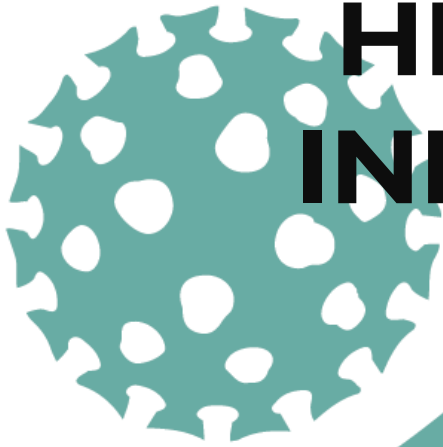


DIAGNÓSTICO DIFERENCIAL DE LAS HEPATITIS AGUDAS EN VIAJEROS E INMIGRANTES. IDENTIFICACIÓN DE AGENTES EMERGENTES



CURSO FORMATIVO DE ACTUALIZACIÓN EN HEPATITIS VIRALES

GABRIEL REINA GONZÁLEZ

GABI@UNAV.ES

10/03/2022



**Clínica
Universidad
de Navarra**

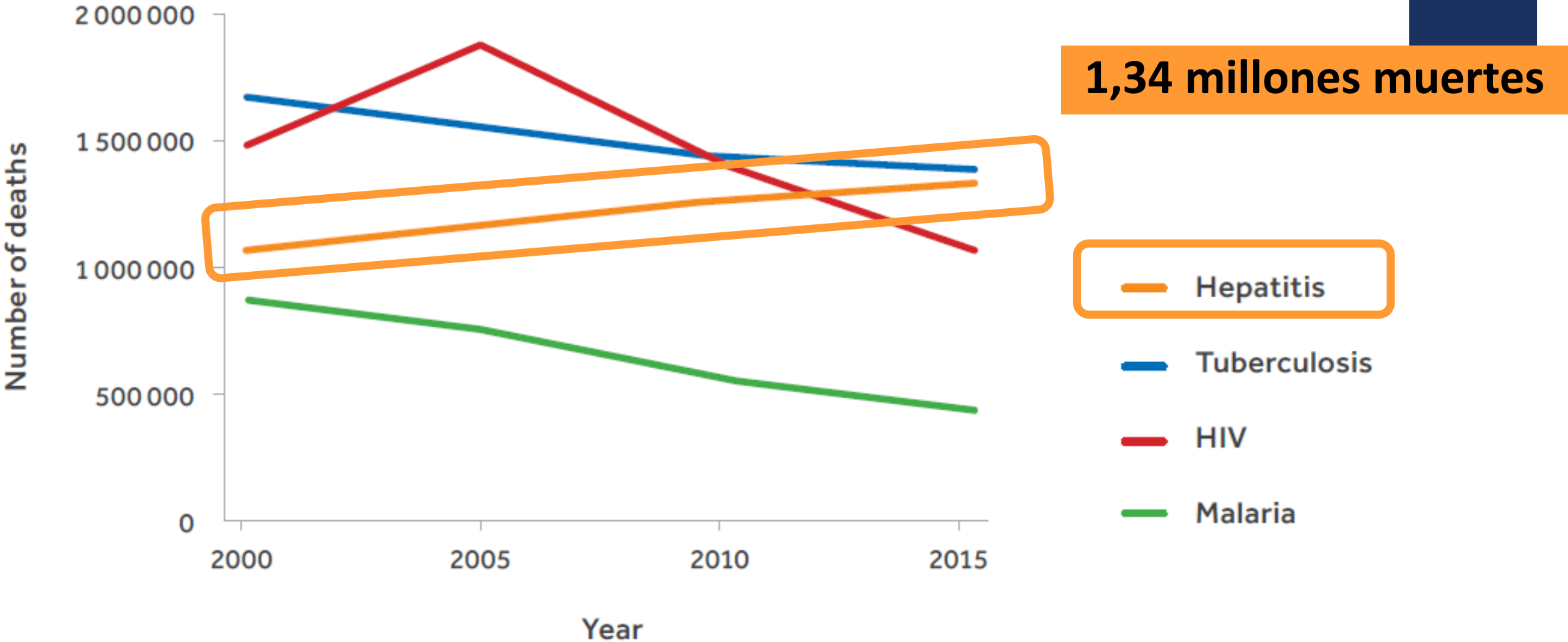


HEPATITIS AGUDA VIAJEROS E INMIGRANTES

- ¿Qué importancia tiene?
- Viajeros/Inmigrantes
- Agentes implicados
- Causas Emergentes



Fig. 2. Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000–2015: unlike HIV, tuberculosis and malaria, the trend in mortality from viral hepatitis is increasing

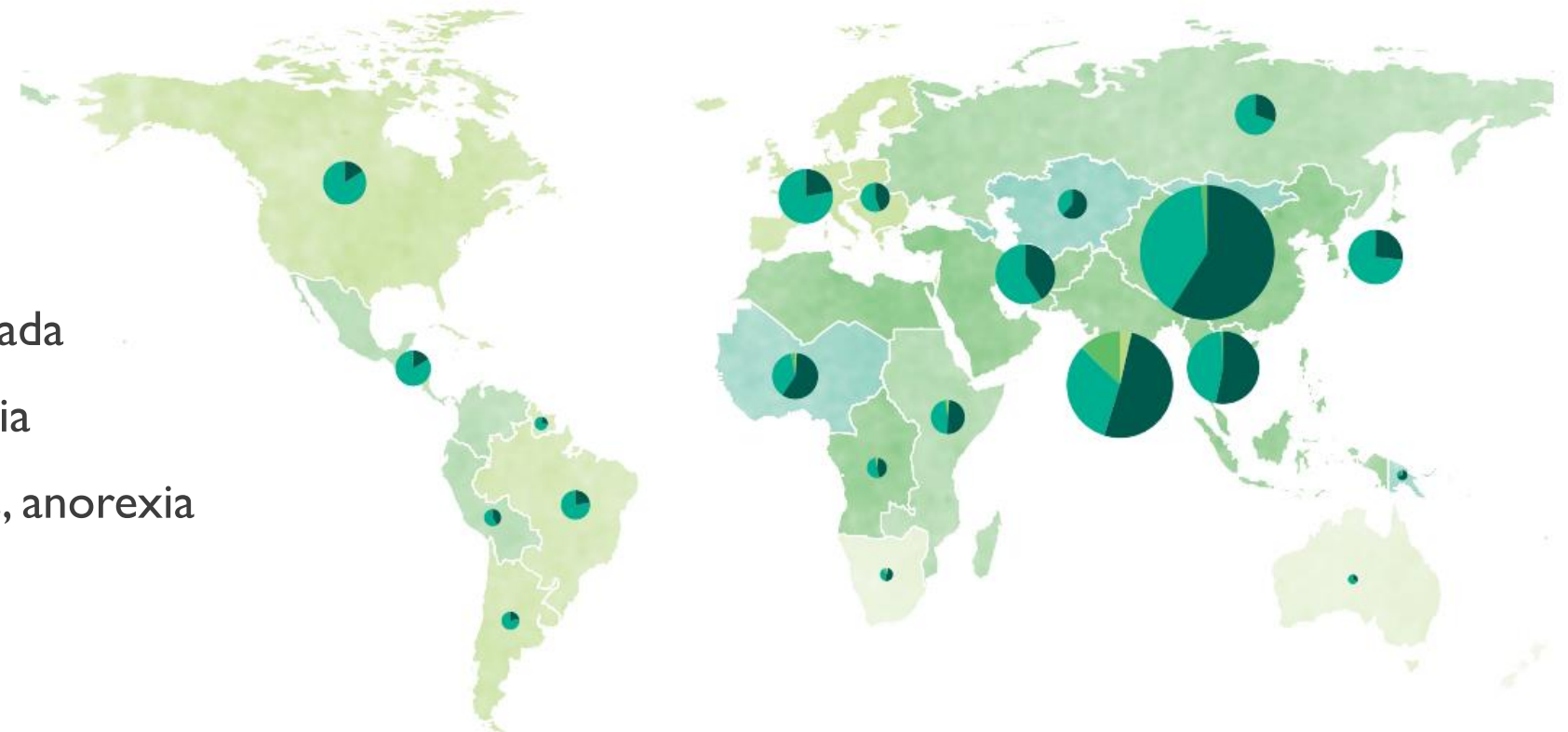


Source: WHO global health estimates (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015. Geneva: World Health Organization; 2016.)

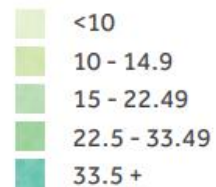
Figure 3. Regional distribution of viral hepatitis deaths

HEPATITIS AGUDA

- Generalmente autolimitada
- Síntomas: ictericia, coluria
- Fiebre, malestar, náuseas, anorexia
- Edad
- Estado inmune



MORTALITY RATE (PER 100,000 PY)



PROPORTION ATTRIBUTABLE TO EACH VIRUS

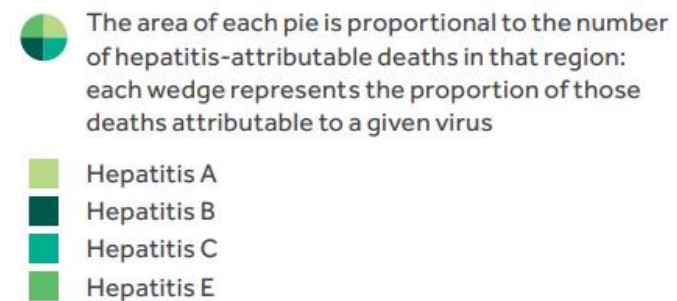
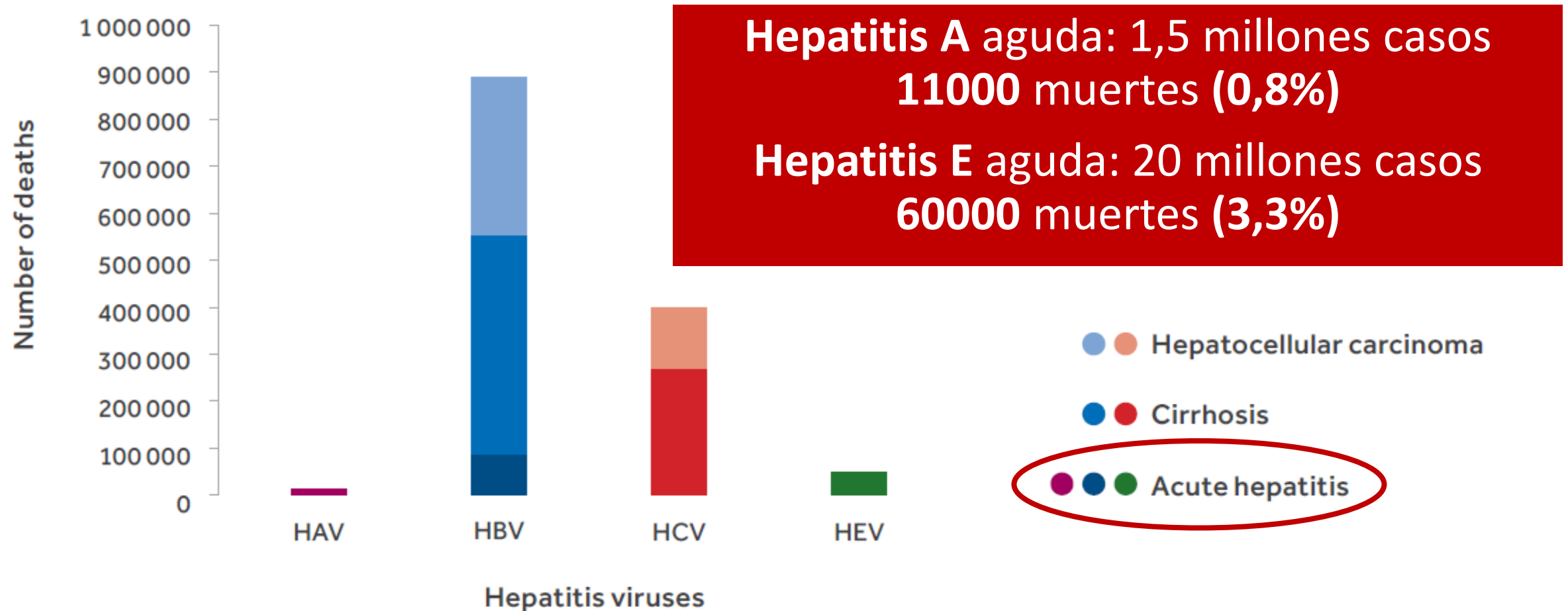


Fig. 1. Deaths from viral hepatitis, by virus and type of sequelae, 2015:
most viral hepatitis deaths are due to the late complications of HBV and HCV infection



HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HEV: hepatitis E virus

Source: WHO global health estimates for 2015 published in 2016 (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000–2015. Geneva: World Health Organization; 2016.)

DIAGNÓSTICO DIFERENCIAL HEPATITIS AGUDA VIAJEROS/INMIGRANTES

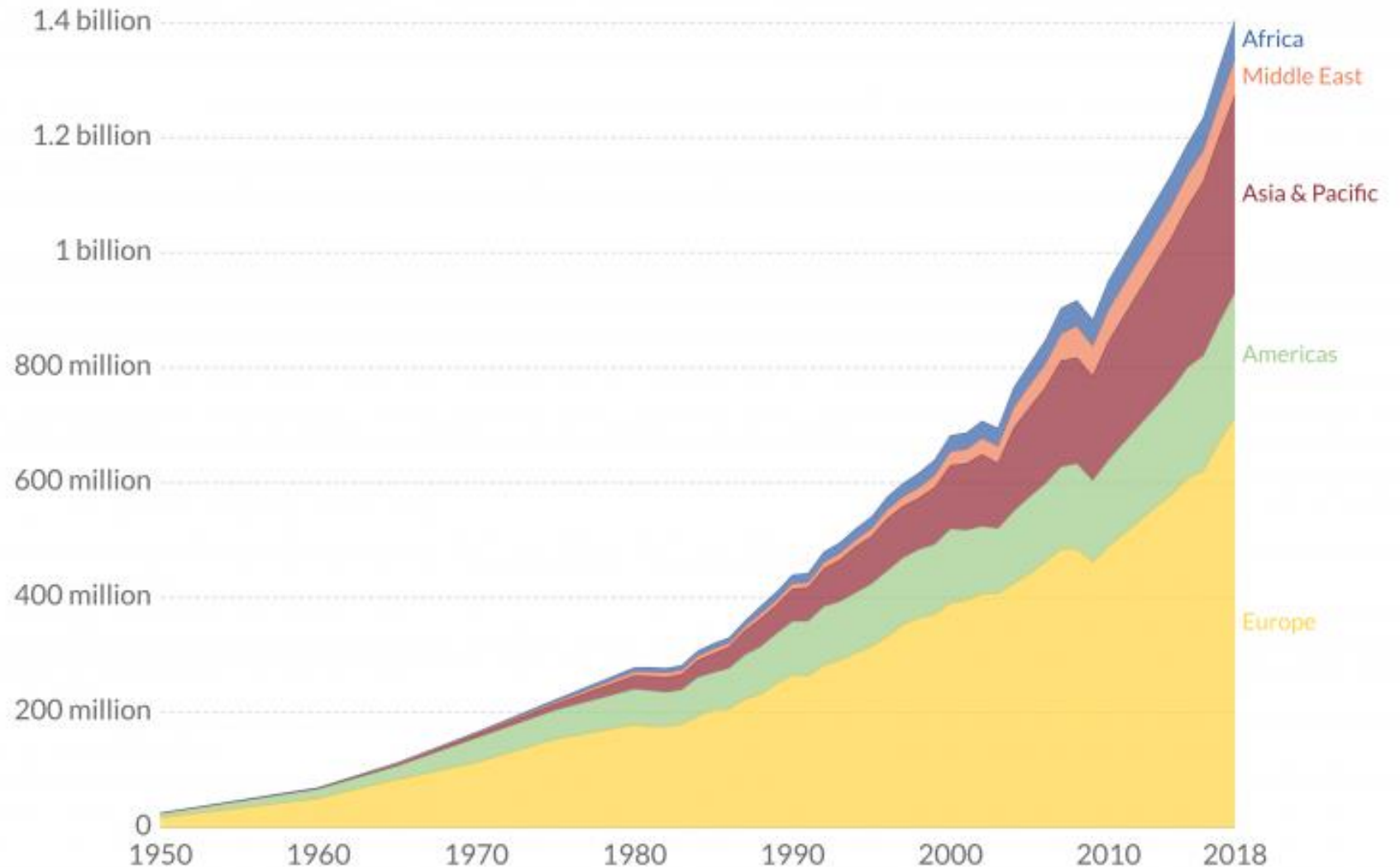
- VHA,VHB,VHC,VHE
- VIH
- CMV,VEB
- Fiebre Amarilla
- Dengue
- Zika
- Chikungunya
- Hidatidosis
- Colangitis ascendente
- Absceso hepático
- Hepatocarcinoma
- Paludismo
- *Rickettsia*
- *Coxiella*
- *Salmonella*
- *Borrelia*
- *Leptospira*
- Parvovirus B19
- Enterovirus
- *Schistosoma*
- *Cryptosporidium*
- *Staphylococcus, Streptococcus*
- Enterobacterias, BGNMF
- *Treponema pallidum*
- *Pneumocystis*
- *Cryptococcus*
- *Toxoplasma*
- Babesiosis
- *Bartonella*
- *Listeria*
- Hantavirus
- Amebiasis

CIFRAS VIAJEROS INTERNACIONALES

- 1950: 25 millones personas
- 2018: 1500 millones personas

International Tourist Arrivals by World Region

Our World
in Data

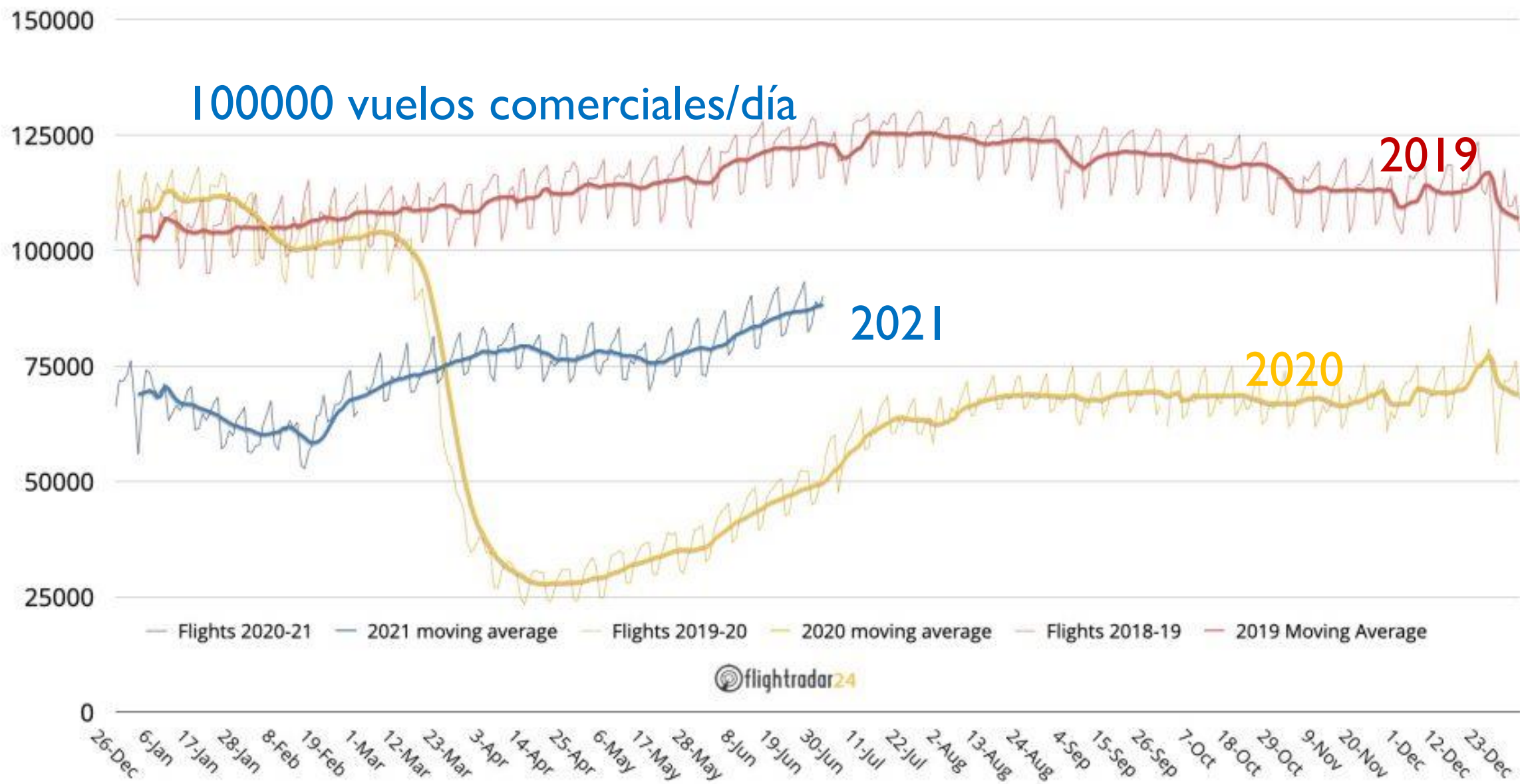


Source: United Nations World Tourism Organization - World Tourism Barometer (2019)

OurWorldInData.org/tourism/ • CC BY

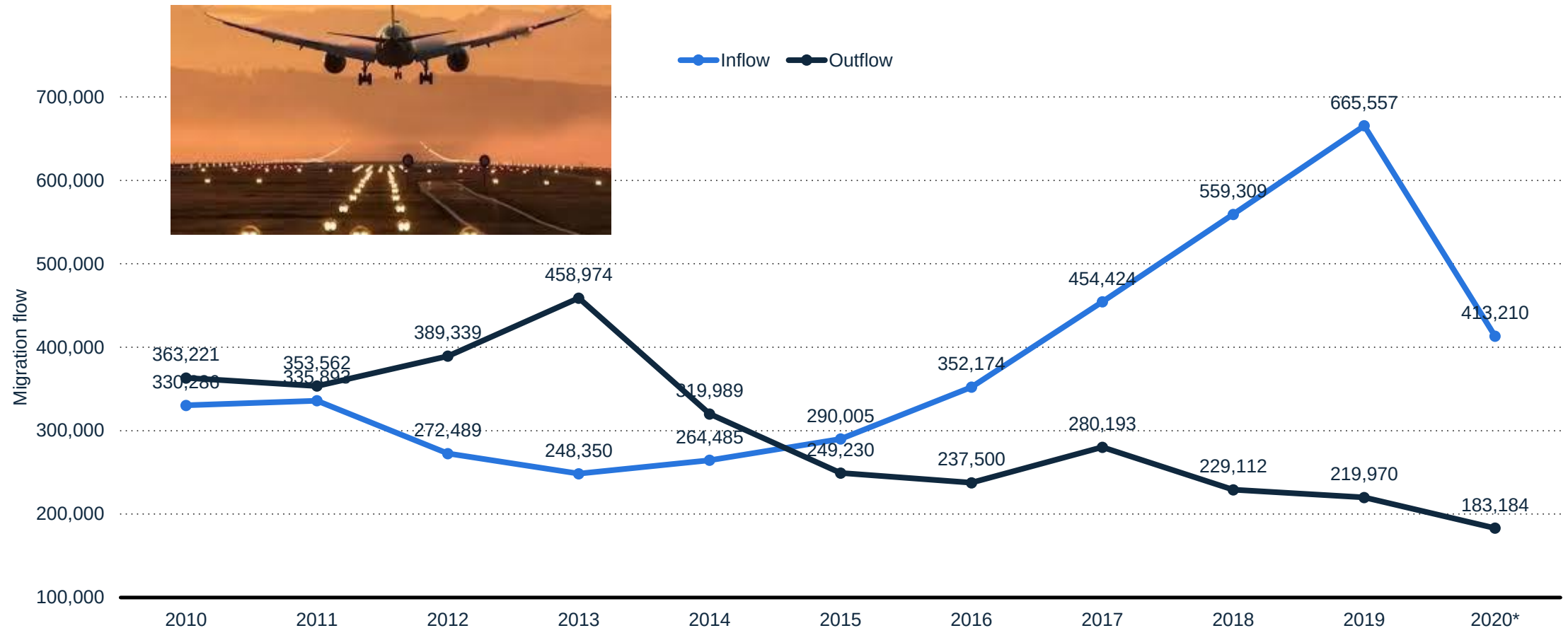


Commercial flights tracked by Flightradar24 2019-2021



Migration flow of foreign nationals in Spain from 2010 to 2020

Migration flow of foreign nationals in Spain 2010-2020



Note(s): Spain; 2010 to 2020

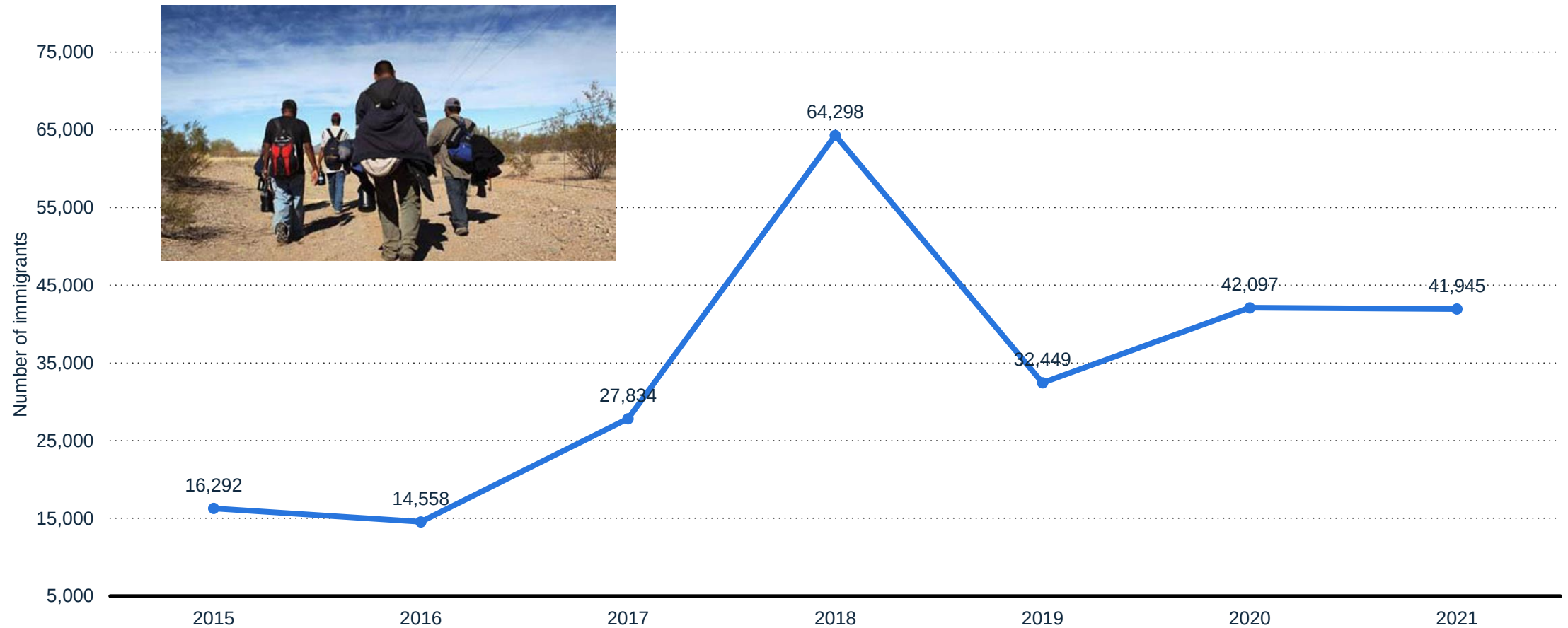
Further information regarding this statistic can be found on [page 8](#).

Source(s): INE (Spain); [ID 445986](#)

2013, 3.2% of the global population (231 million individuals) migrated

Number of foreigners entering Spanish territory without authorization between 2015 and 2021

Number of irregular immigrants arriving in Spain 2015-2021



Note(s): Spain; 2015 to 2021; land and sea arrivals

Further information regarding this statistic can be found on [page 8](#).

