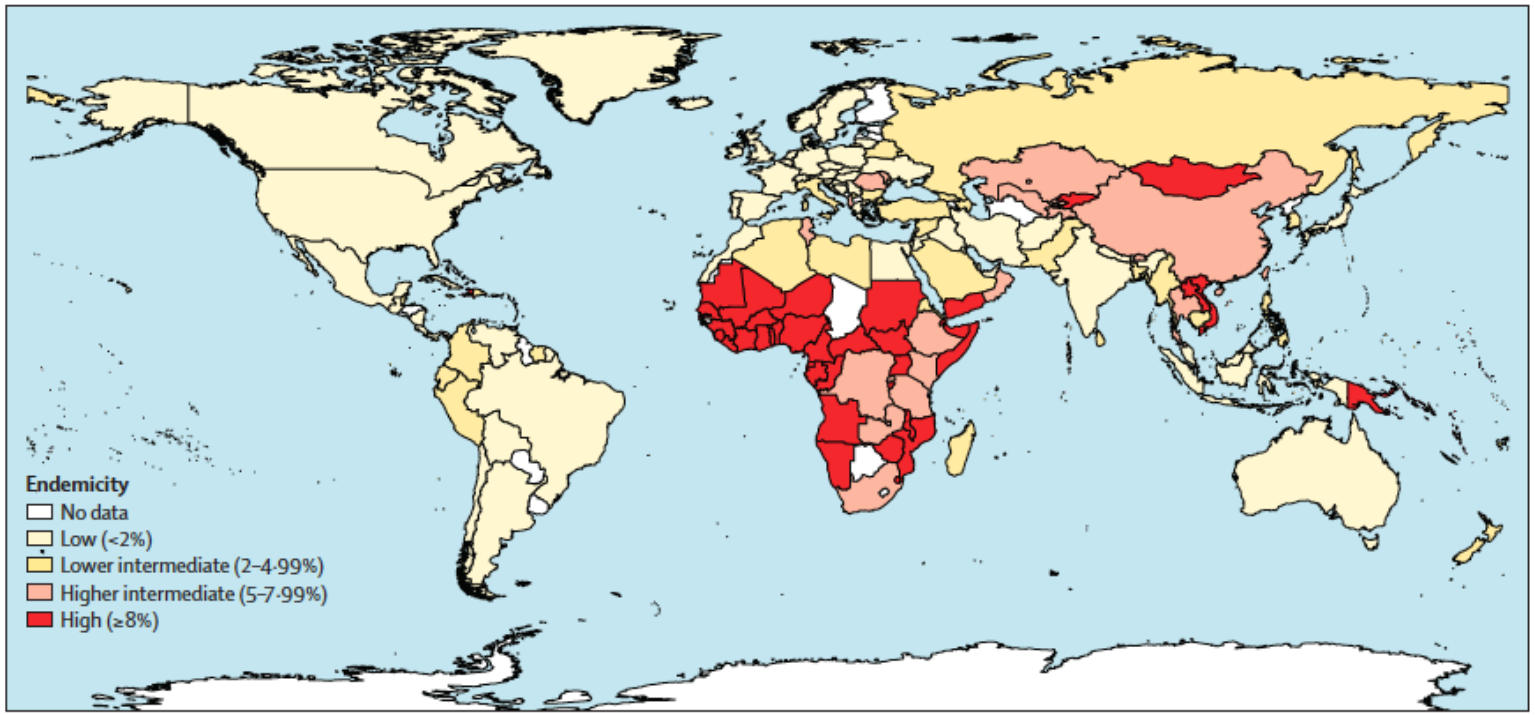
Variables	Multivariate		
	OR	95% CI	*p*
Sex			
Female	1		
Male	1.744	0.648–1.973	0.502
Age (mean years)			0.554
Continent of origin			
North Africa	1		
C/S America	1.300	0.645–2.618	0.463
Eastern Europe	1.533	1.359–2.815	0.001
Asia	1.955	1.631–2.978	0.014
Sub-Saharan Africa	3.762	2.437–5.892	<0.001
Endemic area			
Low	1		
Intermediate	1.481	0.893–2.741	0.071
High	3.625	3.089–5.721	<0.001
Marital status (*n* = 3,722)			
Not single	1		
Single	0.635	0.422–1.371	0.083
Education degree (mean years)			0.340
Religion			
Islamic	1		
Oriental religions	2.554	0.538–3.224	0.642
Other	1.947	0.736–2.385	0.198
Christian	2.149	0.757–2.382	0.158
None	0.825	0.734–1.966	0.581
Legal conditions			
Regular	1		
Irregular/clandestine	0.975	0.271–1.599	0.492
HCV-Ab (*n* = 3,704)			
No	1		
Yes	0.582	0.201–1.672	0.283
Serological tests for syphilis and other treponematoses (*n* = 3,626)			
VDRL–/TPHA–	1		
VDRL–/TPHA+	1.648	0.612–1.957	0.628
VDRL+/TPHA+	1.318	0.682–1.635	0.775

A) Country of origin	HBs Ag+ (%)
Senegal	40/308 (13.0)
China	28/246 (11.4)
Moldova	88/821 (10.7)
Romania	6/161 (3.7)
Brazil	3/91 (3.3)
Egypt	5/234 (2.1)
Pakistan	5/241 (2.1)
Morocco	3/159 (1.9)
Nigeria	5/301 (1.7)
Ukraine	5/460 (1.1)
B) WHO endemic area	**HBs Ag+ (%)**
High	183/1,957 (9.4)
Intermediate	41/1,761 (2.3)
Low	0/10 (0)

HBsAg= hepatitis B surface antigen; WHO= World Health Organization.

El Hamad I et al J Travel Med 2015

5.014.437 immigrants from foreign countries residents in Italy[1]



HBsAg Endemicity[2]	N of resident immigrants[1]	Estimated n of HBsAg+ immmigrants
10-15%	218.864	27.358
5-10%	2.276.415	170.731
2-5%	1.588.397	55.594
< 2%	93.0761	931
Totale		**254.613**

1. Comuni Italiani 2014; 2 Schweitzer A et al. The lancet 2015

Point-of-Care Screening, Prevalence, and Risk Factors for Hepatitis B Infection Among 3,728 Mainly Undocumented Migrants From Non-EU Countries in Northern Italy

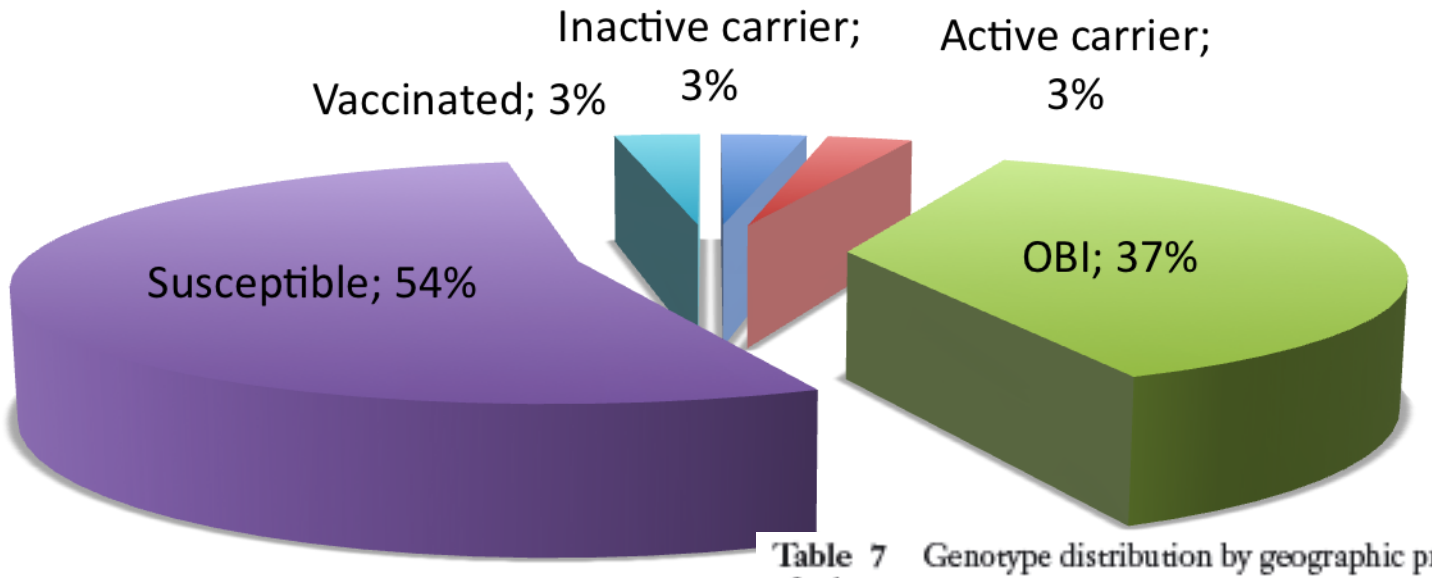


Table 7 Genotype distribution by geographic provenance of migrants

	North Africa ($n = 1$)	SS/S Africa ($n = 3$)	Eastern Europe ($n = 31$)	Asia ($n = 9$)	C/S America ($n = 1$)
Genotype A ($n = 8$)	0	2	5	0	1
Genotype B ($n = 5$)	0	0	0	5	0
Genotype C ($n = 5$)	0	0	1	4	0
Genotype D ($n = 27$)	1	1	25	0	0

El Hamad I et al. J Travel Med 2015

Hepatitis B and immigrants: a SIMIT multicenter cross-sectional study Characteristics of the 3,760 HBsAg-positive patients immigrants versus Italians

	Immigrants	Italians	*p* value
Number of cases, *n* (%)	932 (24.8)	2,828 (75.2)	
Distribution in Italian centers, *n* (%)			<0.001
Northern Italy	336 (36.1)	1,222 (43.2)	
Central Italy	521 (55.9)	603 (21.3)	
Southern Italy	75 (8.0)	1,003 (35.5)	
Region of origin, *n* (%)			
Eastern Europe	330 (35.4)	–	
Asia	346 (37.1)	–	
Sub-Saharan Africa	163 (17.5)	–	
North Africa	51 (5.5)	–	
Other[a]	42 (4.5)	–	
Gender			
Females, *n* (%)	536 (57.5)	876 (31.0)	<0.001
Age at enrollment, median (range)	34 (18–77)	52 (18–93)	<0.001
First observation for HBV			
Incident cases, *n* (%)	319 (34.2)	375 (13.3)	<0.001
Alcohol intake, *n* (%)[b]	315 (41.4)	1,213 (60.0)	<0.001

	Immigrants	Italians	*p* value
Co-infections, *n*/*n* tested (%)			
HDV	39/849 (4.6 %)	190/2,501 (7.6 %)	0.003
HCV	29/903 (3.2 %)	262/2,710 (9.7 %)	<0.001
HIV	73/850 (8.6 %)	354/2,291 (15.5 %)	<0.001
HBV genotype tested, *n* (%)	45 (4.8 %)	181 (6.4 %)	
A	5 (11.1 %)	14 (7.7 %)	
B	5 (11.1 %)	1 (0.6 %)	
C	13 (28.9 %)	2 (1.1 %)	
D	18 (40.0 %)	159 (87.8 %)	
E	3 (6.7 %)	1 (0.6 %)	
F	1 (2.2 %)	4 (2.2 %)	
HBeAg-positives[c]			
n/*n* tested (%)	254/925 (27.5 %)	391/2,792 (14.0 %)	<0.001
HBV-DNA (IU/ml)			
>400	499/844 (59.1 %)	1,089/2,355 (46.2 %)	<0.001
>400 off-therapy	398/499 (77.4 %)	646/1,089 (58.6 %)	<0.001

