Hepatitis Vaccines

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National Taiwan University
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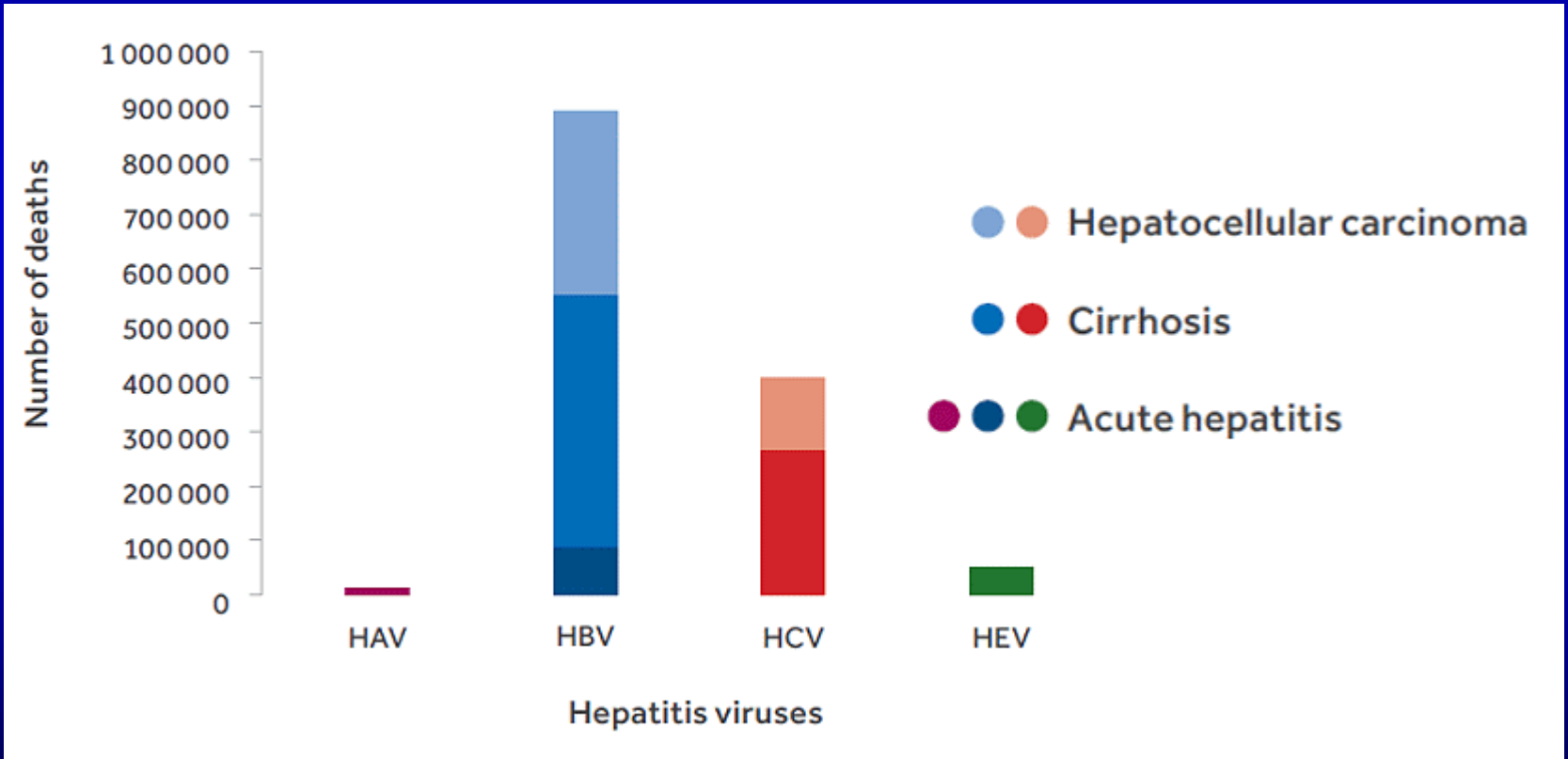
G.Q.