Source(s): Ministerio del Interior (España); [ID 1187486](#)

TRANSMISIÓN HEPATITIS



VHB



■ Fecal-oral

- Hepatitis A
- Hepatitis E



■ Artrópodo vector

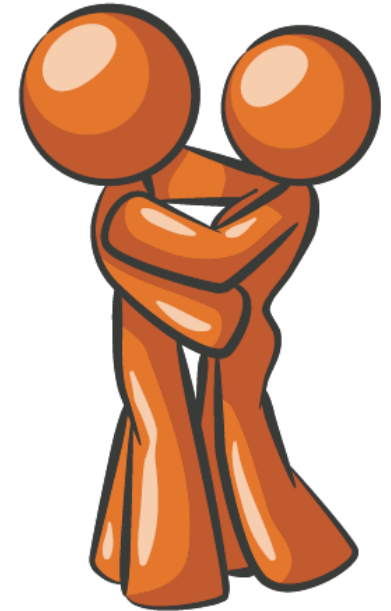
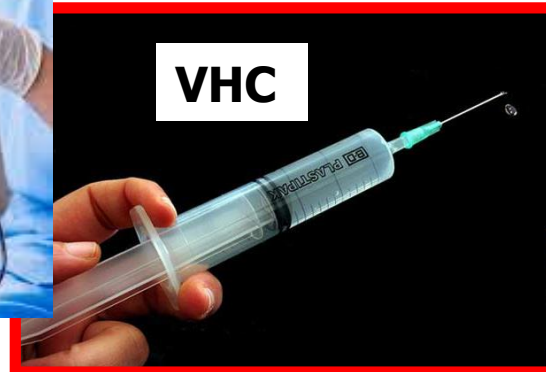
- Dengue
- Fiebre Amarilla
- ...



■ Parenteral/Sexual

- Hepatitis B/D
- Hepatitis C

VHC



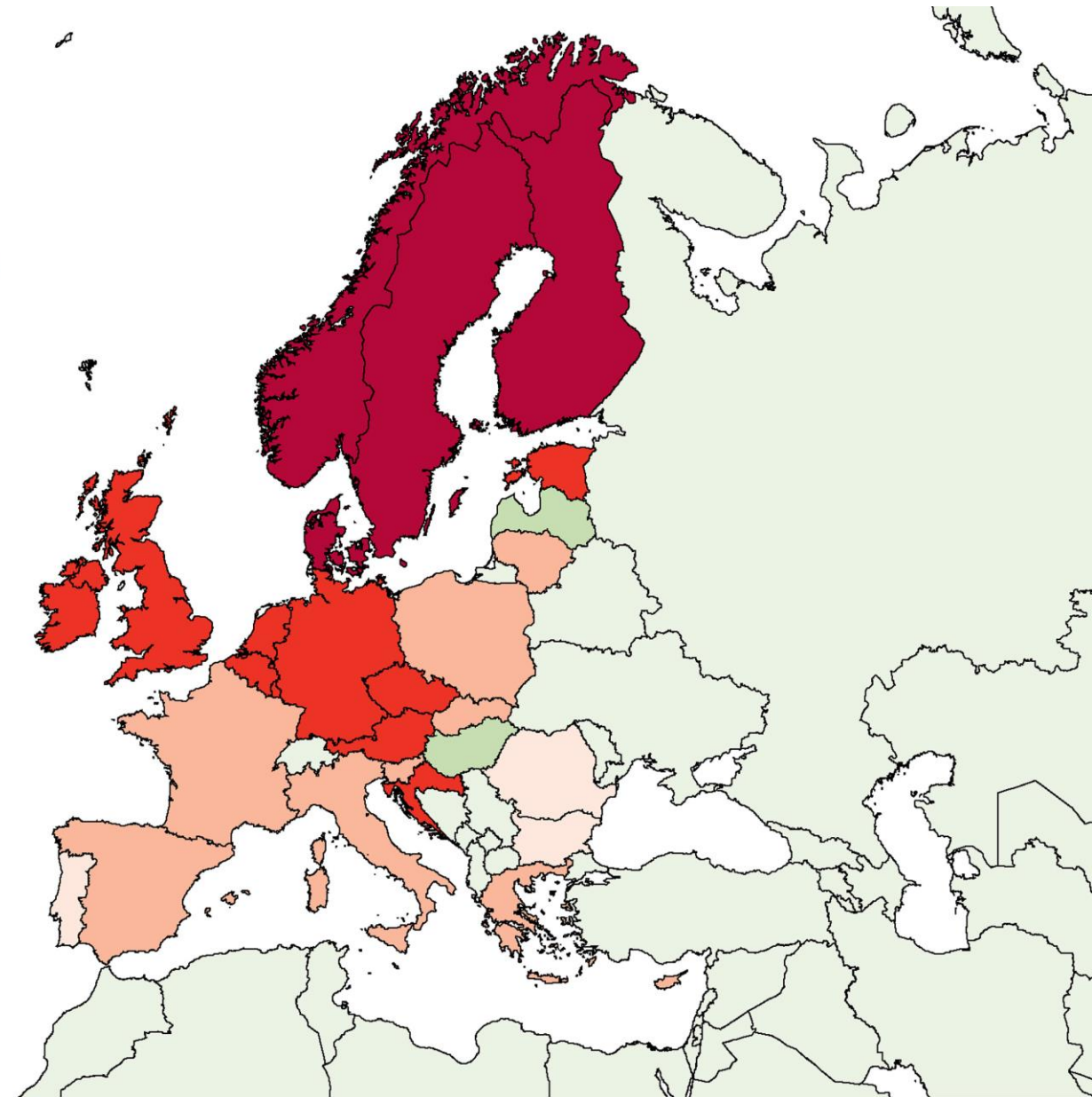
VIAJEROS – ALTA SUSCEPTIBILIDAD HEPATITIS A

- Mejora condiciones higiénico-sanitarias
- España baja endemicidad

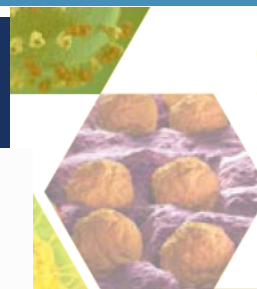
HAV susceptibility
profiles 2000–14



EU or EEA members

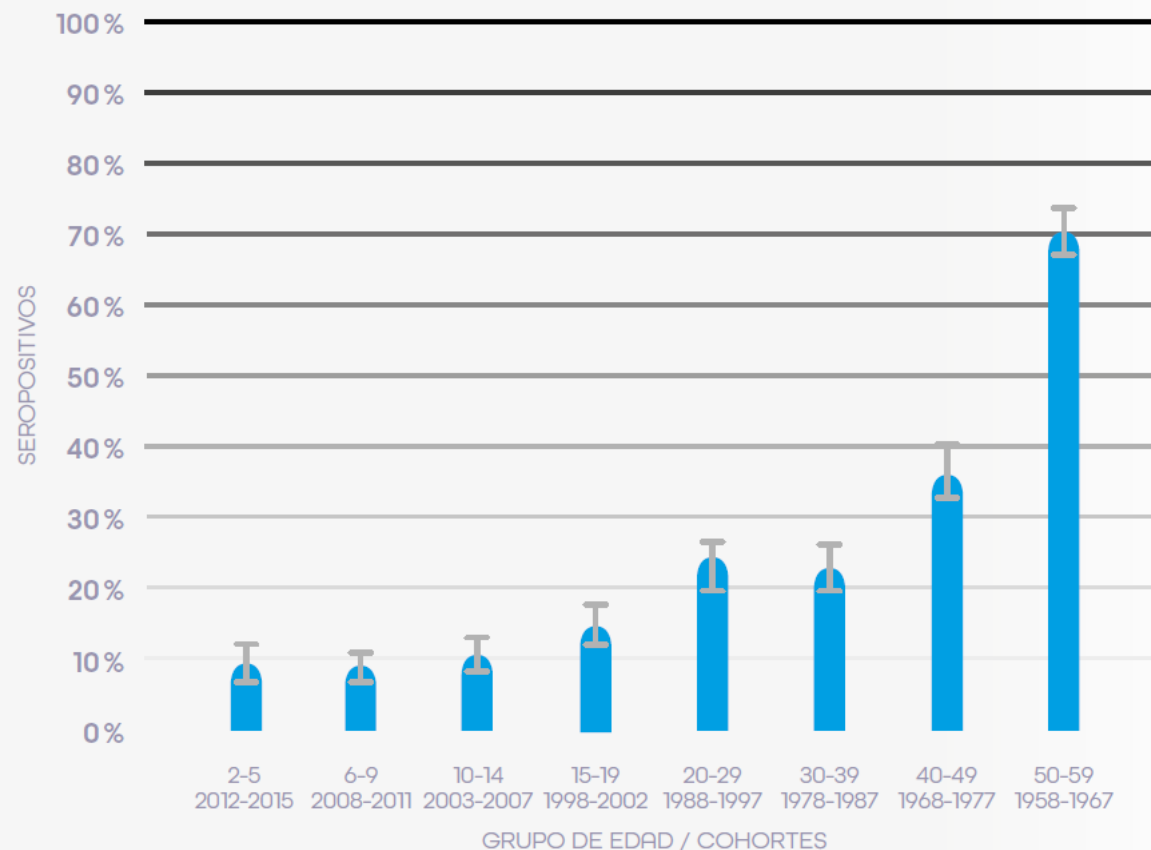


HEPATITIS A



2º ESTUDIO DE SEROPREVALENCIA EN ESPAÑA

SEPTIEMBRE 2020

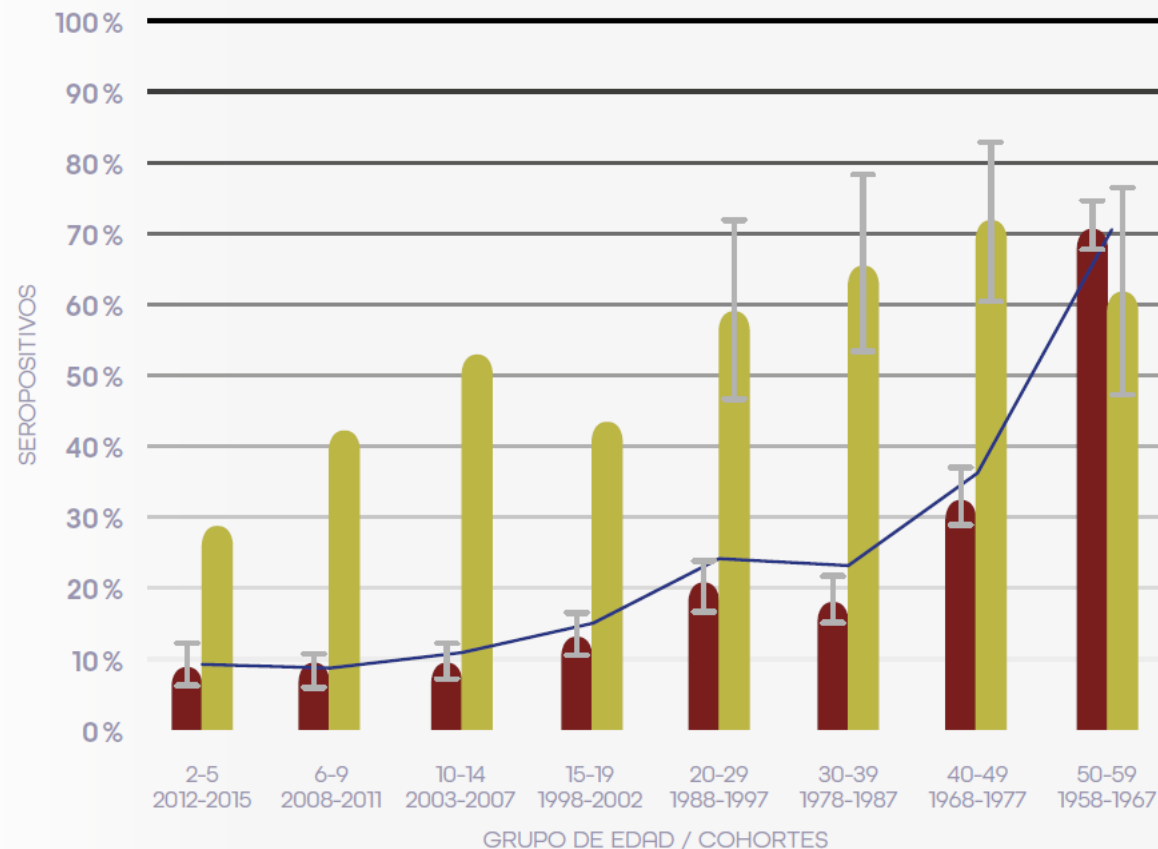


- <15 años: 10%
- 40-49 años: 36%
- 50-59 años: >70%

HEPATITIS A

2º ESTUDIO DE SEROPREVALENCIA EN ESPAÑA

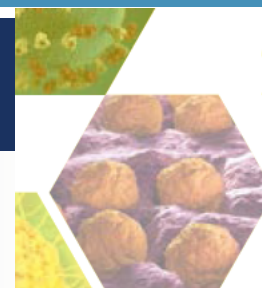
SEPTIEMBRE 2020



- Españoles
 - <40 años: 10-20%
 - 40-59 años: 30-70%
- Extranjeros: 30-60%

* En los grupos de edad de extranjeros entre 2 y 19 años no se calcula el IC debido al bajo número de casos.

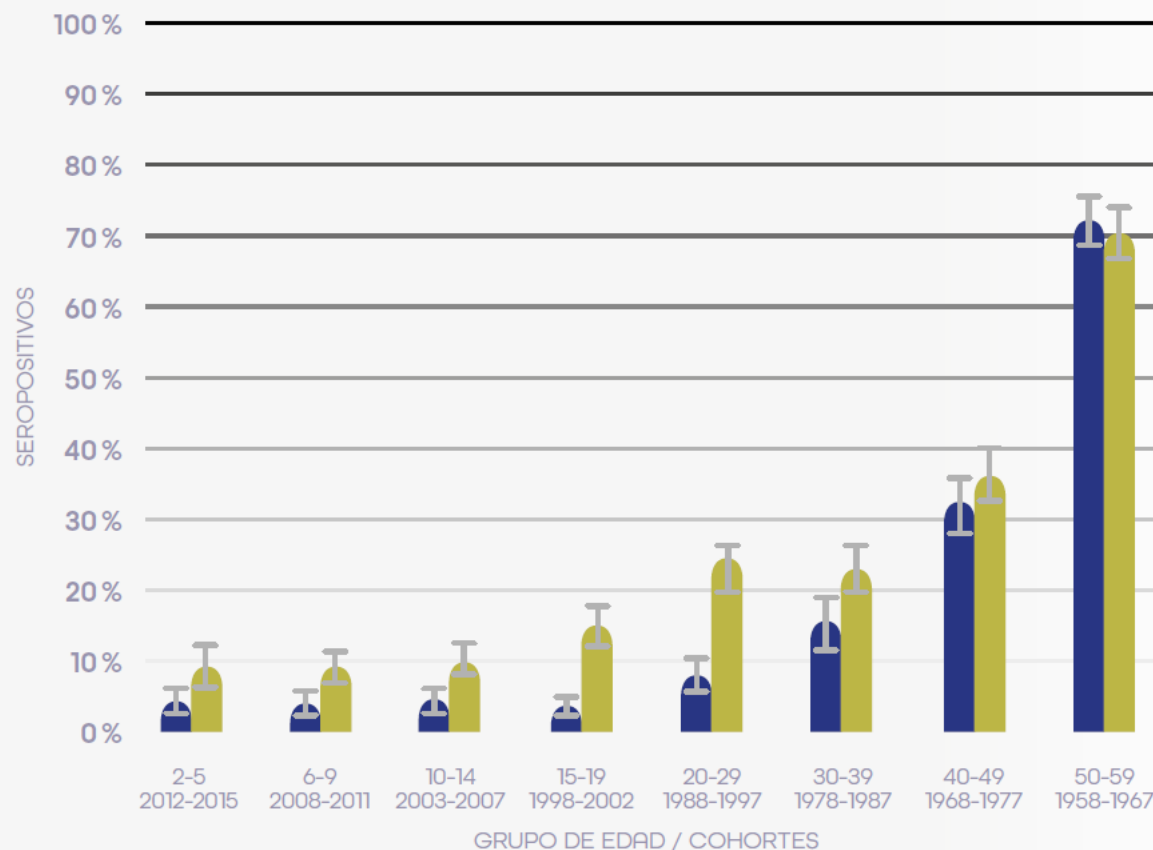
HEPATITIS A



2º ESTUDIO DE SEROPREVALENCIA EN ESPAÑA

SEPTIEMBRE 2020

- Infección natural
 - 3-5% en menores 20 años

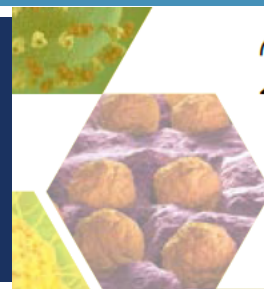


**20 millones españoles
susceptibles**

Hepatitis A

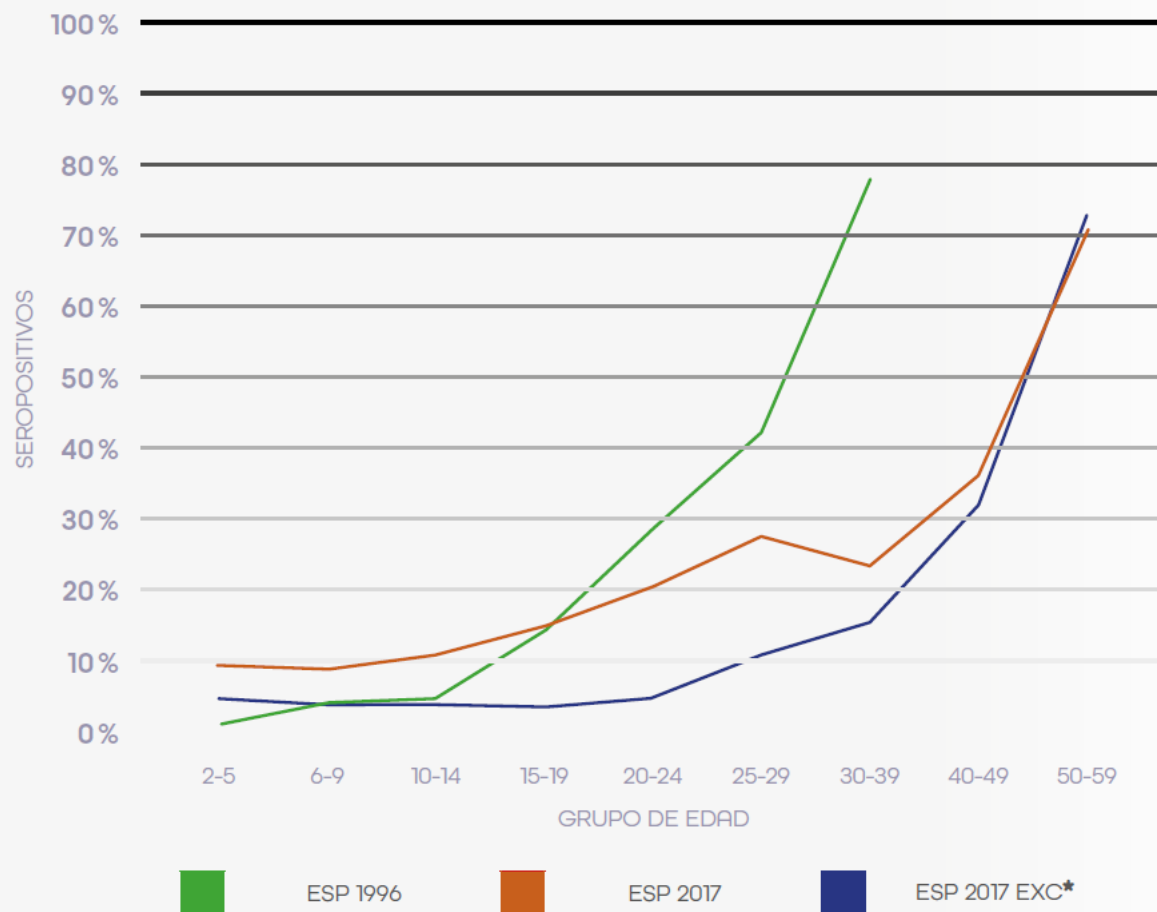
* Población de España excluyendo la población de Cataluña, Ceuta, Melilla y personas nacidas fuera de España.

HEPATITIS A



2º ESTUDIO DE SEROPREVALENCIA EN ESPAÑA

SEPTIEMBRE 2020



* Excluidos Cataluña, Ceuta, Melilla y con país de nacimiento extranjero.

■ Cambios 1994-2017



HEPATITIS A

Travel-associated hepatitis A in Europe, 2009 to 2015

Julien Beauté¹, Therese Westrell¹, Daniela Schmid², Luise Müller³, Jevgenia Epstein⁴, Mia Kontio⁵, Elisabeth Couturier⁶, Mirko Faber⁷, Kassiani Mellou⁸, Maria-Louise Borg⁹, Ingrid Friesema¹⁰, Line Vold¹¹, Ettore Severi^{1,12}

- 28% casos UE importados
- Tendencia decreciente
- África/Asia
- Hombres <25 años
- VACUNA
 - 25% viajeros

TABLE 4

Number of travel-associated cases of hepatitis A, number of nights spent and risk by travel destination, 10 EU/EEA countries^a, 2009–2015 (n=2,416)

Region	Travel-associated cases			Nights		Cases/million nights (95% CI)
	n	%	% <15 years	(million, estimate 2009–15 ^b)		
Total (all regions)	2,416	100	39.8	7,794	100	0.31 (0.30–0.32)
Africa	753	31.2	33.3	357	4.6	2.11 (1.96–2.27)
America						
North America	10	0.4	0.0	412	5.3	0.02 (0.01–0.04)
Central and South America ^c	106	4.4	14.2	228	2.9	0.46 (0.38–0.56)
Asia	705	29.2	50.4	564	7.2	1.25 (1.16–1.35)
Europe						
EU 28	427	17.7	13.6	5,150	66.1	0.08 (0.07–0.09)
Other European countries ^d	410	17.0	56.8	995	12.8	0.41 (0.37–0.45)
Oceania	5	0.2	0.0	88	1.1	0.06 (0.02–0.13)

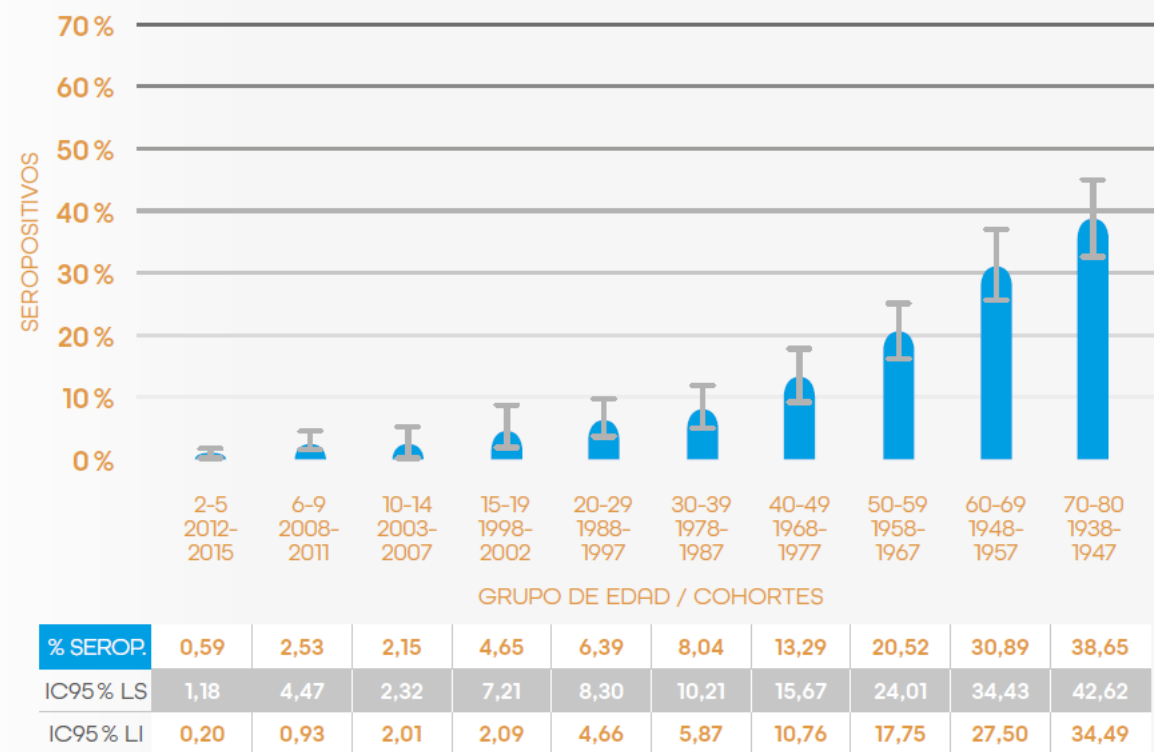


2º ESTUDIO DE SEROPREVALENCIA EN ESPAÑA

SEPTIEMBRE 2020

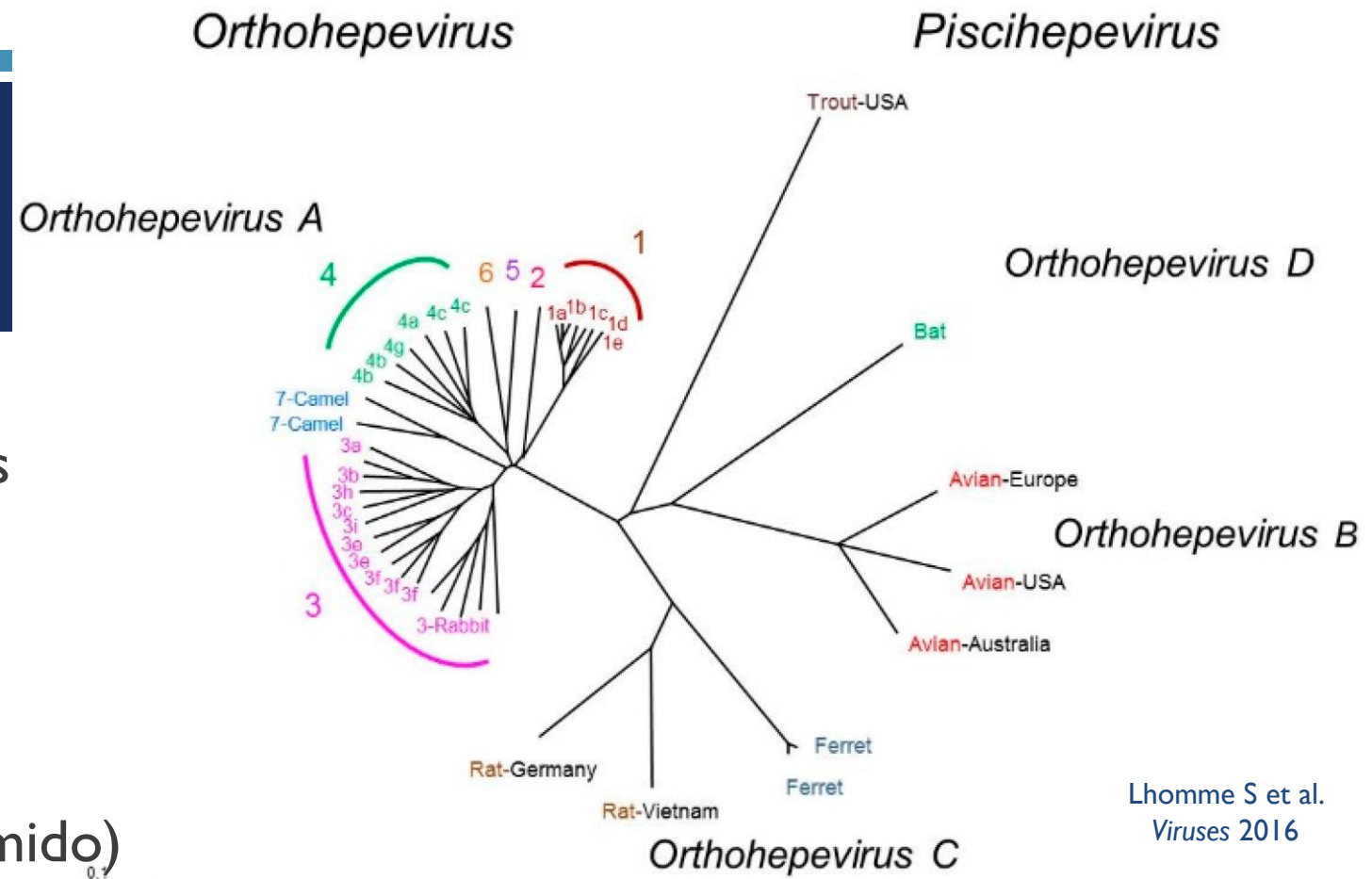
HEPATITIS E

- **Riesgo:**
inmunodepresión/gestantes
(letalidad 25-30%)
- **Prevalencia:**
 - <40 años: <10%
 - >60 años: 30-40%