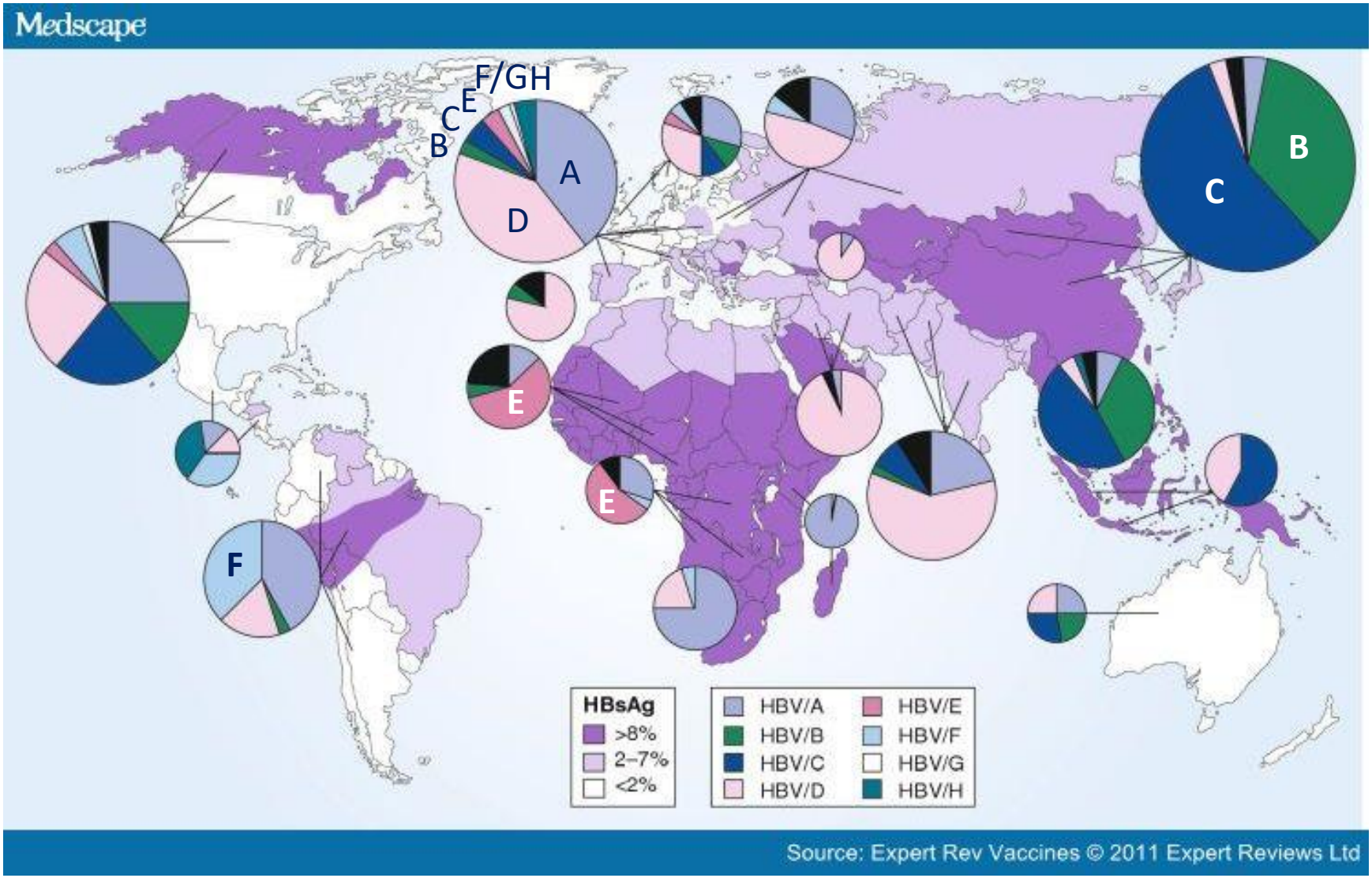
Fasano M et al Infection 2013

Hepatitis B and immigrants: a SIMIT multicenter cross-sectional study Characteristics of the 3,760 HBsAg-positive patients immigrants according to the region of origin versus Italians

	Italians	Eastern Europe	Asia	Sub-Saharan Africa	North Africa	Other	*p* value
Number of cases, *n* (%)	2,828 (75.2)	330 (8.8)	346 (9.2)	163 (4.3)	51 (1.4)	42 (1.1)	
Age (years), *n* (%)							<0.001
18–29	83 (2.9)	122 (37.0)	144 (41.6)	29 (17.8)	4 (2.9)	1 (2.4)	
30–49	1,147 (40.6)	166 (50.3)	187 (54.0)	126 (77.3)	42 (82.4)	33 (78.6)	
50–59	767 (27.1)	31 (9.4)	14 (4.0)	6 (3.7)	4 (7.8)	8 (19.0)	
≥60	831 (29.4)	11 (3.3)	1 (0.3)	2 (1.2)	1 (2.0)	0 (0.0)	
Gender							
Females, *n* (%)	876 (31.0)	189 (57.3)	253 (73.1)	67 (41.1)	16 (31.4)	11 (26.2)	<0.001
Co-infections *n*/*n* tested (%)							
HDV	190/2,501 (7.6)	25/289 (8.7)	4/330 (1.2)	6/148 (4.1)	1/44 (2.3)	3/38 (7.9)	<0.001
HCV	262/2,710 (9.7)	12/319 (3.8)	2/338 (0.6)	3/159 (1.9)	6/47 (12.8)	6/40 (15.0)	<0.001
HIV	354/2,291 (15.5)	10/290 (3.4)	7/320 (2.2)	40/152 (26.3)	6/48 (12.5)	10/40 (25.0)	<0.001
HBeAg							
Positives, *n*/*n* tested (%)	391/2,792 (14.0)	45/327 (13.8)	159/345 (46.1)	30/161 (18.6)	6/51 (11.8)	14/41 (34.1)	<0.001

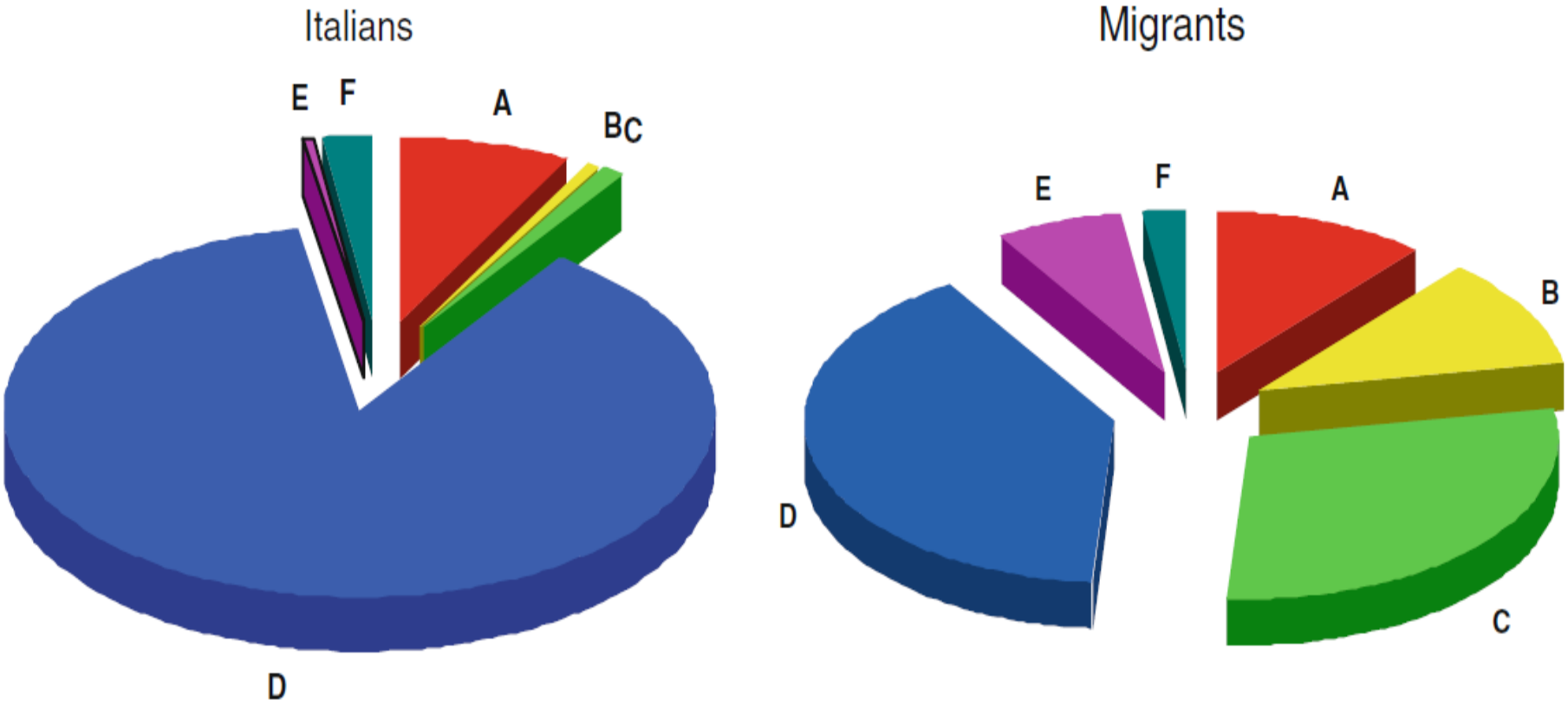
Fasano M et al Infection 2013

This situation is exacerbated by the increased circulation of atypical HBV genotypes, often associated with faster disease progression



Geographical variation in the prevalence of HBV genotypes A–H. Results of a review of genotyping results from 45,000 HBV-infected individuals over a 10-year period

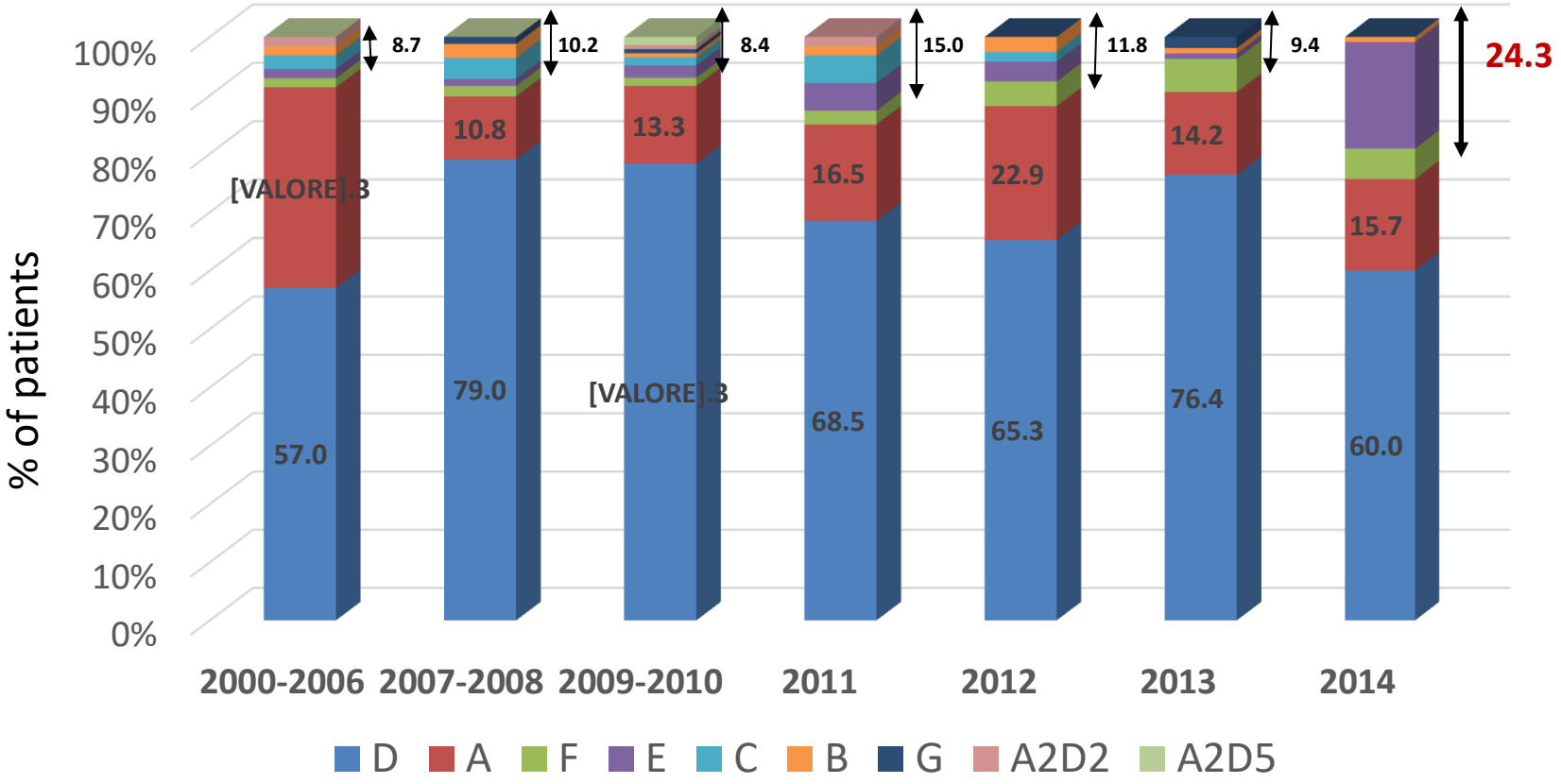
Hepatitis B and immigrants: a SIMIT multicenter cross-sectional study of the 3,760 HBsAg-positive patients