Deaths from viral hepatitis WHO, 2015

Most viral hepatitis deaths are due to the late complications of HBV and HCV infection



Global Hepatitis Report, 2017
(http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/)

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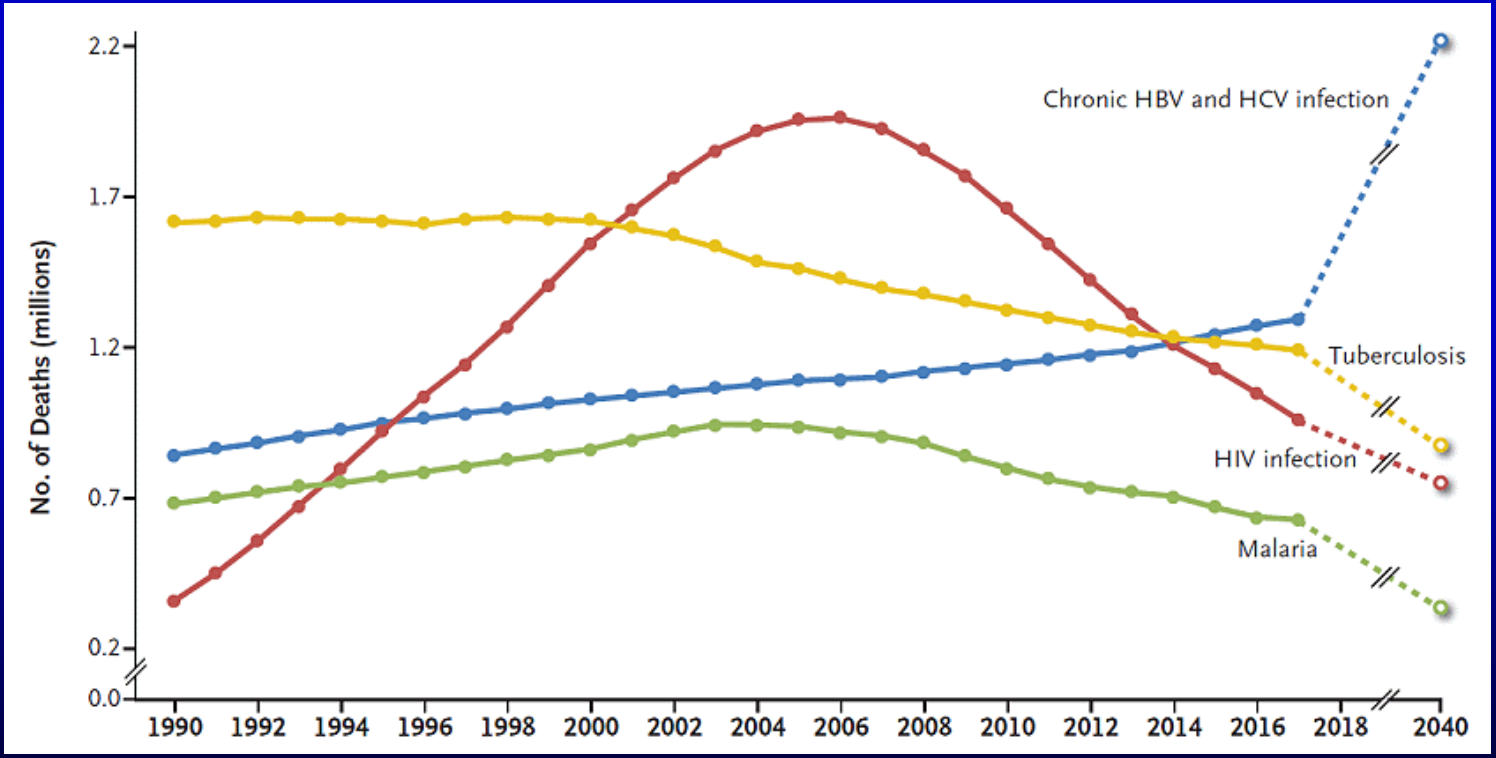
Worldwide deaths from chronic viral hepatitis

Chronic hepatitis kills **1 million** persons every year, accounting for as many global deaths as those due to HIV infection, tuberculosis, or malaria.



G.Q.

Thomas DL. N Engl J Med 2019;380(21):2041.