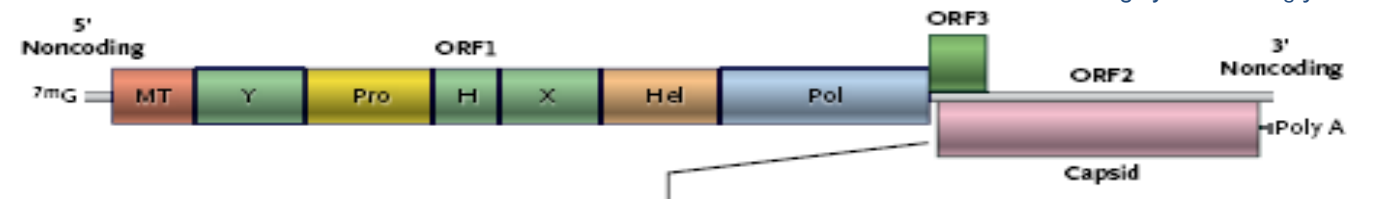


HEPATITIS E

- Distribución global
- Periodo incubación: 2-6 semanas
- Hepatitis aguda
 - >95%:AUTOLIMITADA
 - Fulminante/Extrahepática
- Hepatitis crónica (inmunodeprimido)
- Familia *Hepeviridae*
 - Género *Orthohepevirus* (vertebrados terrestres)
 - 4 especies: A, B, C, D
 - *Orthohepevirus-A*: 8 genotipos
 - Género *Piscihepevirus* (trucha)



Lhomme S et al.
Viruses 2016



Hoofnagle JH et al. *N Engl J Med* 2012

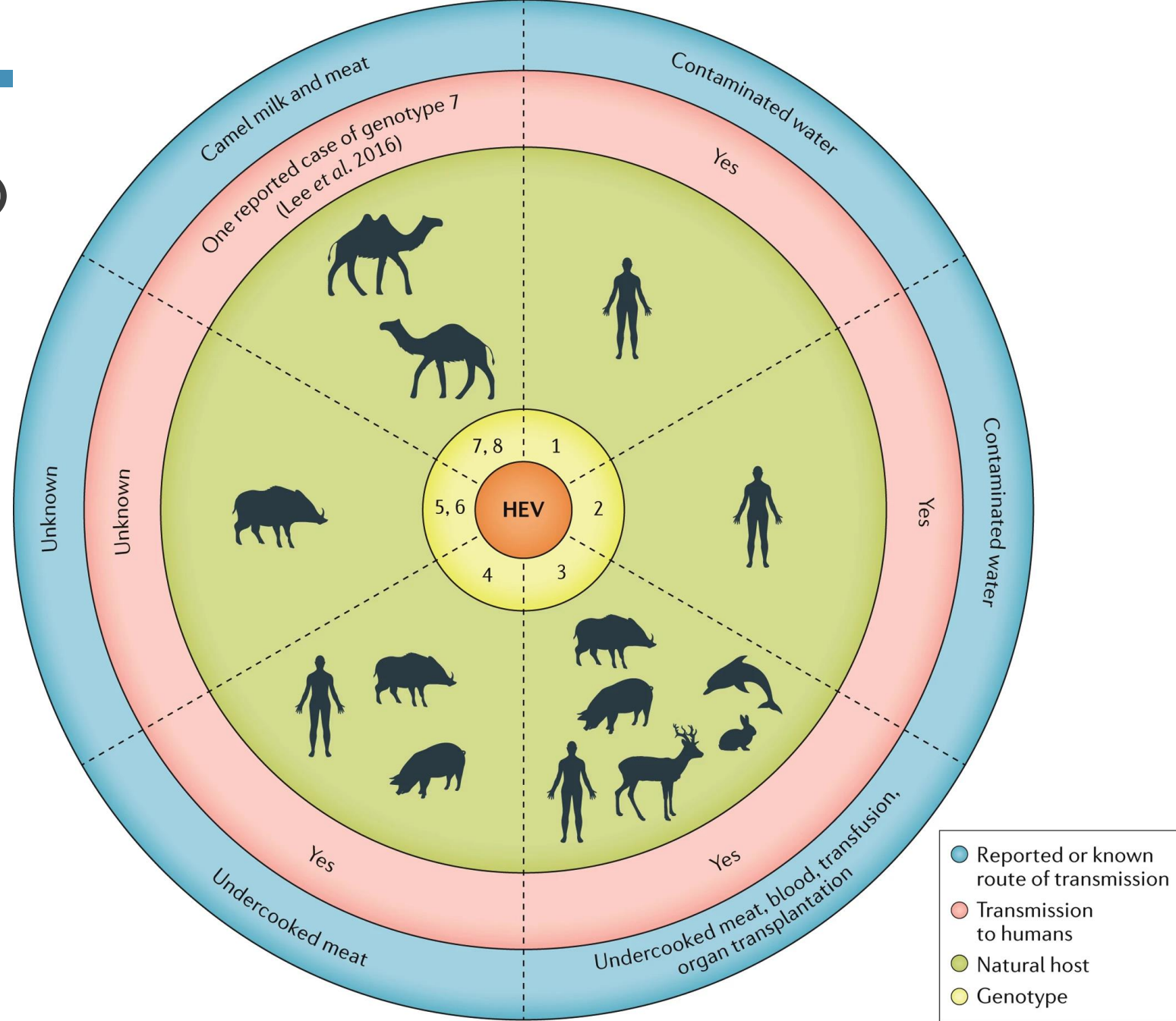
■ Hepatitis E (Orthohepevirus-A)

36 subtipos / 1 serotipo

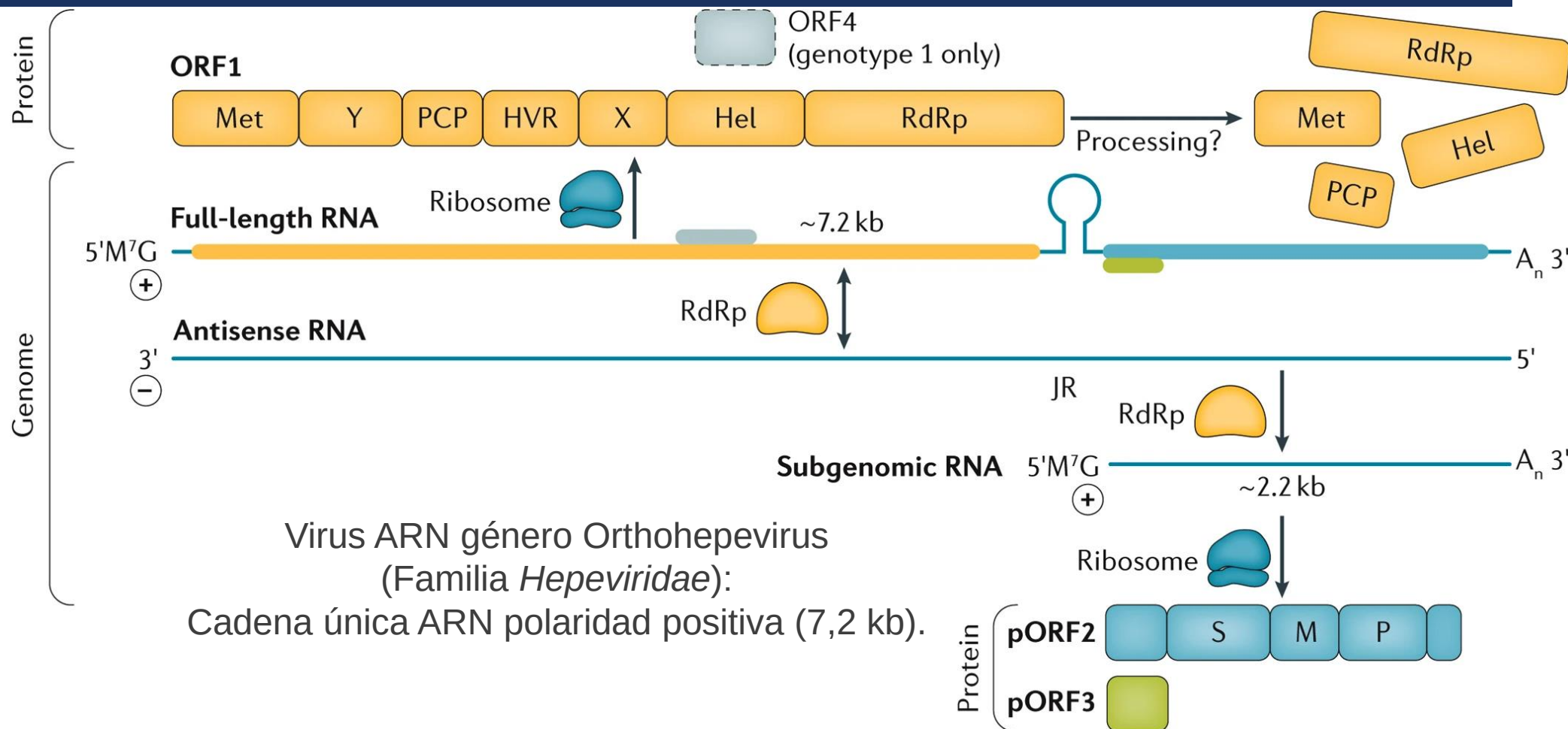
- **Genotipos 1 y 2:** humanos (agua)
- **Genotipo 3 y 4:** animal/humano (carne poco cocinada)
- **Genotipo 5-8:** animales

■ Transmisión

- Consumo agua/carne
- Sangre
- Trasplante órganos

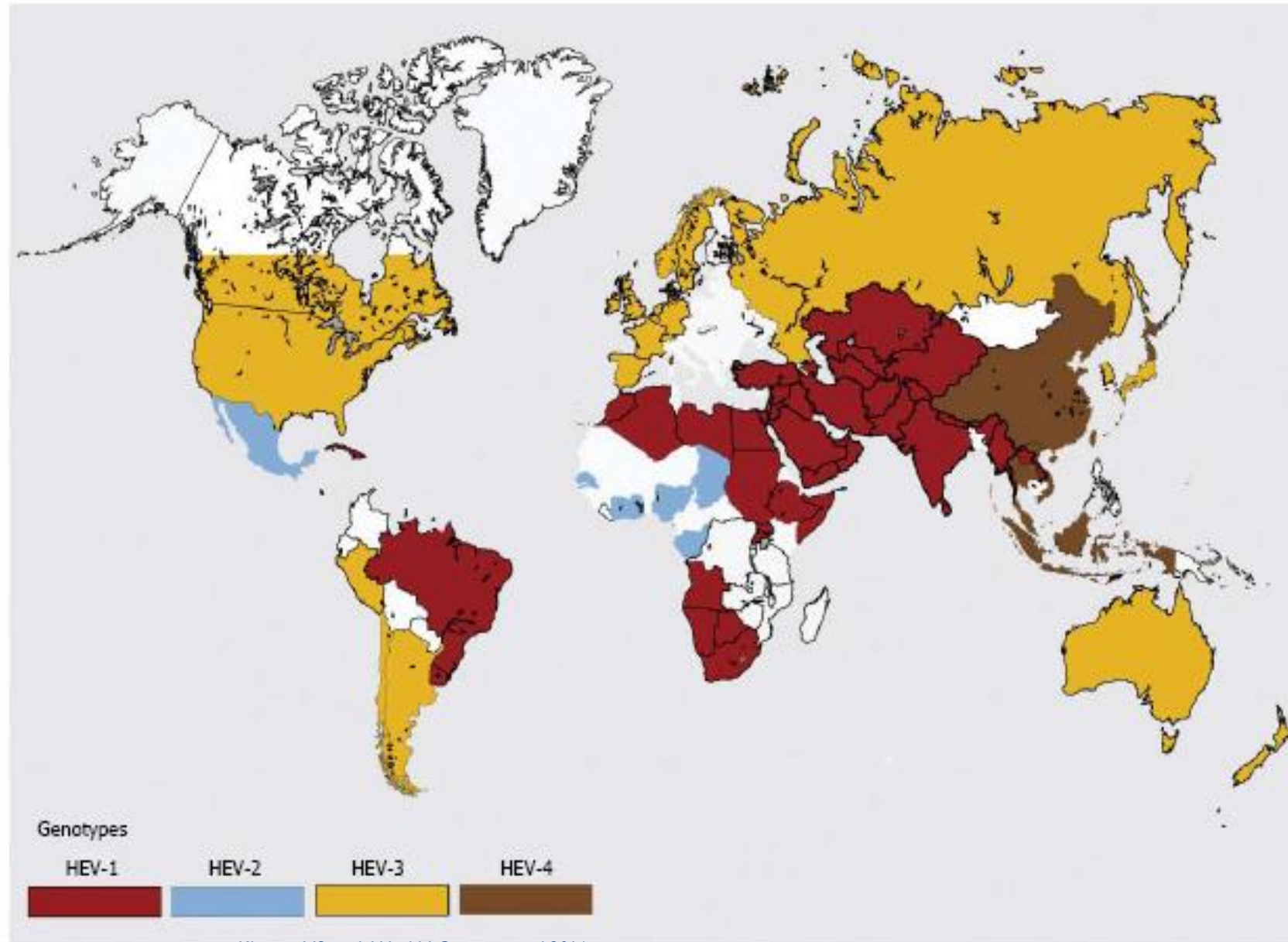


VIROLOGÍA DEL VHE: GENOMA Y VIRIÓN



HEPATITIS E

- Distribución global
- Periodo incubación:
2-6 semanas

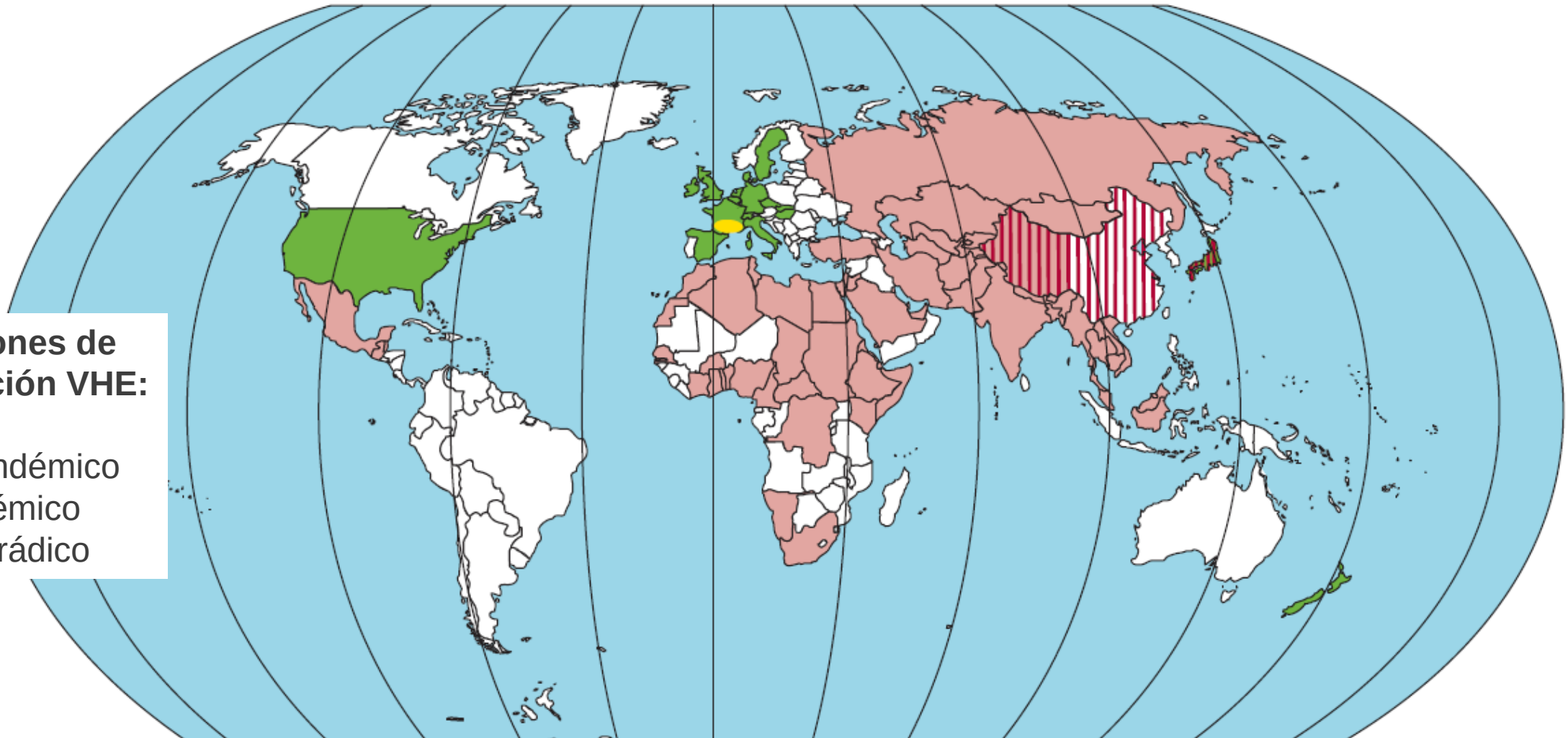


Khuroo MS et al. World J Gastroenterol 2016

Figure 5 Global distribution of hepatitis E virus genotypes. See text under "global distribution" for explanation.

4 patrones de
distribución VHE:

Hiperendémico
Endémico
Esporádico



Epidemiología de la hepatitis E: Distribución mundial

Genotype 1 and 2
• Endemic
• Waterborne

Genotype 3
• Sporadic
• Zoonotic

Genotype 3
• Hyperendemic
area

Genotype 4
• Sporadic
• Zoonotic

Figure 2: Worldwide distribution of clinical cases of HEV infection

Epidemiología

Hepatitis E:

Vías de transmisión

- Agua
- Productos sanguíneos
- Persona-persona
 - Vertical
 - Zoonosis

Modo de transmisión según grado de desarrollo económico.

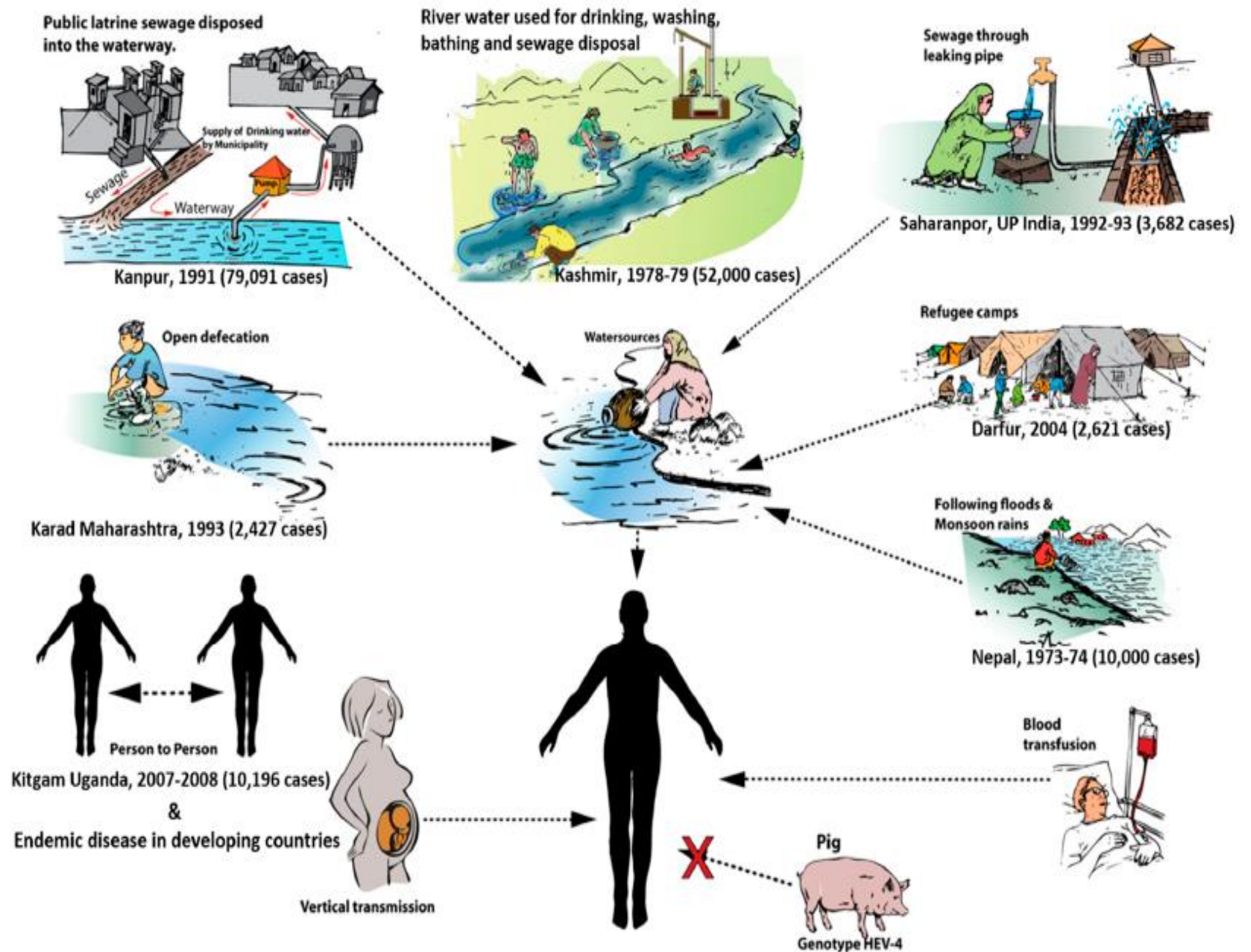
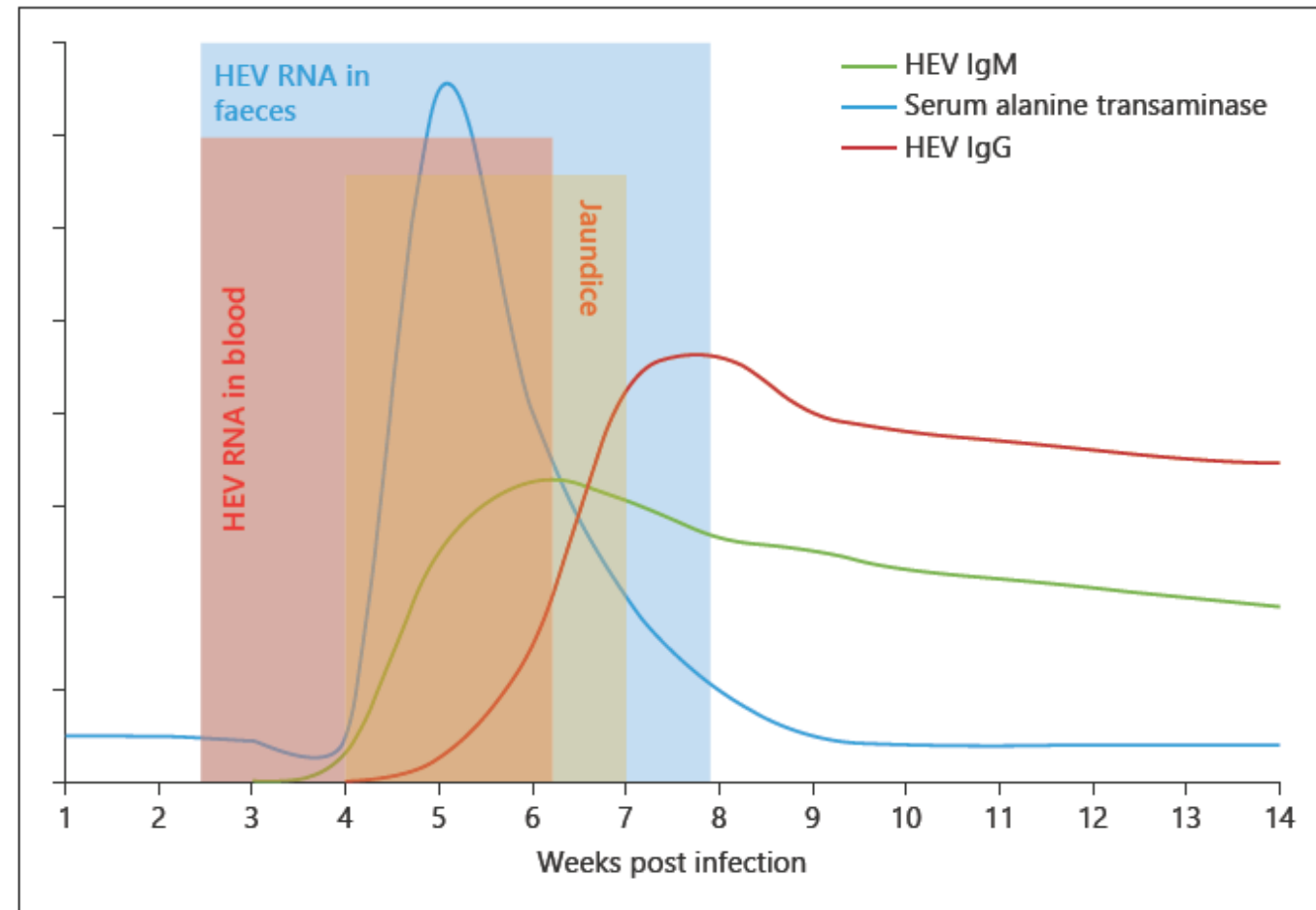


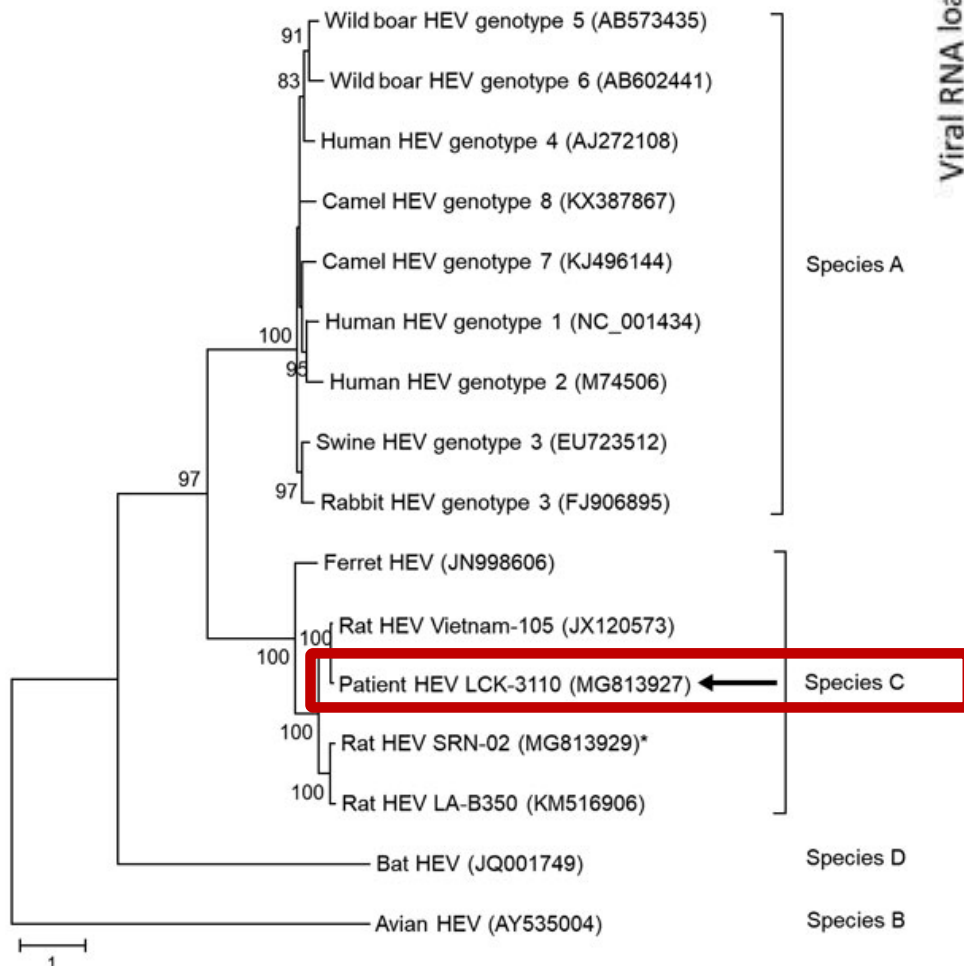
Figure 2. Modes of transmission of hepatitis E in developing countries. The settings for contamination of drinking water have been drawn in sketches, with epidemics reported in each case.