Genotype distribution in the native and foreign-born populations

M. Fasano et al. Infection (2013) 41:53–59

……whose prevalence is increasing over time



The figure reports HBV genotypes stratification per year of collection

Svicher et al 2016

Epatite B: Informazioni e Buone regole

Progetto

Ben informati

Campagna d'Informazione e Sensibilizzazione

Un'iniziativa

SIMIT
SOCIETA' ITALIANA DI MALATTIE INFETTIVE E TROPICALI

乙型肝炎：信息和好良规范

项目

Ben informati

信息传播和提高认知活动

举措实施

SIMIT
SOCIETA' ITALIANA DI MALATTIE INFETTIVE E TROPICALI

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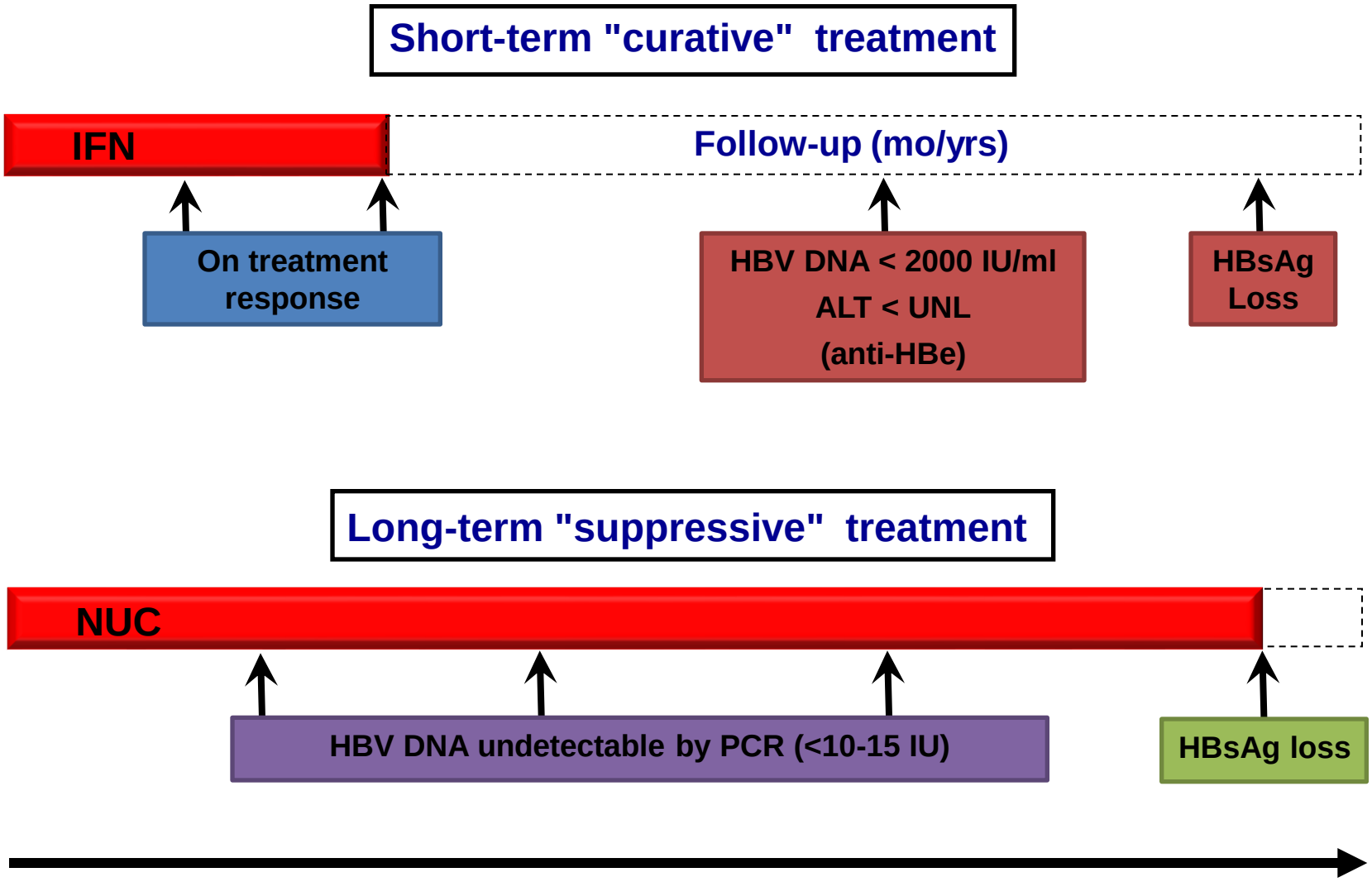
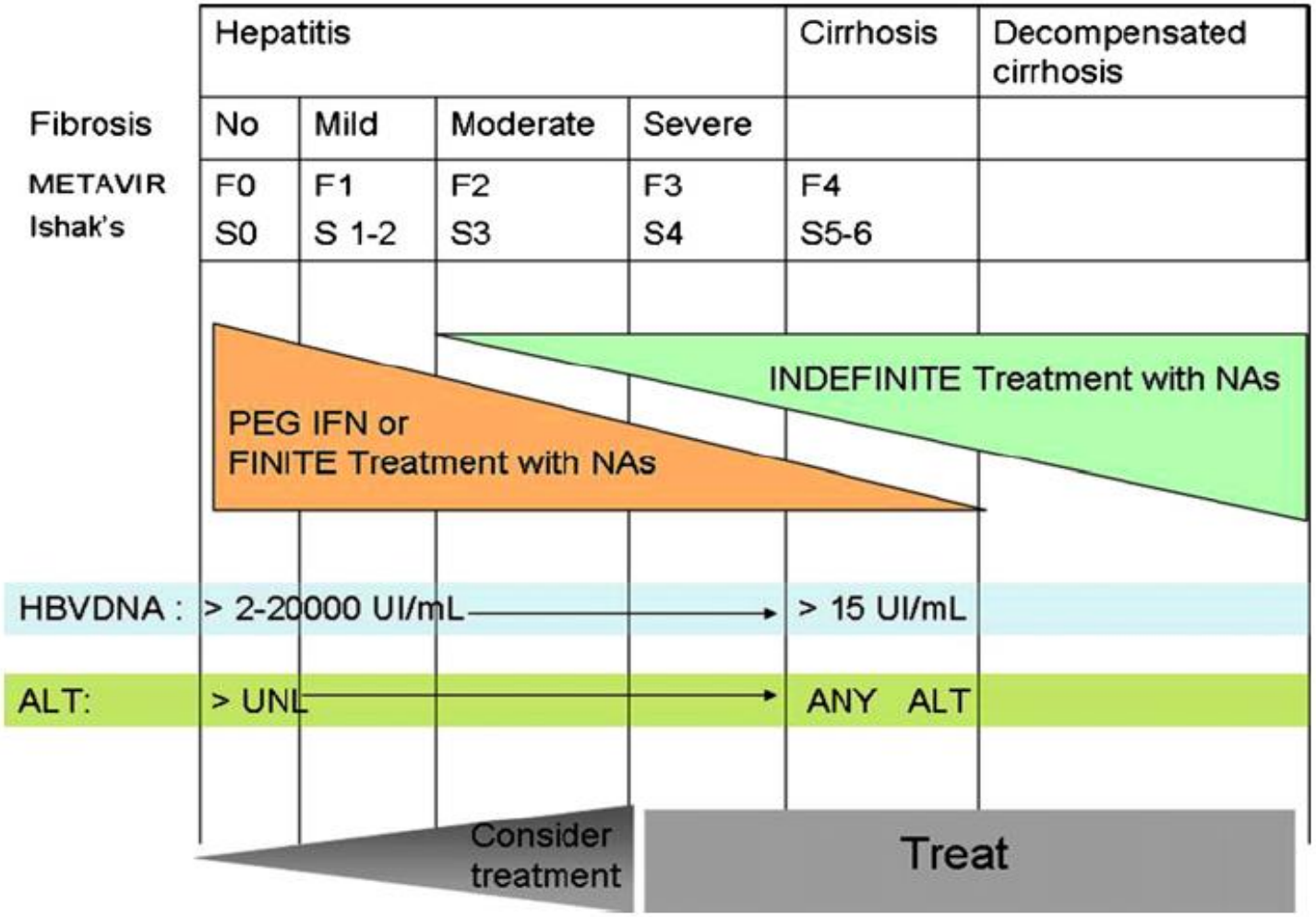
Therapeutic strategies for chronic hepatitis B

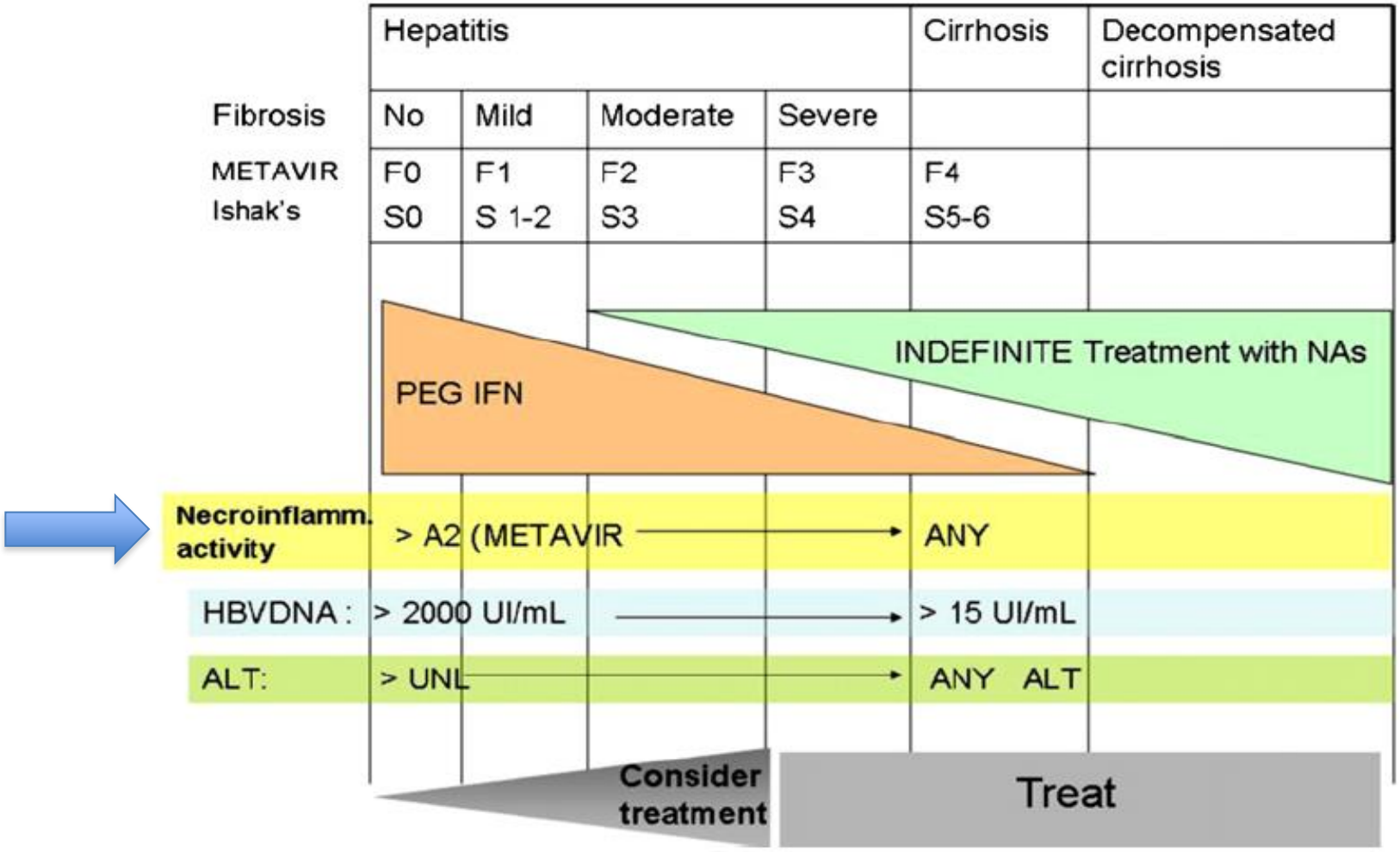


The "Stresa Paradigm" HBeAg positive hepatitis B with or without cirrhosis



(Carosi and Rizzetto, DLD 2011)

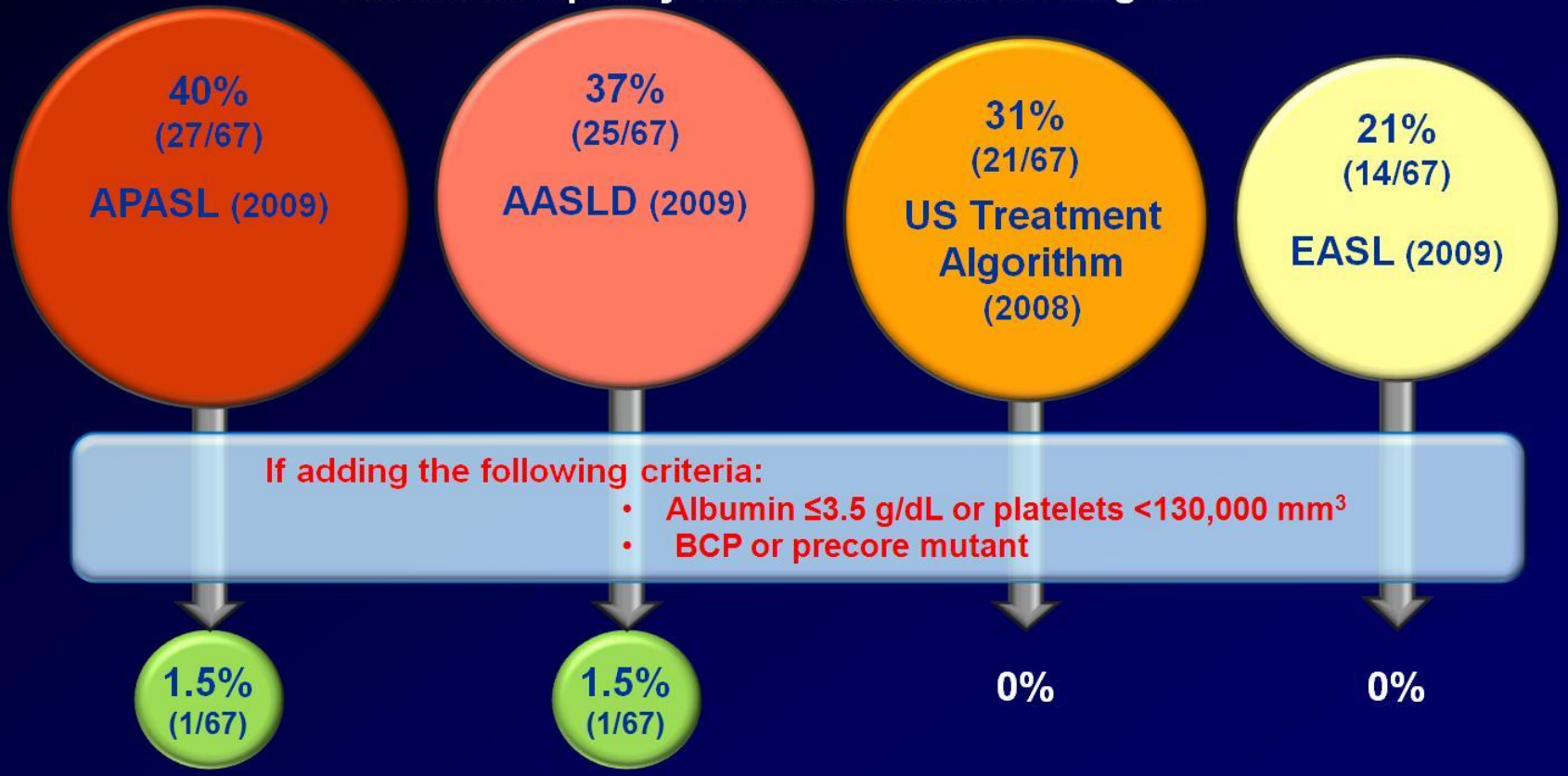
The “Stresa Paradigm” HBeAg negative hepatitis B with or without cirrhosis