Hepatitis elimination WHO, 2017

- Goals: eliminate hepatitis by **2030**

A No. of New Cases

	2015	2020	2030
HBV	4.7 million	3.3 million	470,000
HCV	1.75 million	1.23 million	175,000

30% Reduction

90% Reduction

B No. of Deaths

	2015	2020	2030
HBV	884,000	796,000	309,000
HCV	400,000	360,000	140,000

10% Reduction

65% Reduction

G.Q.

Thomas DL. N Engl J Med 2019;380(21):2041.

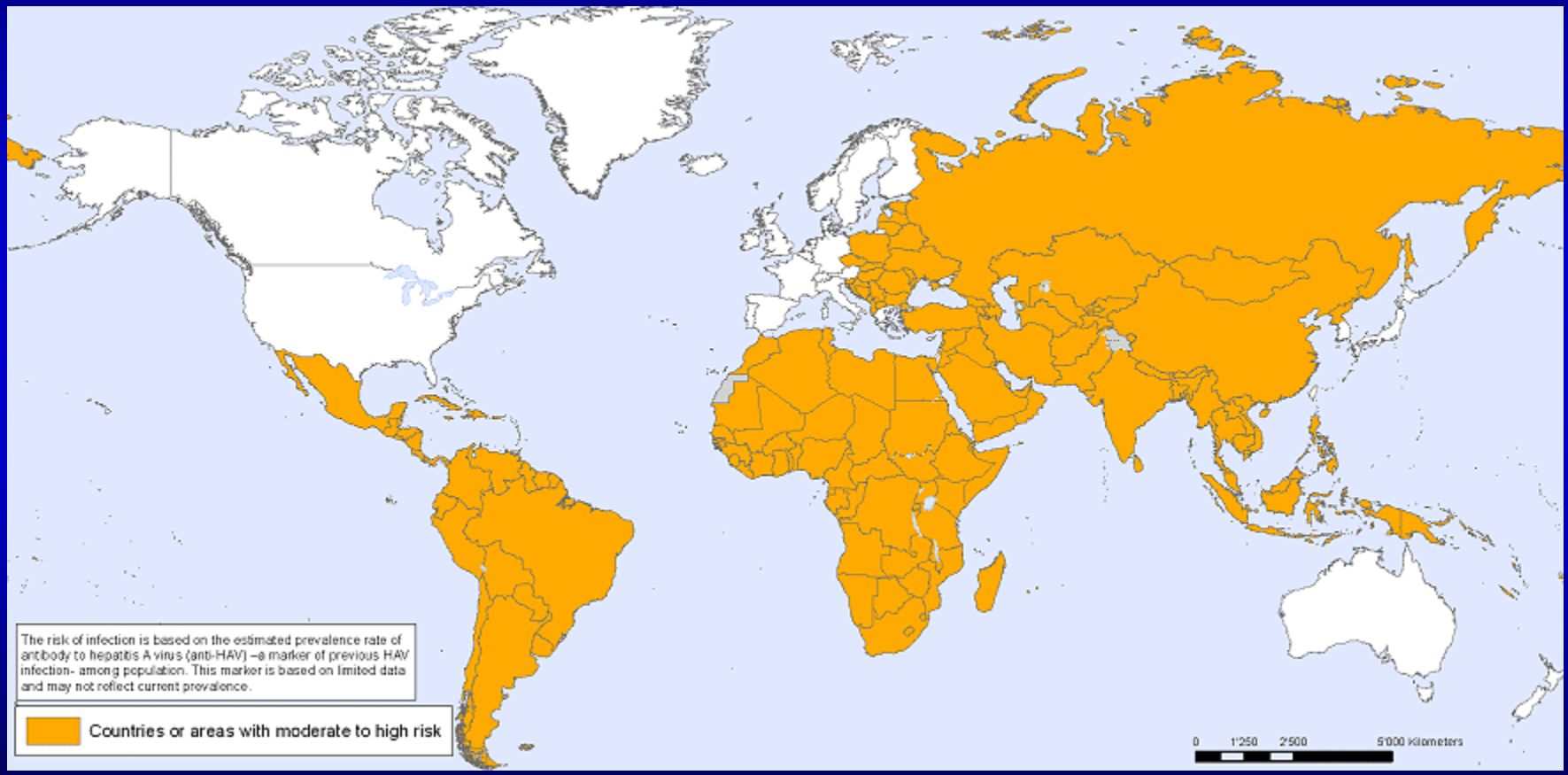
Hepatitis A

HEPATITIS A

- No chronic infection.
- Transmission: fecal-oral route
  - Ingestion of fecal matter, even in microscopic amounts, from close person-to-person contact or ingestion of contaminated food or drinks.
- No available antiviral agent
- Very effective vaccines(+)

G.Q.

