VHPB TECHNICAL MEEETING

The changing context of Hepatitis Delta

28 – 29 October 2021

Does the use of Hepatitis B vaccine prevent Hepatitis Delta?

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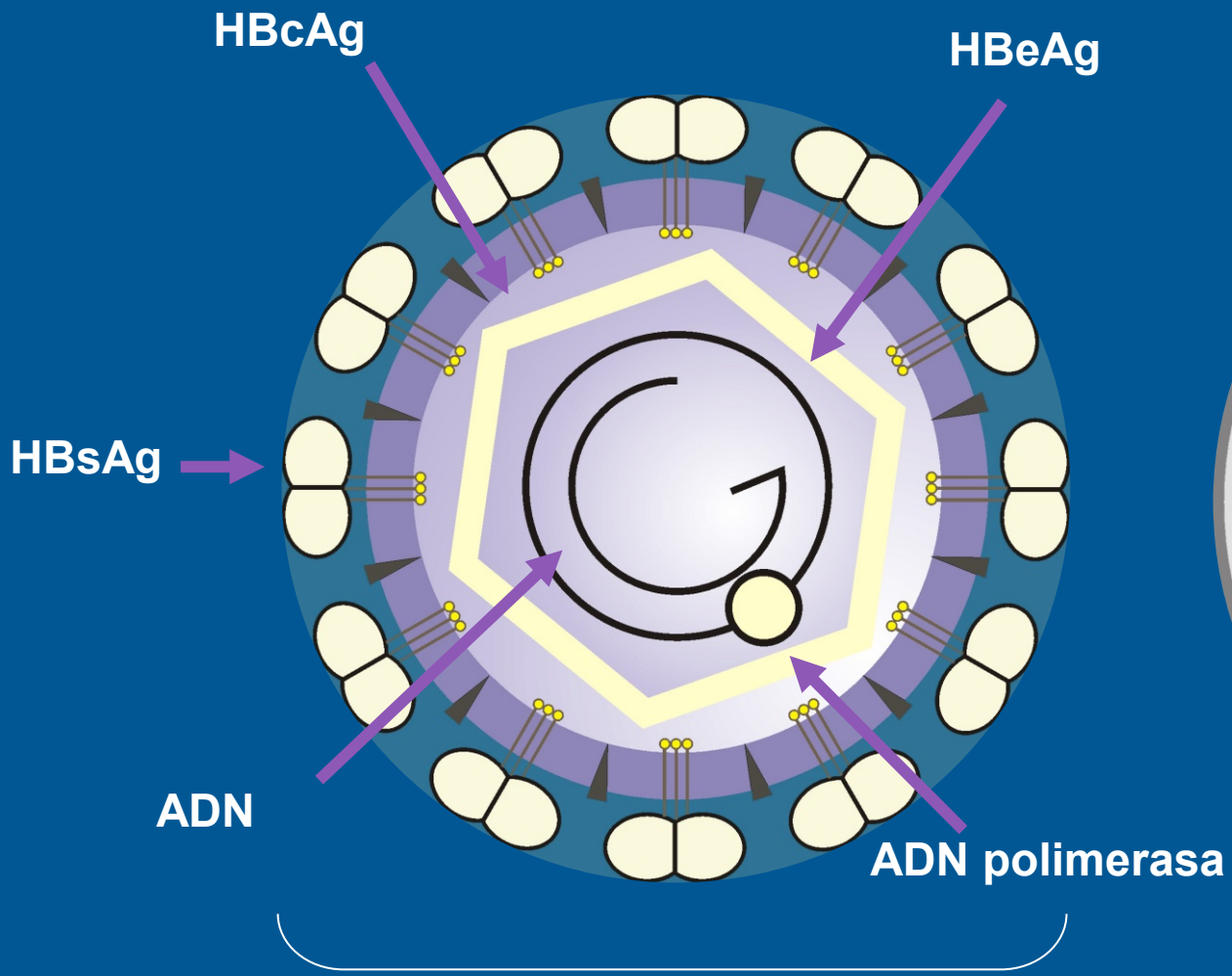
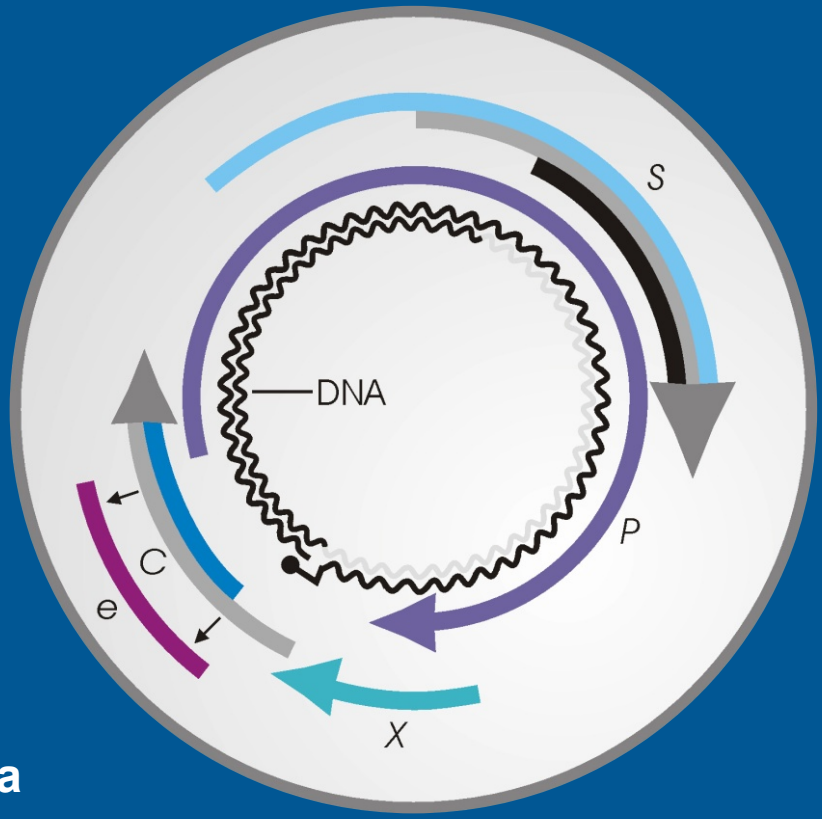
National Institute of Health, Perú

National University of San Marcos

Virus de Hepatitis B



~41 nm (virus de ADN más pequeño conocido)



8 HBV genotypes (A-H) based on ≥8% sequence divergence

Gt **F** (Perú) associated with HCC.

Adaptado de Ganem et al. *N Engl J Med.* 2004;350:1118-1129.
Adaptado de Liang et al. *N Engl J Med*. 2002;347:208-210.
Fung, et al. *Hepatology*. 2004;40:790-792.

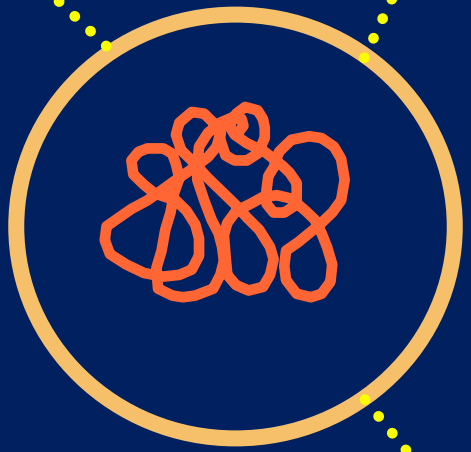
Investigar para proteger la salud.

Hepatitis D (Delta)