(Carosi and Rizzetto, DLD 2011)

Patients Who Developed Serious Liver-related Complications[a] May Be Excluded from Treatment by Current Guidelines/Algorithms

Percent of patients who developed serious liver-related complications but did not qualify for treatment according to:



Percent of patients who would not qualify for treatment with additional criteria

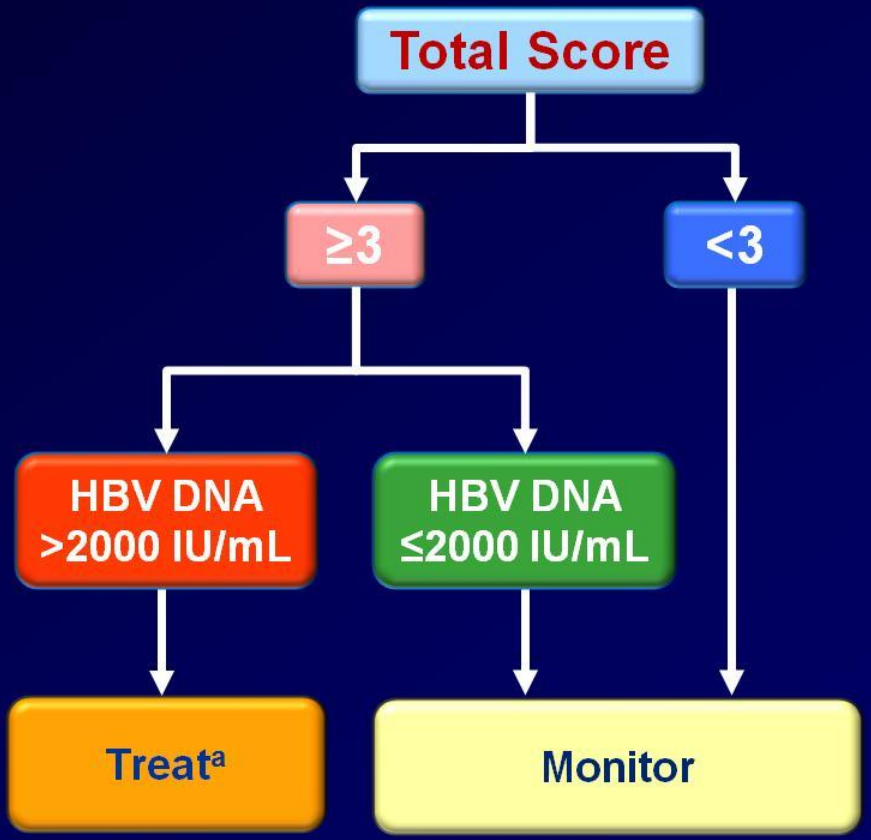
[a]Includes HCC development and non-HCC liver-related deaths.

Adapted from Tong MJ, et al. *J Gastroenterol Hepatol.* 2011;26:829-835.

Evaluation on Patients in the Gray Zone

Conduct liver biopsy if possible.
If not, calculate Risk Impact Score[b]:

Risk Factors	Impact Score
Age ≥40	1
Male sex	1
ALT: male ≥30 U/L or female ≥19 U/L	1
BCP mutation	2
HCC in first-degree relative	3
Albumin ≤3.5 g/dL or Platelet ≤130,000 mm^3	3
Total Score	____ points



[b]This scoring system is based on expert opinion and warrants further clinical experience and validation

Tong MJ, et al. *Dig Dis Sci.* 2011;56(11):3143-3162.

Peg-IFN-a for HBeAg positive patients

HBV Genotype	Consider Peg-IFN in pts with:
A	Either high ALT (≥2x ULN) or low HBV DNA (<9 log cp/ml)
B or C	Both high ALT (≥2x ULN) and low HBV DNA (<9 log cp/ml)
D	Peg-IFN generally not recommended

Recommendations based on an average probability of **SVR of more than 30%**

Buster et al. Gastroenterology 2009

Response-guided therapy using HBsAg levels in Peg-IFN-treated patients: *early stopping rules**

HBeAg-positive

Week 12:

- No decline of HBsAg (A,D)
- HBsAg >20,000 IU/mL (B,C)

Week 24:

- HBsAg >20,000 IU/ml (A,B,C,D)

* 92-100% Negative Predictive Values

HBeAg-negative

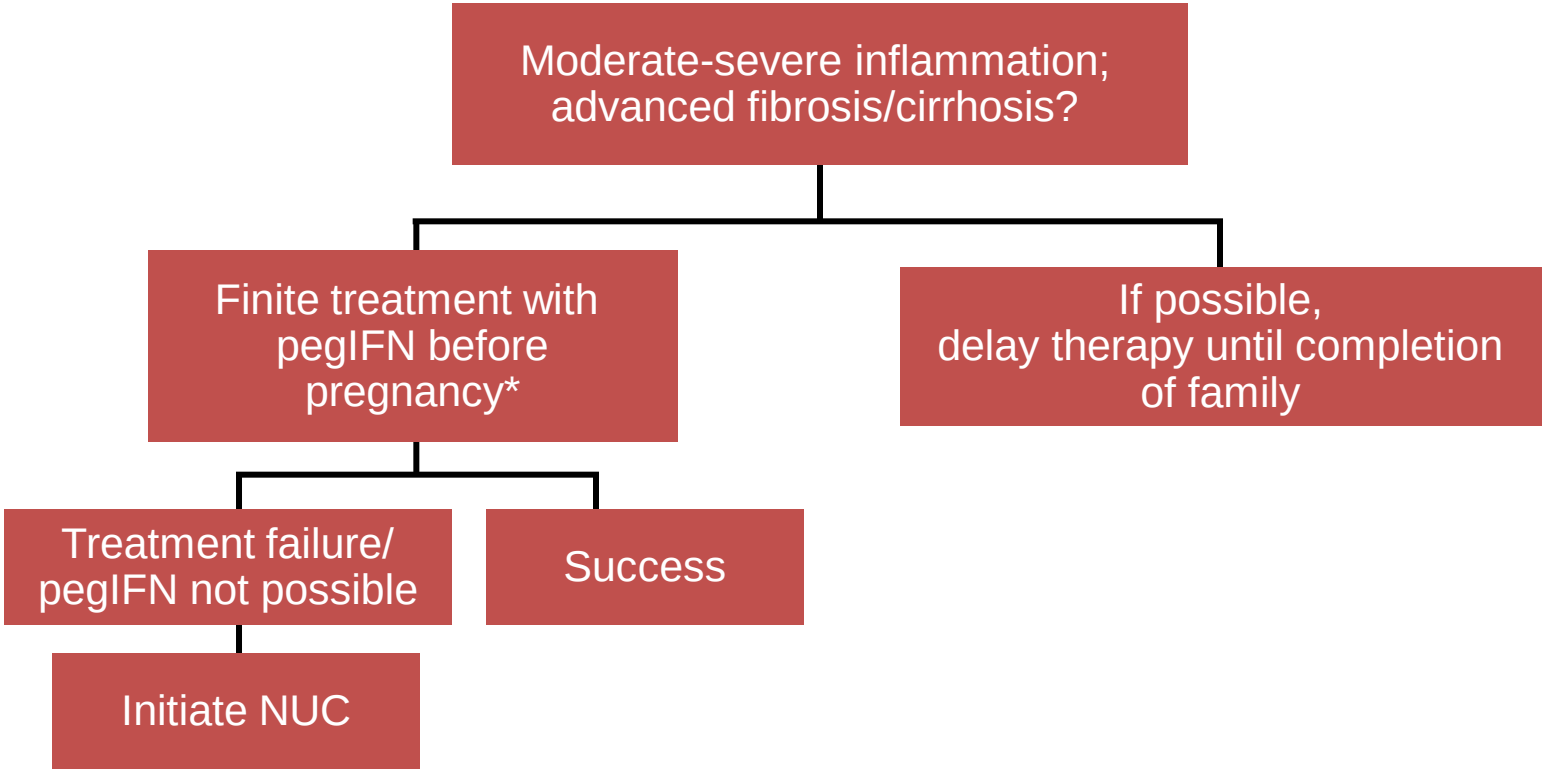
Week 12:

-No decline in HBsAg + <2 log decline in HBV DNA

* 95-100% Negative Predictive Values

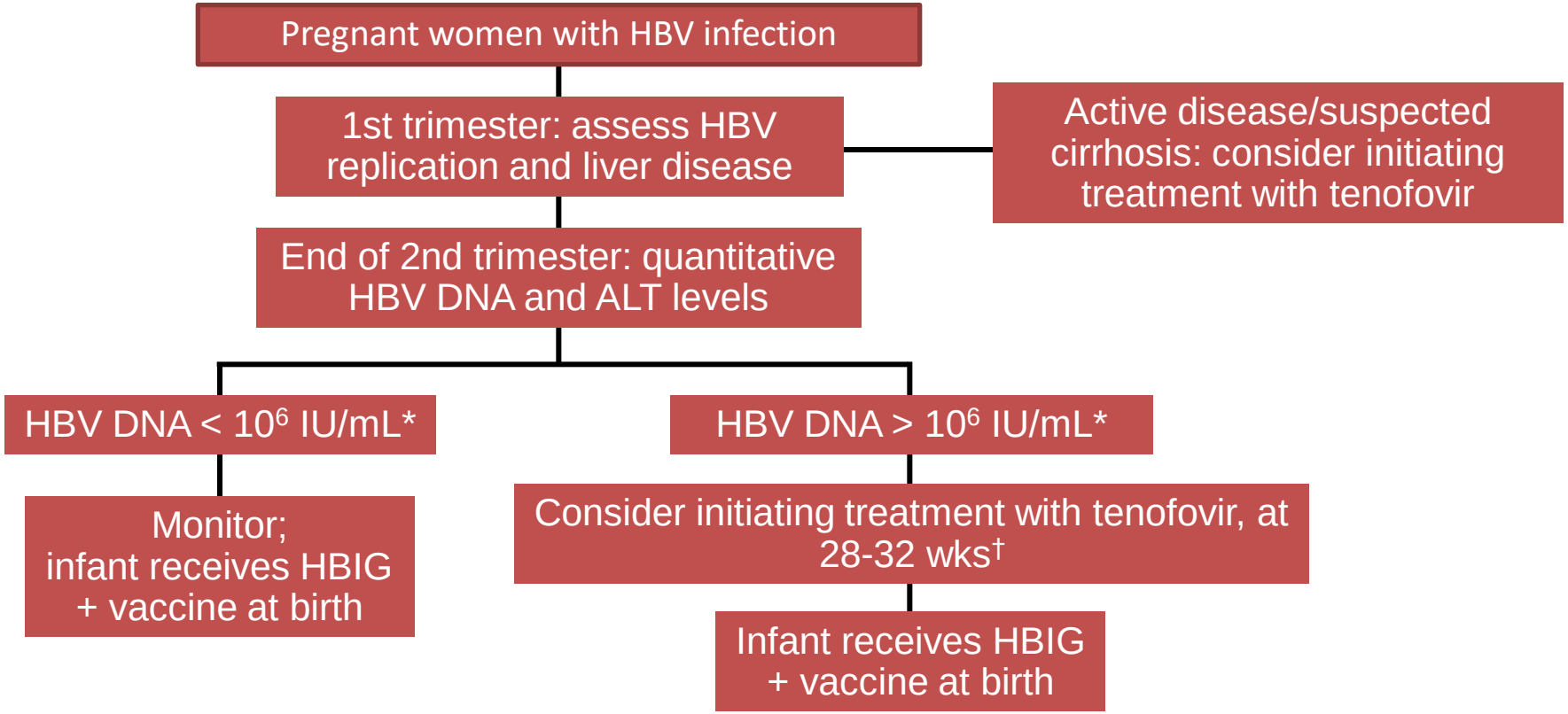
EASL Clinical Practice Guidelines. J Hepatol 2012;57:167-185

Antiviral Therapy for Chronic HBV Infection in Women Starting a Family in Near Future



*Effective contraception indicated.

Algorithm for HBV Management in Women During Pregnancy



*The cut-off level of maternal HBV DNA level for initiation of therapy is unclear, and HBV DNA from 6-8 $\log_{10}$ IU/mL can be considered for therapy based on physician and patient preference.

†Tenofovir is preferred if treatment is expected to be > 12 weeks or if treatment is expected to continue while breastfeeding.