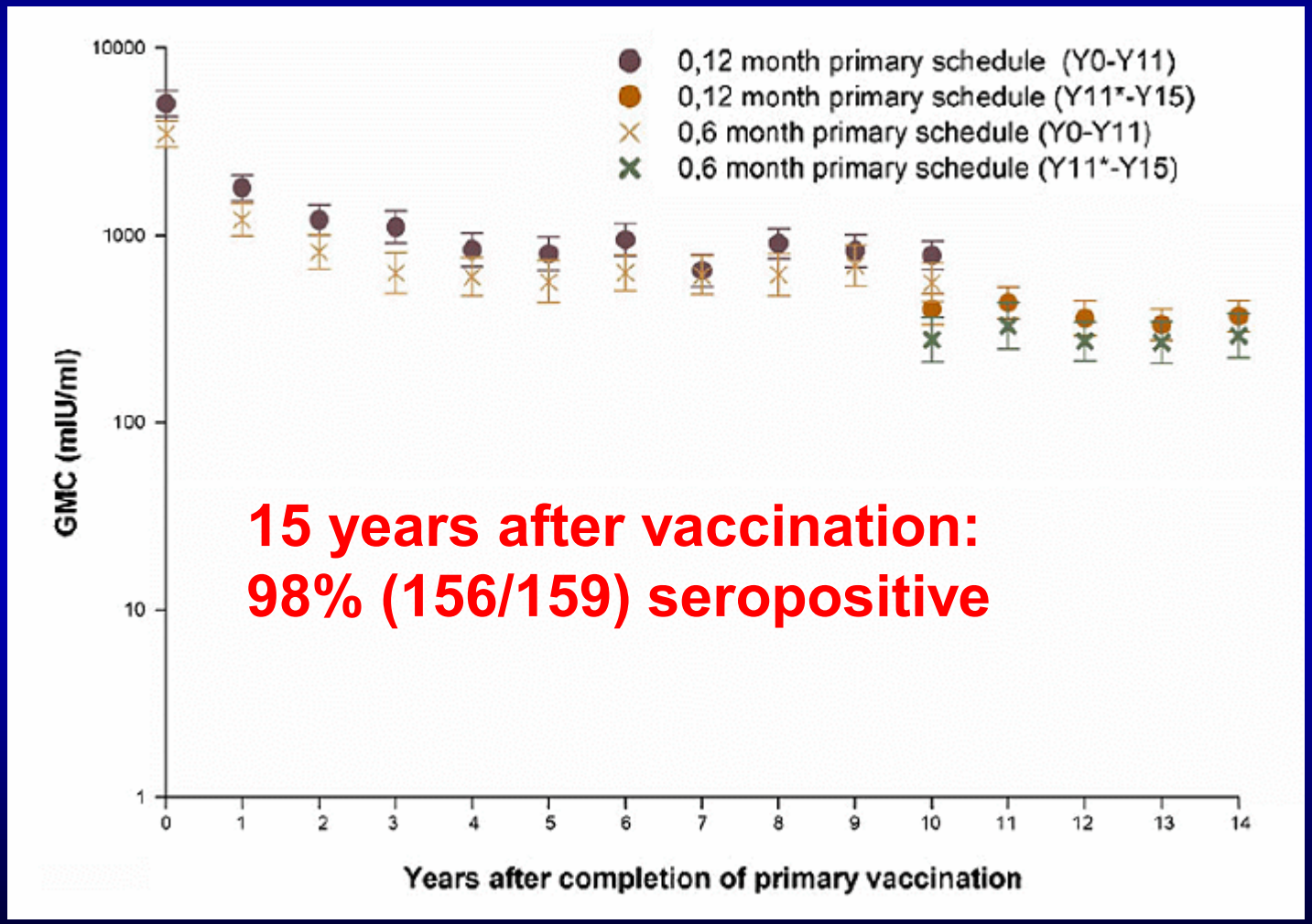
Countries/areas at risk for hepatitis A
2012, WHO



WHO website
(http://gamapserver.who.int/mapLibrary/Files/Maps/Global_HepA_ITHRiskMap.png?ua=1).