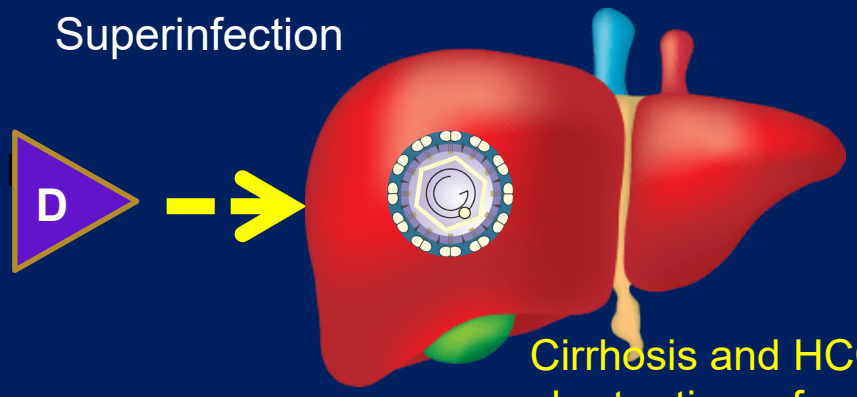
δ antigen

HBsAg

RNA

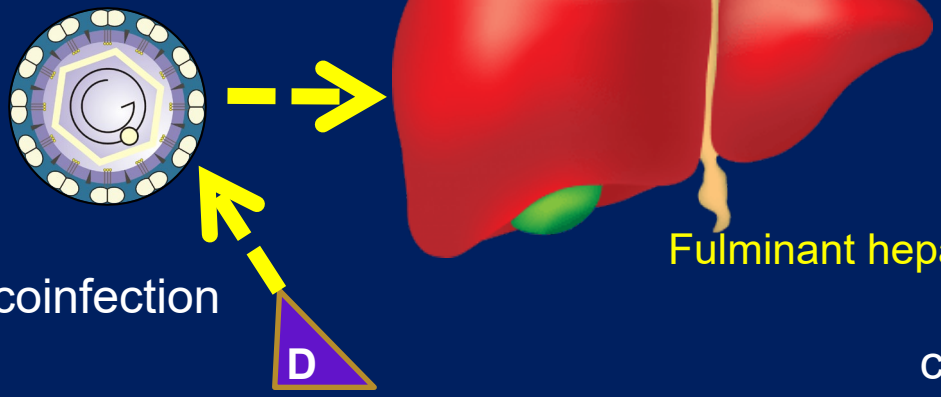


Superinfection



Cirrhosis and HCC in a shorter time of evolution

HBsAg



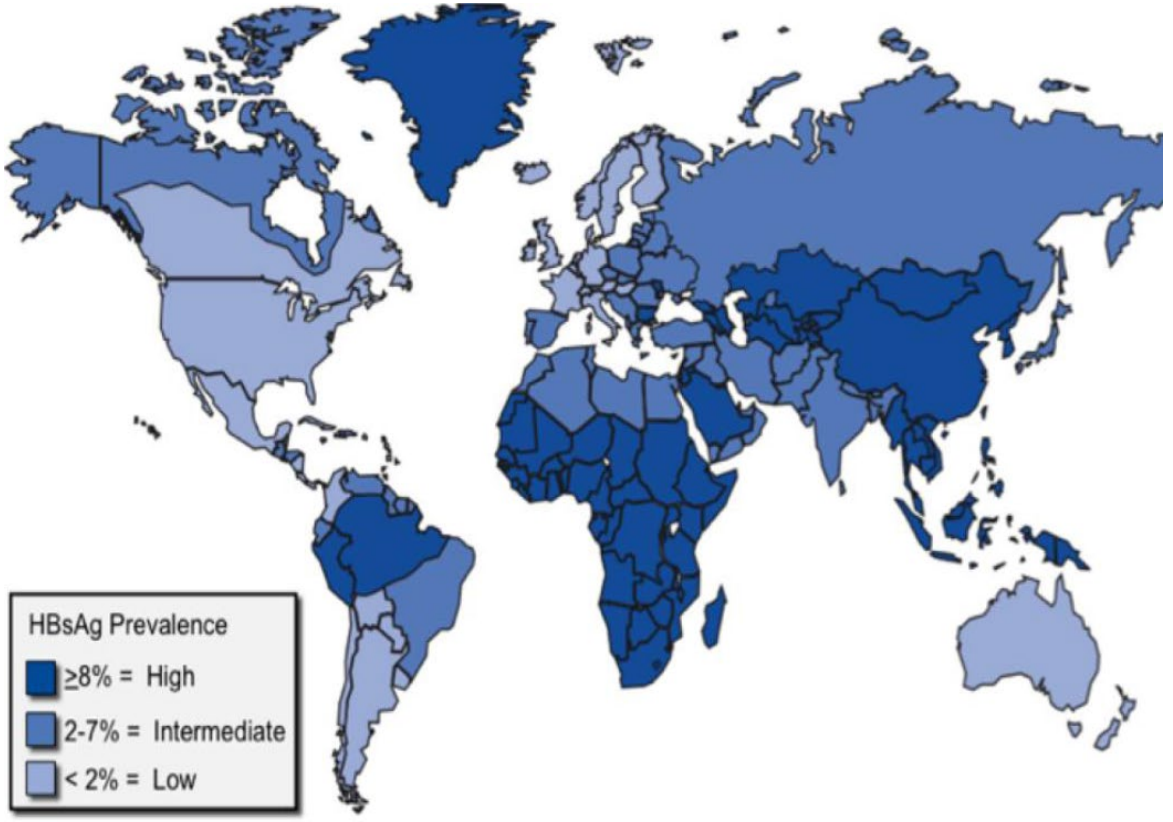
Fulminant hepatitis

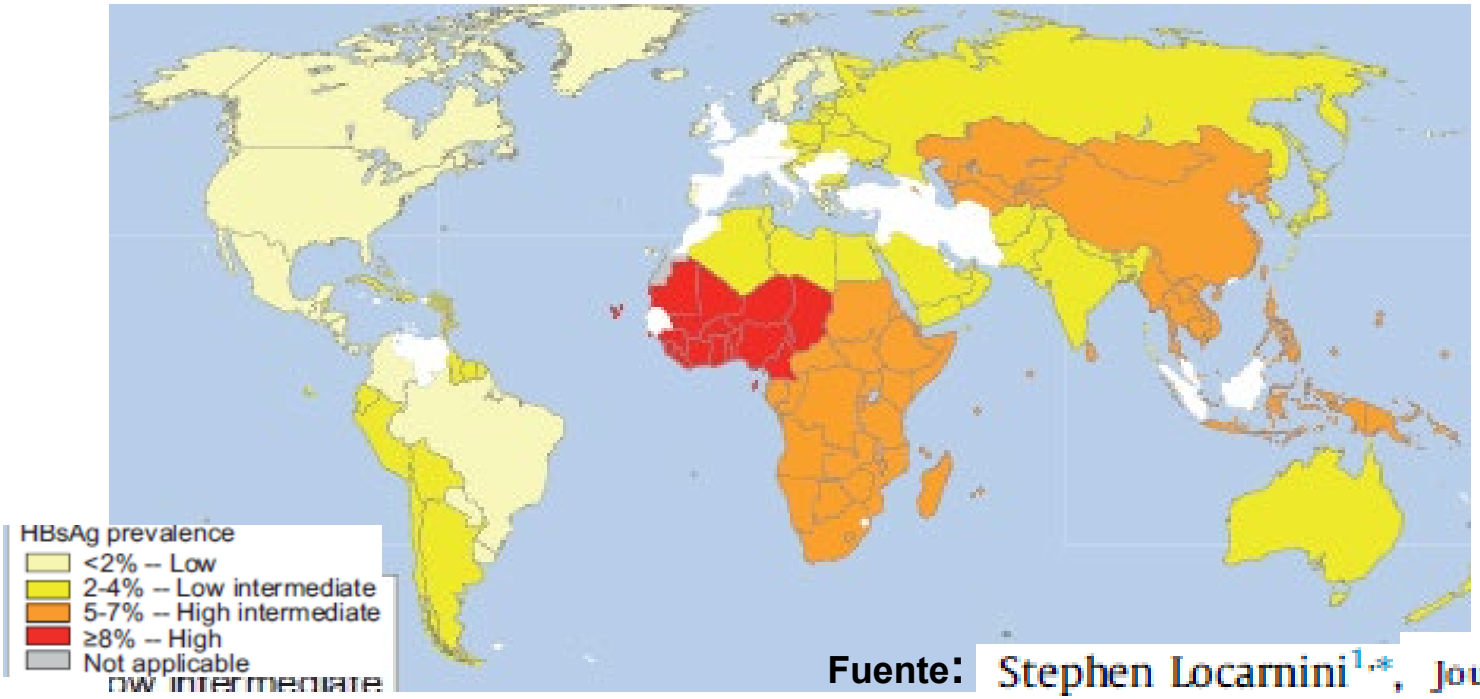
Hepatitis Delta in Peru
Genotype III
in Amazon and Andean Region