DIAGNÓSTICO HEPATITIS E

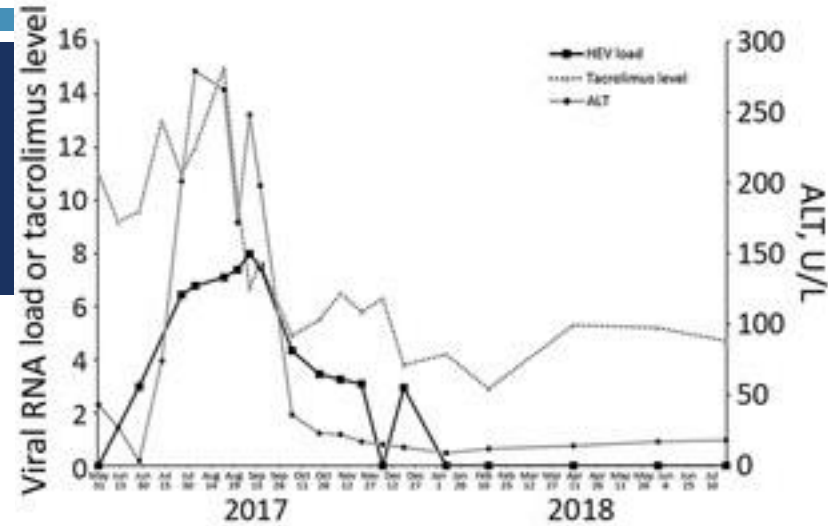
- IgM/IgG (seroconversión)
- ARN VHE: **sangre y heces** antes de la aparición de los síntomas y durante un periodo de tiempo limitado
- ARN VHE **saliva**



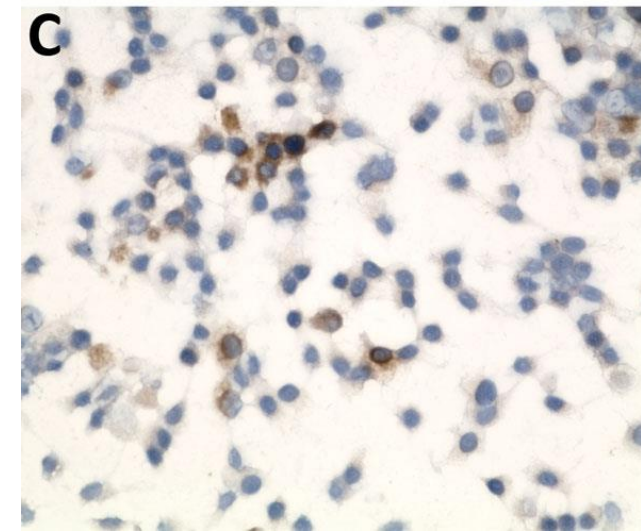
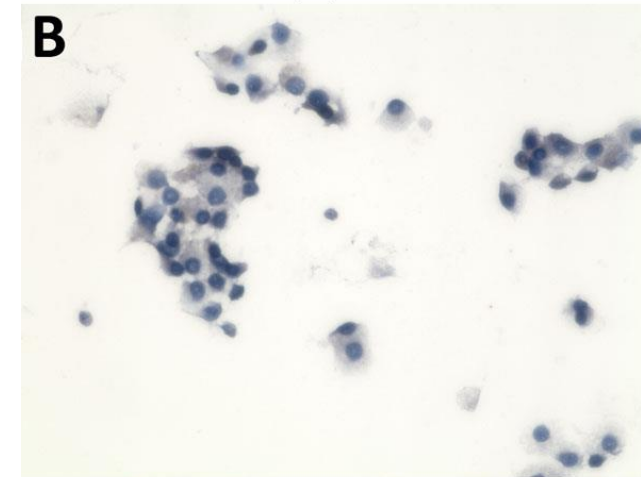
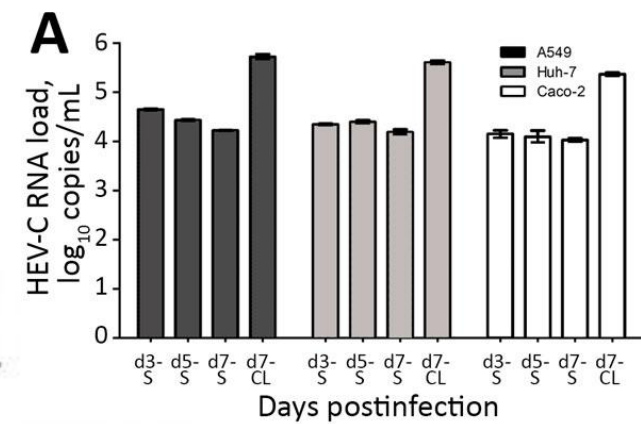
ORTHOHEPEVIRUS C 2017



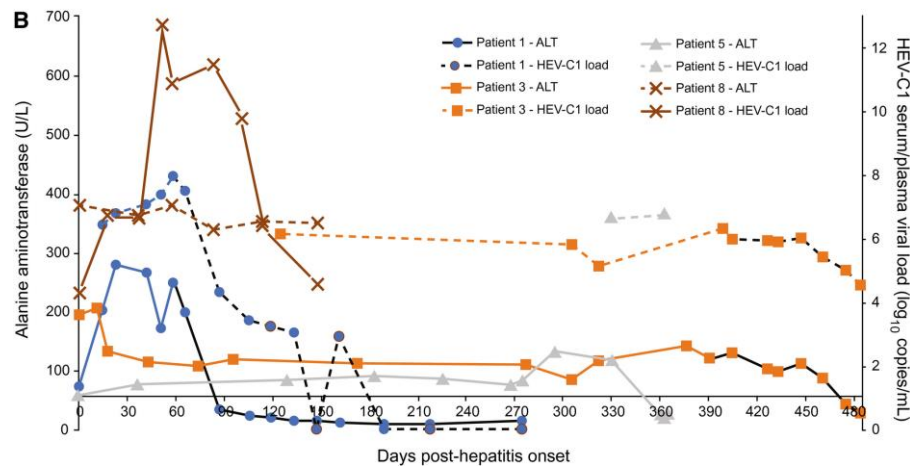
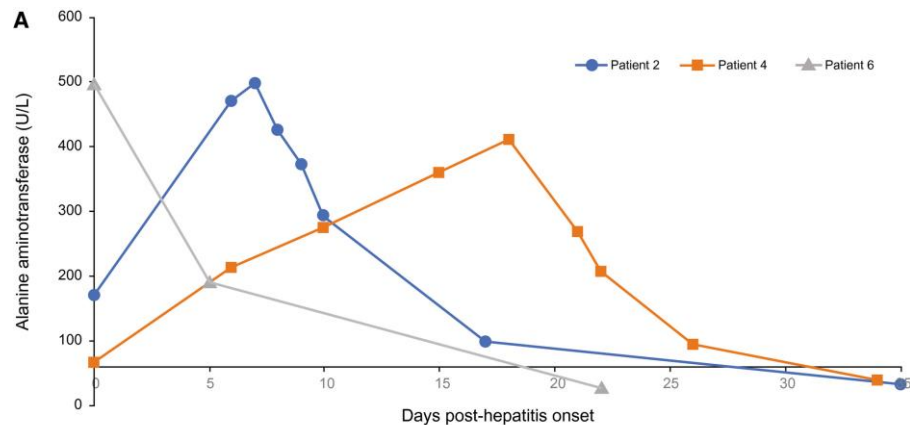
Sridhar et al. *Emerg Inf Dis* 2017



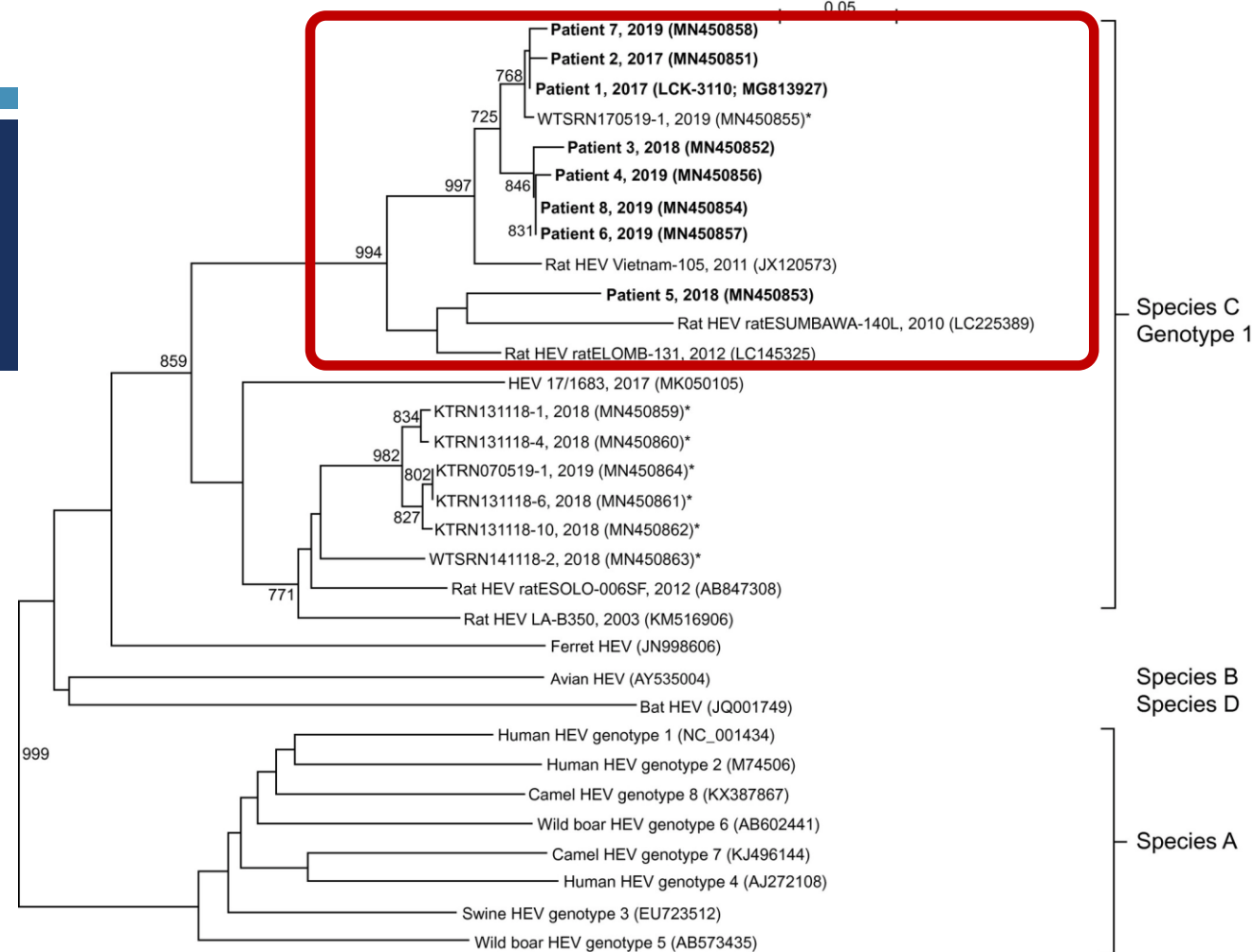
- **2010: Alemania Roedores** (Hospedador Natural)
- **2017 Primer caso humano Hong Kong**
 - Tx Hepático
 - 6meses Ortho-C(+) heces
 - Viable en cultivo celular
 - Muestras ambientales 2017 negativas
 - Muestra 2012 rata Ortho-C (+)



ORTHOHEPEVIRUS C 2017-2019



Sridhar et al. *Hepatology* 2021



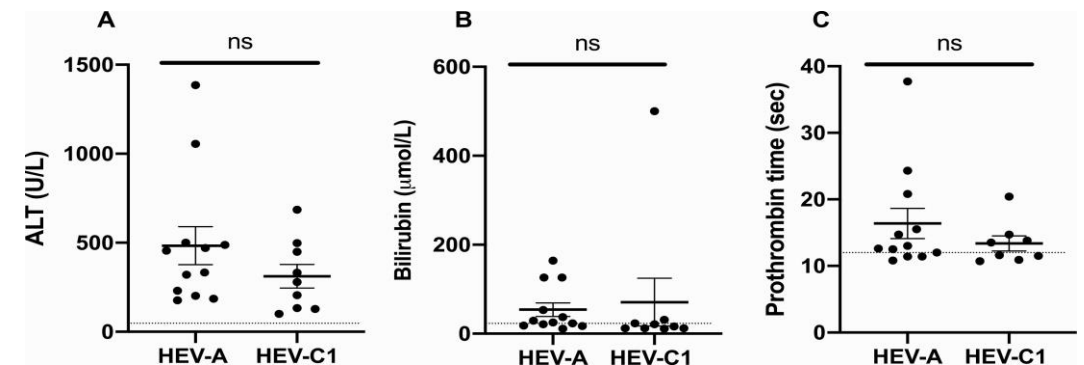
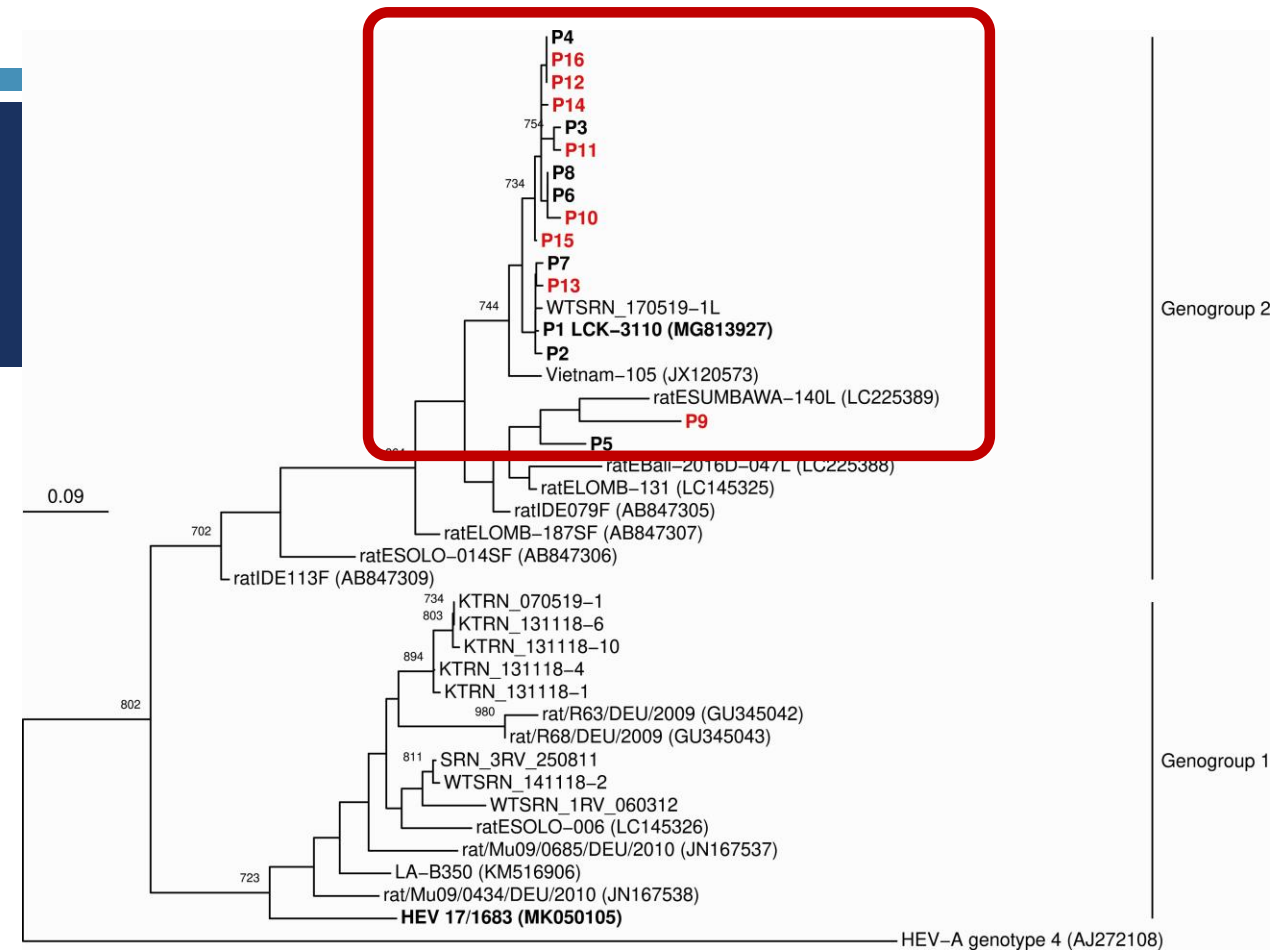
■ Hong Kong 2017-2019

- 2860 muestras humanas (hep.aguda/inmunodep): 7(+) (0,25%)
- 186 muestras ratas: 7(+) (3,8%)
- Casos inmunocompetentes e inmunodeprimidos
- I exitus (Ortho-C en LCR(+))

ORTHOHEPEVIRUS C 2019-2020

■ Hong Kong 2019-2020

- 9/21 (42,9%) (VHE inmunodeprimidos): 7(+) (0,25%)
- Hepatitis persistente:
 - 78% VHE (+)
 - 75% Orthohepevirus-C (+)
- PCR VHE: frecuente neg
- Serología IgM VHE: frecuente neg
- Ribavirina opción terapéutica



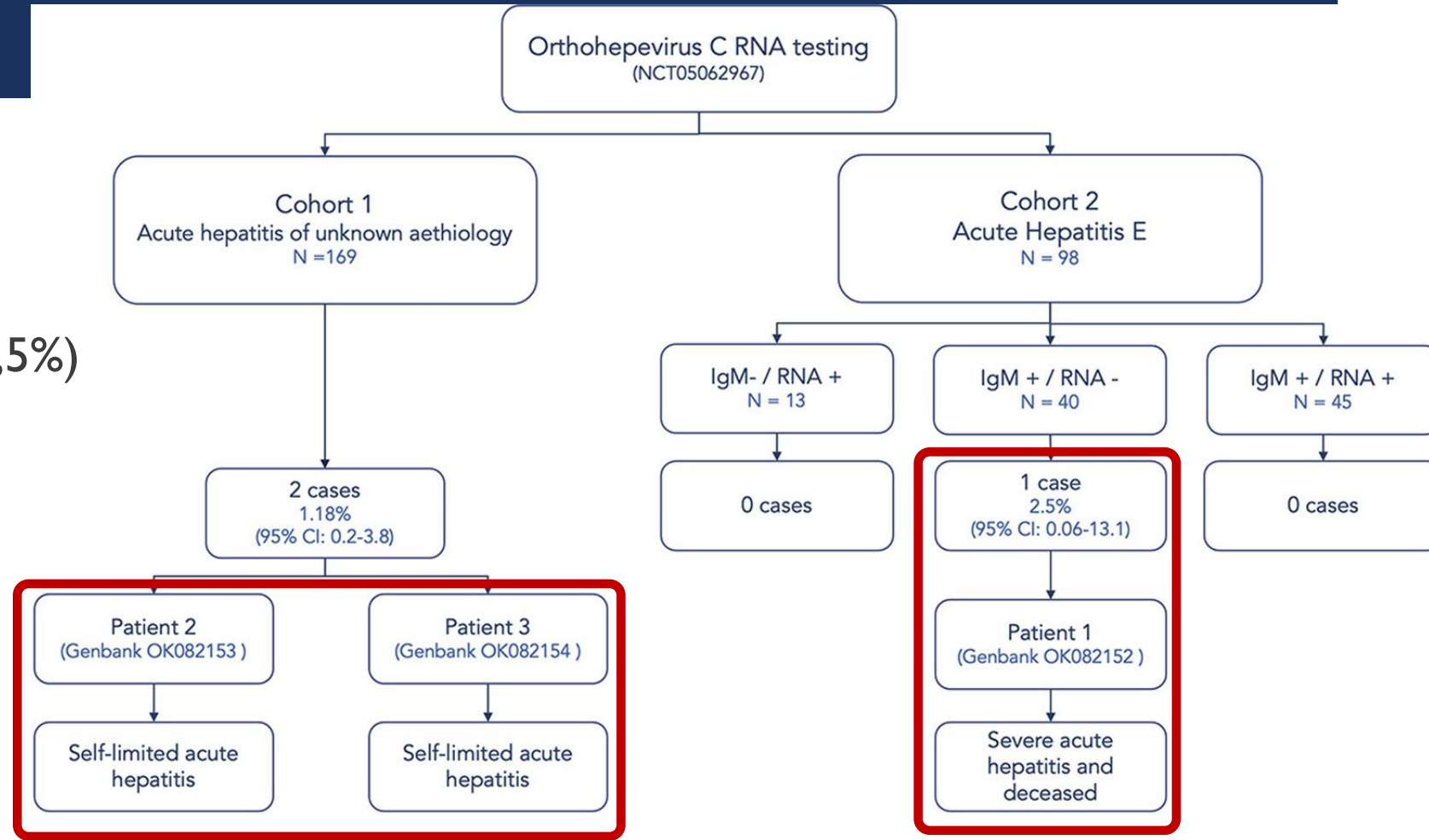
ORTHOHEPEVIRUS C

- Distribución mundial
- ARN Ortho-C roedores 22 paí
 - Germany, France, Denmark, Lithuania, Hungary, Austria, Switzerland, Italy, Spain, Greece, Belgium, Czech Republic, England, Netherlands,
 - USA, Brazil
 - China, Indonesia, Vietnam, Japan
 - Uganda, Kenya



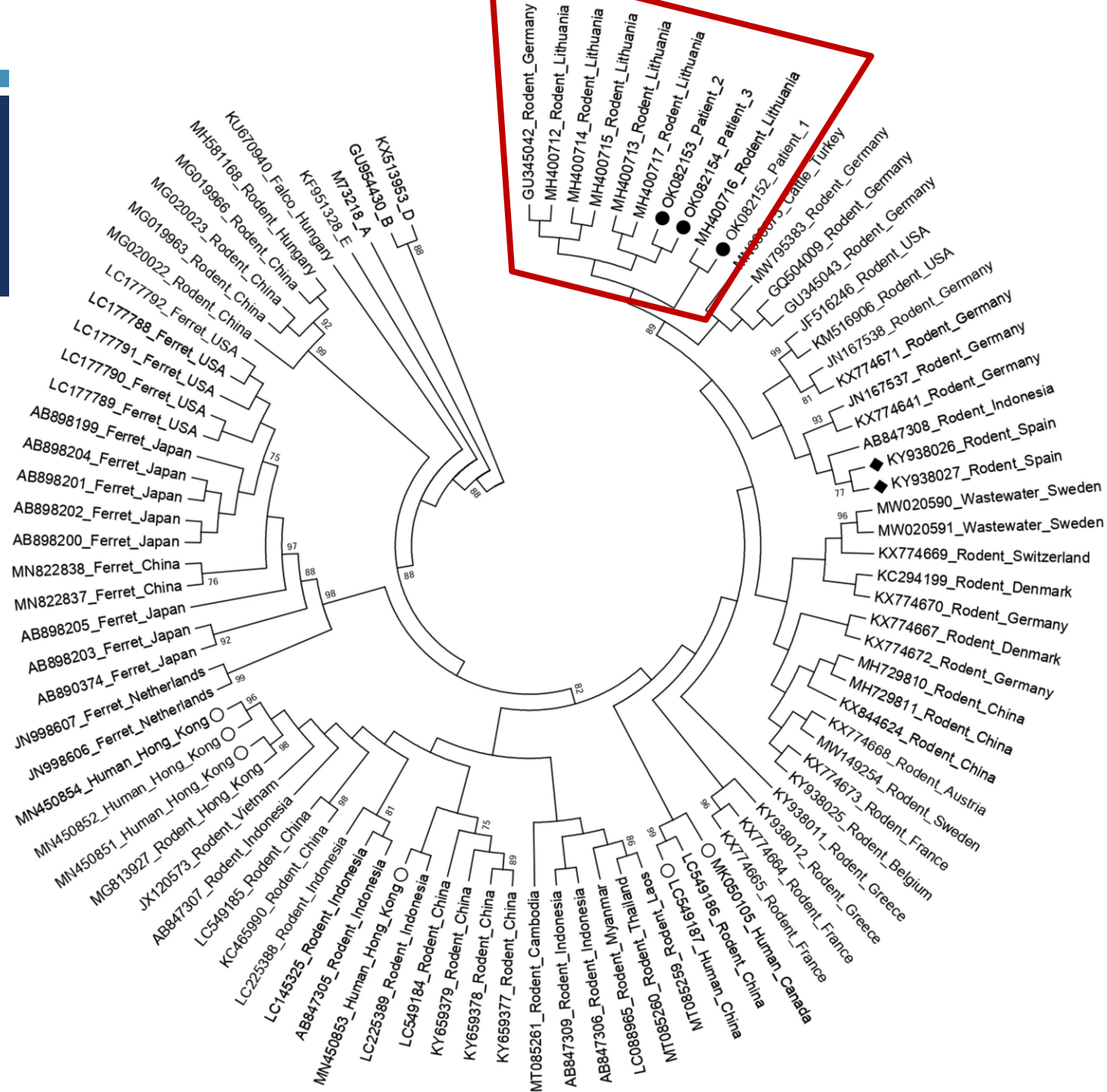
ORTHOHEPEVIRUS C ESPAÑA

- 3 casos humanos
 - 1 casos IgM VHE (+) (2,5%)
 - 2 casos ¿? (1,2%)
- ARN VHE (-)
- ARN Ortho-C (+)



ORTHOHEPEVIRUS C ESPAÑA

- Filogenia cercana roedores del área Andalucía y Europa



LEPTOSPIROSIS COMO CAUSA DE HEPATITIS AGUDA

TABLE 1. *Distribution of leptospiral and viral hepatitis (A–E)-positive cases*

Etiology of acute viral hepatitis	Number	Percentage
HBV	41	16.6%
HCV	06	2.4%
HAV	63	25.5%
HEV	32	12.9%
Leptospira	46	18.6%

LEPTOSPIROSIS

- **Zoonosis** (orina roedores y otros mamíferos reservorios)
- Infección **emergente** e **infravalorada**
- **Cambio climático** puede aumentar la incidencia
- Generalmente **ASINTOMÁTICA** ó cuadro pseudogripal
- **Complicaciones** de pronóstico incierto: Leptospirosis icterohemorrágica / Enf. Weil / Enf. Arrozales
 - Ictericia, fallo renal y hemorragia pulmonar
- **DIAGNÓSTICO** (FOD, trombopenia, hepatitis):
 - 1ª semana infección: PCR/cultivo
 - 2ª semana: IgM

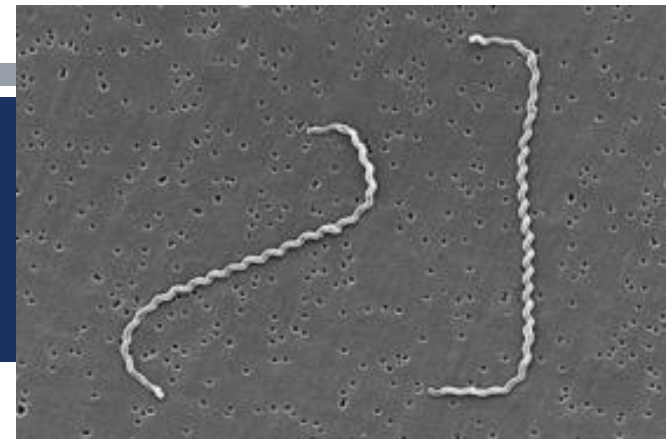


TABLE 2. *Comparison of clinical features of leptospirosis and acute viral hepatitis (AVH)*

Clinical features	Leptospirosis (%) (<i>n</i> =46)	AVH (A–E) (%) (<i>n</i> =142)	<i>P</i> value
Jaundice	35 (76)	134 (94.36)	
Fever	45 (97.8)	88 (61.97)	
Headache	21 (45.6)	22 (15.49)	
Anorexia	27 (58.6)	115 (80.98)	
Nausea/vomiting	17 (36.9)	120 (84.5)	<0.05
Myalgia	16 (34.7)	39 (27.46)	
Hepatomegaly	17 (36.9)	142 (100)	<0.001
Splenomegaly	5 (10.86)	82 (57.7)	<0.01
Conjunctival suffusion	6 (13)	...	<0.001
Diarrhoea	4 (8.6)	...	
Abdominal pain	31 (67.3)	52 (36.6)	
Respiratory symptoms	9 (19.5)	...	
Oliguria	26 (57.2)	...	<0.01
Chills	34 (74.3)	26 (19.7)	<0.001