Another critical issue is represented by HDV

- Although HBV vaccination is active also against HDV, HDV stills remains a cause of **severe acute and chronic liver illness**

- **Anti-HBV drugs cannot interfere with the production of HBV surface antigens, therefore they do not affect HDV replication**

- **HDV-driven disease evolves quite frequently to HCC**

- There are **no antiviral drugs against HDV**
  - So far, Interferon alfa is used to treat the most severe forms, but results are disappointing

Strategie terapeutiche attuali nel migrante con epatite virale

- Epatiti virali prima causa di morte per infezione nel mondo con maggioranza dei decessi nei paesi a risorse limitate
- Elevata prevalenza infezioni da HBV e HCV negli immigrati
- Infezione da HBV:
  - prevalenza correlata ad area di origine
  - Vaccinazione immigrati: molto resta da fare
  - Differenze cliniche: maggior numero di soggetti giovani HBeAg+
  - Problemi clinici: indicazioni al tratamento in HBeAg+ gestione giovani donne HBeAg+

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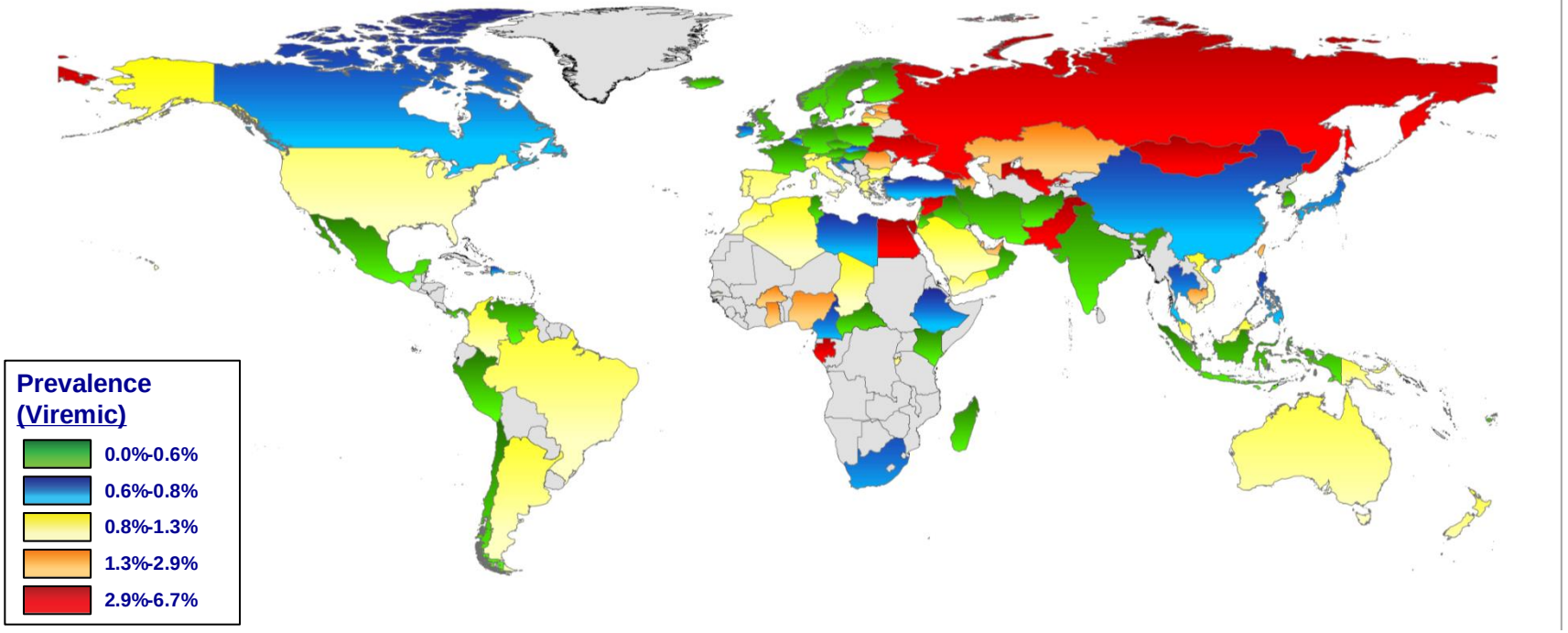
An Estimated 70 -130 Million are Infected with HCV (Viremic)

Countries with HCV Epidemiology Data

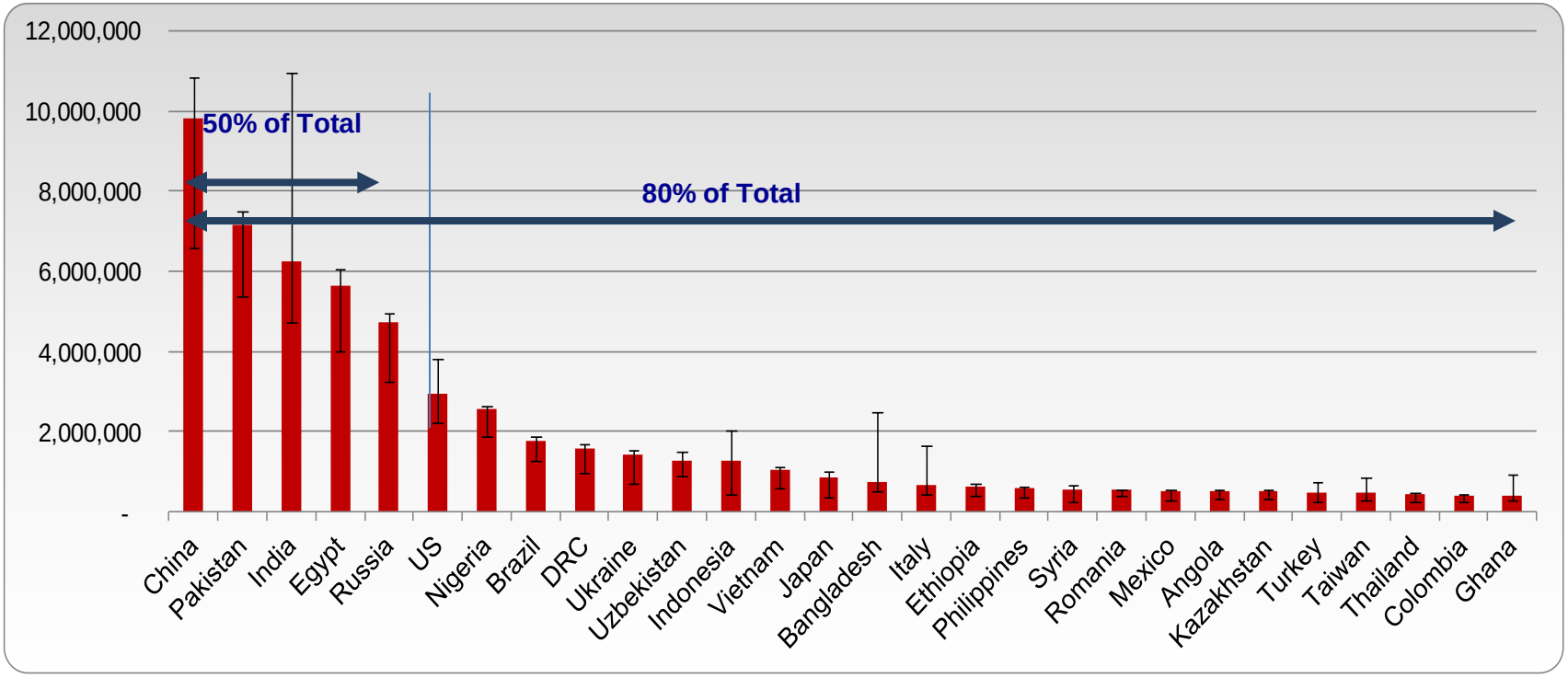


HCV burden was verified in 59 countries; 33 others modeled using published data

Polaris Observatory (http://www.polarisobservatory.com/)

Twenty-Eight Countries Account for 80% of HCV Infections

Viremic HCV Infections (2016)



Source: Polaris Observatory (http://www.polarisobservatory.com/)

WHO Global Health Sector HCV Strategy

Global targets for 2030

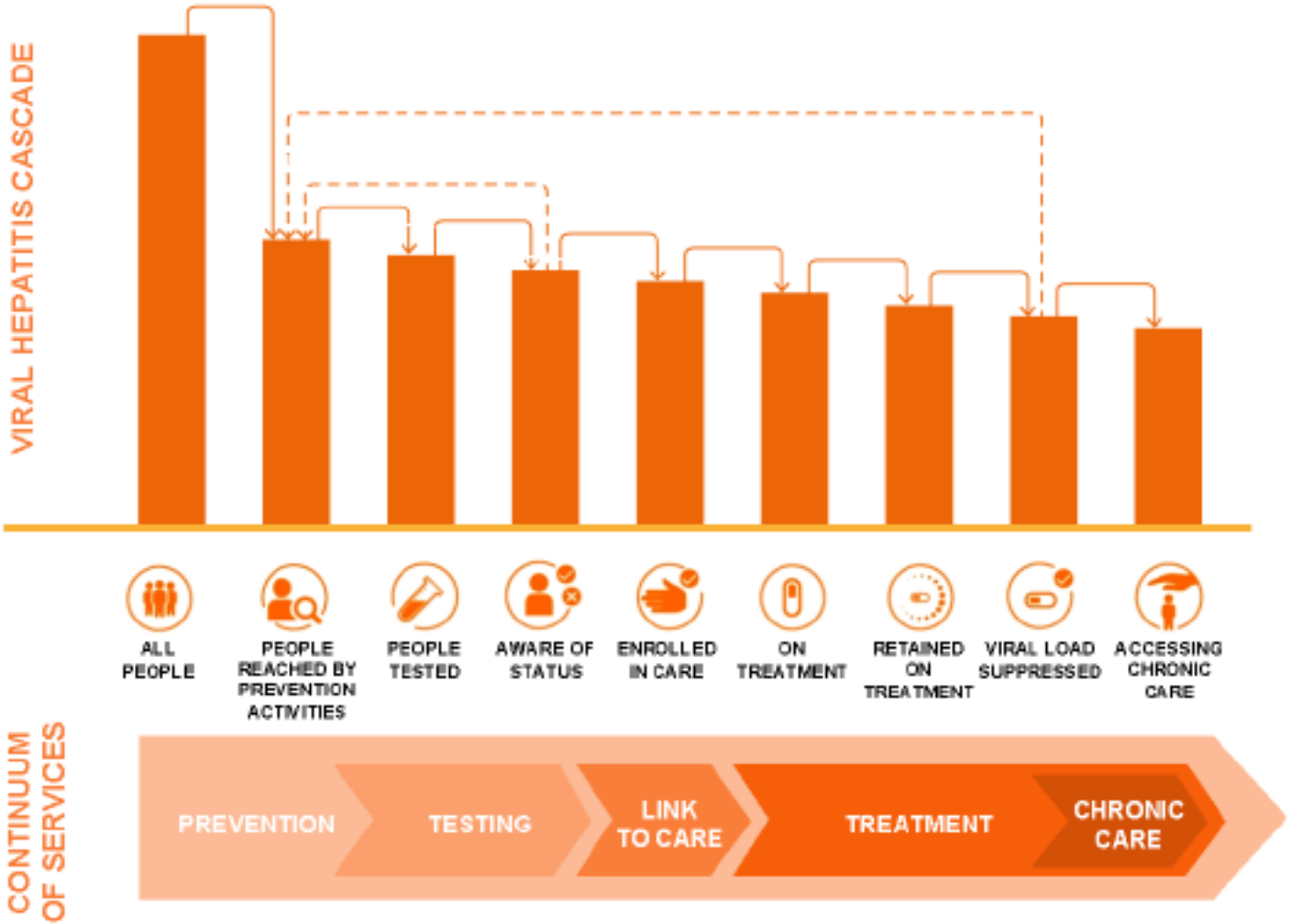
- **90%** diagnosed
- **90%** of eligible people treated
- **90%** of those treated are cured
- **50%** of PWID covered by harm reduction services by 2020

- **70%** reduction in HCV incidence
  - 50% reduction by 2020
- **Zero** new infections due to unsafe blood transfusions
- **75%** reduction in new infections due to unsafe medical practices by 2020

- **60%** reduction in HCV-related deaths

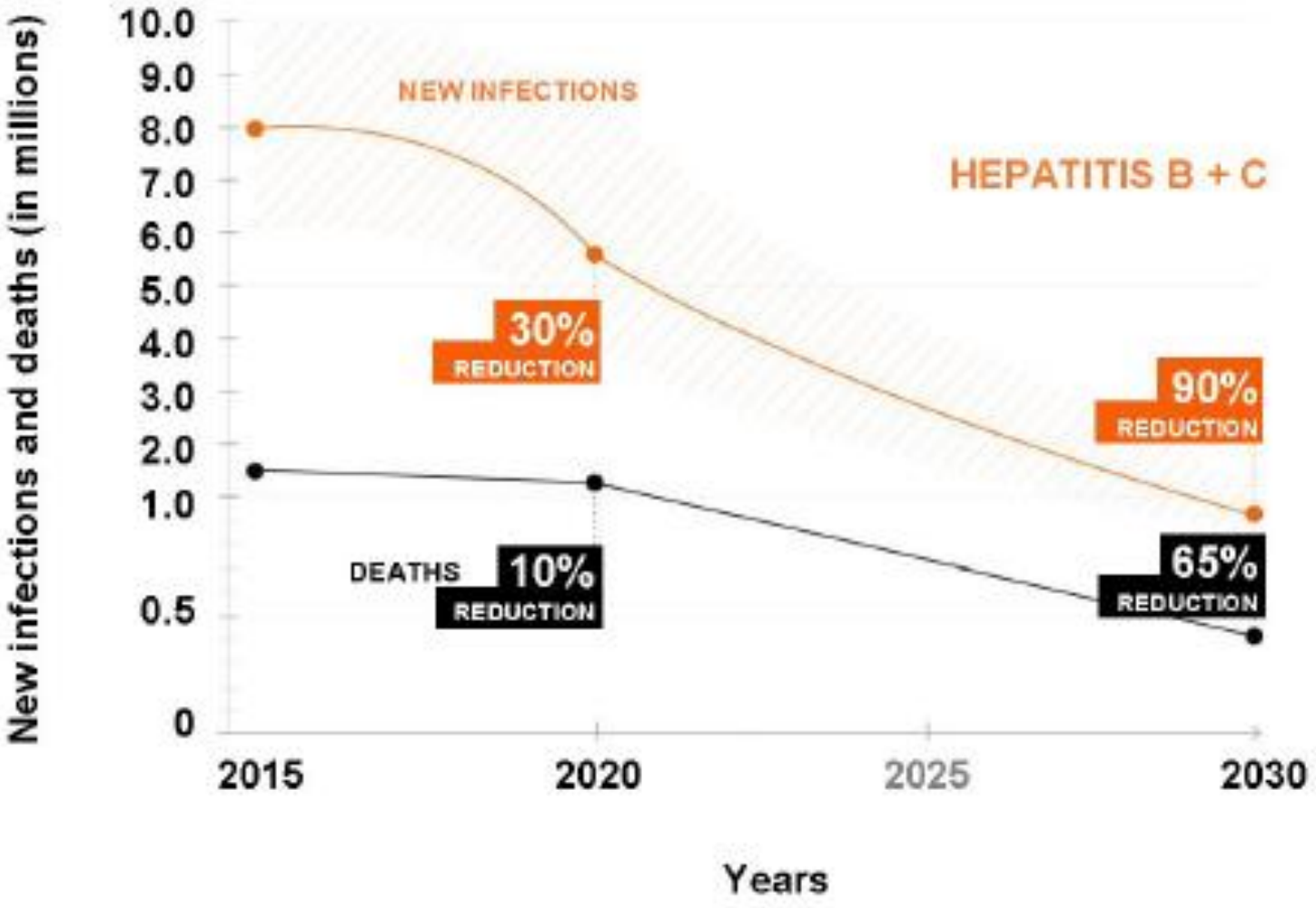
WHO. Draft global health sector strategy on viral hepatitis, 2016–2021. Available at: www.who.int/hepatitis/news-events/strategy2016-2021/Draft_global_health_sector_strategy_viral_hepatitis_13nov.pdf?ua=1 (accessed January 2016)