J Infect Dis. 1996 Nov;174 (5):920-6

cacs

Global endemicity of HBV 1996

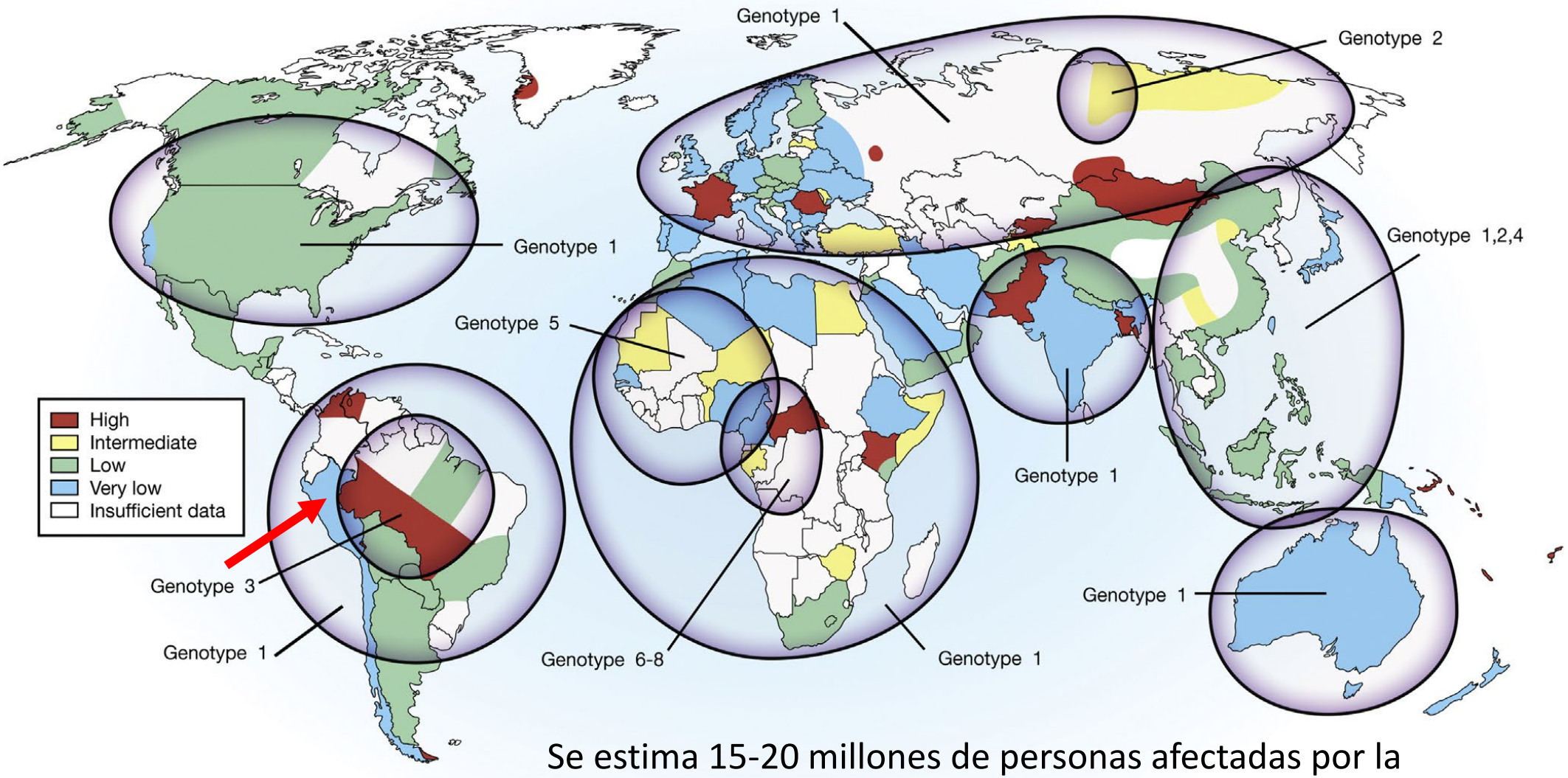




Global prevalence of HBV, 2005

Fuente: Stephen Locarnini[1,*], Journal of Hepatology 2015 vol. 62 | S76–S86

Distribución Mundial de la Hepatitis D y sus genotipos

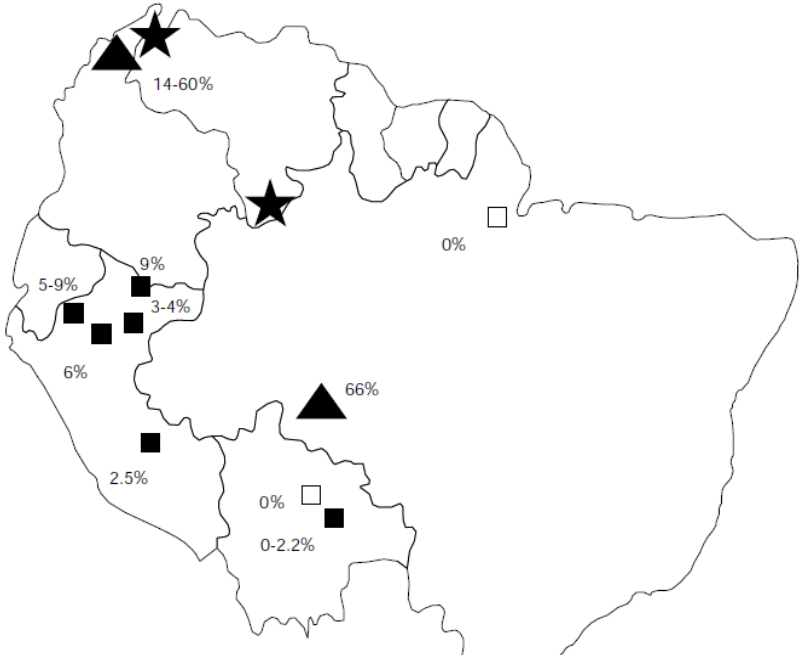


Se estima 15-20 millones de personas afectadas por la infección por HDV en el mundo

Fuente: Koh C. Gastroenterology 2019;:1–16

HDV distribution in South America

Geographical distribution of HDV in the Amazon and neighboring ecosystems.



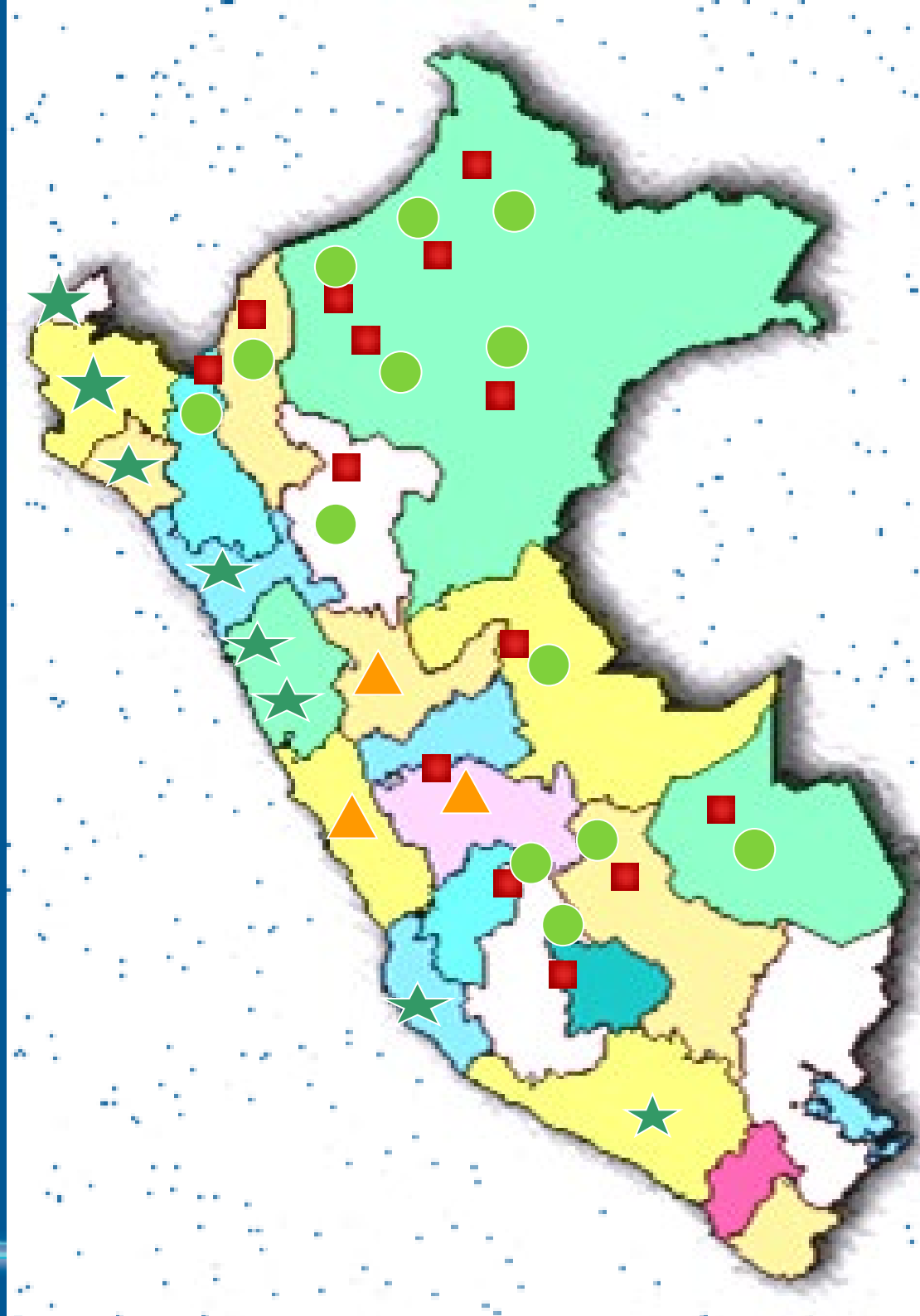
Country	Area	% positive for Anti-HBc	HBsAg	Anti-HDV*
Bolivia	Chapare, Santisima Trinidad	34-84	0-4.8	0-2.2
Brazil	Acre, Amazonas	66.1		66.6
	Pará	18-85	0-14.4	0
Colombia	Sierra de Santa Marta	35-93	1.8-23.0	Up to 60
Peru	Marañón, Madre de Dios	69-74	3.9-12.1	2.5-9.0
Venezuela	Sierra de Perijá	62-71	5.6-11.1	14.2-42.8

* Among HBsAg carriers.