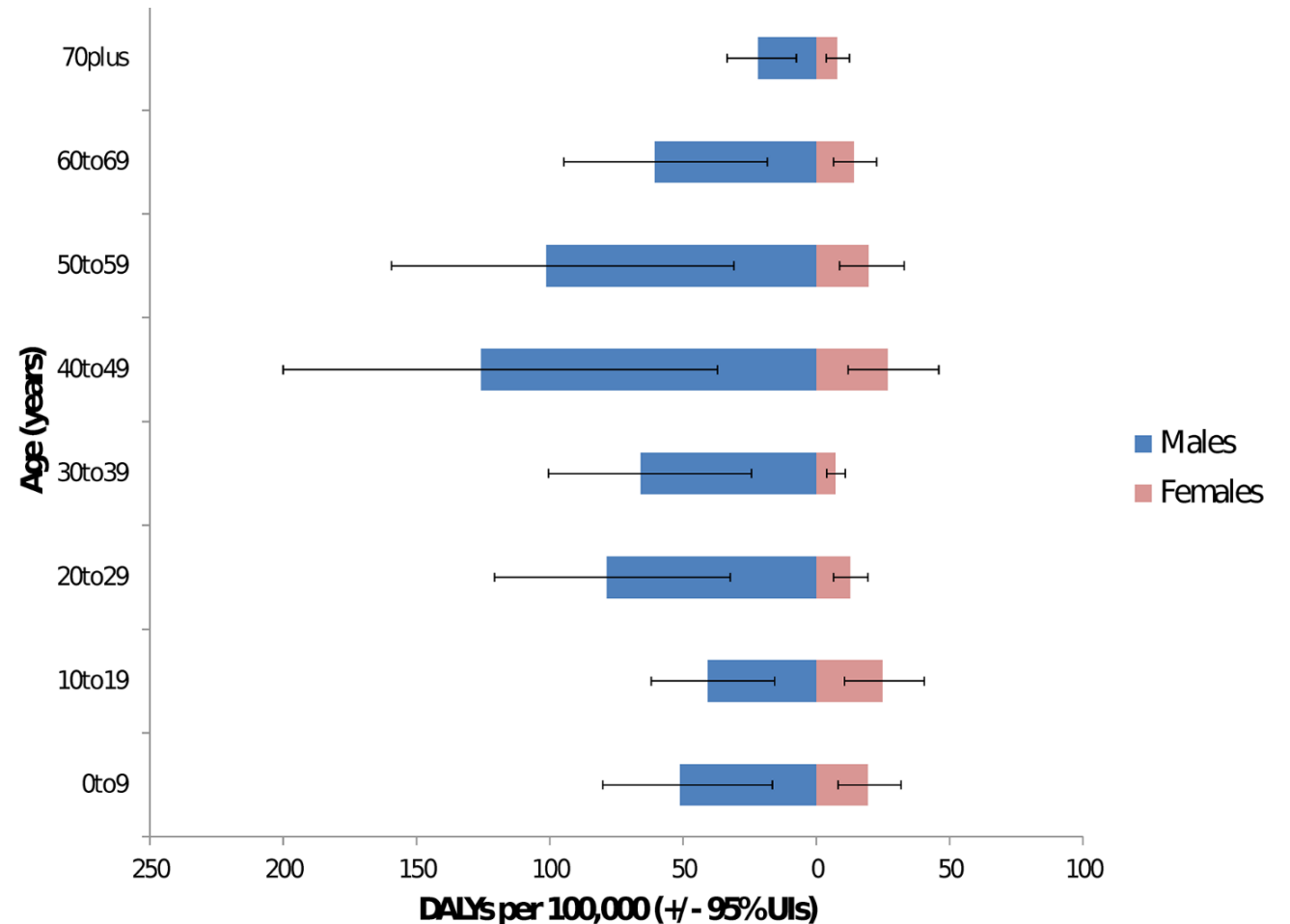
LEPTOSPIROSIS DISTRIBUCIÓN MUNDIAL

- 1,03 millones casos anuales
- 60000 muertes
- 2,90 millones DALYs
- Hombres jóvenes LMIC
- Zoonosis más perjudicial

RESEARCH ARTICLE

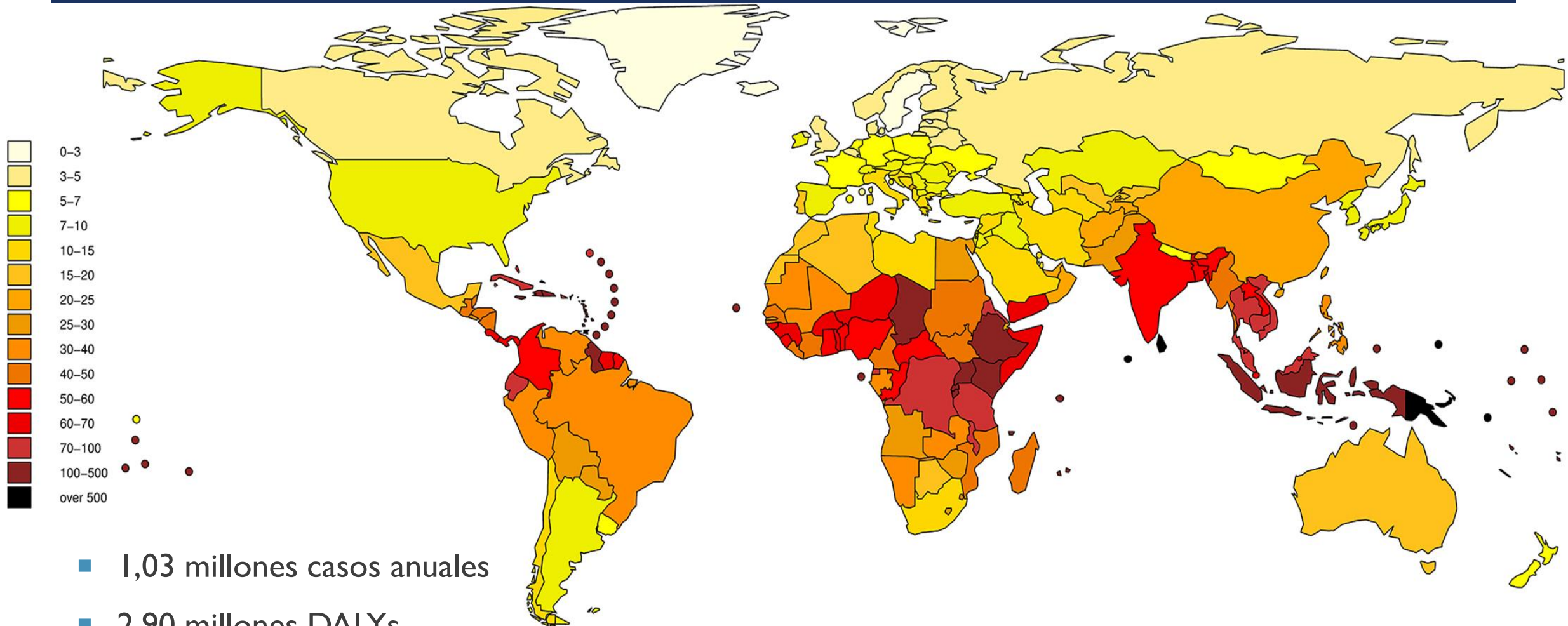
Global Burden of Leptospirosis: Estimated in Terms of Disability Adjusted Life Years

Paul R. Torgerson¹, José E. Hagan^{2,3}, Federico Costa^{2,3,4}, Juan Calcagno², Michael Kane⁵, Martha S. Martinez-Silveira², Marga G. A. Goris⁶, Claudia Stein⁷, Albert I. Ko^{2,3}, Bernadette Abela-Ridder^{8*}



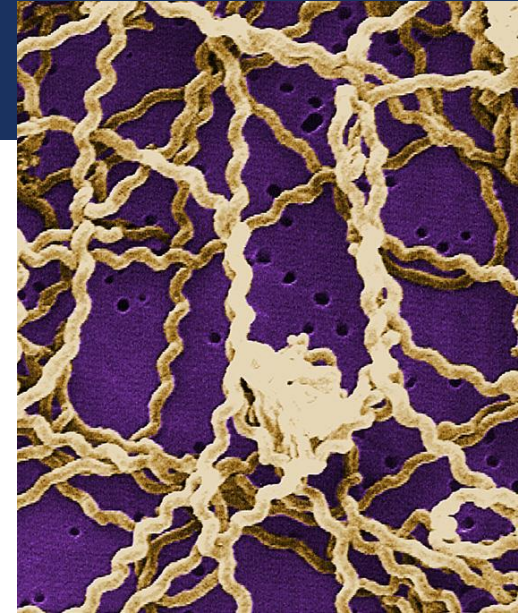
LEPTOSPIROSIS

DISTRIBUCIÓN MUNDIAL



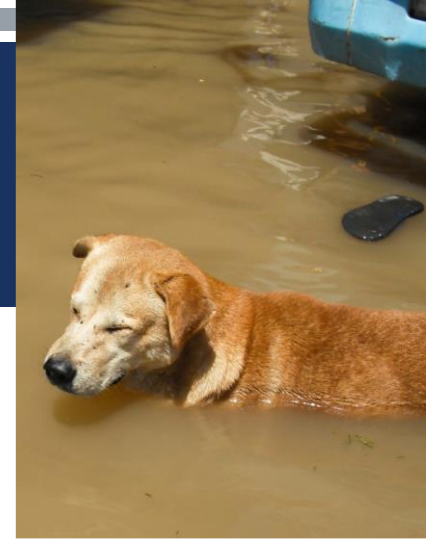
LEPTOSPIROSIS GENERALIDADES

- 10 especies patógenas *Leptospira* spp
 - Más de 250 serovars patogénicas
- Distribución mundial (>1 millón casos al año): 60000 muertes
 - Mayor incidencia Zona Tropical
- USA: 100-150 casos/año (Puerto Rico/Hawaii)
- Brotes: lluvias torrenciales, inundaciones



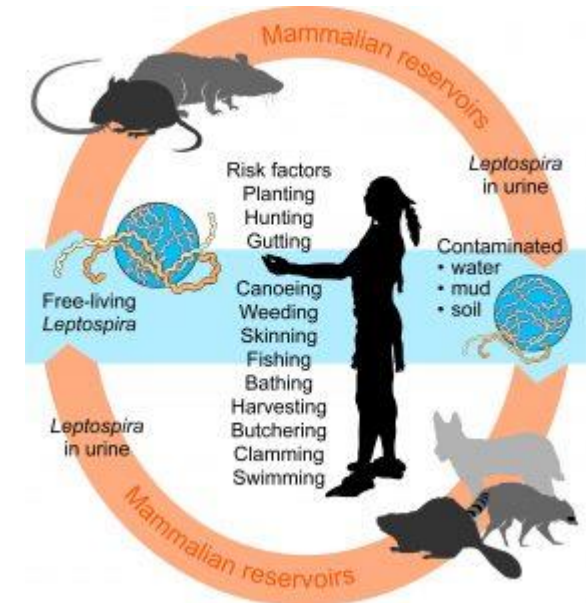
LEPTOSPIROSIS TRANSMISIÓN

- **Agua** contaminada con **orina de animales**
- Sobrevive semanas-meses en agua y tierra contaminada
- Tipos de infección
 - Contacto directo orina/fluidos reproductivos animales
 - **Contacto agua contaminada (agua estancada, ríos, rías, alcantarillas) y tierra húmeda**
 - Ingestión comida/agua contaminada
 - Mamíferos intermediarios
- Vía transmisión:
 - Mucosas
 - **Conjuntiva**
 - **Cortes/abrasiones piel**



LEPTOSPIROSIS TRANSMISIÓN

- ¿Human-to-human?: Raro
 - Relaciones sexuales/Lactancia materna. Mordeduras animales
- Actividades alto riesgo transmisión:
 - Caminar, nadar, navegar en aguas contaminadas
 - Mayor riesgo: inmersión prolongada, sumergir cabeza, tragar agua
- Otras:
 - Contacto directo con animales
 - Abrasión piel + exposición agua/tierra contaminada (trekking, jardinería)

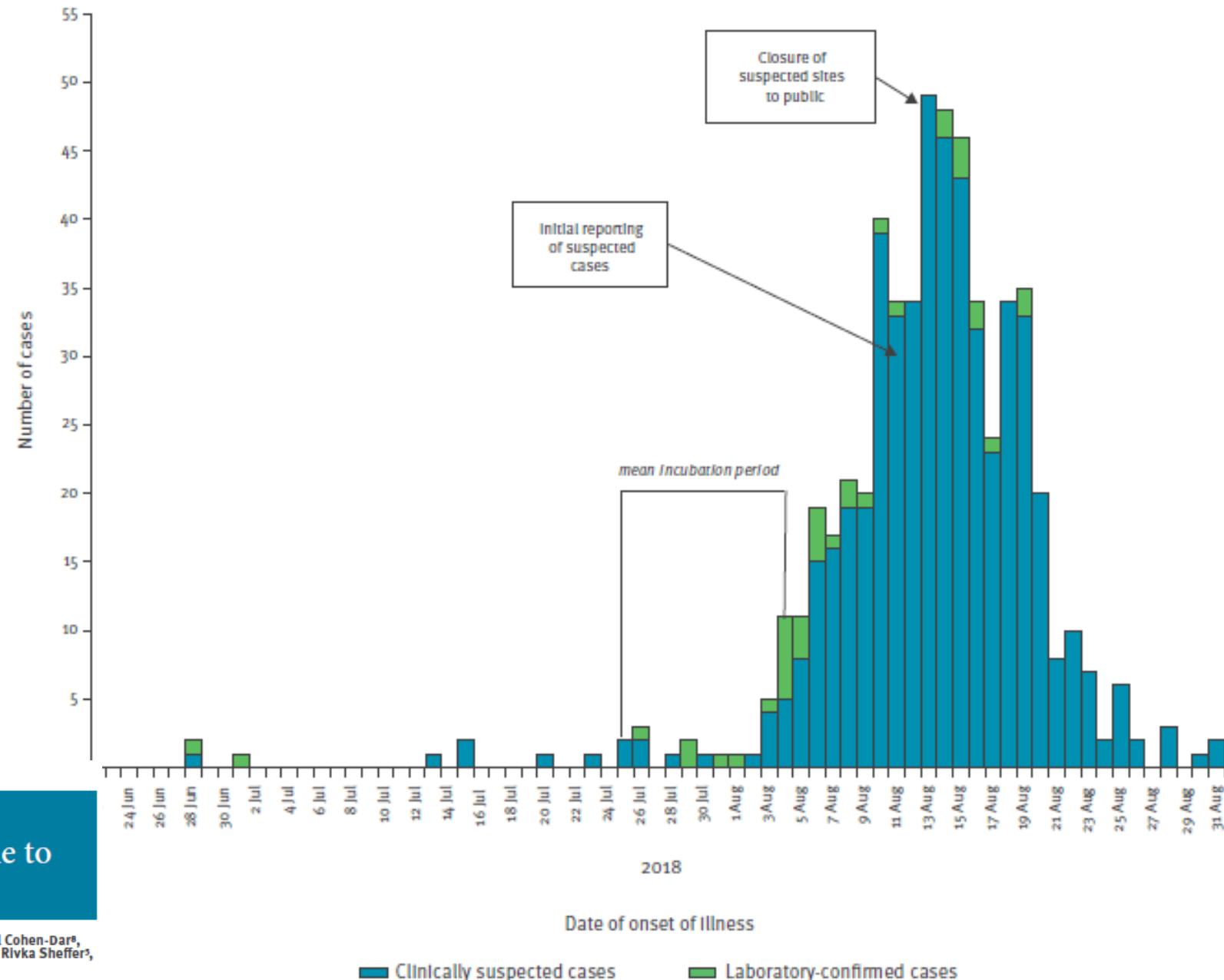


LEPTOSPIROSIS ENFERMEDAD EMERGENTE



- Israel
 - Antes 2018: 10 casos/año
 - 2018: 583 casos

FIGURE 1
Epidemic curve for human leptospirosis in Northern Israel, June–August 2018 (n = 619)



RAPID COMMUNICATION

Outbreak of human leptospirosis linked to contaminated water bodies in Northern Israel, June to August 2018

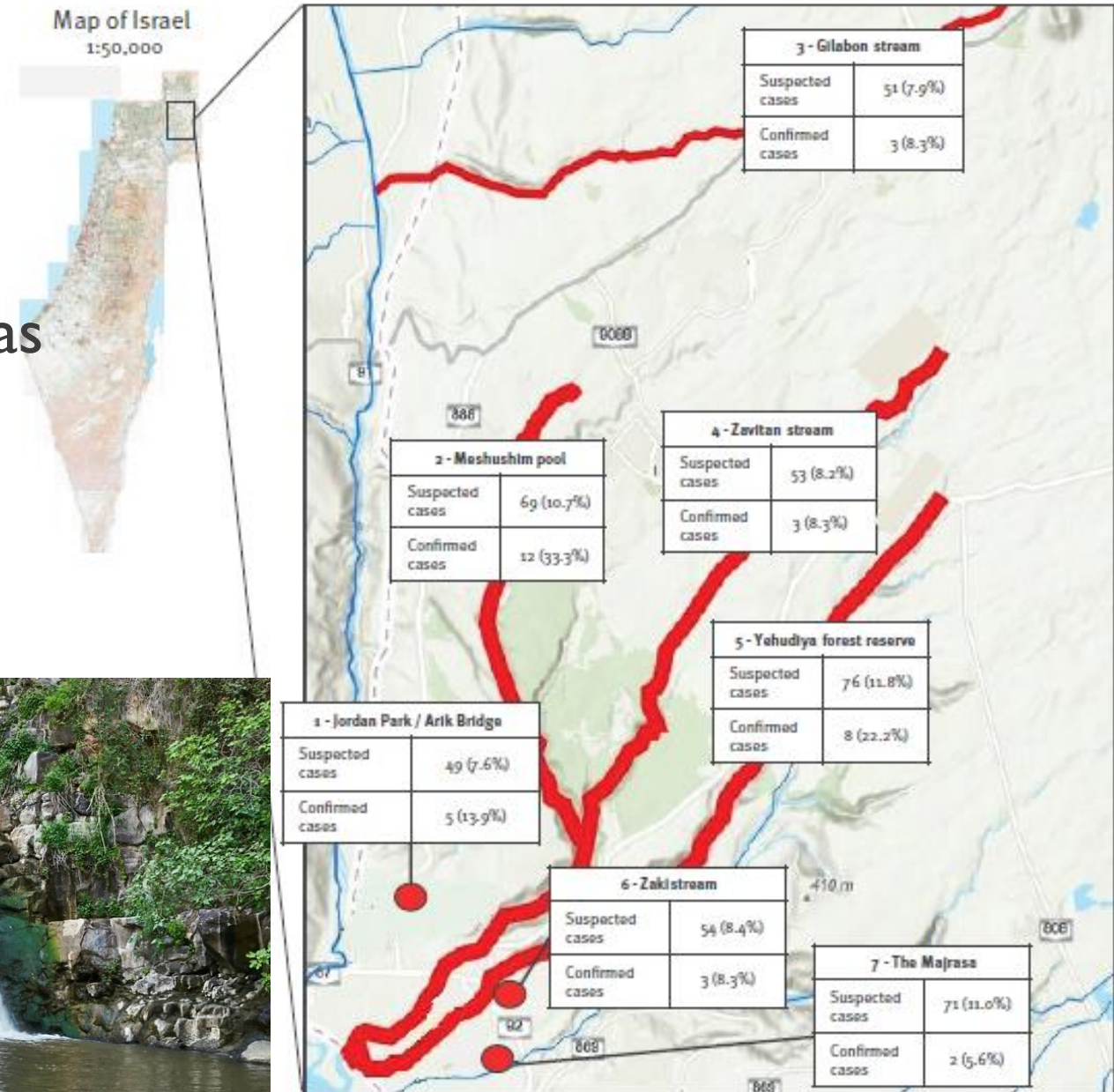
Yuval Dadon^{1,2,3}, Eric J. Haas^{2,3,4}, Ehud Kaliner⁵, Emilla Anis^{2,4}, Shepherd Roee Singer^{2,4}, Yafit Atiya-Nasagi⁷, Michal Cohen-Dar⁸, Eva Avramovich⁹, Roni King¹⁰, Oded Sued¹¹, Tamir Goshen¹², Sharon Amit¹³, Ian Miskin¹⁴, Efrat Gino¹⁵, Ruth Yishai¹⁶, Rivka Sheffers¹⁷, Itamar Grotto^{1,4}, Jacob Moran-Gilad^{1,4,5}

LEPTOSPIROSIS ENFERMEDAD EMERGENTE

- Cierre piscinas naturales sospechosas
- Información población
- AB (empírica, profilaxis)



FIGURE 2
Spatial distribution of leptospirosis cases in Northern Israel, June–August 2018 (n = 540)



LEPTOSPIROSIS ENFERMEDAD EMERGENTE

■ Vigilancia contaminación fecal

- Umbral: 1000 a 400 UFC/100mL

■ Animales reservorio



FIGURE 3

Faecal contamination of water bodies in Northern Israel, June–August 2018

Water source	Contamination Level (Faecal coliforms / 100mL)						
Day count	0	16	17	24	25	29	31
Date in 2018	22 Jul	7 Aug	8 Aug	15 Aug	16 Aug	20 Aug	22 Aug
1. Jordan Park / Arik Bridge	820	400			1000	1200	470
2. Meshushim pool ^a	620	300		1100	880	1110	1000
3. Gilabon stream	640	500			1440	1600	3200
4. Zavitan stream ^a	60		3600	500		310	360
5. Yehudiya forest reserve	440	600		1170		4560	2560
6. Zaki stream	2170	900	1500	4400		4000	3840
7. The Majrasa	520	250			800	2480	1100

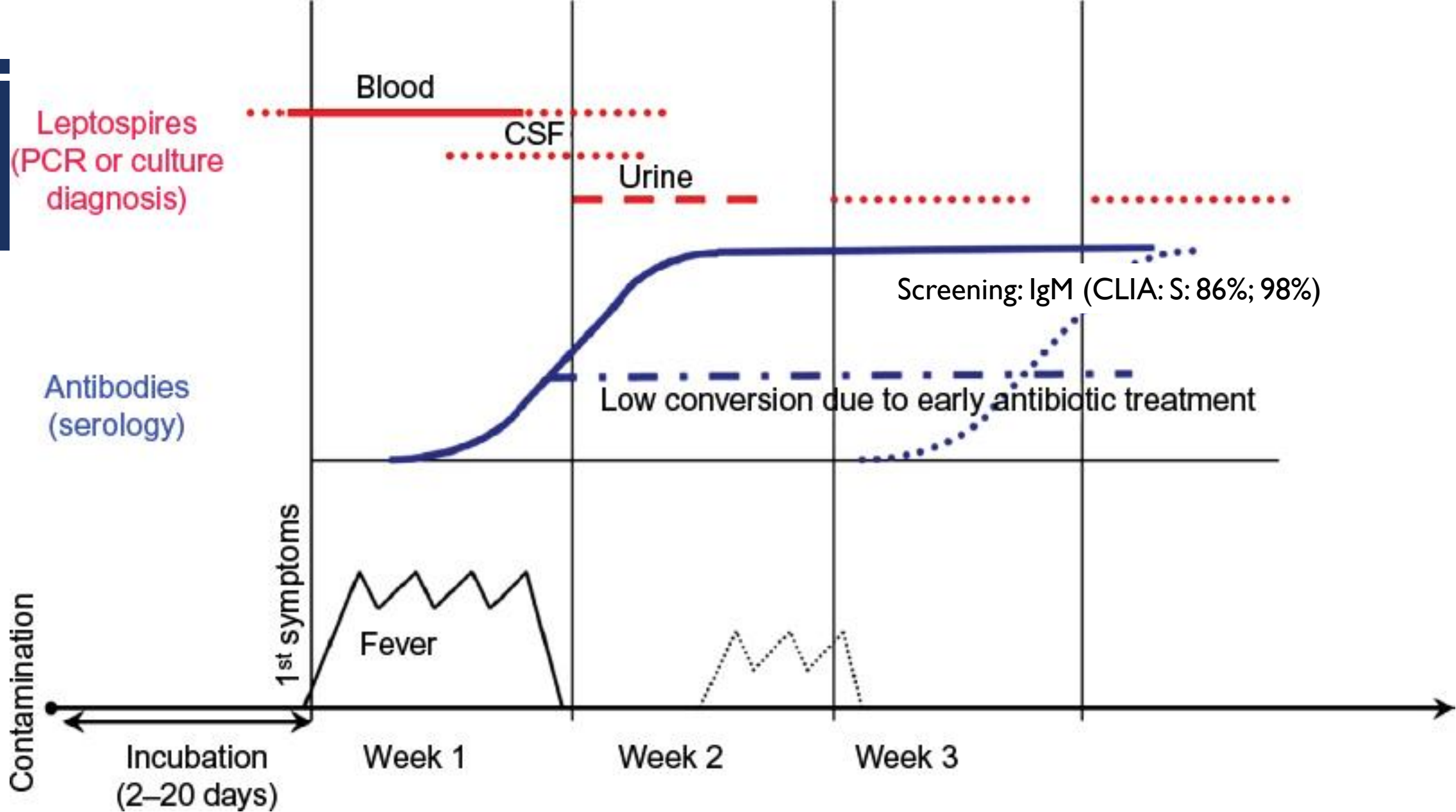
^aWater bodies tested positive for pathogenic *Leptospira* by real-time PCR.

LEPTOSPIROSIS DIAGNÓSTICO

- FASE AGUDA (semana 1)
 - Sangre total (PCR, cultivo) / Suero (IgM)
- FASE CONVALECIENTE (a partir de semana 2)
 - Suero y orina
- Bacteriemia 4-6 días iniciales
- Bacteriuria intermitente tras 7 días infección
- Anticuerpos 3-10 días tras inicio síntomas
 - Fase aguda y convaleciente



LEPTOSPIROSIS



TRANSMISIÓN HEPATITIS

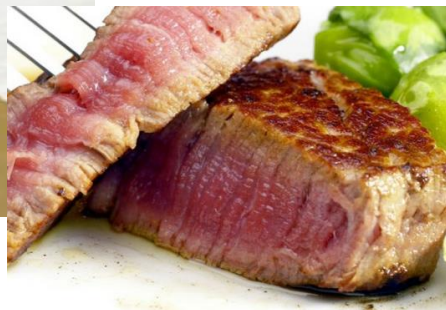


VHB



■ Fecal-oral

- Hepatitis A
- Hepatitis E



■ Artrópodo vector

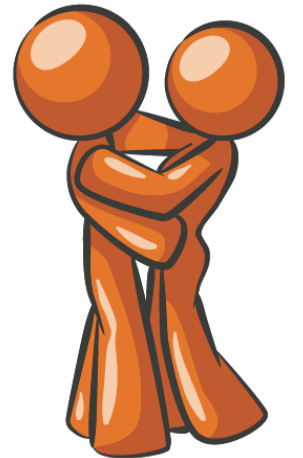
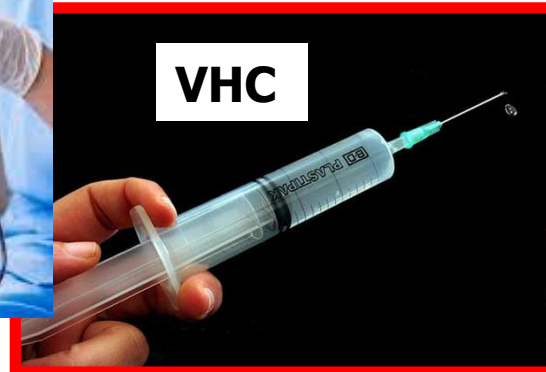
- Dengue
- Fiebre Amarilla
- ...



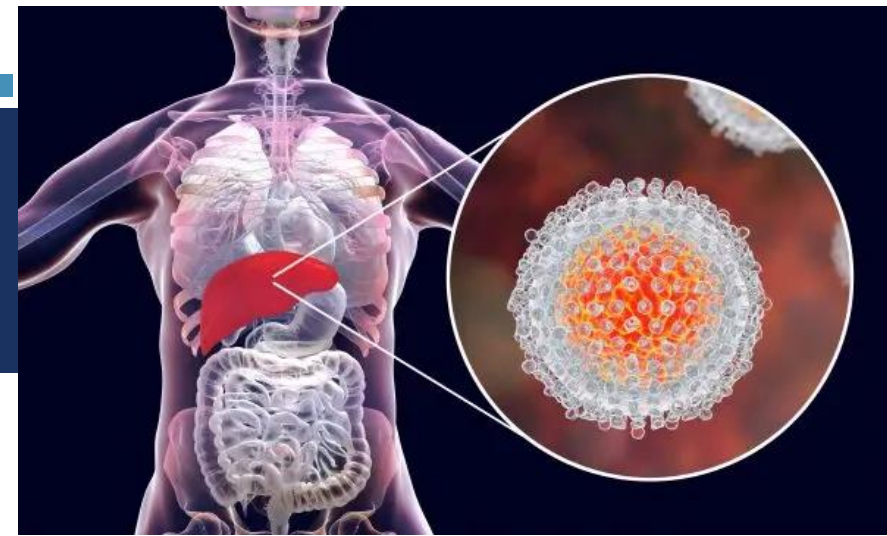
■ Parenteral/Sexual

- Hepatitis B/D
- Hepatitis C

VHC



FLAVIVIRUS VIRUS ARN ICOSAÉDRICOS



- a. Hepatotropos: **Virus Hepatitis C** y **Hepatitis G**.
- b. Arbovirus productores de fiebre hemorrágica y encefalitis.

Transmisión por mosquito *Aedes aegypti* o *Aedes albopictus*:

- Virus **Dengue**: arbovirosis más frecuente en el mundo. 1) Dengue clásico (autolimitado); 2) Dengue hemorrágico (30% mortalidad)
- Virus **Zika**: microcefalia en recién nacido (Brasil 2015)
- Virus **Fiebre Amarilla**: vacuna obligatoria



Transmisión por mosquito *Culex* spp:

- **West Nile Virus**, encefalitis (reservorio: aves).

Transmisión por garrapatas:

- **Encefalitis transmitida por garrapatas** (Europa Central).