G.Q.

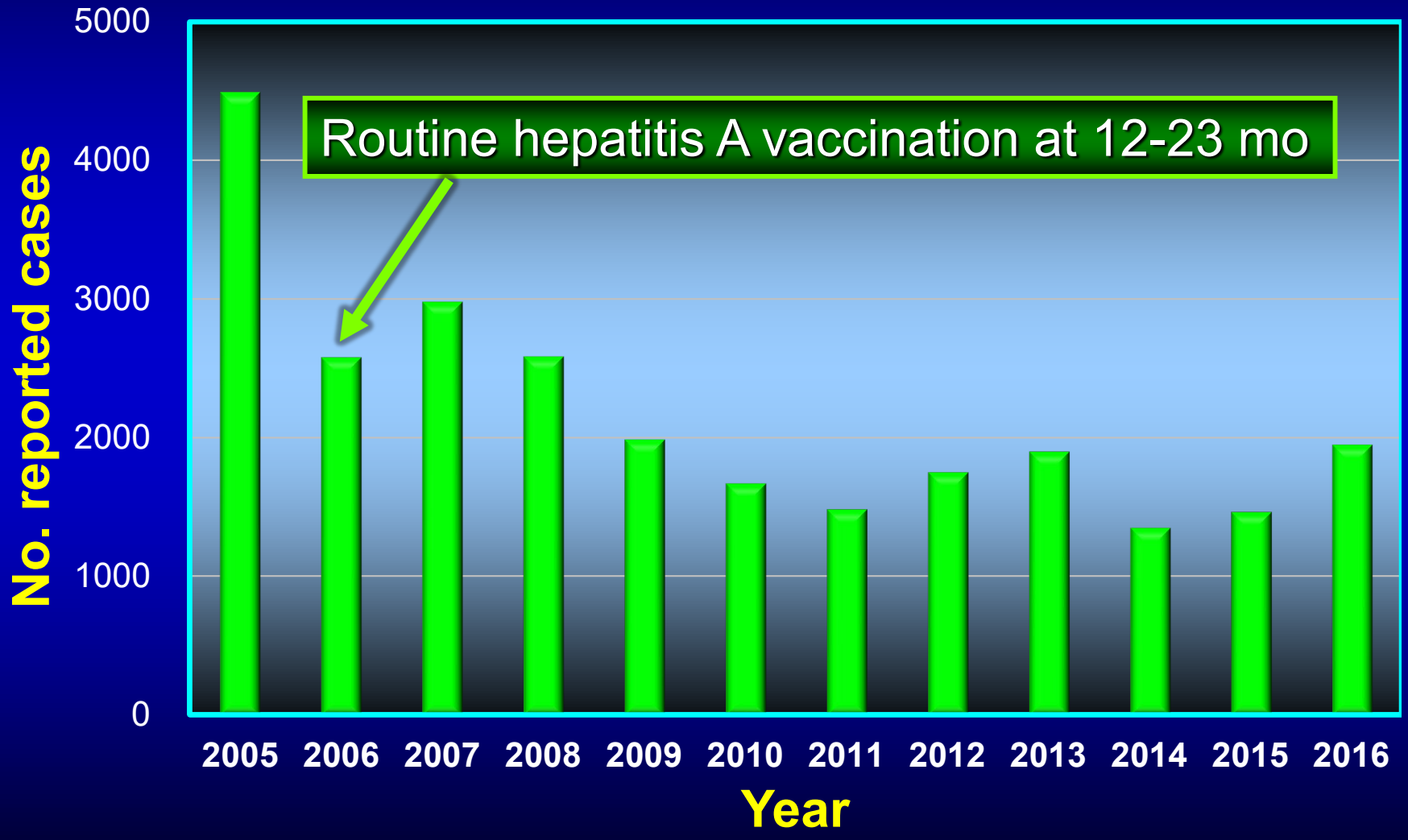
Long-term persistence of hepatitis A antibody after receiving 2 doses of inactivated hepatitis A vaccine N=159, adults, Belgium



G.Q.