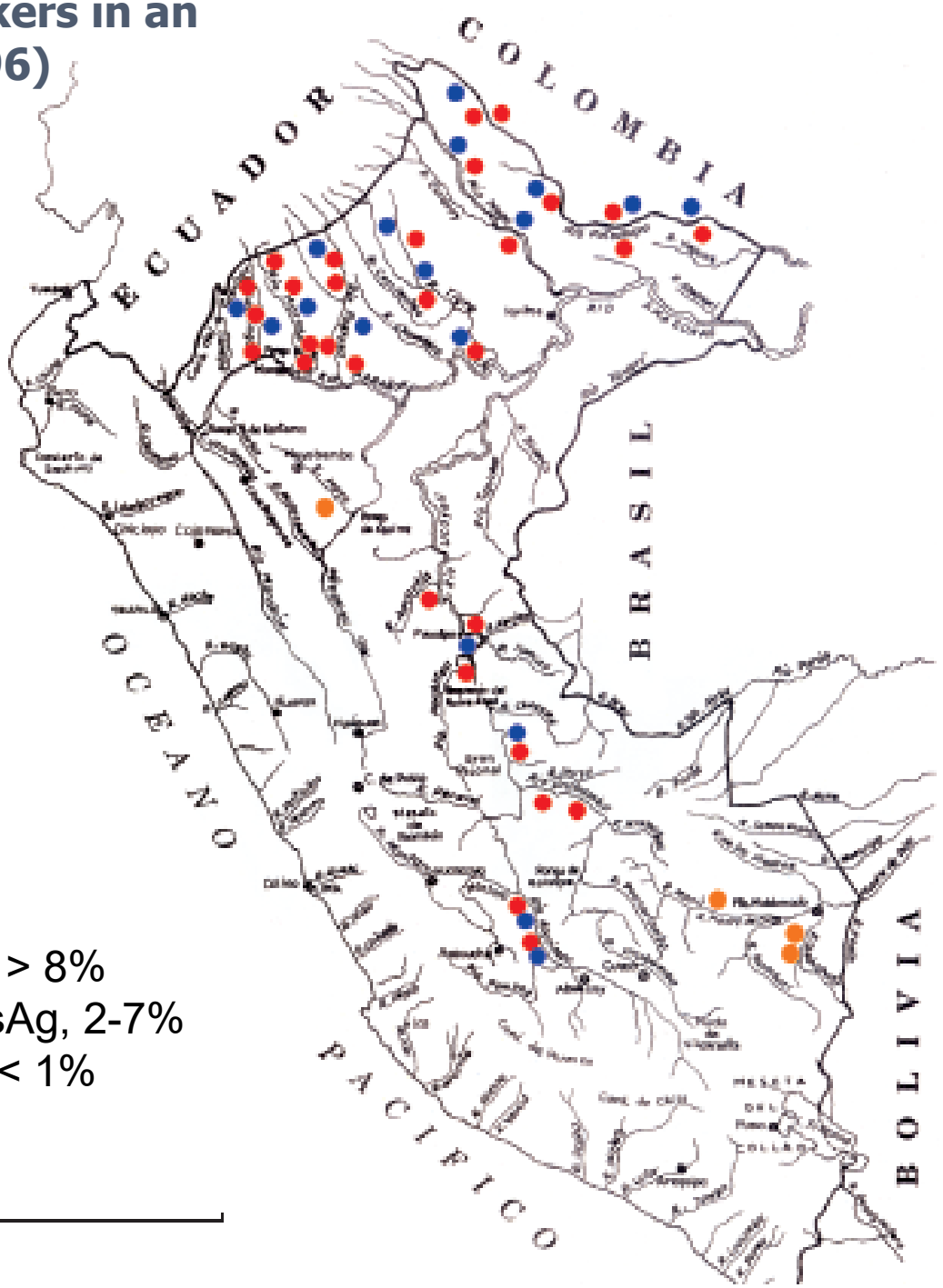
Cad. Saúde Pública, Rio de Janeiro, 19(6):1583-1591, nov-dez, 2003

HEPATITIS B and D IN PERU before 1991

- High endemicity, HBsAg > 8%
- Medium endemicity, HBsAg, 2-7%
- Low endemicity, HBsAg < 1%
- Hepatitis Delta



Prevalence of HBV and HDV serological markers in an Amazon basin Population in Peru (1996)



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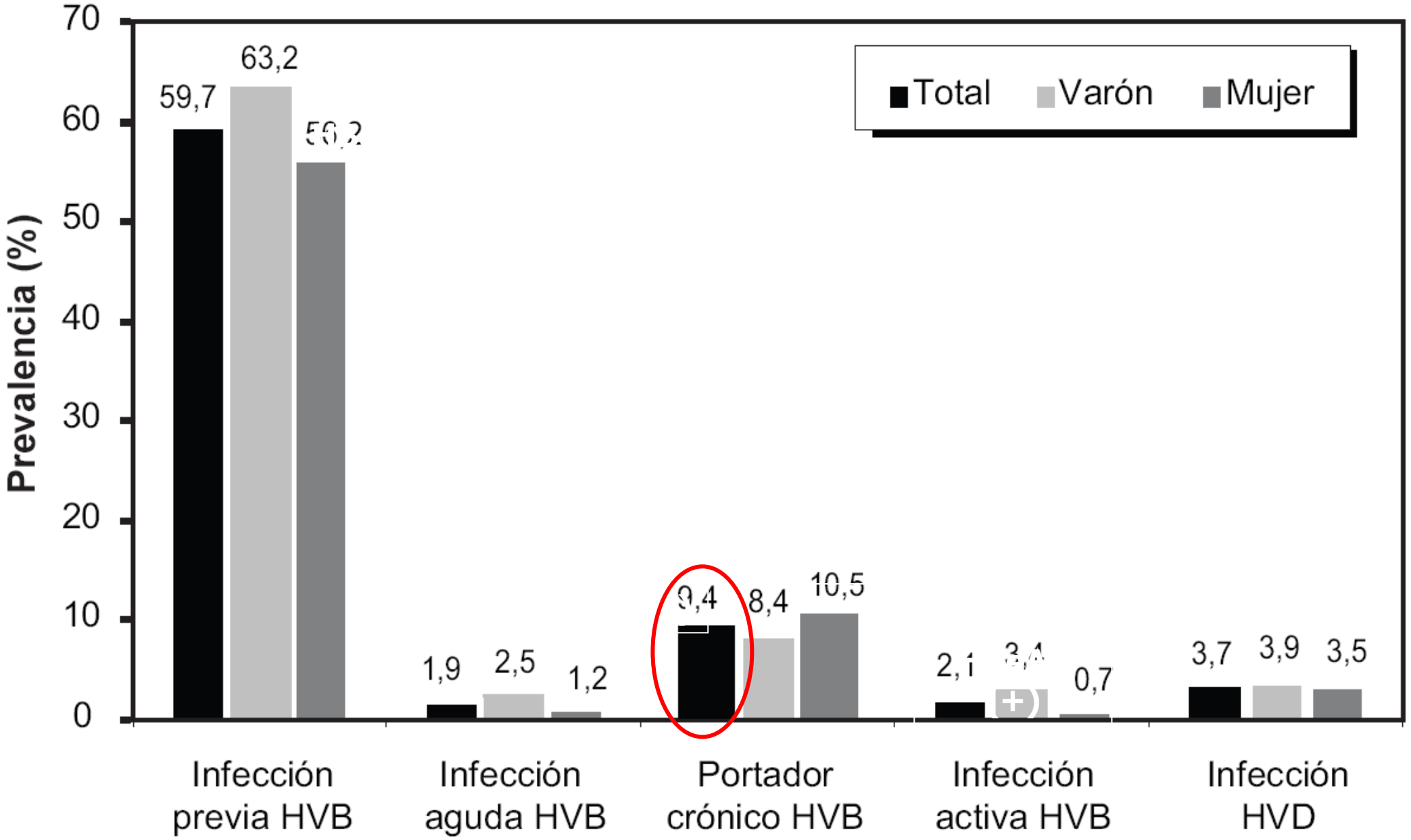