DIAGNÓSTICO: **serología** (IgG, IgM). **PCR** sangre/LCR (viremia de corta duración)

VIRUS DENGUE

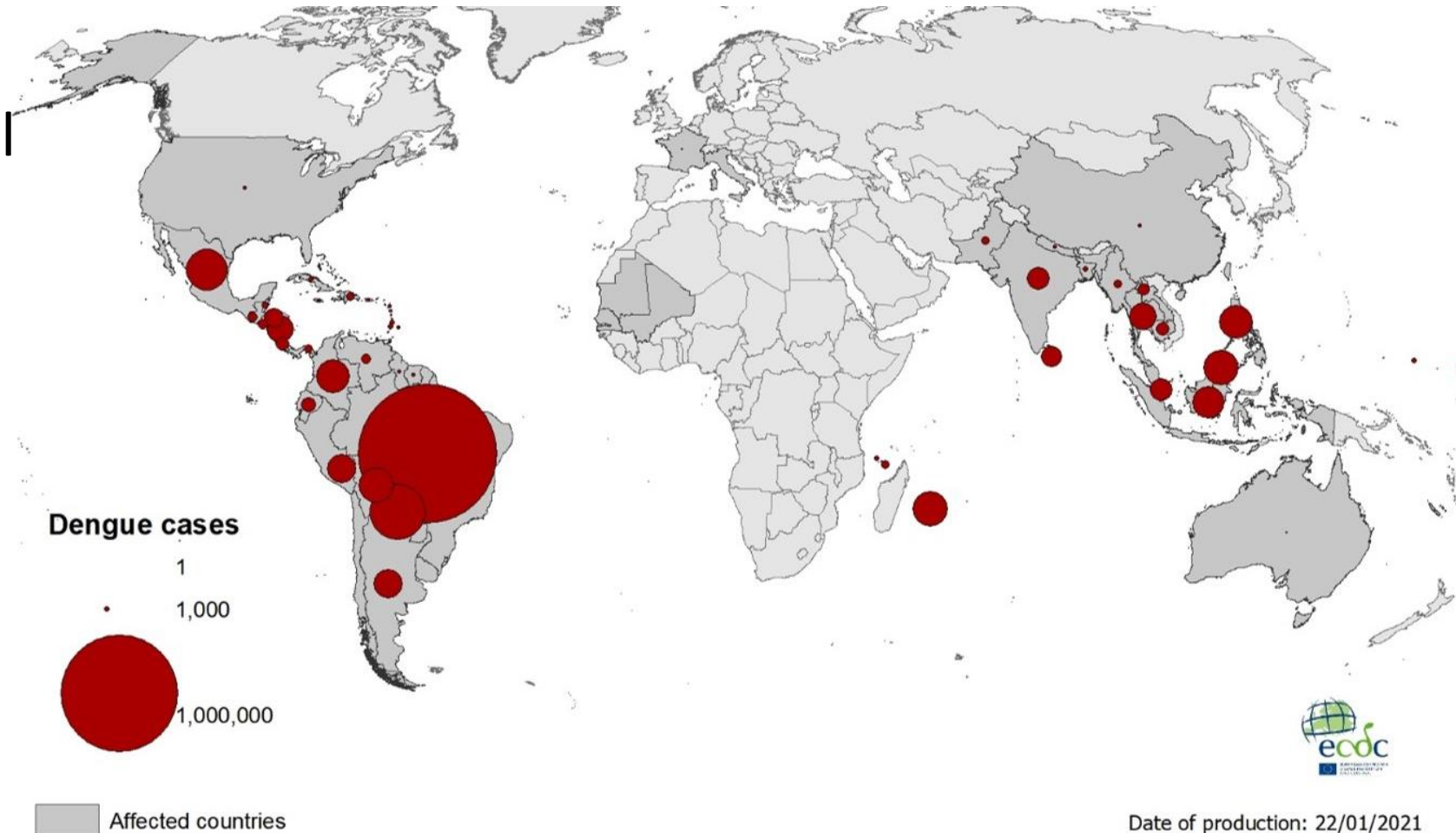
- Género *Flavivirus* (familia *Flaviviridae*)
- Hebra de ARN de polaridad positiva
- 4 serotipos de virus: 1, 2, 3 y 4
 - Inmunidad de larga duración contra SEROTIPO infectante
 - No protegen frente a otros serotipos
- TRANSMISIÓN: picadura de HEMBRAS del mosquito género *Aedes*
 - *Aedes aegypti* → vector principal nivel mundial
 - *Aedes albopictus*





DISTRIBUCIÓN GEOGRÁFICA

- Zonas tropicales y subtropicales de todo el mundo
- OMS → endémico en 5 de sus 6 regiones
 - África
 - Mediterráneo Oriental
 - Asia Sudoriental
 - América
 - Pacífico Occidental



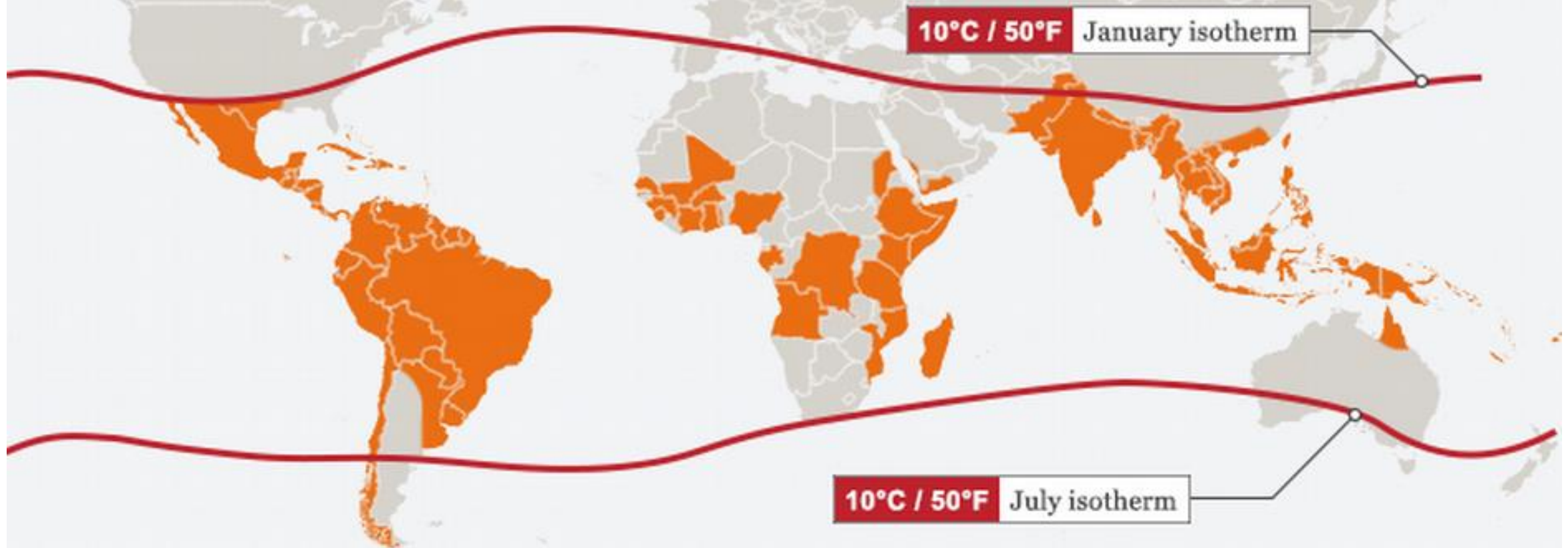
Date of production: 22/01/2021

Riesgo de salud pública para territorios no endémicos + presentes mosquitos del género *Aedes* → varios países de la región Europea

Dengue fever worldwide prevalence (2013)

■ The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of *Aedes aegypti*, the principal mosquito vector of dengue viruses.

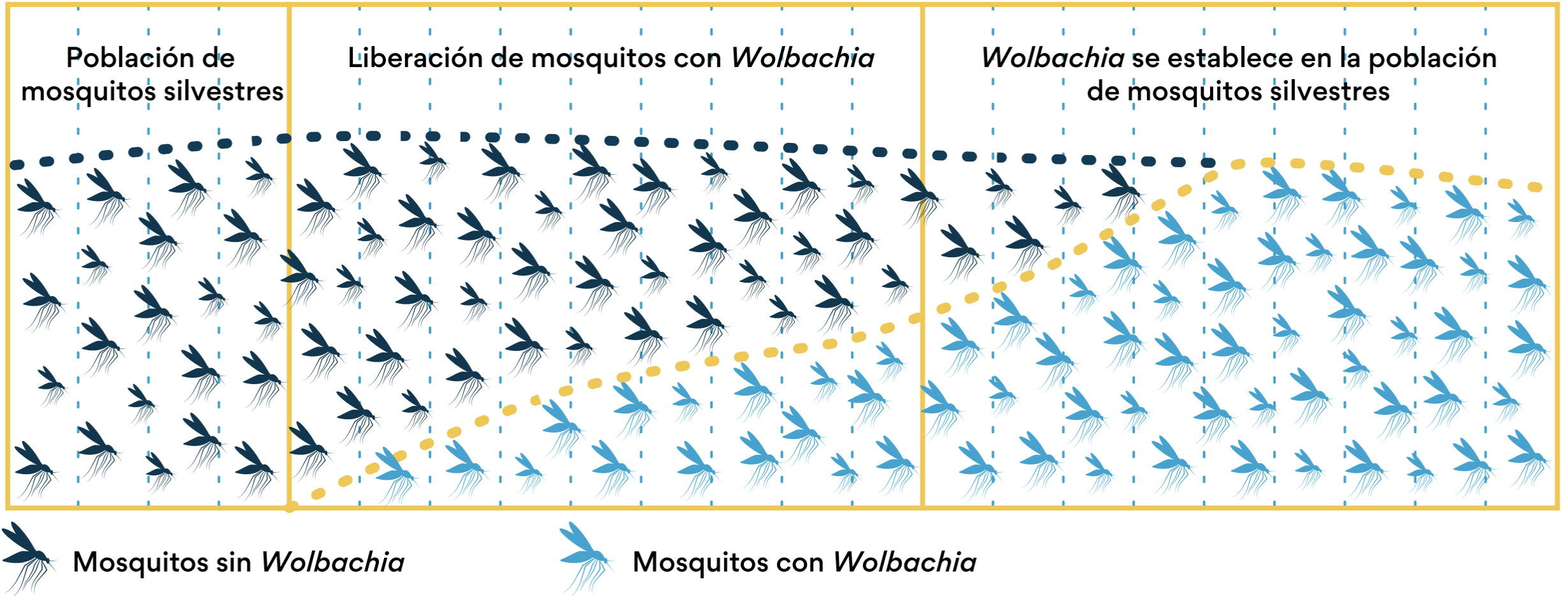
■ Countries or areas where dengue has been reported



Source: WHO

© DW

PERIODO DE LIBERACIÓN

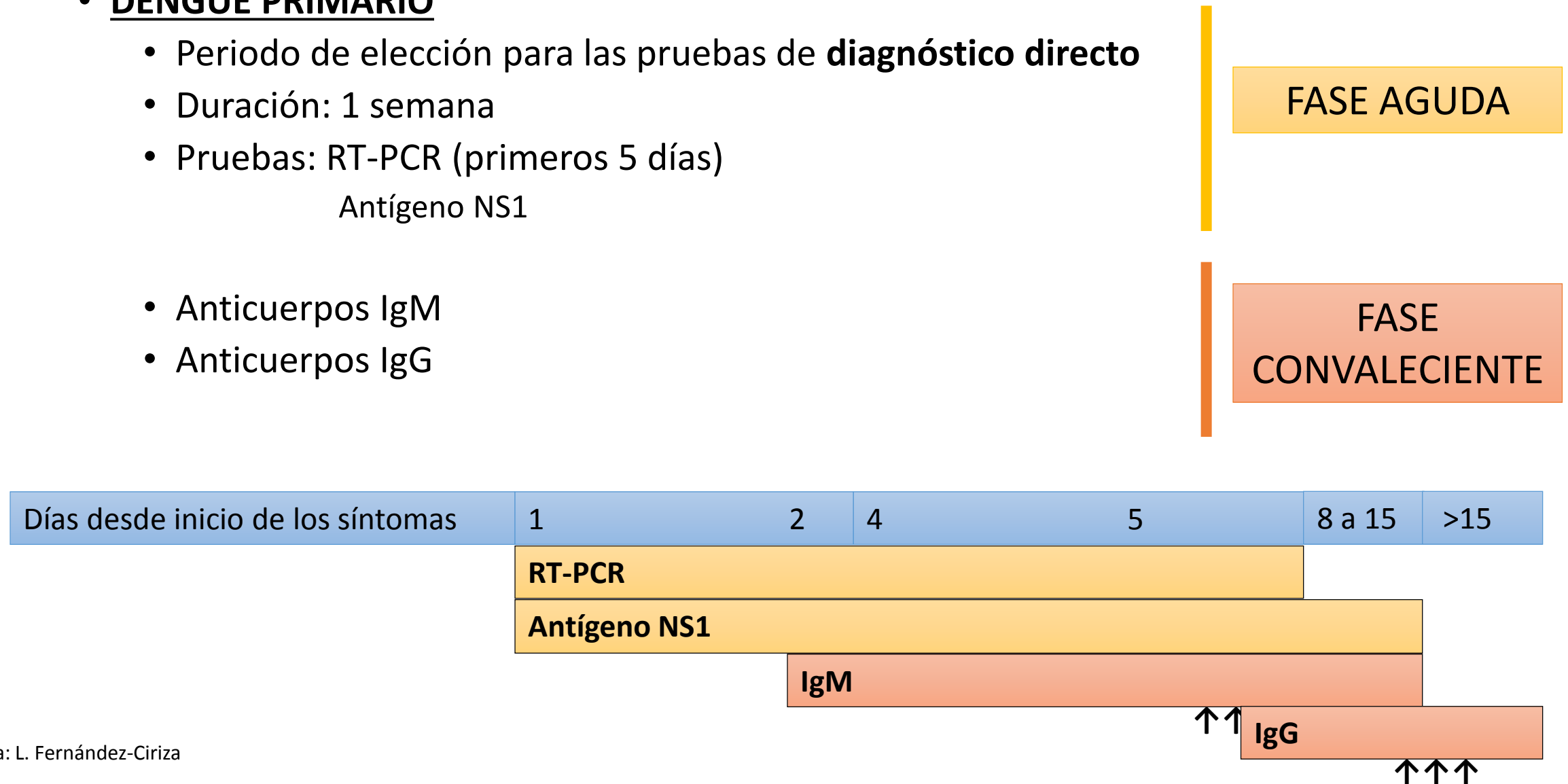


Reemplazo de Mosquito Aedes (con *Wolbachia*): no transmisor de Dengue, Zika, Fiebre Amarilla, Chikungunya

➤ CINÉTICA DE LOS MARCADORES DE INFECCIÓN

• DENGUE PRIMARIO

- Periodo de elección para las pruebas de **diagnóstico directo**
- Duración: 1 semana
- Pruebas: RT-PCR (primeros 5 días)
Antígeno NS1
- Anticuerpos IgM
- Anticuerpos IgG



FIEBRE AMARILLA

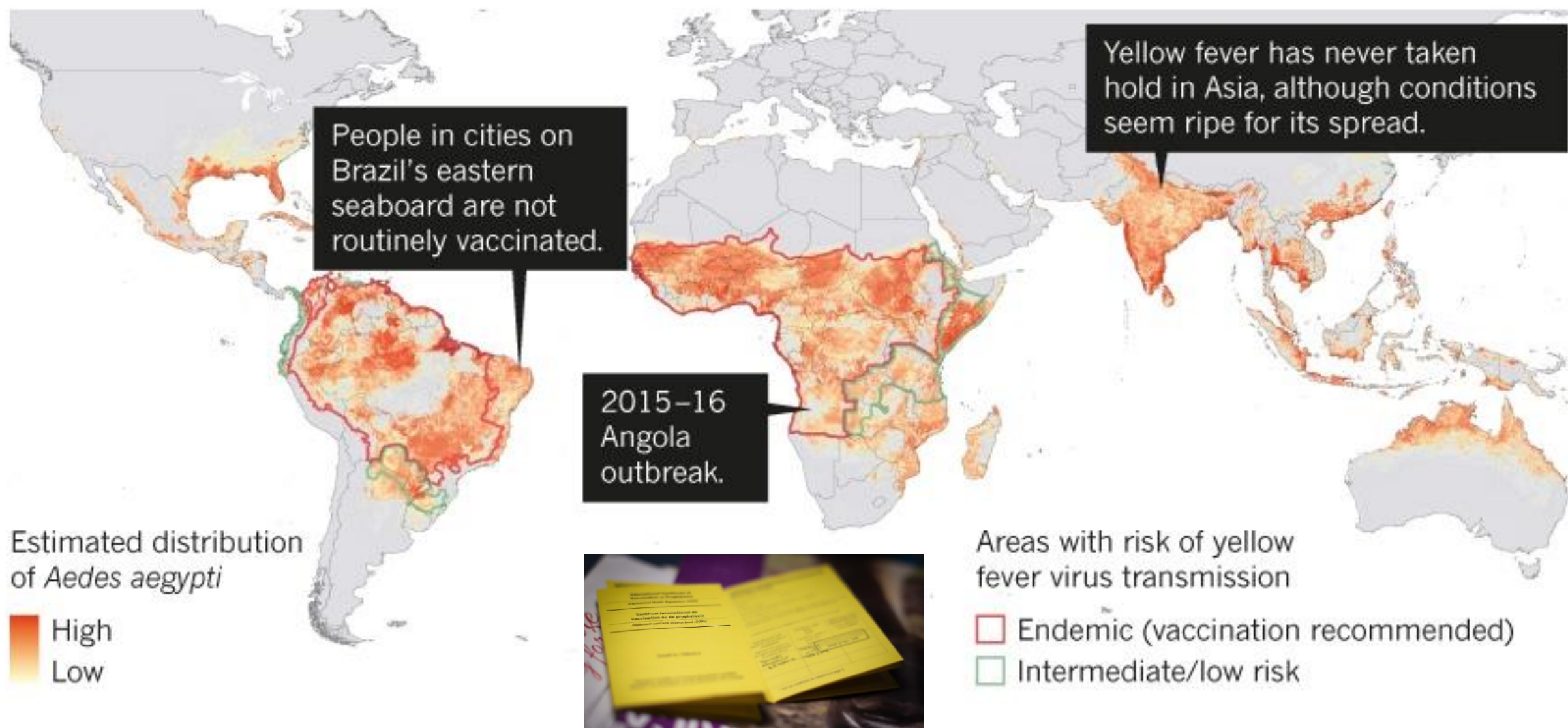
- Género *Flavivirus* (familia *Flaviviridae*)
- Valorar zona de viaje
- DIAGNÓSTICO:
 - IgG / IgM
 - Neutralización
 - RT-PCR viremia inferior a síntomas
 - Inmunohistoquímica
- Vacunación Obligatoria en determinados países



WHERE MIGHT YELLOW FEVER GO NEXT?

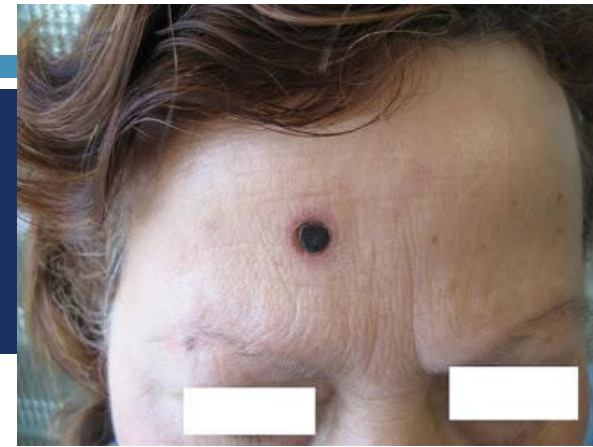
©nature

An ongoing outbreak of yellow fever in Angola has scientists worried that the virus might spread to cities that harbour its urban carrier, the *Aedes aegypti* mosquito.



RICKETTSIAS

- Parásito Intracelular Obligado
- Zoonosis (excepto *R.prowazekii*)
- Transmisión por artrópodos (excepto *C.burnetti*)
- Diagnóstico: **serología**
- Tratamiento: **doxiciclina**



Especie	Transmisión	Síndrome clínico
<i>R. conorii</i>	Garra pata (<i>Rhipicephalus sanguineus</i>)	Fiebre Botonosa Mediterránea (fiebre, mialgias, mancha negra)
<i>R. ricketsii</i>	Garra pata	Fiebre Montañas Rocosas
<i>R. prowazekii</i>	Piojos (<i>Pediculus humanus</i>)	Tifus Exantemático Epidémico
<i>R. typhi</i>	Pulga rata	Tifus Exantemático Endémico
<i>C. burnetti</i>	AÉREA	Fiebre Q - Aguda: hepatitis, neumonía - Crónica: endocarditis

TRANSMISIÓN HEPATITIS



VHB



■ Fecal-oral

- Hepatitis A
- Hepatitis E



■ Artrópodo vector

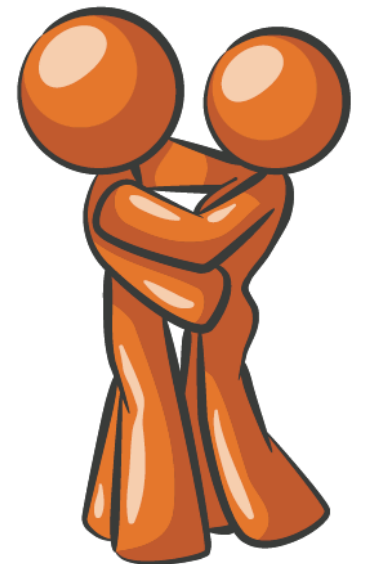
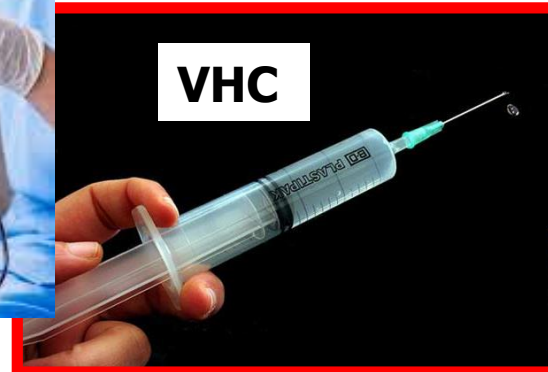
- Dengue
- Fiebre Amarilla
- ...

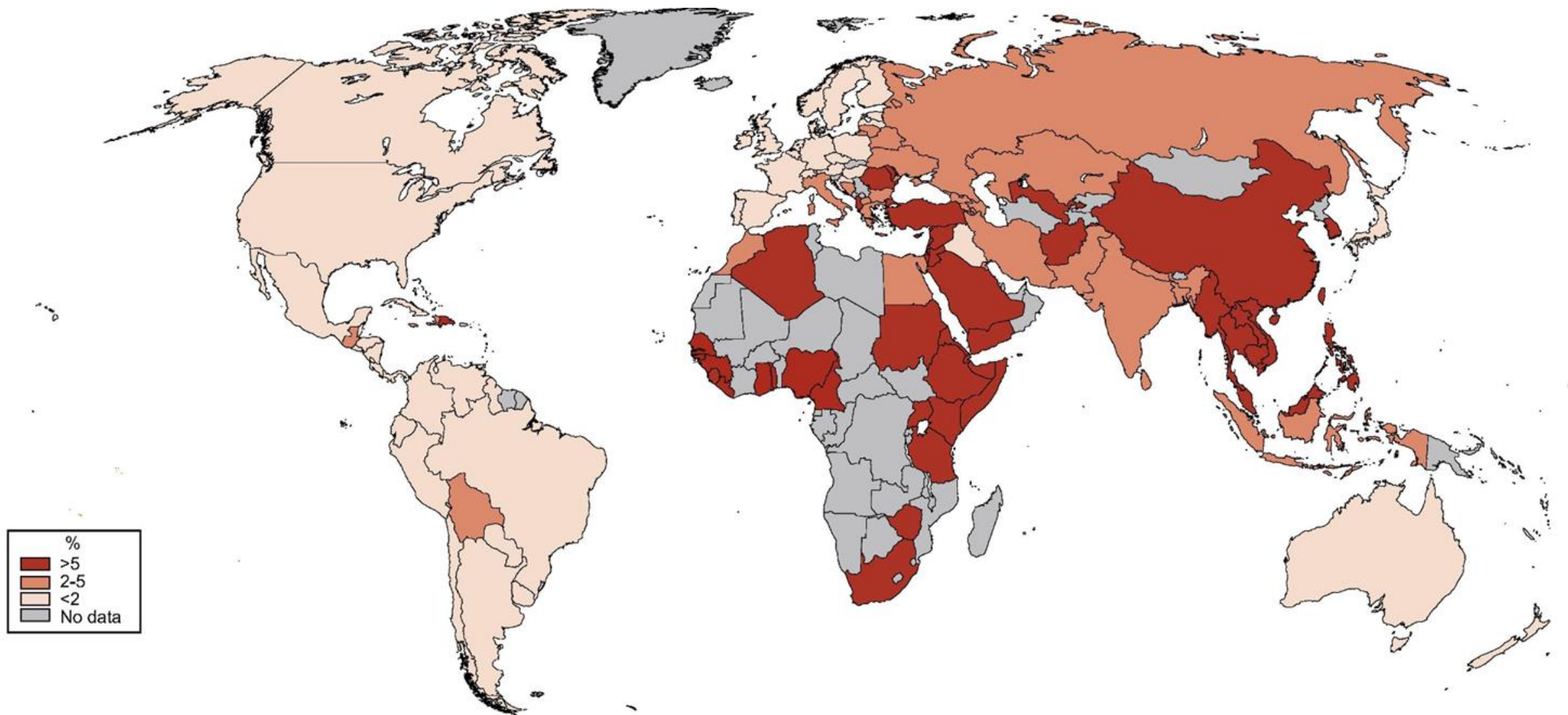


■ Parenteral/Sexual

- Hepatitis B/D
- Hepatitis C

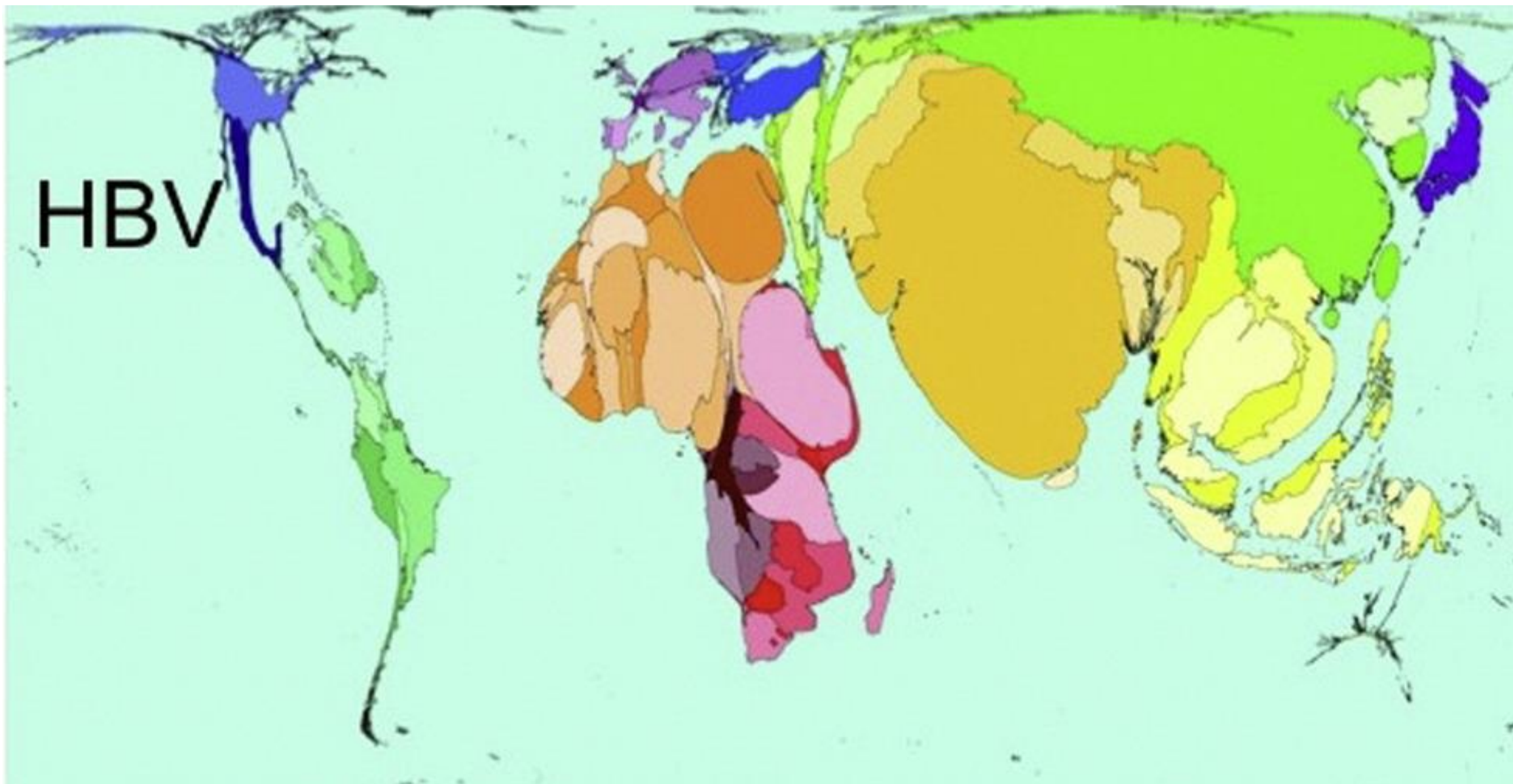
VHC





Global HBV Prevalence

Sharma, et al. *Journal of Hepatology*, 2015.