The continuum of viral hepatitis services and treatment cascade



World Health Organization

Targets for reducing new cases and deaths from chronic viral hepatitis B and C infections



World Health Organization

Prisons and HCV: hidden epidemic

Worldwide 15% of the prisoners are HCV Ab +

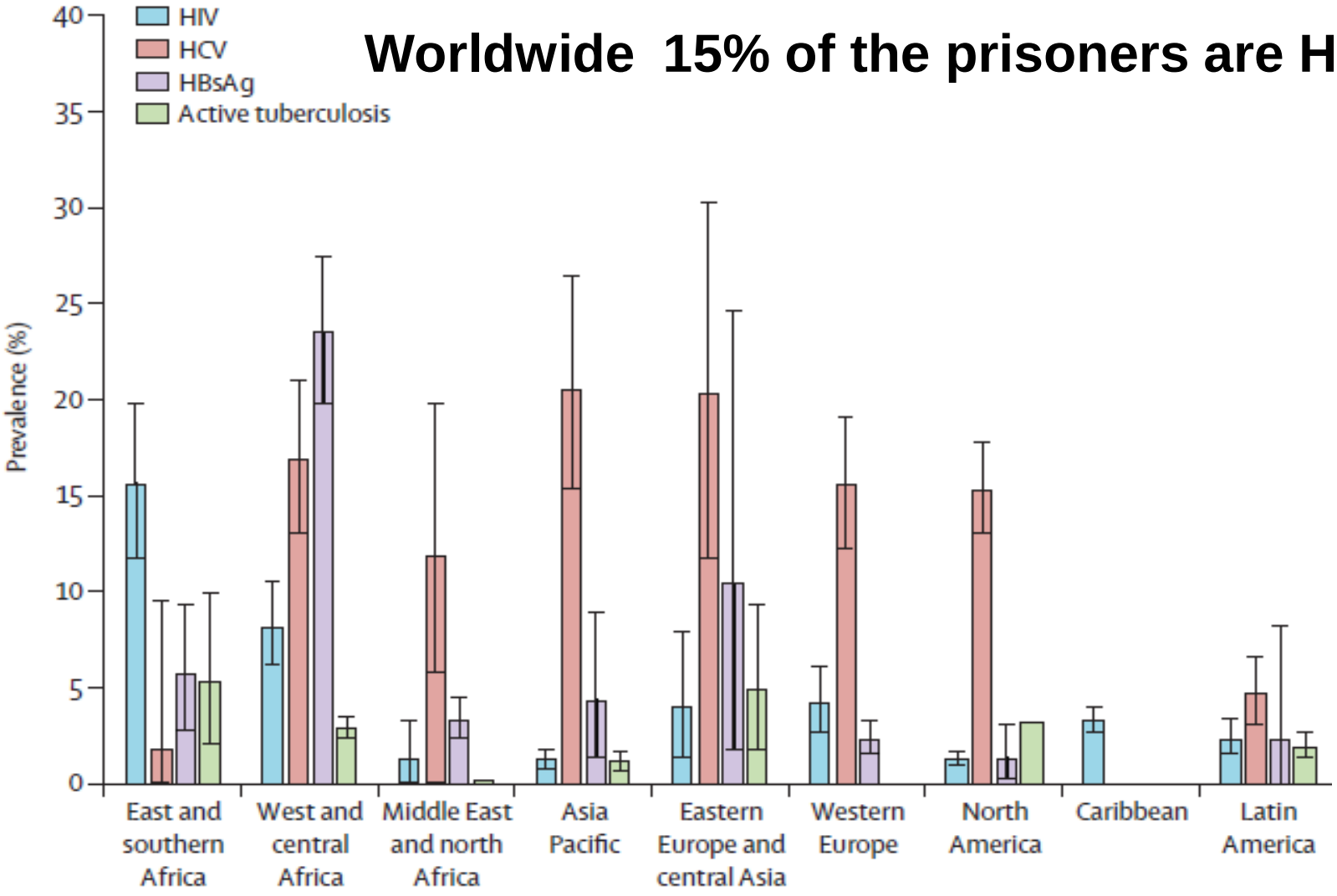


Fig. Regional prevalence of hepatitis, TB in prisons between 2005 and 2015

Dolan, K et al. Lancet 2016

Principle of an RDT

Example of the Oraquick Test

HCV Antibody RDTs

Assay	Manufacturer	Specimen	Volume	Duration
Oraquick® HCV	Orasure	Serum, plasma Whole blood Oral fluid	20-40 mL	20-40 min
Toyo® HCV	Turklab	Serum, plasma Whole blood	10-30 mL	5-15 min
Labmen® HCV	Turklab	Serum, plasma Whole blood	10 mL	15 min
Multisure HCV	MP Biomedicals	Serum, plasma Whole blood	25 mL	15 min
Assure® HCV Rapid Test	MP Biomedicals	Serum, plasma Whole blood	5-50 mL	15 min
Signal HCV v2.0	Span Diagnostics	Serum, plasma	100 mL	10 min
First Response HCV Card Test	Premier Medical Corp. Ltd.	Serum, plasma Whole blood	35 mL	20-30 min
SD Bioline HCV	Standard Diagnostics	Serum, plasma Whole blood	10 mL	5-20 min

Performance of HCV RDTs
Meta-analysis 2015

- 30 studies included
- >17,000 specimens tested

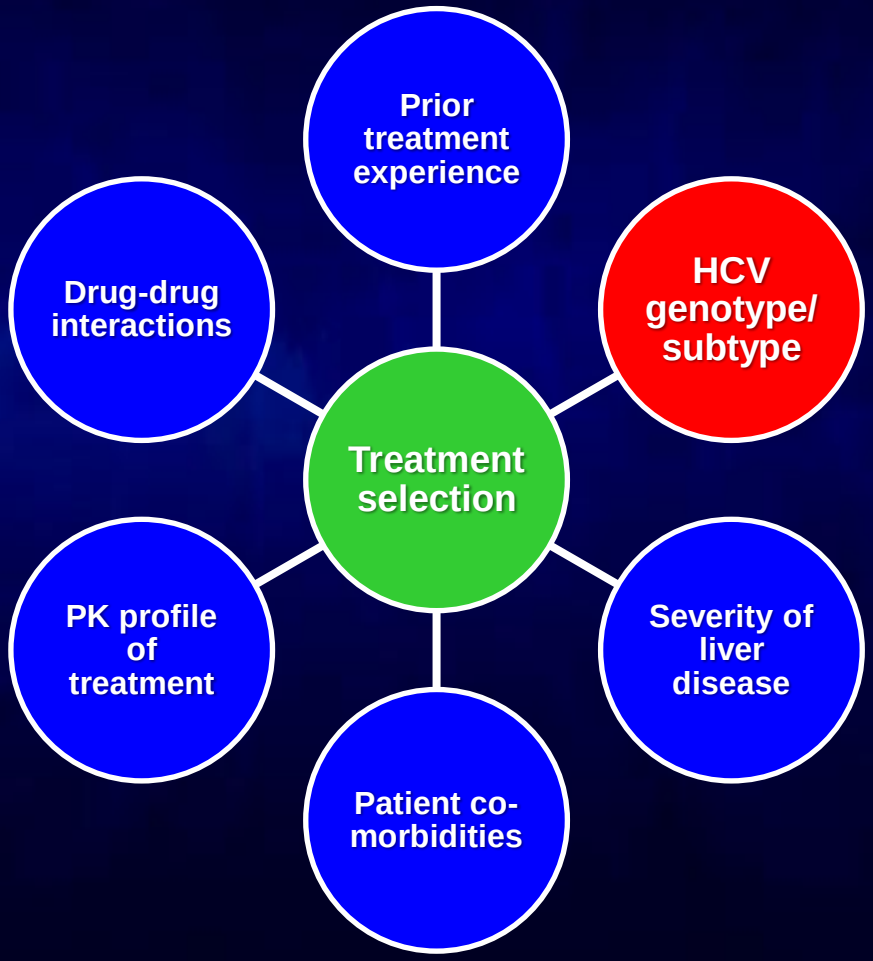
Variable	Subgroups	Specificity	Sensitivity
Year	<2005	98.0%	96.5%
	≥2005	99.0%	95.8%
Location	Developing country	98.4%	91.6%
	Industrialized country	99.1%	97.4%
Fluid	Serum	99.0%	96.5%
	Whole blood	98.6%	94.7%
	Plasma	99.0%	97.6%
	Oral fluid	98.6%	93.9%

(Khuroo et al., PLoS One 2015;10:e0121450)

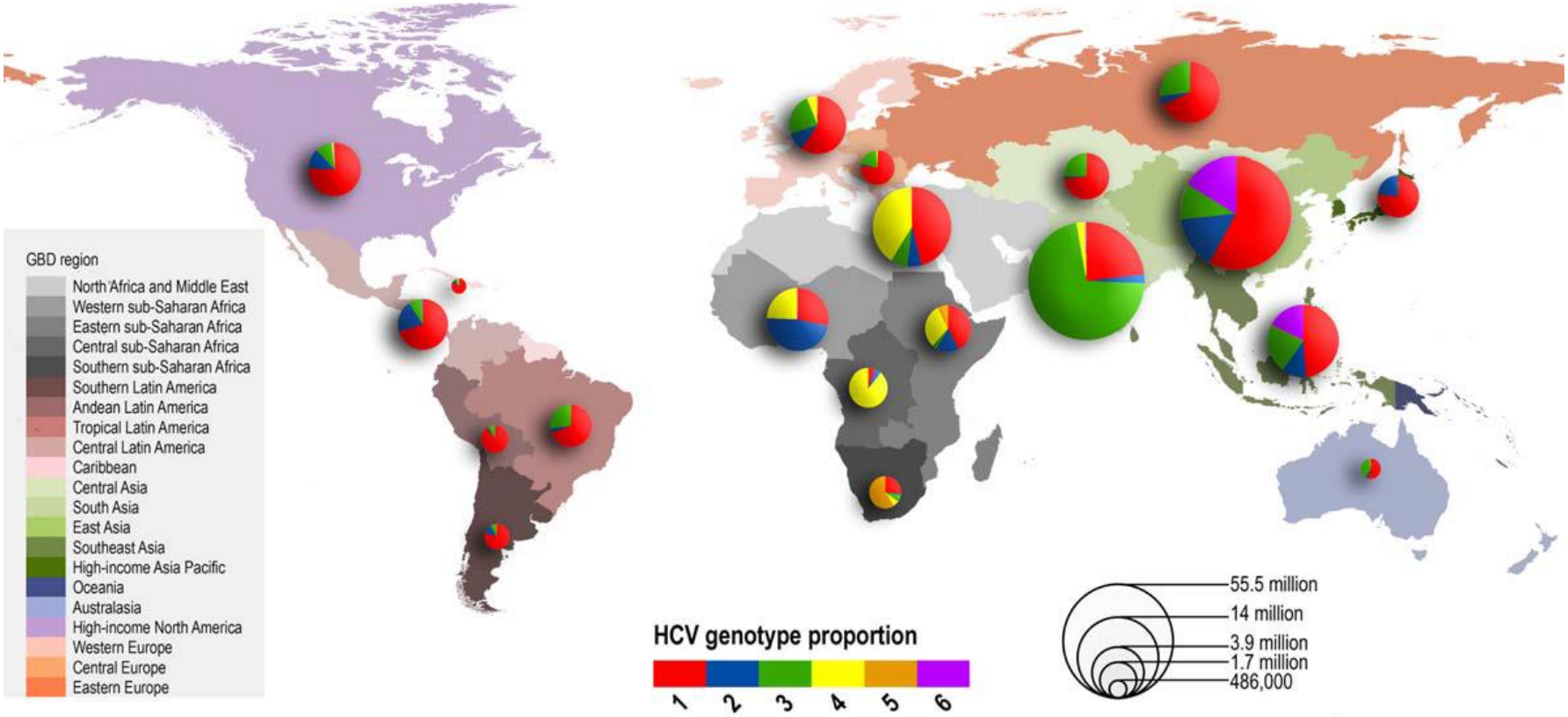
Strategie terapeutiche attuali nel migrante con epatite virale