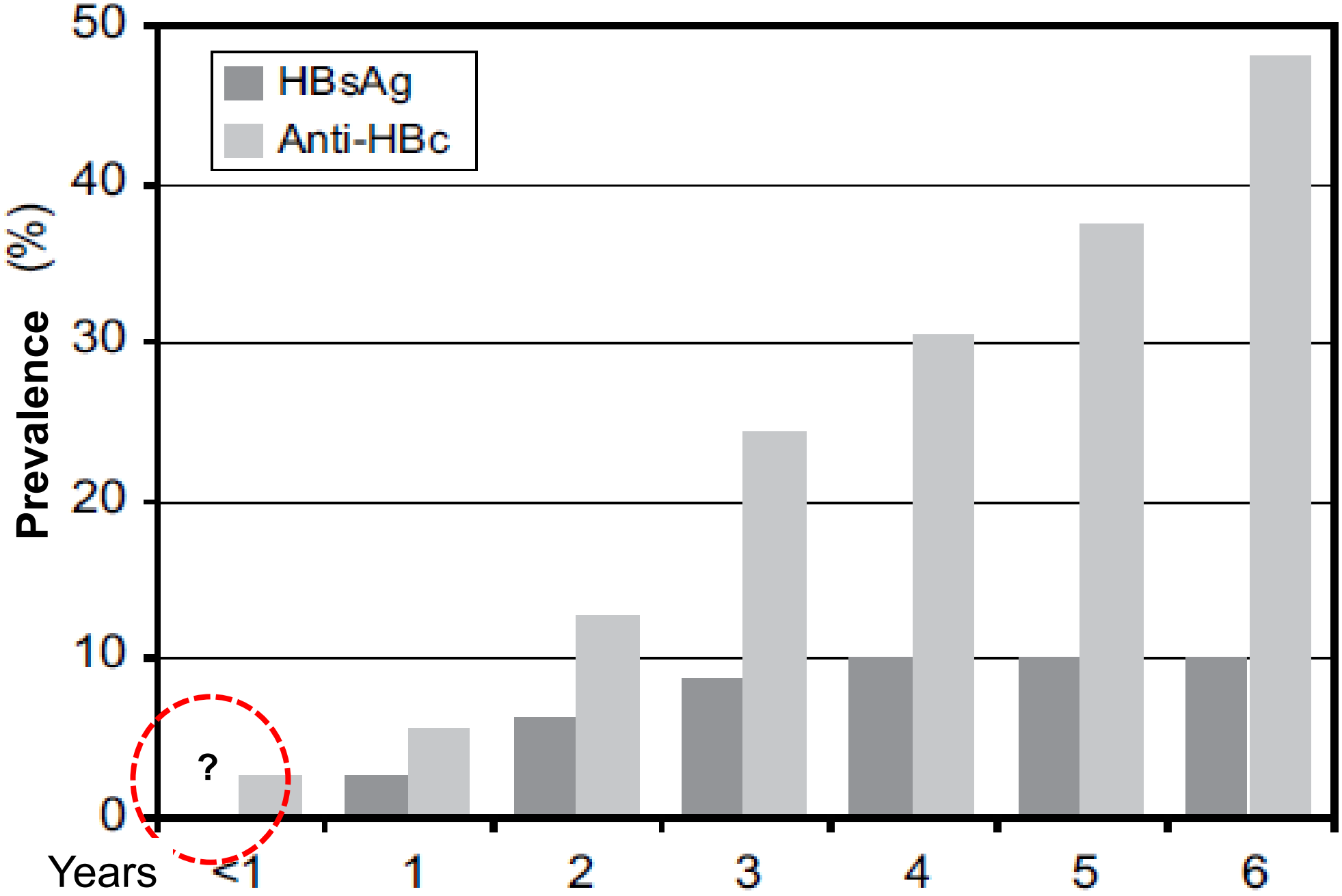
Cabezas C. et al. Rev Peru Med Exp Salud Publica 2006;23(2):114-122

HBV transmission

Through exposure to blood and / or body fluids

- Sexual
- Parenteral
- Perinatal (vertical)
- Horizontal (Saliva vehicle)
- Vectors: Biological, mechanical

(Mosquitoes, bats)



Prevalence of HBV infection in children from Huanta (Peru) 1994

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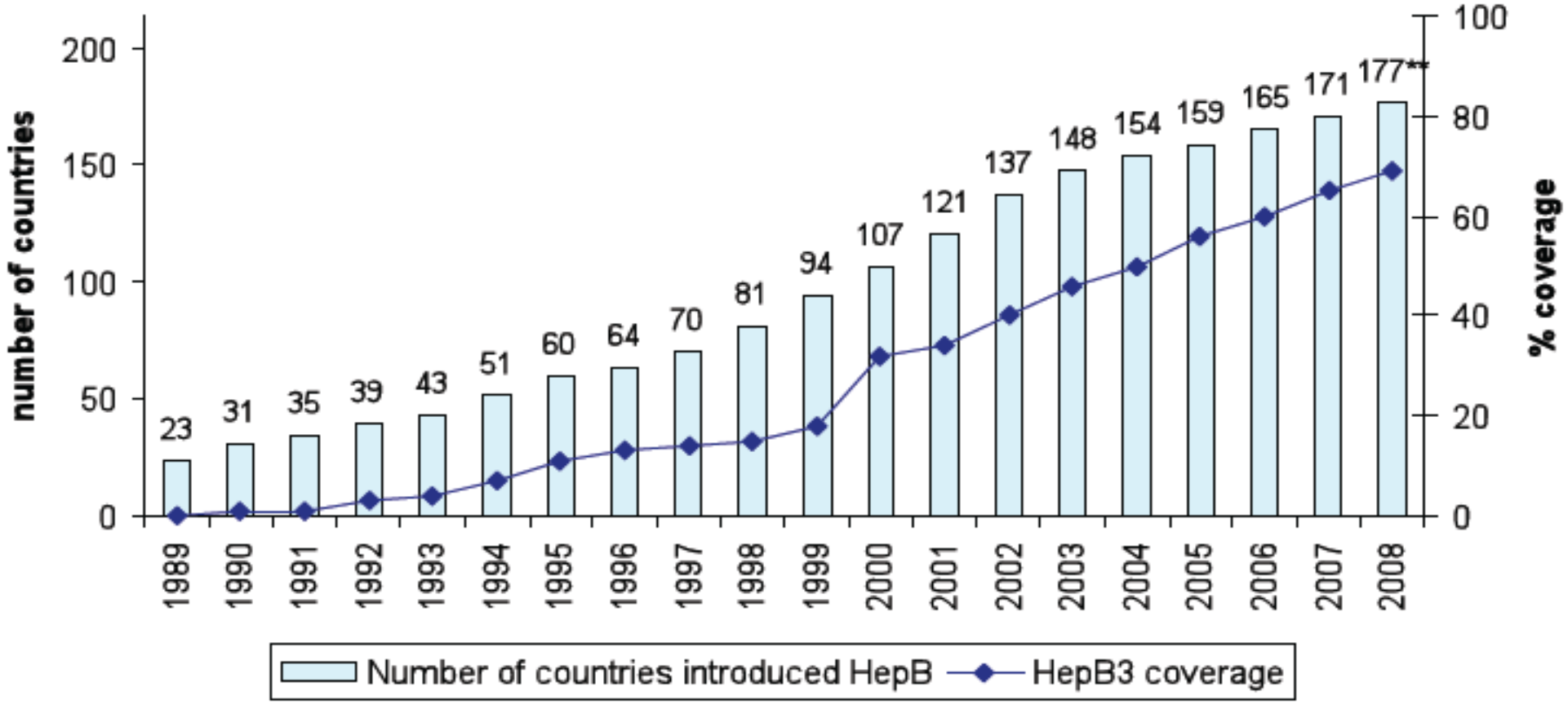
MINISTERIO DE SALUD
Salud


FUERZA AEREA DEL PERU

Number of countries having introduced HepB vaccine* and global infant HepB3 coverage, 1989-2008



* Year of introduction can be the year of partial introduction

** Includes India and Sudan with partial introduction

Source: WHO/UNICEF coverage estimates 1980-2008, August 2009, 193 WHO Member States. Date of slide: 11 August 2009 excluding 3 countries where HepB administered for adolescence

World Health Organization

Recombinant DNA HBV VACCINES

Dose: <15 years: 10 ug; > 15 years: 20 ug, 3
DosesScheme: Newborn, Children: 2, 4, 6 months
Adults: 0.1.2 months.
Route of administration: Intramuscular

The process of introducing the HBV vaccine in Peru

YEAR	INTERVENTION
1991	Immunization against HBV in children under 5 years of age, Abancay (Apurimac)
1994	Immunization against HBV in children under 5 years of age, Huanta (Ayacucho)
1996	Immunization against HBV in children under 1 year of age, from hyperendemic areas of Peru
1997- 2004	Universal immunization against HBV in children under 5 year of age in Peru
2008	Immunization campaign against HBV in children under 18 years of age in Peru


ye a tu hijo AHORA!
APOYO DE HUANTA
MINSA OPS UPCH
FONCODES
LA HEPATITIS "B" MATA!!!

BENEFITS OF THE CAMPAIGN AGAINST HBV, 2008

Programmed Population 2 to 19 years 10'126,086

IF YOU DON'T GET VACCINATED

People are exposed to infection by the Hepatitis B Virus

Considering that Peru on average has a level of medium endemicity (3-7%)

567,060 chronic HBV carriers would occur

10% Evolutionary Liver Cancer (56,706 people)

30% to Cirrhosis (170,118 people))

1 Situación epidemiológica de la Hepatitis B y Delta en el Perú y Bases para su control, César Cabezas y Col. Instituto Nacional de Salud

2 Guan Zhiqiang, Dong Zhaohui, Wang Qinhuan, Cao Dexian. Cost of Chronic Hepatitis B, Infection in China,J Clin Gastroenterol Volume 38, Supp. 3, November/December 2004.