Mapas proporcionales a prevalencia infección

Matthews et al, *J Clin Virol* 2014



Know Hepatitis B

Campaign Materials in
multiple languages +

Professional Resources

About the Campaign

About our Partner

Spread the Word

Contact Us

[Read more information](#)
on viral hepatitis from
CDC.



愛家人從關愛自己開始

가족 사랑의 첫 걸음은
당신의 건강을 돌보는 일입니다.

Yêu thương gia đình bắt đầu bằng sự
chăm sóc cho bản thân.

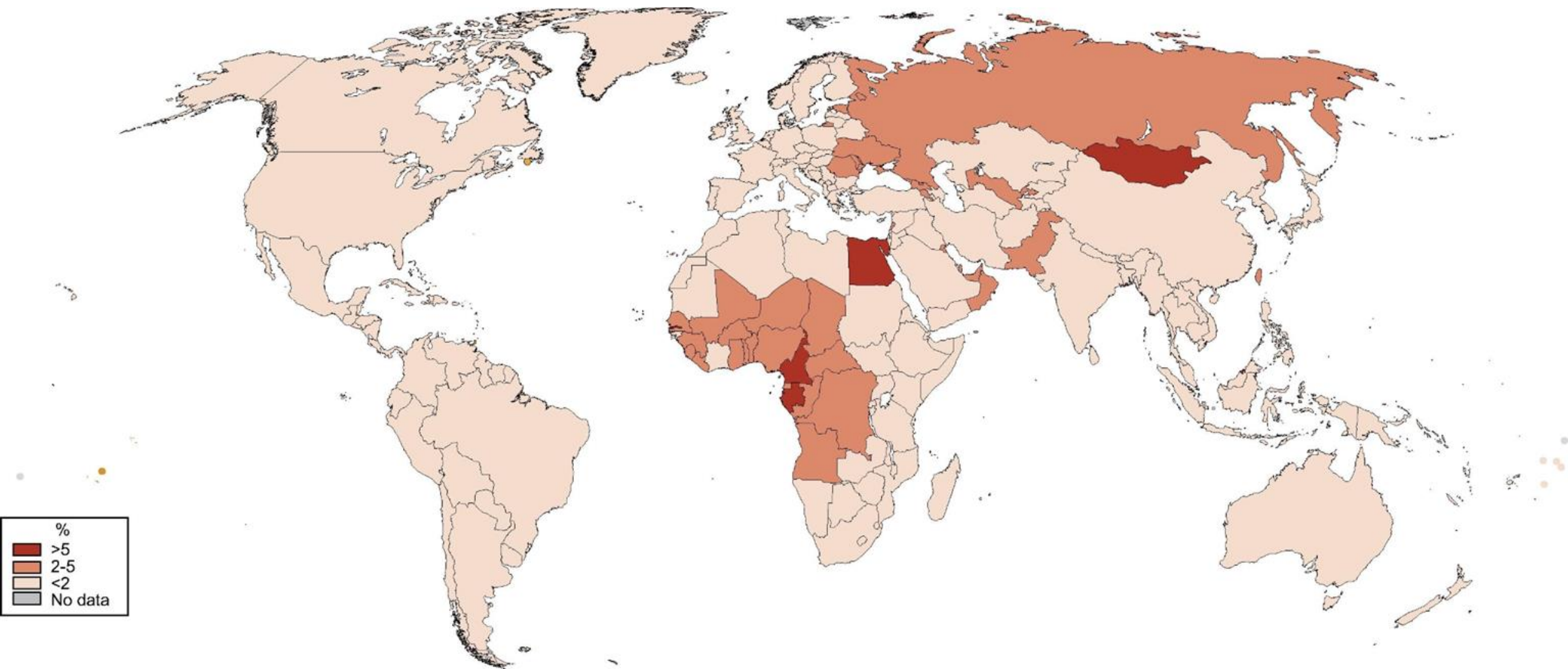


Get tested for Hepatitis B.
Treatments are available that can save your life.



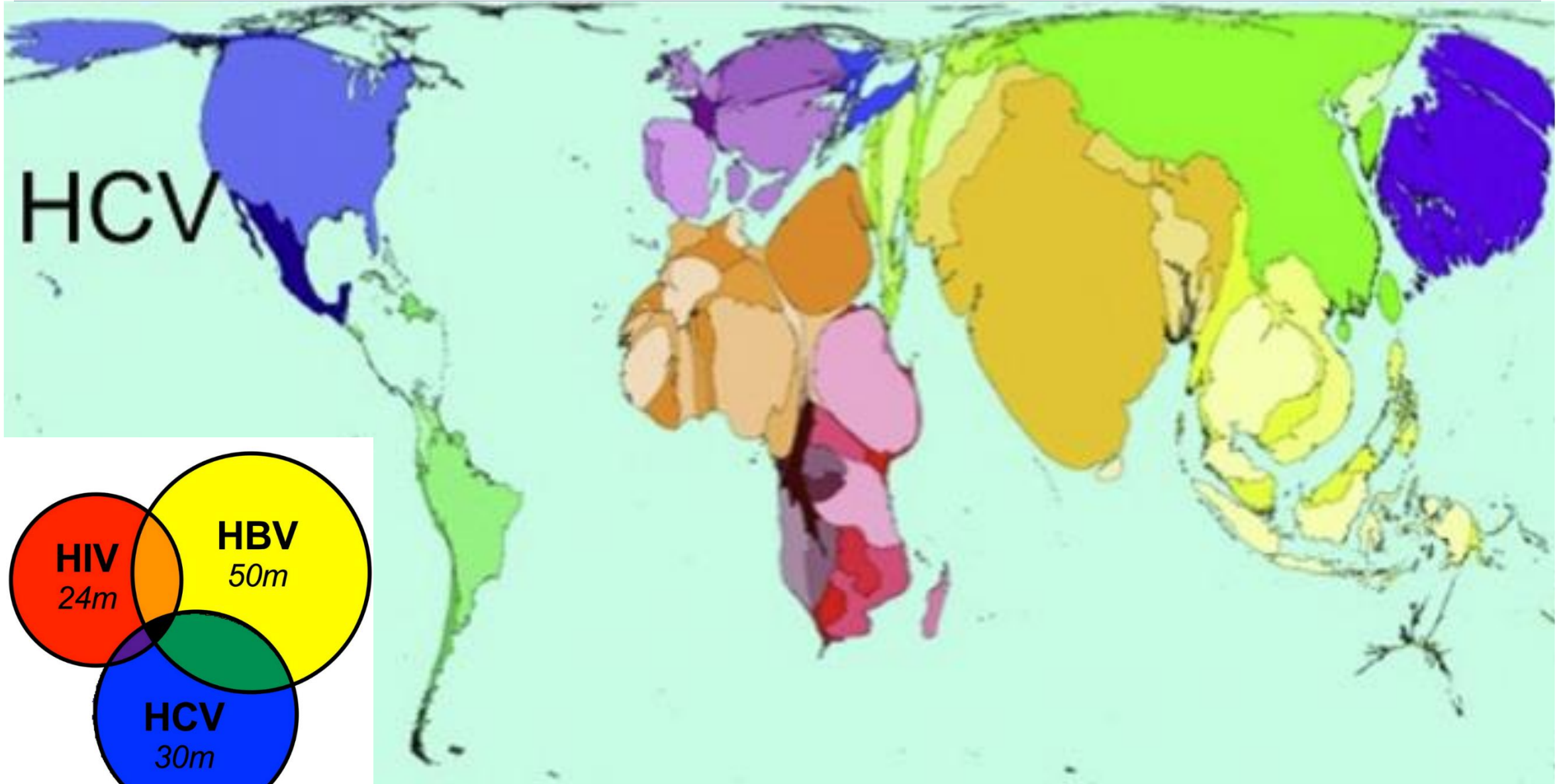
Hepatitis B disproportionately affects Asian Americans

Hepatitis B is common worldwide, especially in many parts of Asia and the Pacific Islands. In the United States, hepatitis B disproportionately affects Asian Americans. While Asian Americans make up 6% of the US population, they account for more than 60% of Americans living with hepatitis B.



Global HCV Prevalence

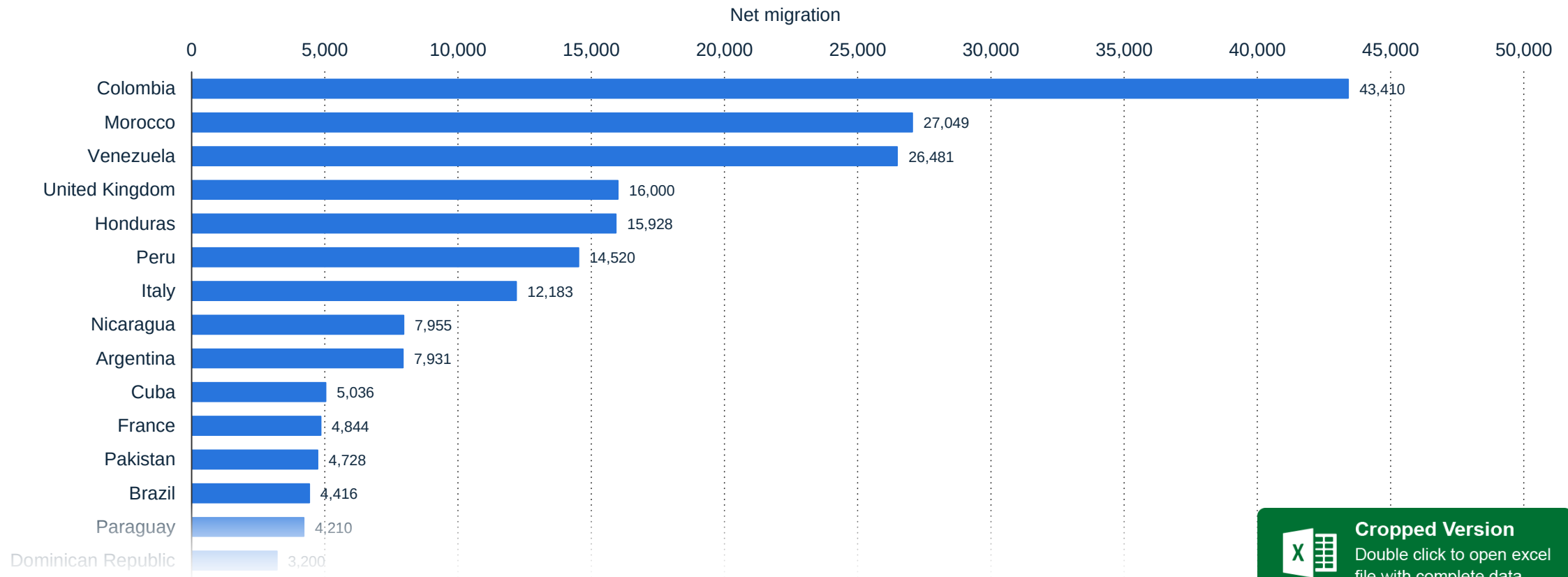
Sharma, et al. *Journal of Hepatology*, 2015.



SSA: 20% VHC global

Net migration of foreign nationals to Spain during 2020, by nationality

Net migration of foreign nationals to Spain 2020, by nationality



Cropped Version

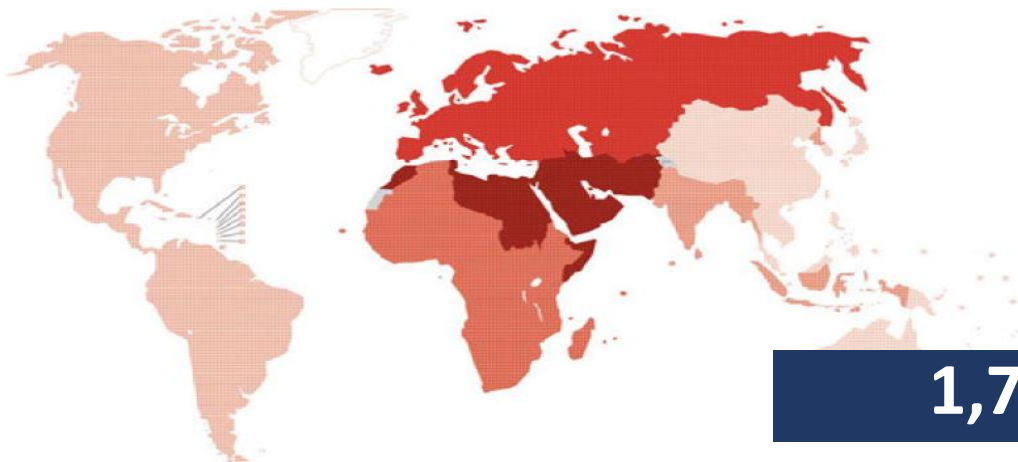
Double click to open excel file with complete data

Note(s): Spain; 2020

Further information regarding this statistic can be found on [page 8](#).

Source(s): INE (Spain); [ID 446008](#)

Table 3 (with map). Incidence of HCV infection in the general population, by WHO region, 2015:
1.75 million new infections in 2015



INCIDENCIA VHC

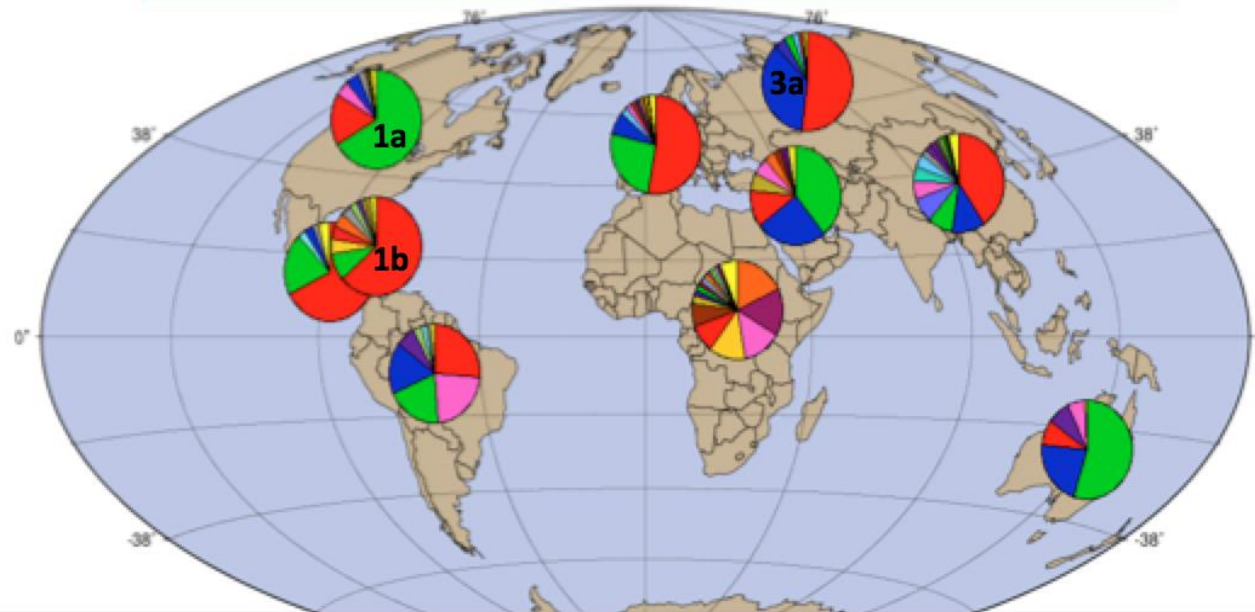
1,75 millones nuevos casos VHC en 2015

WHO region	Map key	Incidence rate (per 100 000)		Total number (000)	
		Best estimate	Uncertainty interval	Best estimate	Uncertainty interval
African Region		31.0	22.5–54.4	309	222–544
Region of the Americas		6.4	5.9–7.0	63	59–69
Eastern Mediterranean Region		62.5	55.6–65.2	409	363–426
European Region		61.8	50.3–66.0	565	460–603
South-East Asia Region		14.8	12.5–26.9	287	243–524
Western Pacific Region		6.0	5.6–6.6	111	104–124
Global		23.7	21.3–28.7	1 751	1 572–2 120

Unacceptably low SVR rates in African patients with unusual HCV sub-genotypes: Implications for global elimination

The distribution of HCV subtypes differs between Africa and other regions

Distribution of global HCV subtypes within the Los Alamos HCV database



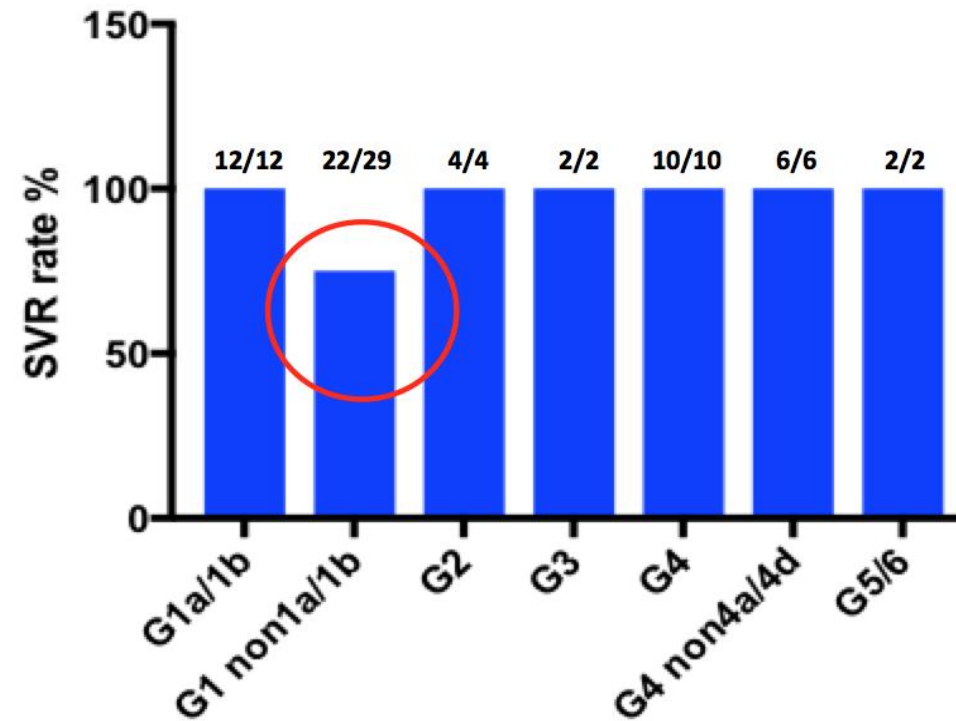
HCV database data suggests the majority of **G1 non 1a/1b** and **G4 non 4a/4d** sequences originate from Africa. We will refer to these as '*distinct subtypes*'.

Unacceptably low SVR rates in African patients with unusual HCV sub-genotypes: Implications for global elimination

K. Childs, C. Davis, S. Montague, M. Cannon, D. Smith
G. [Dusheiko](#), E. Thomson, K. Agarwal



Overall SVR rate of 75% in Distinct G1 Subtypes



Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study



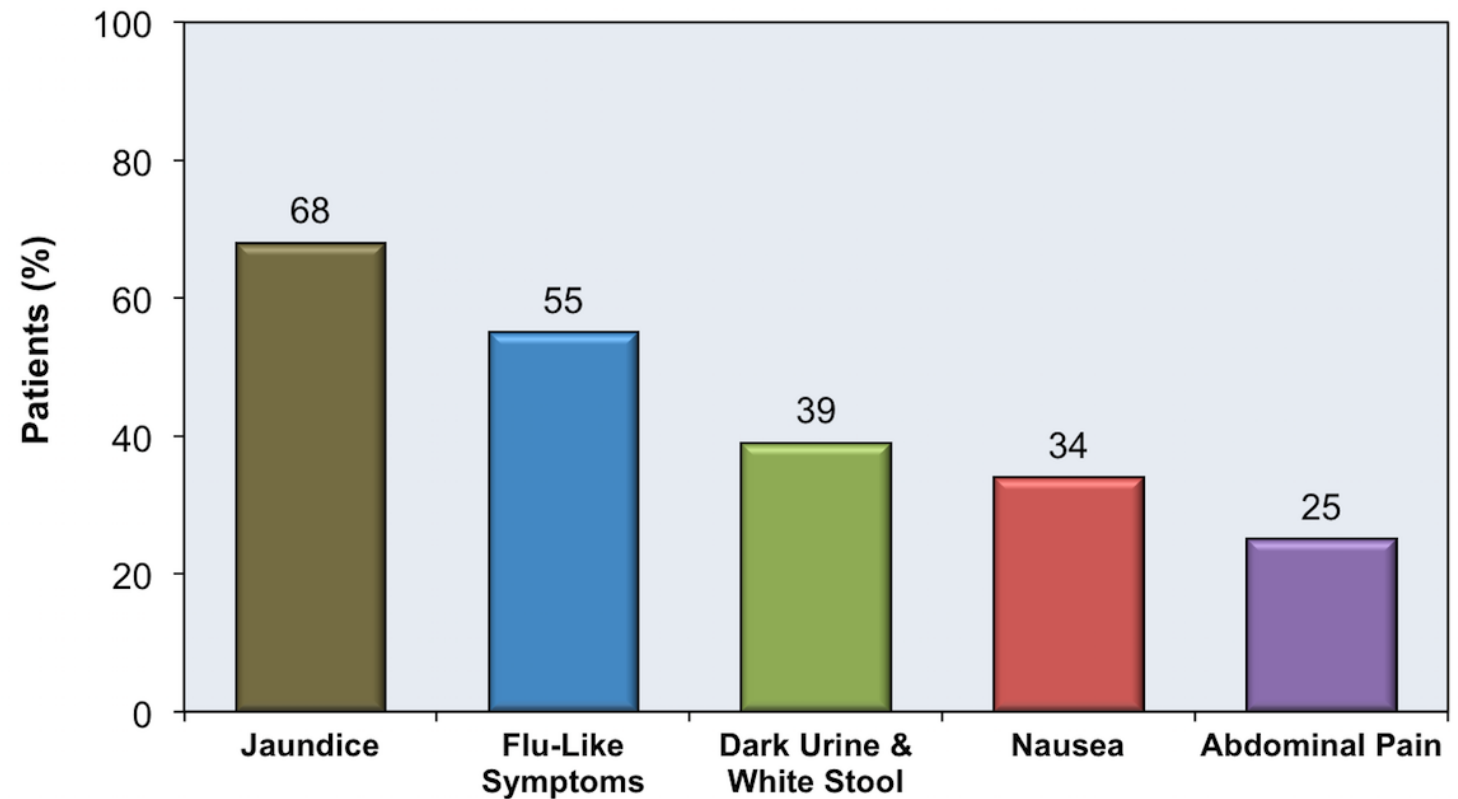
The Polaris Observatory HCV Collaborators*



INFECCIÓN AGUDA POR VHC

GENERALIDADES

- Hepatitis C de menos de 6 meses de evolución
- Diagnóstico:
 - Seroconversión
 - ARNVHC(+) sin anticuerpos
 - FRENAR TRANSMISIÓN
- 75-85% ASINTOMÁTICA
- Síntomas: semana 4-12



Estimating Acute Viral Hepatitis Infections From Nationally Reported Cases

- Conocer modo transmisión
- Control de brotes
- Problema: cifras no reales
- Diagnóstico inadecuado



FIGURE 1—Steps used to estimate new infections of viral hepatitis among adults: United States, 2011.

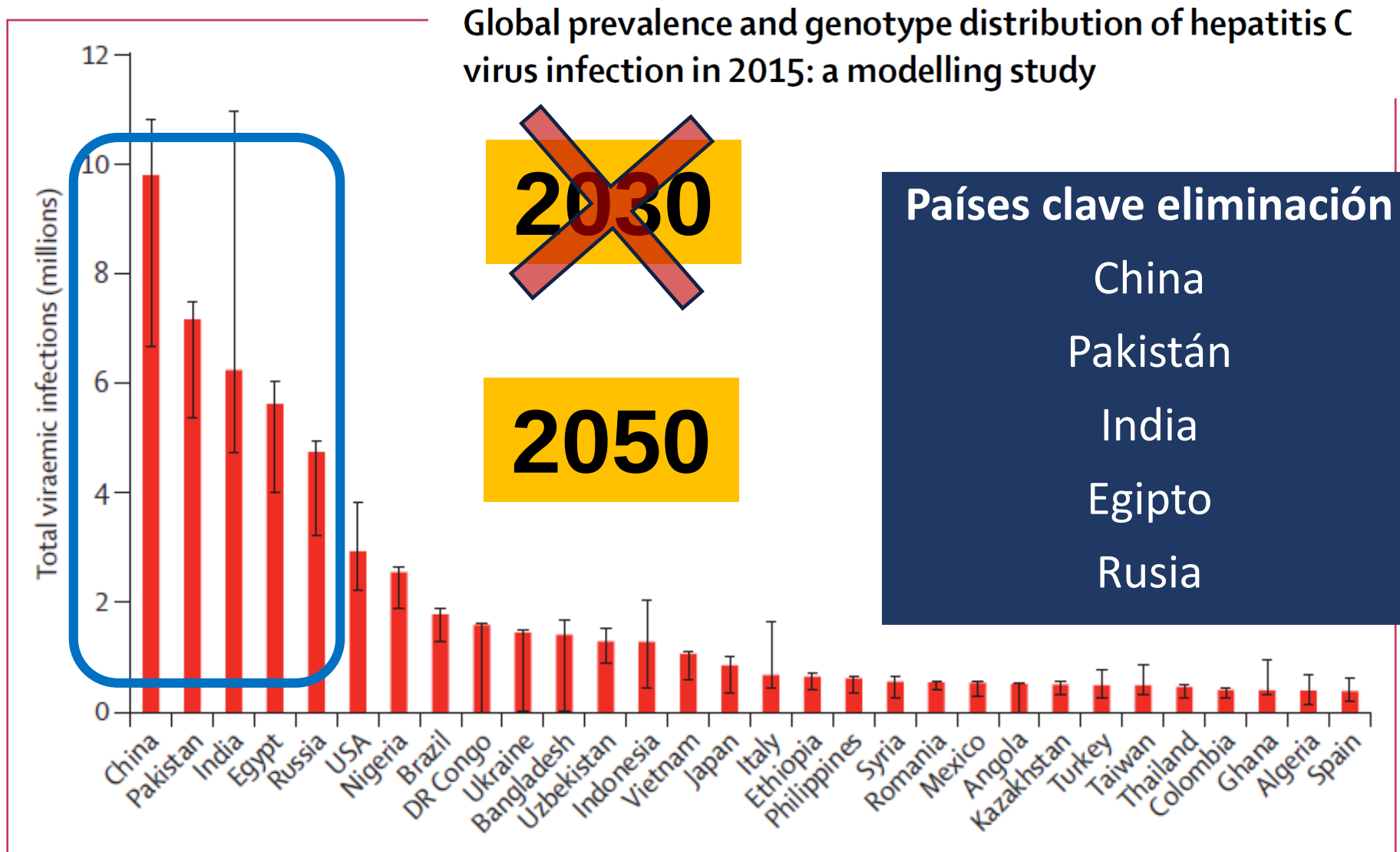
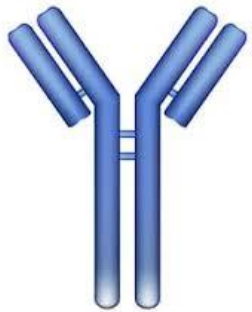
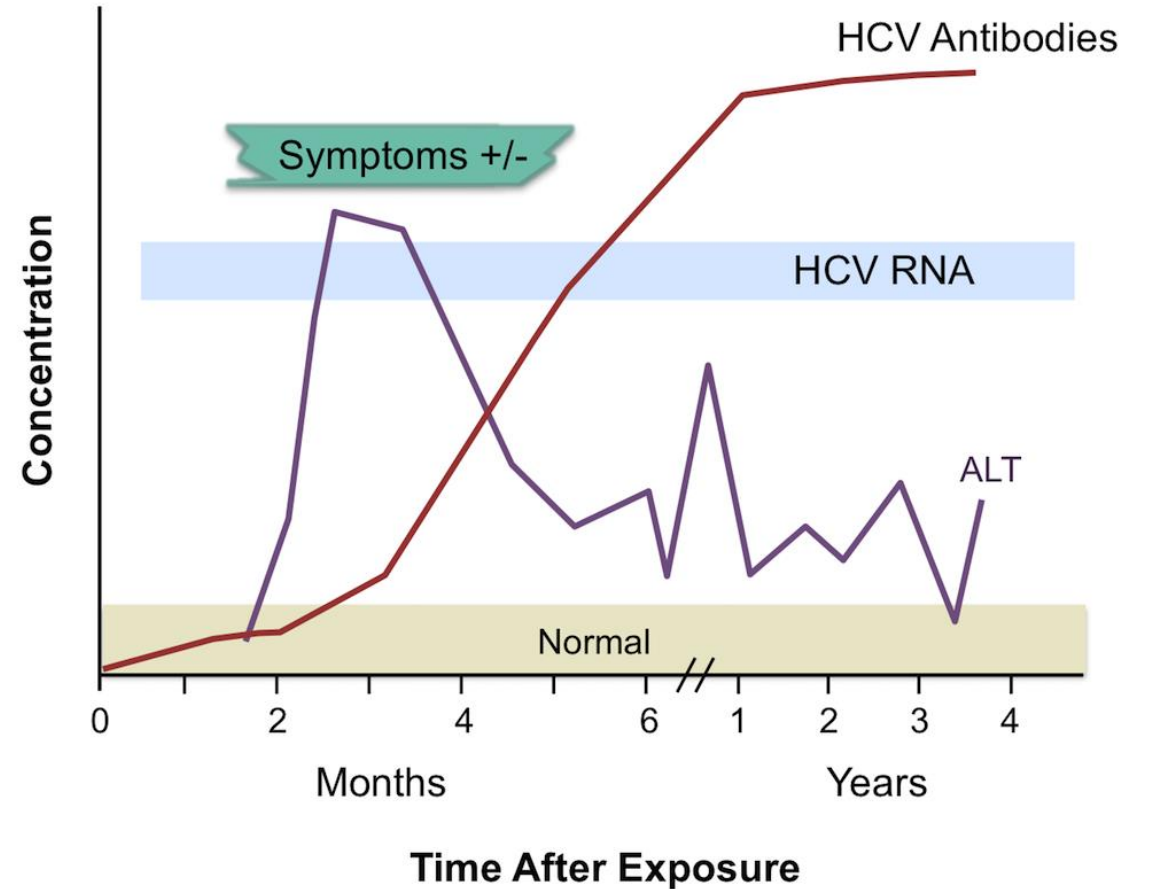


Figure 2: Countries accounting for 80% of the total viraemic HCV infections

HCV=hepatitis C virus.