- Epatite come causa di morte nei paesi a risorse limitate
- HBV nei migranti
  - Epidemiologia
  - Differenze nell'indicazione al trattamento
- HCV nei migranti
  - Prevalenza
  - Trattamento il ruolo del genotipo HCV

Characteristics that Inform Treatment Option Selection



Seven HCV Genotypes and 67 Sub-Genotypes Vary in Prevalence Globally

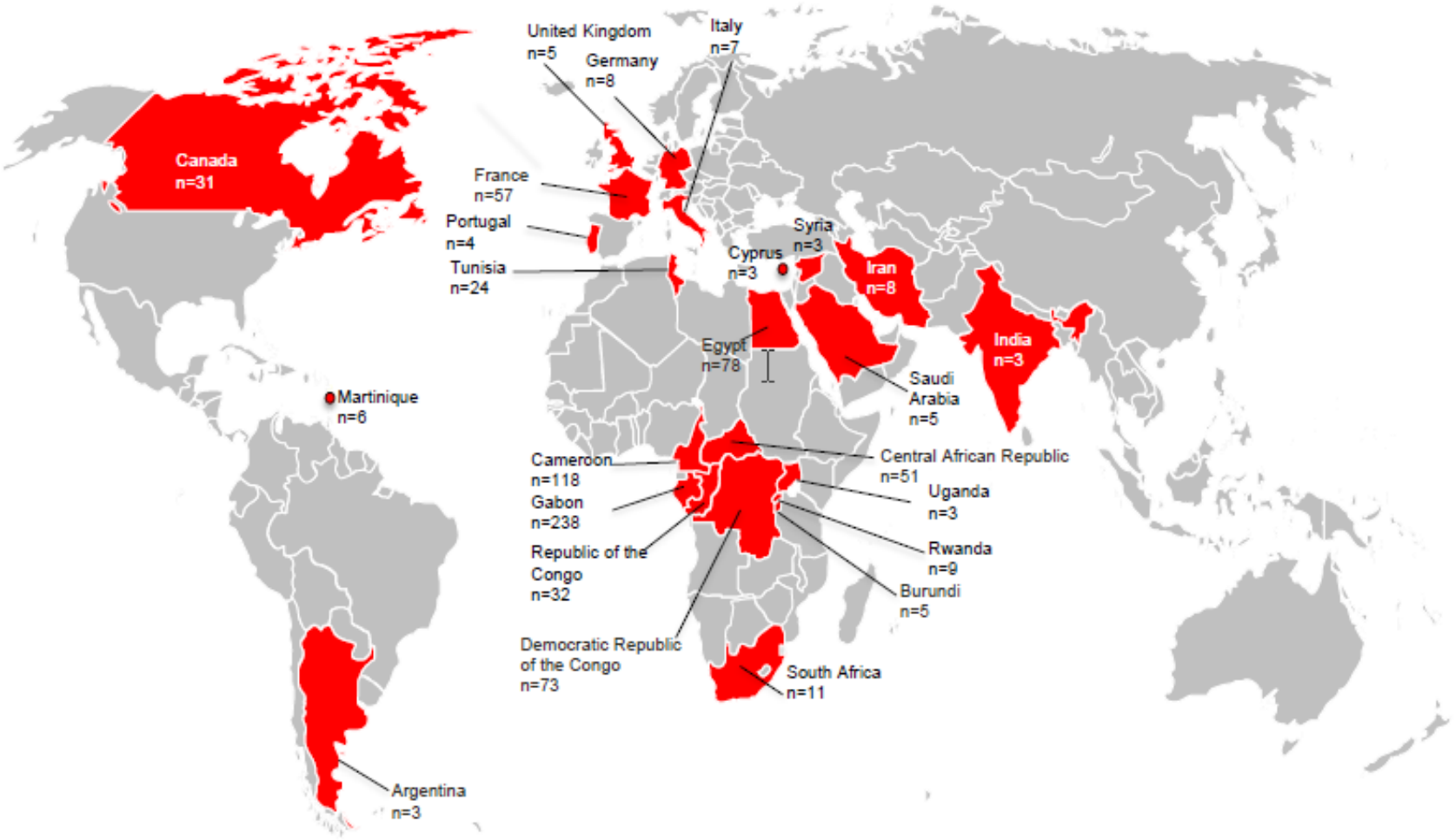


Genotype 1 : 46.2% (83.4 M)
1a: 31%; 1b: 68%
Genotype 3 : 30.1% (54.3 M)

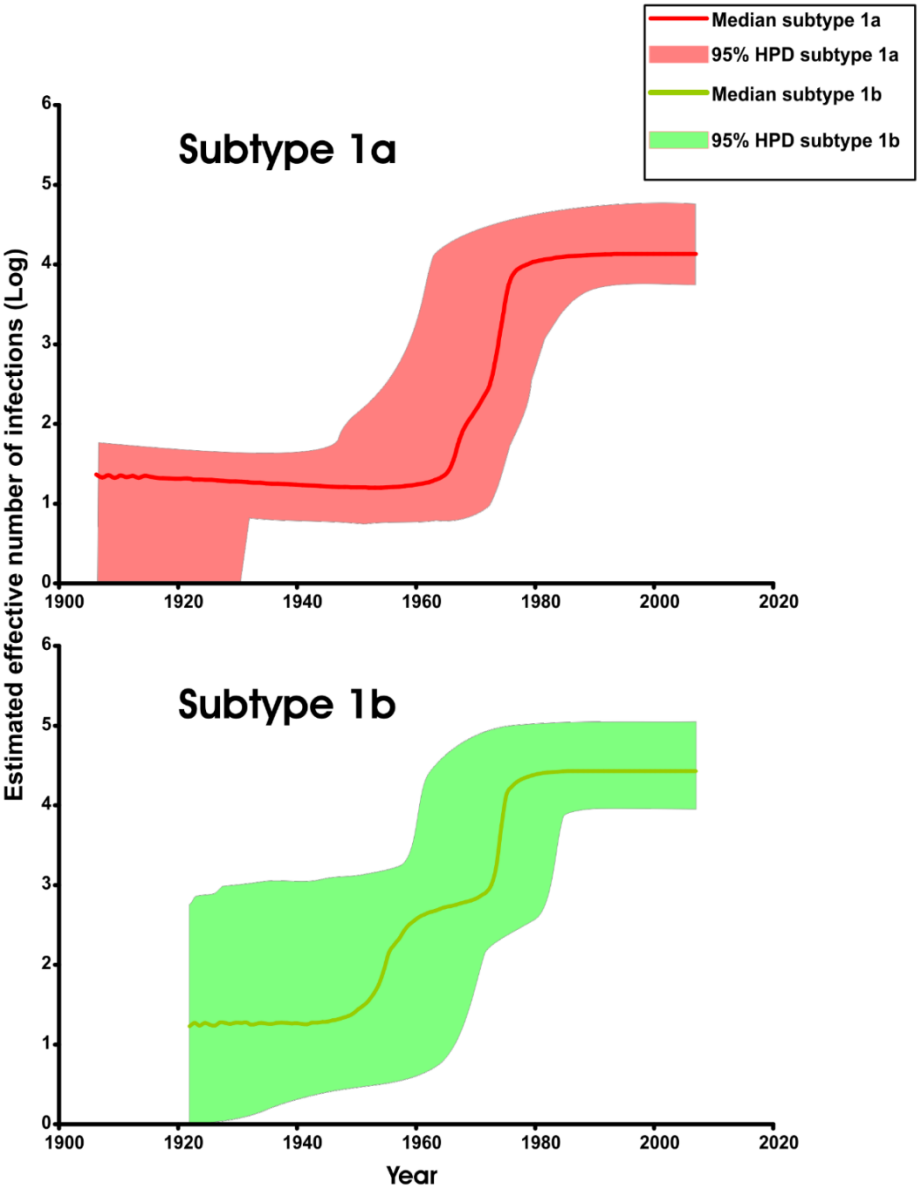
Genotype 2, 9.1% (16.5M)
Genotype 4: 8.3% (15.0M)
Genotype 6: 5.4% (9.8M)
Genotype 5: <1% (1.4M)

Messina JP, et al Hepatology. 2015 Jan; 61(1): 77–87

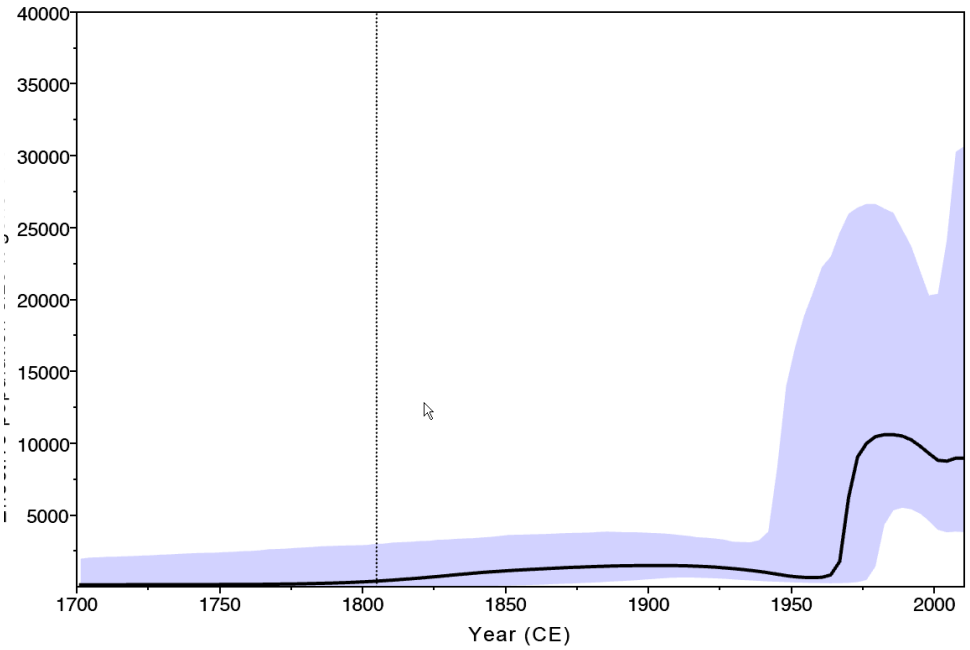
Genotype 4 distribution



Genotype 1 epidemiology in Europe



Genotype 4 epidemiology in Central Africa



Iles *et al.*, 2014 (Virology. 2014 **464-465**:233-43)

People in Africa also inject drugs

Courtesy of Annie Leprêtre, 2015

	Senegal	Tanzania	Kenya
Estimated number of IDUs	1,323 DU in Dakar	15,000 in Dar el Salem	20-30,000 In Kenya
HCV prevalence	39%	53%	39-59%

Leprêtre, A et al. JAIDS 2015 Mohammed, Z et al. Shah R et al. unpublishe

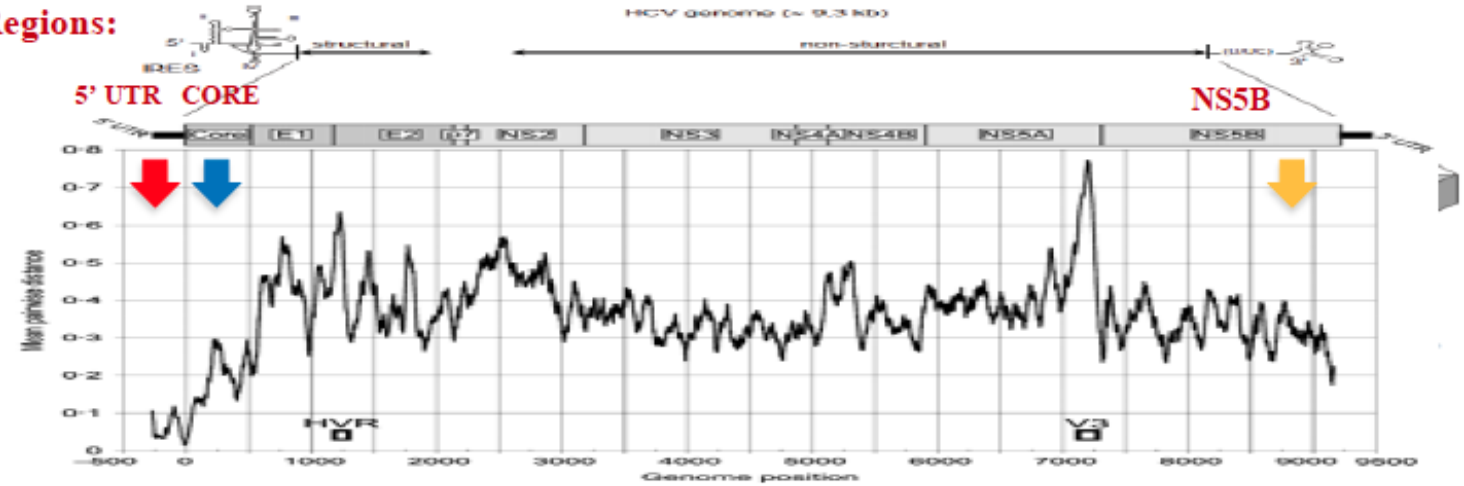
IFN-Free Treatment Options

Combination regimen	GT1	GT2	GT3	GT4	GT5-6
SOF + RBV	No	Suboptimal	Suboptimal	No	No
SOF/LDV ± RBV	Yes	No	No	Yes	Yes
SOF/VEL ± RBV	Yes	Yes	Yes	Yes	Yes
OBV/PTV/r + DSV (3D) ± RBV	Yes	No	No	No	No
OBV/PTV/r (2D) ± RBV	No	No	No	Yes	No
GZR/EBR ± RBV	Yes	No	No	Yes	No
SOF + DCV ± RBV	Yes	Yes	Yes	Yes	Yes
SOF + SIM ± RBV	Suboptimal	No	No	Yes	No