Impact of 20 Years of Implementation of an Immunization Program for HBV in Huanta, Peru: First Clues of Elimination of Hepatitis Delta Virus

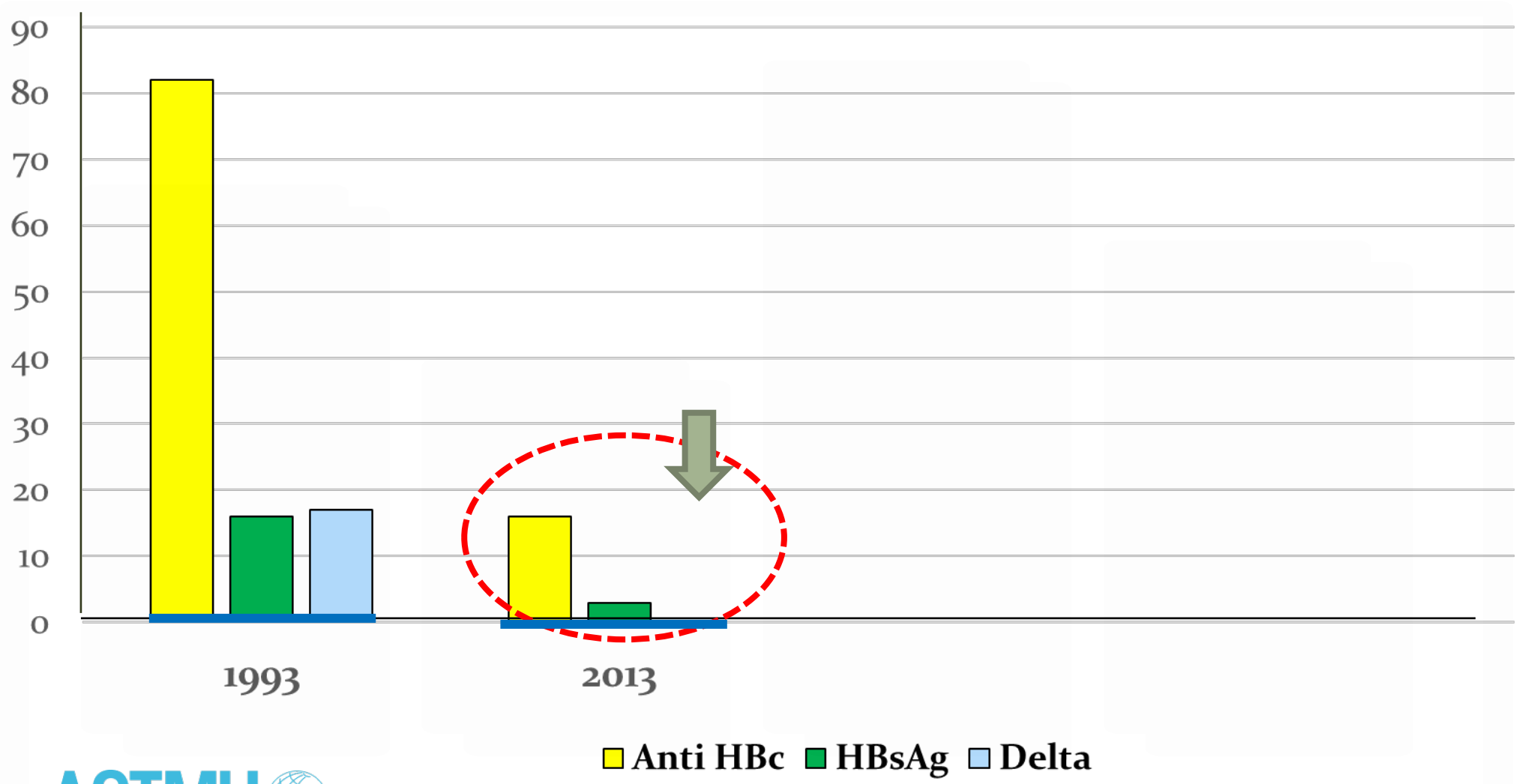
Background: Huanta is an inter-Andean valley of Peru, located at 2627 meters above the sea level with a population of 45,561 inhabitants. For many decades, it has been considered an hyperendemic area for HBV and HDV, with a lethality rate of 8% due to fulminant hepatitis, cirrhosis and hepatocarcinoma associated with infection by HBV and HDV. An immunization program against HBV has been established in children under 5 years of age since 1994.

Methods: We evaluated and compared the prevalence of HBV and HDV infection in healthy school children and adolescents in Huanta, in 1993 with the one found after 20 years of implementation of the immunization program, in 2013 in the same age group. In both surveys (1993 and 2013), the study population was representative of this region, as its selection was randomized. Epidemiological information was collected and the presence of biological markers of infection by HBV and HDV was evaluated determining HBsAg, total anti HBc, IgM anti HBc, , and anti HDV IgM-IgG in serum by means of the ELISA tests for each of the included subjects

Results: A total of 143 children/adolescents participated in the 1993 study. The average age was 13.2 years (7-20 years). In this group, we found 23 chronic HBsAg carriers (16.0%). Previous infection with HBV (total HBc) was detected in 117 (82%) and HDV infection was found in 21/117 (17.9%) individuals infected with HBV. In the 2013 survey, we included 412 subjects, with an average age of 13.1 years (7-20 years), finding 3 chronic carriers of HBsAg (0.72%). Previous HBV infection (total anti HBc) was detected in 64 (15.5%) and not a single case of HDV infection was detected

Conclusion: Twenty years after having implemented a program of childhood vaccination against HBV in a hyperendemic area of Hepatitis B and D, a significant reduction on the prevalence of HBV infection is observed, and the absence of HDV infection in the studied group. This indicates a trend towards the elimination of both infections in the study area.

Impact of 20 Years of Implementation of an Immunization Program for HBV in Huanta, Peru: First Clues of Elimination of Hepatitis Delta Virus



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ADVANCING GLOBAL HEALTH SINCE 1903

2018

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

Trends in mortality burden of hepatocellular carcinoma, cirrhosis, and fulminant hepatitis before and after roll-out of the first pilot vaccination program against hepatitis B in Peru: An analysis of death certificate data

Max Carlos Ramírez-Soto [a,b,*,1], Gutia Ortega-Cáceres [c,1], César Cabezas [a,d]

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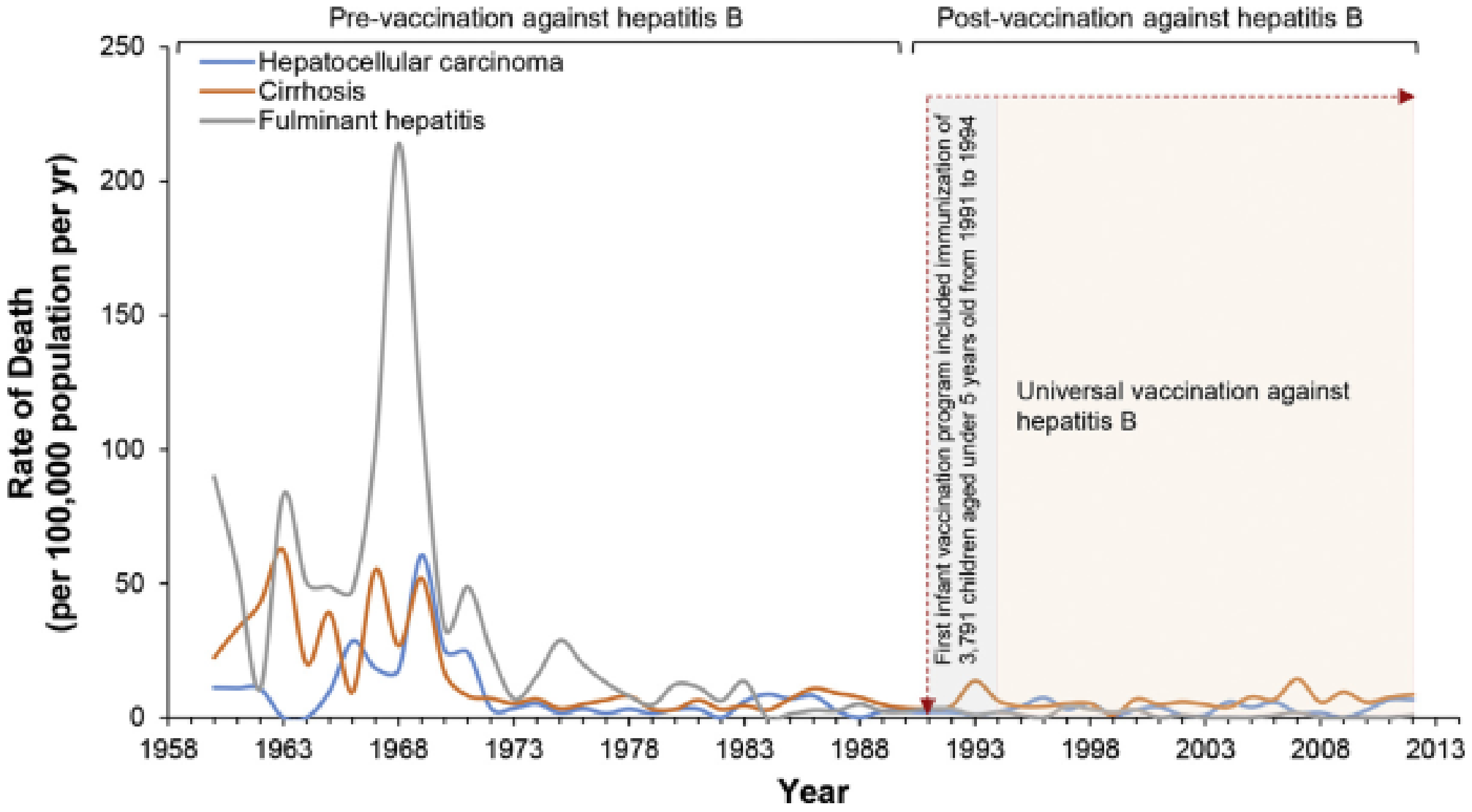
[b] Fondo Nacional de Desarrollo Científico y Tecnológico y de Innovación Tecnológica (FONDECYT), CONCYTEC, Lima, Peru
[c] Escuela de Posgrado, Universidad Ricardo Palma, Lima, Peru
[d] Instituto Nacional de Salud, Lima, Peru

Trends in mortality burden of HCC, cirrhosis, and fulminant hepatitis before and after roll-out of the first pilot vaccination program against hepatitis B in Abancay province in Peru for the period of 1960–2012.