DIAGNÓSTICO



Seroconversión anti-VHC (antes de 12 meses)
ARN VHC(+)/Ag VHC y Acs anti-VHC (-)
Estrategias novedosas (Afinidad, NGS)



HEPATITIS AGUDA EN VIAJEROS E INMIGRANTES

TAKE HOME MESSAGES

- Viajes internacionales/Inmigración: tendencia ascendente
- Alta susceptibilidad población española **Hepatitis A** (95% menores 20 años y sólo el 25% de viajeros se vacuna): **IgM**
- **Hepatitis E**: genotipo infectante según región (**IgM/PCR**)
- **Orthohepevirus-C** hepatitis humana similar VHE origen zoonótico y distribución mundial (**PCR**)
- Leptospirosis: causa emergente relacionada con baño y contacto aguas conminadas (PCR/IgM)
- Hepatitis a partir de arbovirosis (Dengue, Fiebre Amarilla, Zika, Chikungunya) (IgM/neutralización)
- Hepatitis B y C, riesgo de viaje/inmigración áreas hiperendémicas. Afectación por subtipos poco frecuentes de VHC

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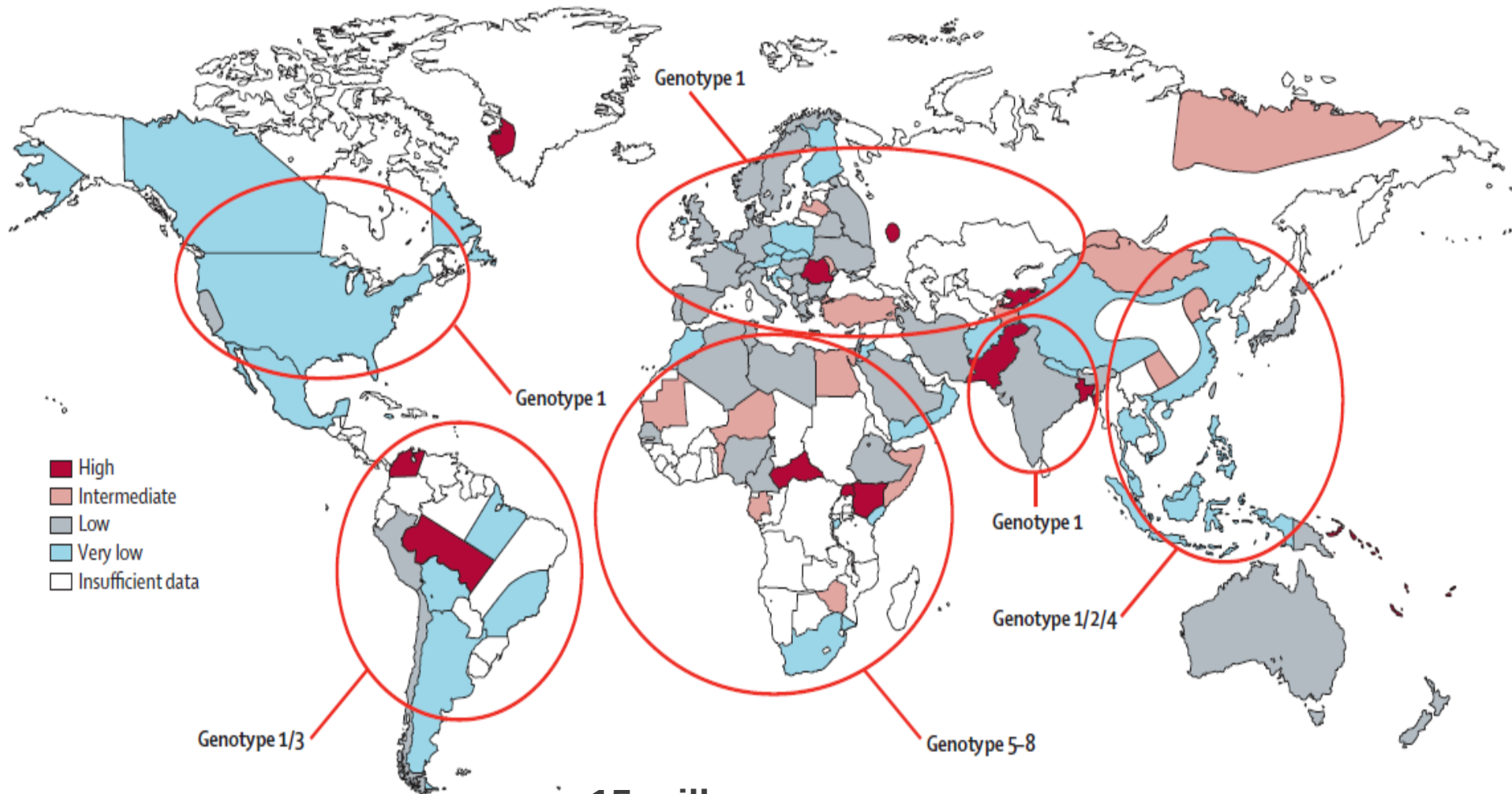
Muchas gracias

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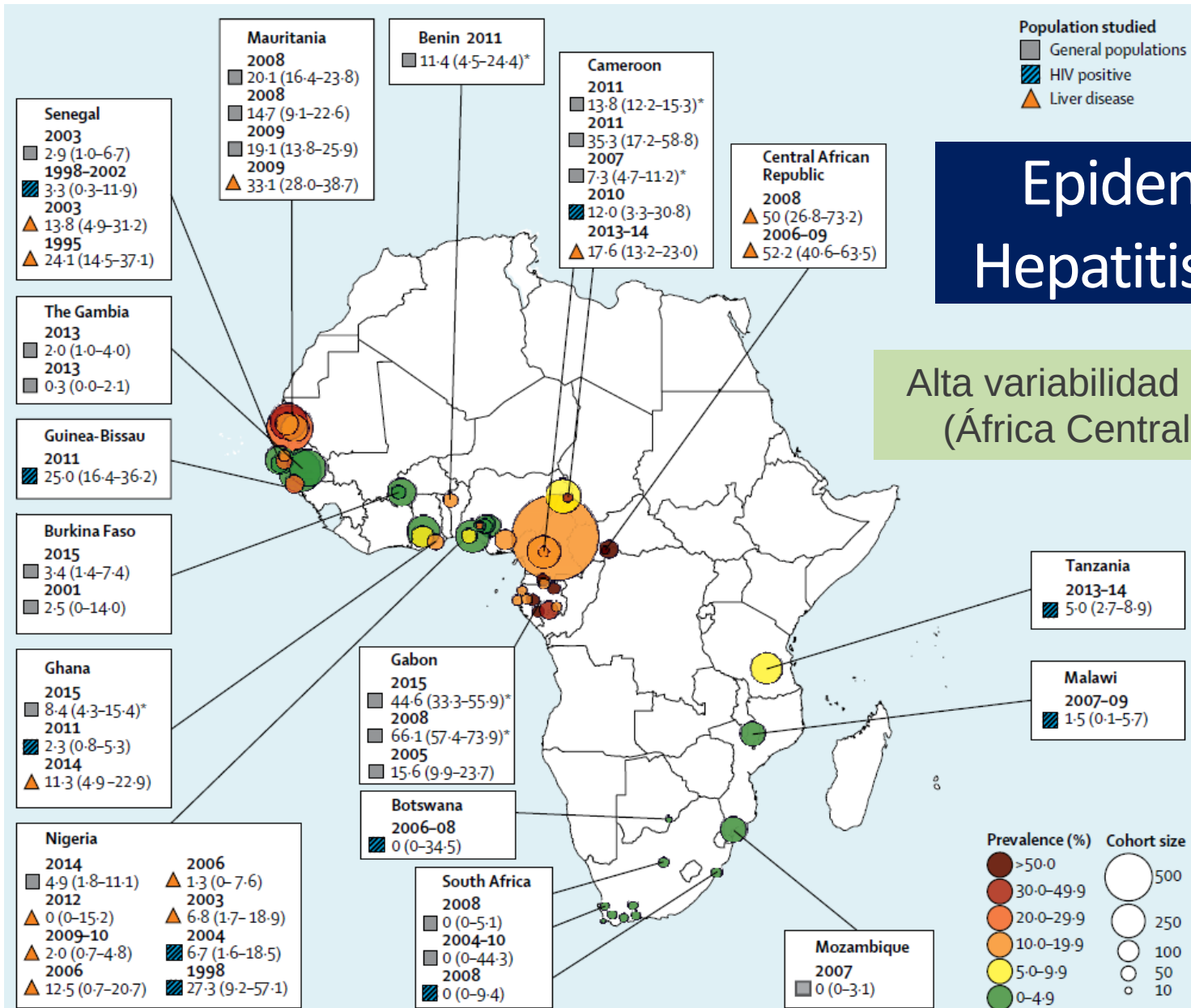
Epidemiología de la Hepatitis D: 8 GENOTIPOS



**15 millones personas
infectadas VHD**

Epidemiología Hepatitis D: Africa

Alta variabilidad seroprevalencia
(África Central y Occidental)



- 
- × 2013, 3.2% of the global population (231 million individuals) migrated

- 
- × 1,4 millones muertes por hepatitis viral cada año
 - × Inequalities in access to healthcare
 - × Reaching at risk populations
 - × Providing access to screening and effective treatment
 - × Stigma
 - × COVID-19 paso atrás

Dunn R et al. Viral hepatitis in 2021: The challenges remaining and how we should tackle them. World J Gastroenterol. 2022

Travelers' Health

Travelers Health > CDC Yellow Book > Contents



Travelers Health

Destinations

Travel Notices +

Find a Clinic +

Travel Advice and Resources +

Disease Directory +

CDC Yellow Book -

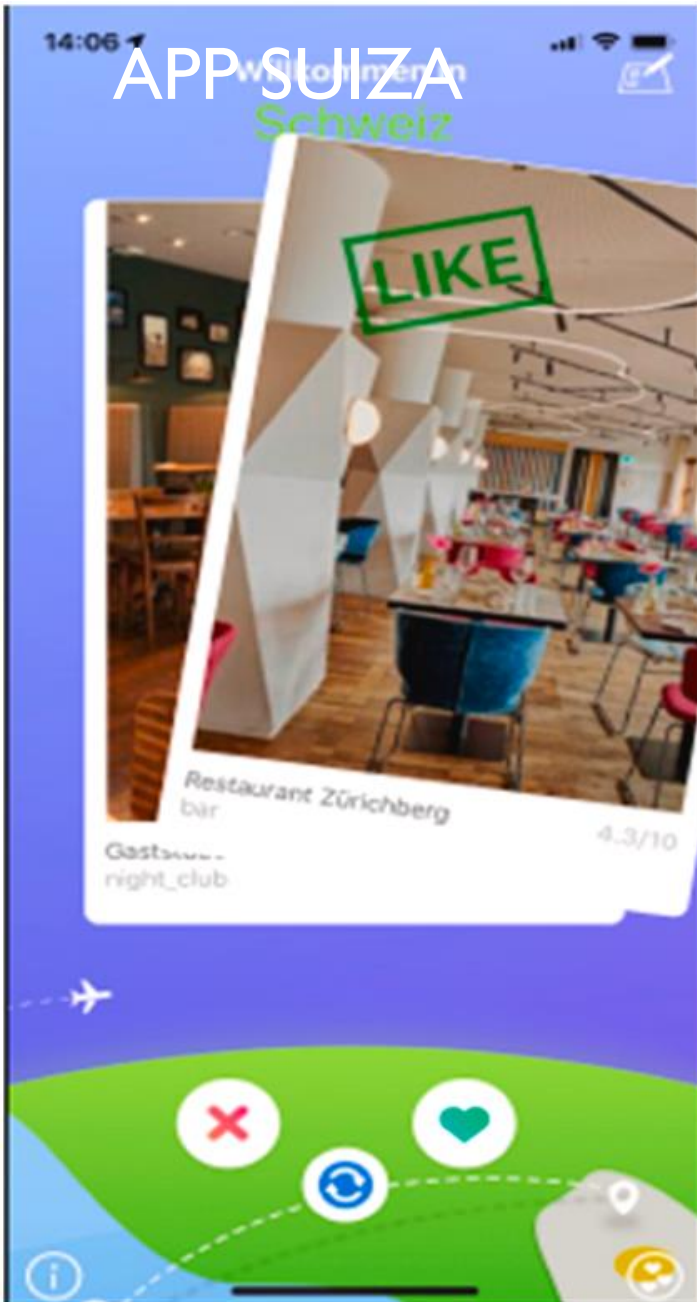
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APP SUIZA



14:08

Aktivitäten

10. Ich bin heute mit einem Fahrrad/Motorrad/Tuk-Tuk/Bajaj/Mototaxi gefahren
(bitte alles Zutreffende ankreuzen):

11. Ich hatte heute Geschlechtsverkehr ohne Kondom
(bitte alles Zutreffende ankreuzen):

12. Jetzt folgen einige Fragen über einen Unfall oder eine Verletzung, welche Sie heute möglicherweise erlebt haben.
Alles Zutreffende bitte nach Schweregrad bewerten (0: kein Ereignis, 1: Mild, 2: Moderat, 3: Moderat-Schwer, 4: Schwer)

Verkehrsunfall Moderat-Schwer

Knee fracture

Sturz o. Verstauchung Kein Ereignis

Sportunfall Kein Ereignis

Wunde, Schnittverletzung

14:06

Info

Tourist App

☒ Erinnerung täglich um 18:00

Diese App wurde von antavi GmbH für die Universität Zürich und das Schweizerische Tropen- und Public Health-Institut entwickelt.

Notfallnummer bei medizinischen Notfällen
+41 61 2848 144
Swiss TPH (24h besetzt). Kostenpflichtig nach Ärztetarif TarMed.

Kontakt für studienspezifische Fragen

Tourist Studie

Zürich
tourist@ebpi.uzh.ch
Oder besuchen Sie unsere [Website](#)

Basel
tourist@swisstph.ch
Oder besuchen Sie unsere [Website](#)

User Info
7A597501-9B86-4937-A655-613F416EAC59
v4

TRAVEL APPLICATION (APP) FOR REAL-TIME DATA MONITORING DURING TRAVEL

Background: The adoption of mHealth technology in travel medicine is a relatively new and unexplored field. We have further developed a **TRAVEL application (app) for real-time data monitoring during travel**. In this manuscript we report on the feasibility using this new app in a large and diverse cohort of travellers to three continents.

Methods: We enrolled **1000 participants from the travel clinics of Zurich and Basel, Switzerland**, aged ≥ 18 years, travelling to **Thailand, India, China, Tanzania, Brazil and Peru between 09/2017–01/2019**. Participants included healthy travellers, individuals with pre-existing chronic diseases and elderly travellers (≥ 60 years). Participants completed an app-based daily survey on risk behaviours/health incidents pre-, during and after travel. Simultaneously, **GPS locations were tightly collected and linked to environmental data**.

Results: **793 (79%) travellers answered at least one questionnaire during their trip**. Participants' median age was 34 years (range 18–84 years); 8% were aged ≥ 60 years; 55% female; **32% had pre-existing chronic diseases**. Completion rates were similar in younger and elderly travellers and in those with and without pre-existing diseases.

Conclusions: **The use of a smartphone app is a feasible method for collecting behavioural and health data in elderly travellers and individuals with chronic diseases travelling to three continents.**

- ✗ Methods: All medical students who had performed an elective in the tropics between July 2006 and December 2008 were sent an informative email asking them to complete a web-based questionnaire.
- ✗ Results: 180 of 242 (74%) students completed the questionnaire. Regarding the risk of bloodborne viral infection: 67% of all students and 32% of junior students engaged in procedures that constitute a risk of exposure to bloodborne viral infection, often in countries with high HIV prevalence rates. None of nine students who experienced possible or certain mucosal or percutaneous exposure to potentially infectious body fluids reported the exposure at the time it occurred and none used PEP. Regarding other health risks: 8 of 40 (20%) students stopped using mefloquine due to adverse effects. This left a sizeable proportion unprotected in countries that are hyperendemic for malaria. Post-travel screening for schistosomiasis, tuberculosis (tuberculin skin test) and carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) encompassed approximately half of all students who should have been screened.
- ✗ Conclusions: Based on the results of this study we have adopted an integral set of measures to reduce the health risks associated with an elective abroad. The pre and post-travel consult has been centralized and standardized as well as the distribution of PEP. In addition we have developed a mandatory module on Global Health for all medical students planning an elective abroad.

Sharafeldin et al. BMC Medical Education 2010. Health risks encountered by Dutch medical students during an elective in the tropics and the quality and comprehensiveness of pre-and post-travel care



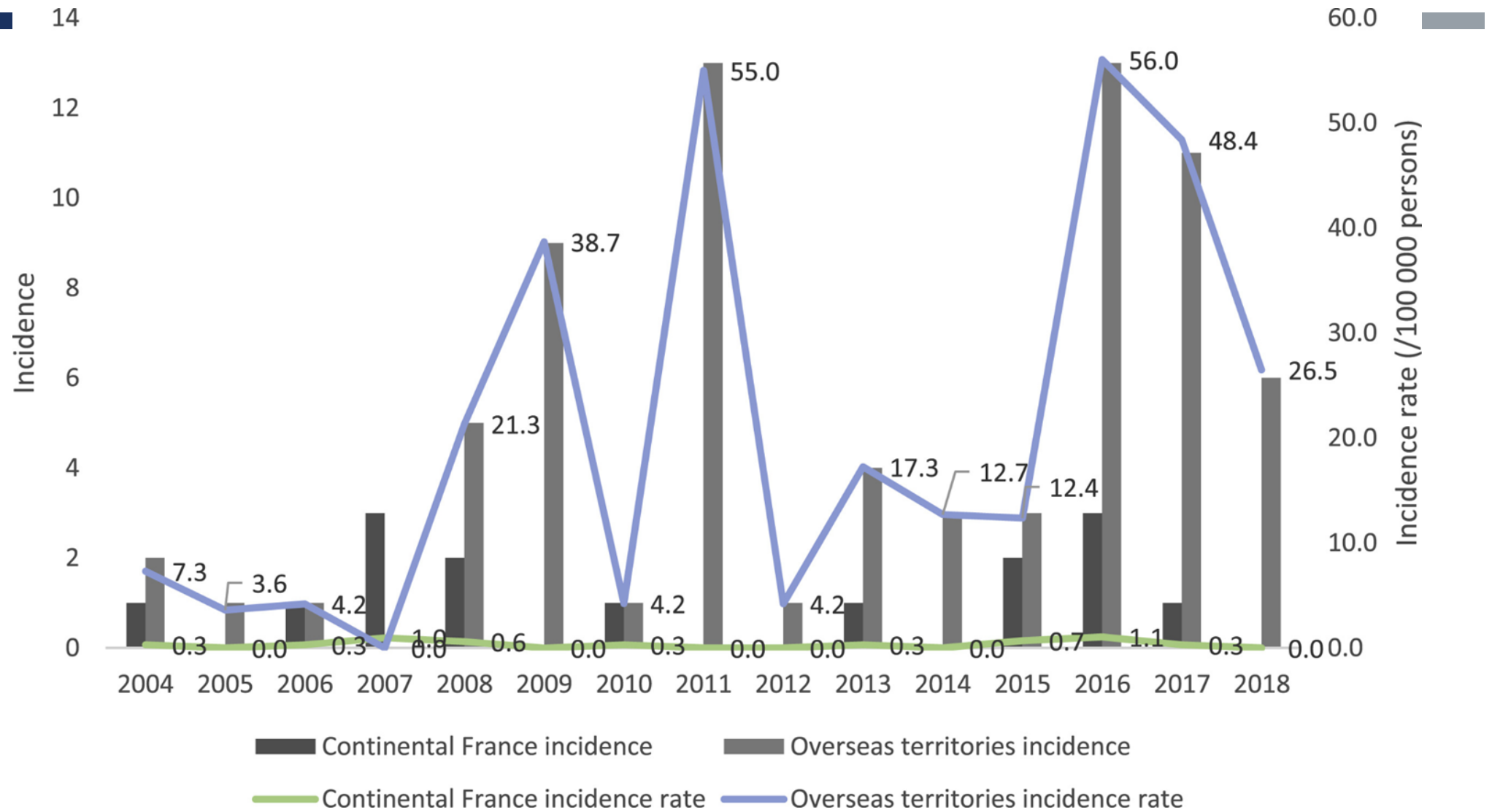
Results

Eighty-eight cases of leptospirosis were reported, 15 cases in continental France and 73 cases in overseas (including 42 cases in the French West Indies). The global leptospirosis incidence rate in continental France was 0.3/100,000 person-years and in overseas 24/100,000 person-years with the higher incidence rate in Martinique (99/100,000 person-years) and in Mayotte (36.9/100,000 person-years).

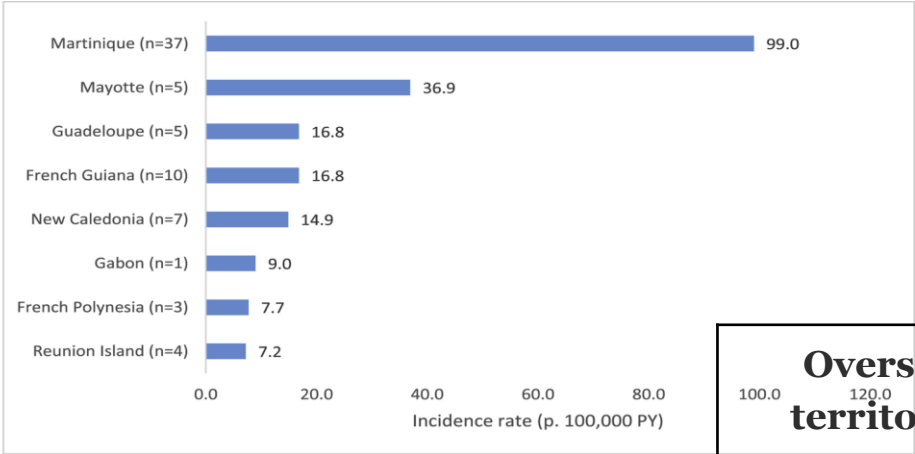
For the clusters in Martinique, between January and June 2009, 7 cases were declared; between 2016 and 2018, 16 cases were reported, high proportions of severe cardiac, renal and neurological forms (6/16) and hospitalizations (9/16).

Conclusion

The occupational risk is real in French Armed Forces, particularly in malaria-free intertropical areas where chemoprophylaxis by doxycycline is not applied. Prevention can be optimized by the use of practical tools such as tables and cartographies, leading to a better leptospirosis risk assessment and application of preventive recommendations.



Gentile, et al. *Travel Med Infect Dis*, 2021



FAF: French Armed Forces; IR: incidence rate; PY: person-years

PY: Person-years.

IR: incidence rate.

FAF: French Armed Forces.

TABLE 2. AVERAGE LEPTOSPIROSIS INCIDENCE RATE IN FRENCH ARMED FORCES AND IN GENERAL POPULATION DIAGNOSED BY NATIONAL REFERENCE CENTER FOR LEPTOSPIROSIS IN 2014–2017.

Overseas territories	Average leptospirosis IR in FAF in 2014–2017 (/100,000 PY)	Average leptospirosis IR in general population diagnosed by National Reference Center for Leptospirosis in 2014–2017 (/100,000 PY)
Martinique	145.8	31.1
Guadeloupe	11,1	31.9
French Guiana	55.0	26.8
Reunion Island	13.6	6.2
Mayotte	37.8	66.5
French Polynesia	9.2	53.7
New Caledonia	7.9	20.0
Total French overseas territories	38.3	27.1

STRENGTHENING SCREENING FOR INFECTIOUS DISEASES AND VACCINATION AMONG MIGRANTS IN EUROPE: WHAT IS NEEDED TO CLOSE THE IMPLEMENTATION GAPS?

- ✗ **Migration** to the European Union (EU)/European Economic Area (EEA) **affects the epidemiology of infectious diseases**, including tuberculosis (TB), HIV, hepatitis B/C, and parasitic diseases.
- ✗ Some **sub-populations** of migrants are also considered to be an **under-immunised group** and thus at **risk of vaccine-preventable diseases**. Providing high-risk migrants access to **timely and efficacious screening and vaccination, and understanding how best to implement more integrated screening and vaccination programmes** into European health systems ensuring linkage to care and treatment, is key to improving the health of migrants and their communities, alongside meeting national and regional targets for infection surveillance, control, and elimination.
- ✗ There is a need now to leverage the increasing momentum around migrant health to both strengthen the evidence-base and to advocate for **universal access to health care for all migrants** in the EU/EEA, **including undocumented migrants**. This should include **voluntary, confidential, and non-stigmatising screening and vaccination that should be free of charge and facilitate linkage to appropriate care and treatment**.

STRENGTHENING SCREENING FOR INFECTIOUS DISEASES AND VACCINATION AMONG MIGRANTS IN EUROPE: WHAT IS NEEDED TO CLOSE THE IMPLEMENTATION GAPS?

Hepatitis B

- × **Screening and treatment** for hepatitis B (HBsAg and anti-HBc, anti-HBs) to migrants from **intermediate** ($\geq 2\%$) or **high** ($\geq 5\%$) HBsAg prevalence countries.
- × Hepatitis B **vaccination** series to all migrant **children and adolescents** from intermediate ($\geq 2\%$) or high ($\geq 5\%$) HBsAg prevalence countries who do not have evidence of vaccination or immunity.

Hepatitis C

- × Hepatitis C **screening** to detect HCV antibodies to migrant populations from **HCV-endemic countries** ($\geq 2\%$) and subsequent RNA testing to those found to have antibodies. Those found to be HCV RNA positive should be linked to care and treatment.

Vaccine-preventable diseases

- × **Vaccination** vs measles/mumps/rubella (**MMR**) to all migrant **children and adolescents** without immunisation records as a priority.
- × **Vaccination** to all **adult** migrants without immunisation records with either one dose of **MMR** or in accordance with the MMR immunisation schedule of the host country.



PATHOG DIS. 2019 MAR 1;77(2):FTZ018. DOI: 10.1093/FEMSPD/FTZ018.

EMERGING ZOOONOTIC VIRAL INFECTIONS OF OCCUPATIONAL HEALTH IMPORTANCE

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PAOLA TOMAO ¹

- × Noori, et al. *Travel Med Infect Dis*, 2021
- × Baroutsou_TMID2021_TOURIST2_Tracking of urgent risks in swiss travellers smartphone App
- × Sharafeldin et al. *BMC Medical Education* 2010. Health risks encountered by Dutch medical students during an elective in the tropics and the quality and comprehensiveness of pre-and post-travel care
- × Gentile, et al. Incidence of leptospirosis in the French armed forces from 2004 to 2018: a retrospective analysis. *Travel Med Infect Dis*, 2021
- × <https://wwwnc.cdc.gov/travel/yellowbook/2020/table-of-contents>
- × Nicoletta Vonesch, Alessandra Binazzi, Michela Bonafede, Paola Melis, Anna Ruggieri, Sergio Iavicoli, Paola Tomao, Emerging zoonotic viral infections of occupational health importance, *Pathogens and Disease*, Volume 77, Issue 2, March 2019, ftz018, <https://doi.org/10.1093/femspd/ftz018>