Several commercial assays are available for determining genotype/subtype

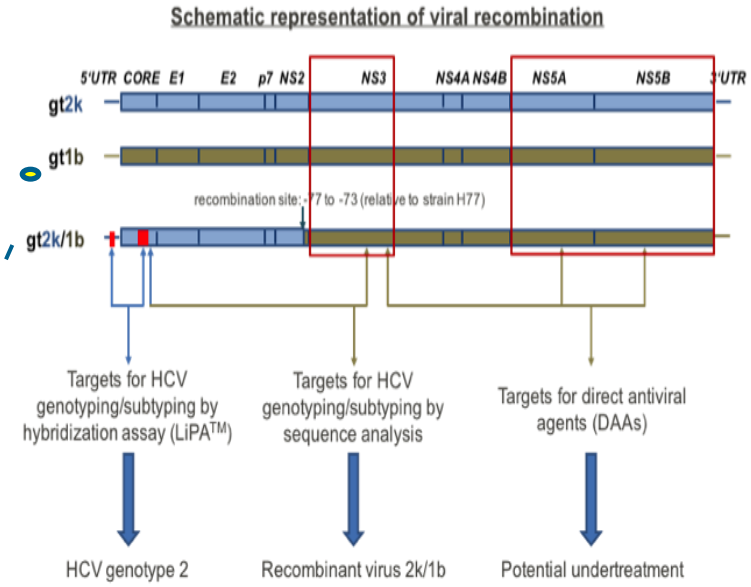
All assays target the 5'NCR gene for genotypes 1-6, in addition, **the 2 assays more used in diagnostics, Abbott and INNO-LiPA/Versant HCV-2.0, target also the NS5B and the core gene**, respectively, providing additional information also in subtyping: for genotype 1 (1a/1b, both), and for all genotypes (only Innolipa).

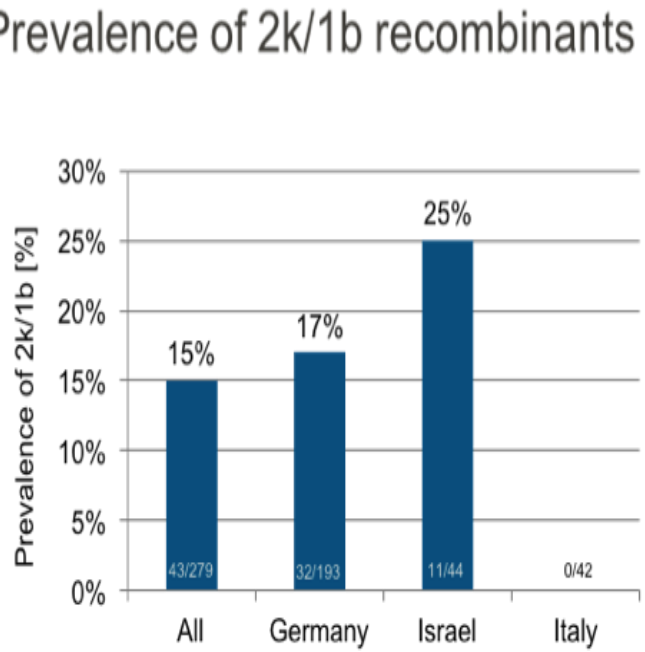
Target HCV Regions:



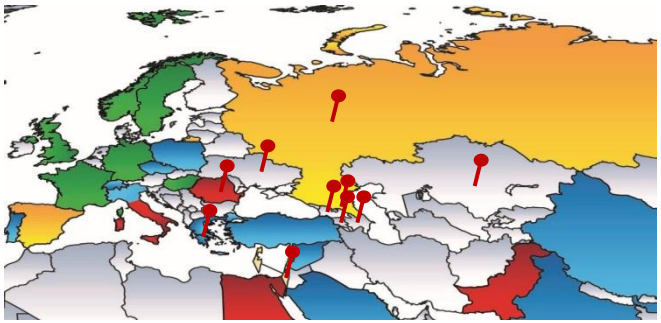
←	**Trugene HCV Genotyping assay**	Direct sequencing
←	**INNO-LiPA HCV 1.0**	Reverse hybridization
← ←	**INNO-LiPA HCV 2.0**	Reverse hybridization
←	**Abbott RealTime HCV Genotype II assay**	Real time PCR →

PREVALENCE AND CLINICAL IMPORTANCE OF HEPATITIS C VIRUS GENOTYPE 2 K/1B CHIMERAS





Inno LIPA I & II: HCV G2
Abbott Real Time HCV Genotype 2 assay : HCV G1



Source: Center for Disease Analysis (http://www.centerforda.com/hcv.htm)

S. Susser, et al EASL 2016 #PS001

Russia	(n=14)
Georgia	(n=8)
Ukraine	(n=4)
Azerbaijan	(n=3)
Israel	(n=2)
Kazakhstan	(n=2)
Armenia	(n=1)
Chechnya	(n=1)
Greece	(n=1)
Romania	(n=1)

Genotype 1a Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/LDV ± RBV	8-12 wk	12 wk + RBV*¶	12 wk	12 wk + RBV*¶
SOF/VEL ± RBV	12 wk	12 wk	12 wk	12 wk
OBV/PTV/r + DSV (3D) ± RBV	12 wk + RBV	12 wk + RBV	24 wk + RBV	24 wk + RBV
GZR/EBR ± RBV	12 wk if HCV RNA ≤800,000 or 16 wk + RBV if HCV RNA >800,000¶	12 wk if HCV RNA ≤800,000 or 16 wk + RBV if HCV RNA >800,000¶	12 wk if HCV RNA ≤800,000 or 16 wk + RBV if HCV RNA >800,000¶	12 wk if HCV RNA ≤800,000 or 16 wk + RBV if HCV RNA >800,000¶
SOF + DCV ± RBV	12 wk	12 wk + RBV*¶	12 wk	12 wk + RBV*¶

*24 wk without RBV if RBV contraindicated or poorly tolerated
¶Only if presence of NS5A RASs at baseline, if resistance testing available

Genotype 1b Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/LDV	8-12 wk	12 wk	12 wk	12 wk
SOF/VEL	12 wk	12 wk	12 wk	12 wk
OBV/PTV/r + DSV (3D)	8-12 wk	12 wk	12 wk	12 wk
GZR/EBR	12 wk	12 wk	12 wk	12 wk
SOF + DCV	12 wk	12 wk	12 wk	12 wk

Genotype 2 Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/VEL	12 wk	12 wk	12 wk	12 wk
SOF + DCV	12 wk	12 wk	12 wk	12 wk

Genotype 3 Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/VEL ± RBV	12 wk	12 wk + RBV*¶	12 wk + RBV*¶	12 wk + RBV*¶
SOF + DCV ± RBV	12 wk	12 wk + RBV*¶	24 wk + RBV	24 wk + RBV

*24 wk without RBV if RBV contraindicated or poorly tolerated
¶Only if presence of NS5A RAS Y93H at baseline, if resistance testing available

Genotype 4 Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/LDV ± RBV	12 wk	12 wk	12 wk	12 wk + RBV Or 24 wk
SOF/VEL	12 wk	12 wk	12 wk	12 wk
OBV/PTV/r (2D) + RBV	12 wk + RBV	12 wk + RBV	12 wk + RBV	12 wk + RBV
GZR/EBR ± RBV	12 wk	12 wk if HCV RNA RR 16 wk + RBV if NR or BT	12 wk	12 wk if HCV RNA RR 16 wk + RBV if NR or BT

*24 wk without RBV if RBV contraindicated or poorly tolerated

Genotype 5-6 Options

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Rx-naïve	Rx-exp[d]	Rx-naïve	Rx-exp[d]
SOF/LDV ± RBV	12 wk	12 wk + RBV*	12 wk	12 wk + RBV*
SOF/VEL ± RBV	12 wk	12 wk	12 wk	12 wk
SOF + DCV ± RBV	12 wk	12 wk + RBV*	12 wk	12 wk + RBV*

*24 wk without RBV if RBV contraindicated or poorly tolerated

EASL RECOMMENDATIONS 2016
HCV Resistance testing prior to First Line DAA

Knowledge based medicine approach

Resistance testing not available

↓

Optimize therapy
To avoid treatment failure

↓

SOF/LDV, SOF/DCV, SOF/SIM
Add RBV in GT 1a, 4,5,6 TE
SOF VEL: add RBV in G3 TE patients and cirrhotics
GZR/EBR use 16 weeks with RBV in HCV GT1a HCVRNA > 800.000

Precision Medicine approach

Resistance testing Available, reliable, interpretable understandable

↓

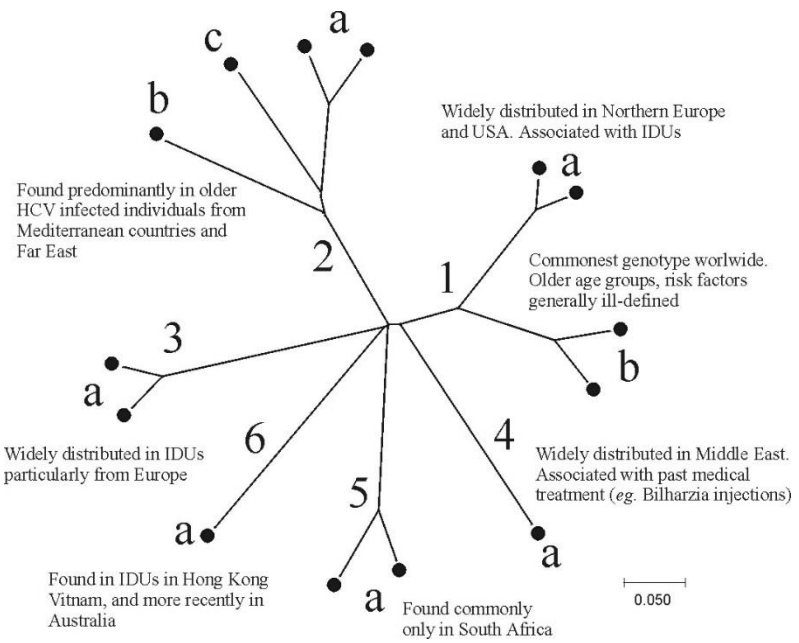
Presence of NSAs RASs (10-15%) Conferring high level resistance (popseq or NGS > 15%)

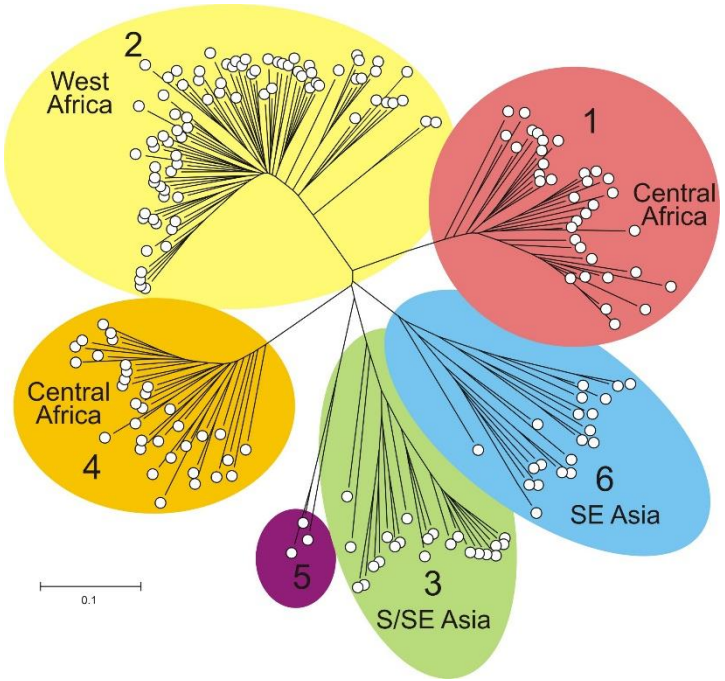
↓

Add ribavirin and or increase treatment duration in patients with NS5As RASs

Genotype diversity of HCV

- Epidemic pattern
  - Spread of certain HCV variants in 20th century
  - Association with new parenteral risk factors
  - Restricted number of (named) subtypes
- Endemic pattern
  - Long term presence
  - Diversity in subtype range
  - One genotype predominant in each region





Strategie terapeutiche attuali nel migrante con epatite virale

- Epatiti virali prima causa di morte per infezione nel mondo con maggioranza dei decessi nei paesi a risorse limitate
- Elevata prevalenza infezioni da HBV e HCV negli immigrati
- Infezione da HBV:
  - prevalenza correlata ad area di origin
  - Vaccinazione immigrati: molto resta da fare
  - Differenze cliniche: maggior numero di soggetti giovani HBeAg+
  - Problemi clinici: indicazioni al tratamento in HBeAg+ gestione giovani donne HBeAg+
- Infezione da HCV
  - Elevata prevalenza in focus group: Paesi ad elevata endemia (Egitto, Pakistan) e prigioni
  - Tests rapidi possono esere la risposta
  - Trattamento: attenzione alla genotipizzazione pre terapia e nella valutazione dei tests di resistenza