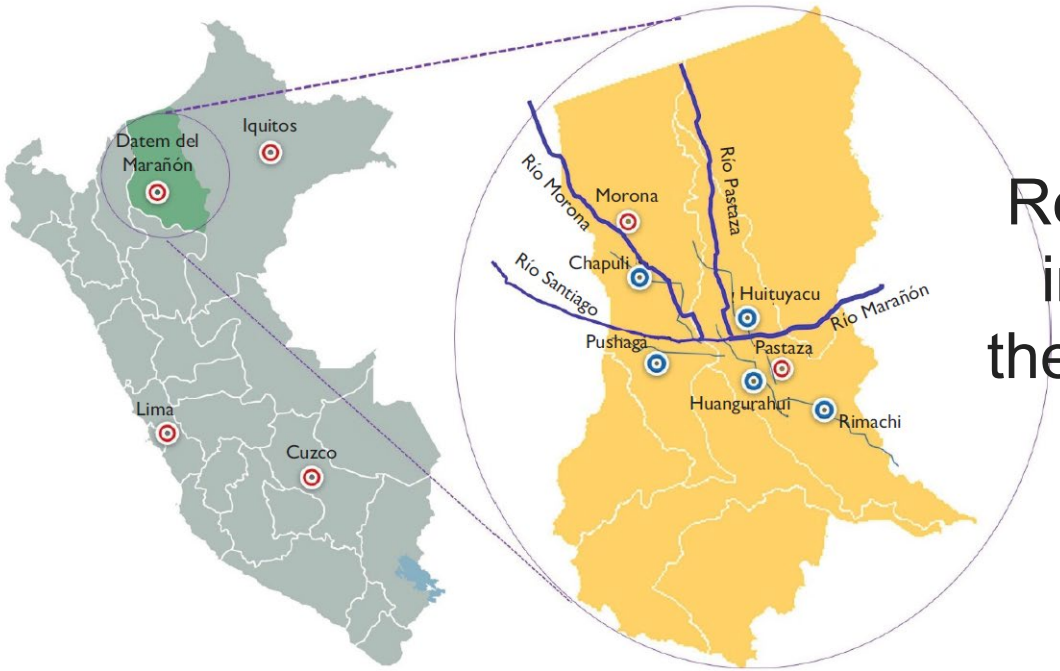


Figura 1. Cuencas de los ríos Pastaza y Morona en los distritos Pastaza y Morona de la provincia del Datem del Marañón, Loreto, Perú

Reduction in HBV and HDV Infection in two Indigenous populations from the Peruvian Amazon after Hepatitis B Vaccination

N = 2,944 inhabitants of 67 indigenous Kandozi and Chapra communities
Prevalence of HBsAg: 2.3%, anti-HBc IgG: 39%, anti-HBs: 50%> 10IU and anti-HDV: 2.0%

Prevalence of HBsAg in children <11 years was zero. Among HBsAg carriers, the prevalence rates of HDV superinfection and acute HBV infection were 2.11% (all were> 14 years) and 11.94%, respectively

Salud Publica Mex. 2020;62:237-245.
https://doi.org/10.21149/11128

RESEARCH ARTICLE

Decrease in the prevalence of hepatitis B and D virus infections in an endemic area in Peru 23 years after the introduction of the first pilot vaccination program against hepatitis B

Cesar Cabezas[1,2]*, Omar Trujillo[3], Johanna Balbuena[1], Flor de Maria Peceros[1], Manuel Terrazas[1], Magna Suárez[1], Luis Marin[1], Janet Apac[4], Max Carlos Ramírez-Soto[1]

1 Centro Nacional de Salud Puública, Instituto Nacional de Salud, Lima, Peru, **2** Facultad de Medicina, Universidad Nacional Mayor de San Marcos, Lima, Peru, **3** Centro Nacional de Salud Intercultural, Instituto Nacional de Salud, Lima, Peru, **4** Dirección de Epidemiología, Dirección Regional de Salud de Apurímac, Apurímac, Peru

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PLoS ONE 15(8): e0236993. https://doi.org/10.1371/journal. pone.0236993

Decrease in the prevalence of hepatitis B and D virus infections in an endemic area in Peru 23 (1991) years after the introduction of the first pilot vaccination program against hepatitis B

Entre 3165 participantes de 0 a 94 años de edad, la prevalencia de Hepatitis B fue:

HBsAg: 1.2% [95% confidence interval (CI) 0.85–1.64%],
Anti-HBc : 41.67% (95% CI 39.95–43.41%)
Anti-HBs en niveles protectores (10 mUI/ml) en HBsAg and anti-HBc negativos fué 66.36% (95% CI 64.15–68.51%).
Prevalencia de HBsAg en niños <15 años de edad fue nula
En menores de 30 años no se detectaron casos de hepatitis Delta.
En portadores de HBsAg mayors de 30 años la prevalencia de hepatitis D fue 5.26% (2/38; 95% CI 0.64–17.74).

*Cabezas C, et al .**PLoS ONE 15(8): e0236993**.* https://doi.org/10.1371/journal.

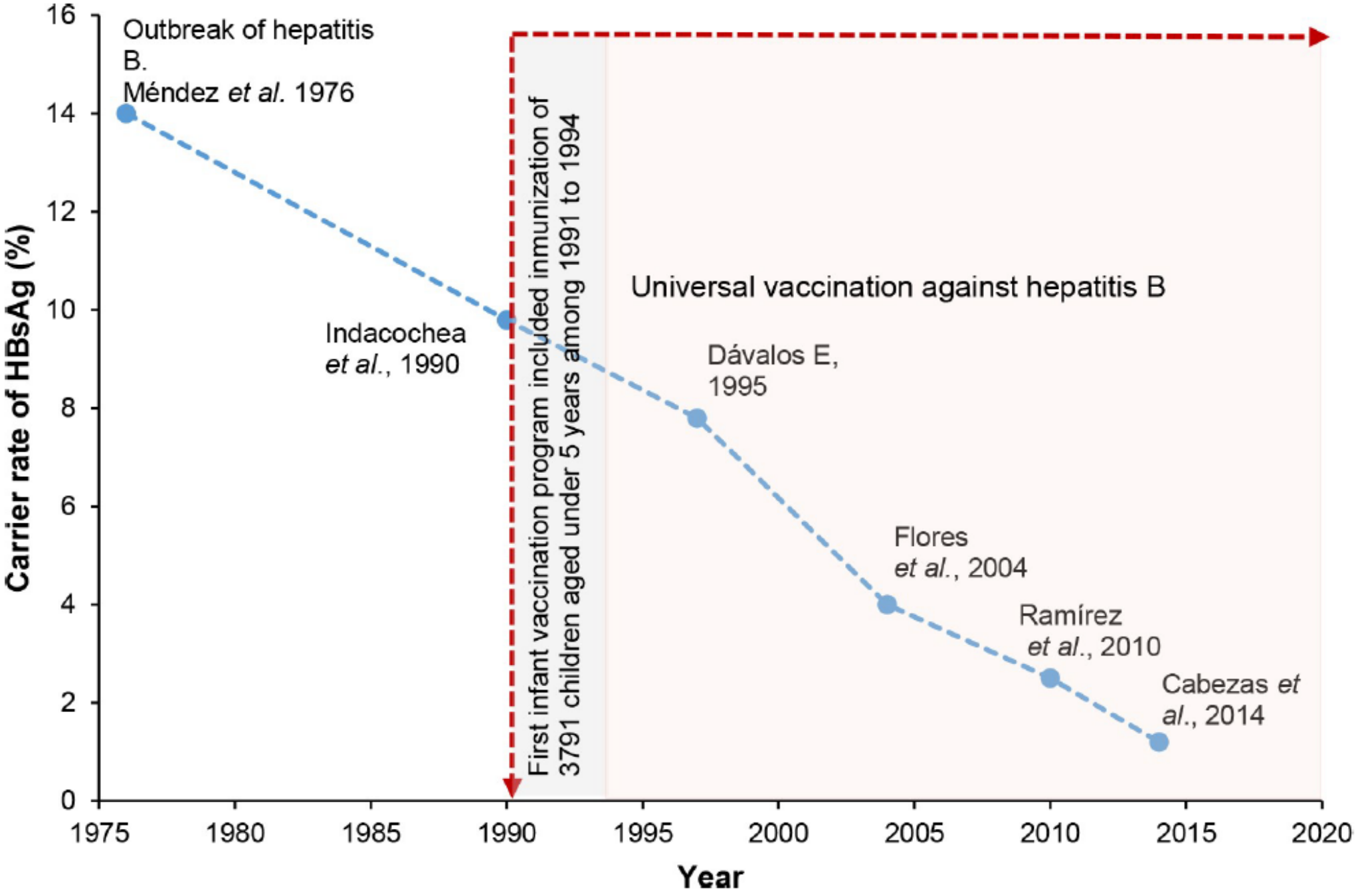
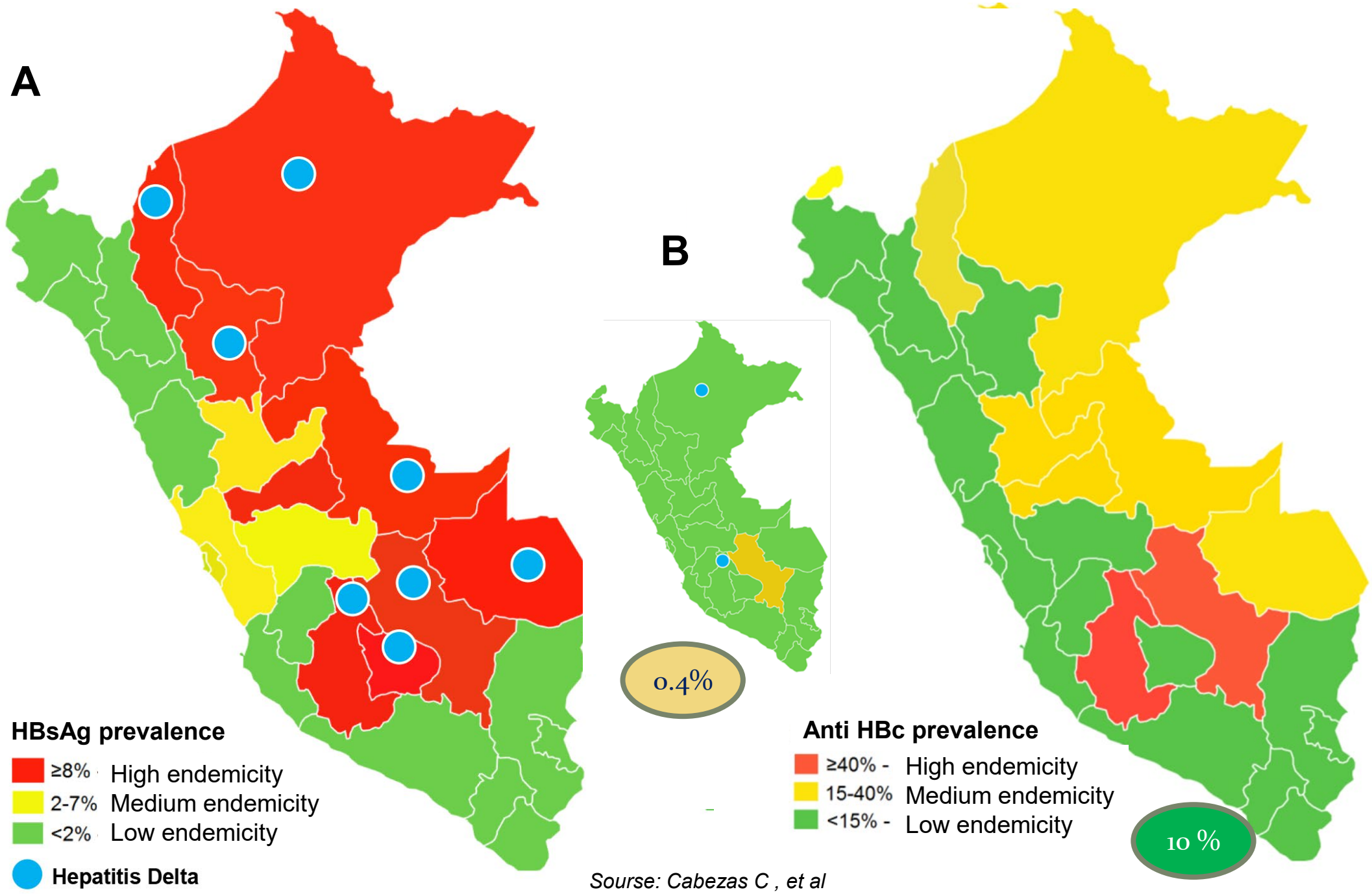


Fig 2. Carrier rates of HBsAg, compared with HBsAg carrier rates reported from previous studies, in Abancay province in Peru [11,12,16–18].

https://doi.org/10.1371/journal.pone.0236993.g002

Prevalence of HBsAg and hepatitis Delta before (A) and after the implementation of the vaccination program against hepatitis B in Peru (B).

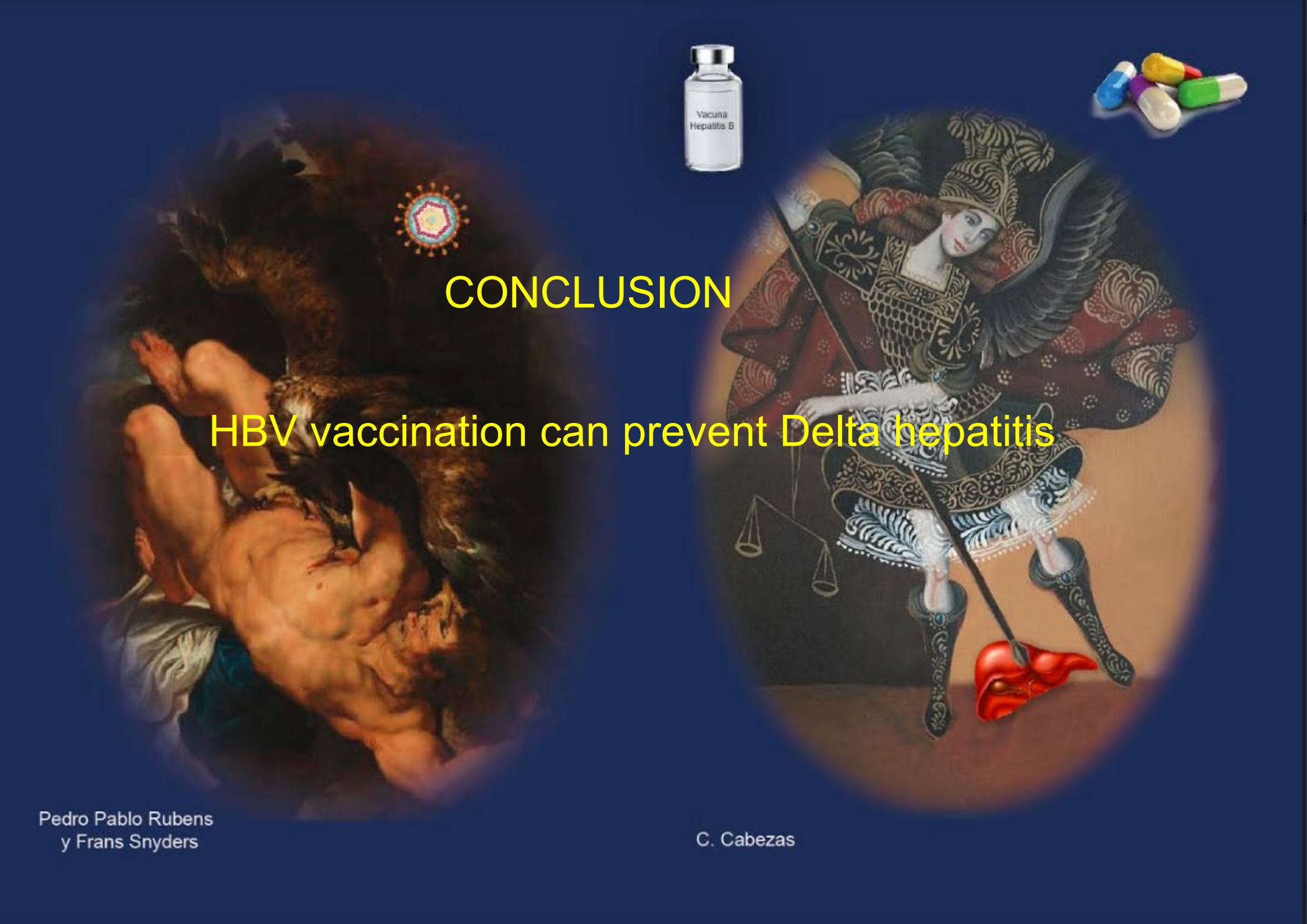


Sourse: Cabezas C , et al

Investigar para proteger la salud.

Eliminating endemic hepatitis B and D in Ayacucho, Peru

Update: As the story was being published, on 18 December 2018, Peru's Ministry of Health approved new national guidelines for the prevention, diagnosis and treatment of hepatitis. The new guidance includes the use of rapid diagnostic tests for screening and diagnosis and pan-genotypic direct acting antivirals for the treatment of hepatitis C (HCV) available to all those living with HCV, in line with WHO recommended guidance. With an estimated population of 220 000 people living with HCV, the new guidelines will make it possible for patients to access hepatitis C cure at US$4 500 or less as opposed to the previous price of over US$10 000. The policy is hoped to lead to even further reductions in such high prices, as the treatment had become much more affordable in many other regions of the world.



CONCLUSION

HBV vaccination can prevent Delta hepatitis

Pedro Pablo Rubens
y Frans Snyders

C. Cabezas