Van Herck K. J Med Virol 2011;83(11):1185.

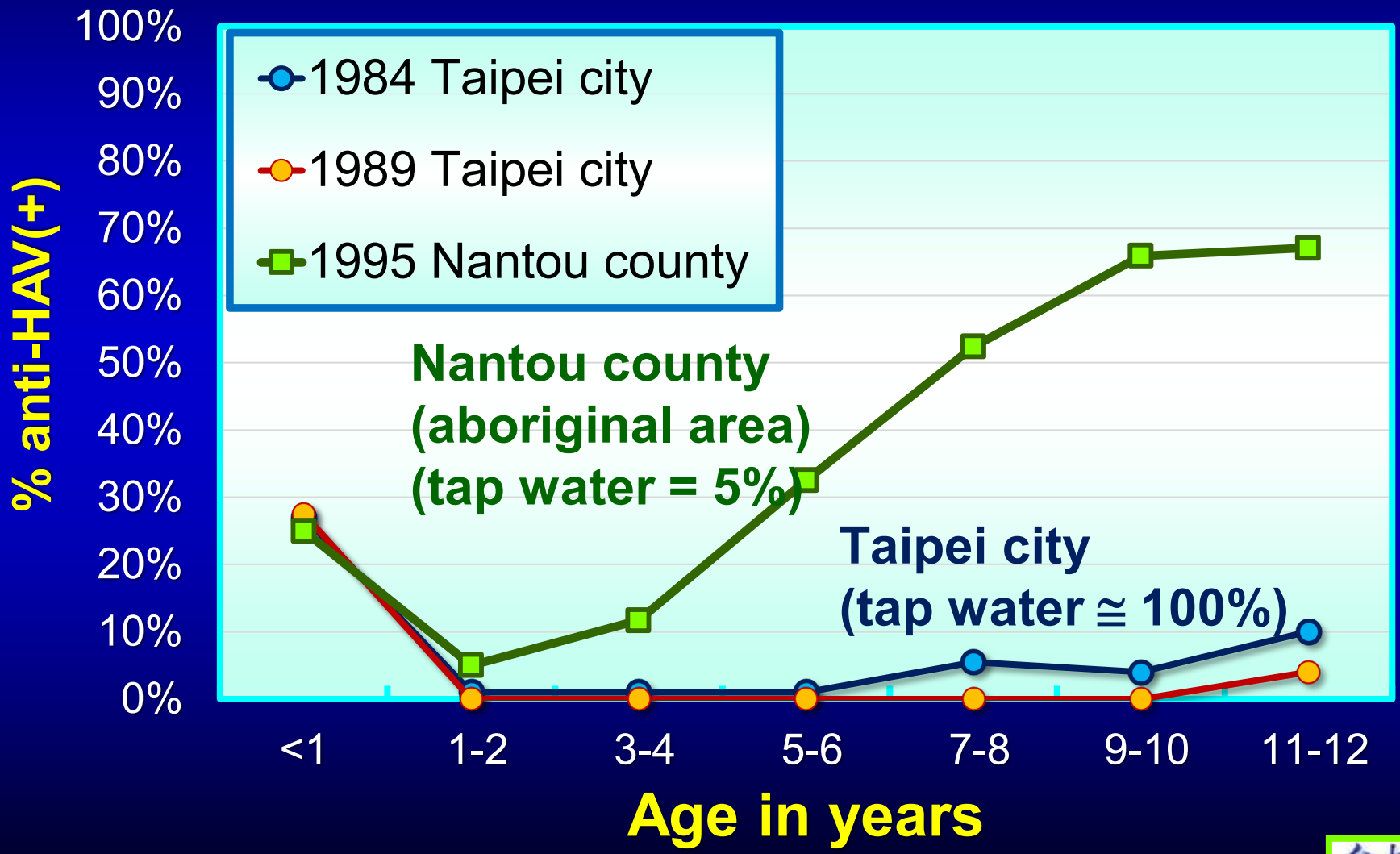
Disease burden from hepatitis A in the United States CDC, USA.



G.Q. CDC web site (https://www.cdc.gov/hepatitis/hav/havfaq.htm#general)

Seroprevalence of hepatitis A

Taiwan



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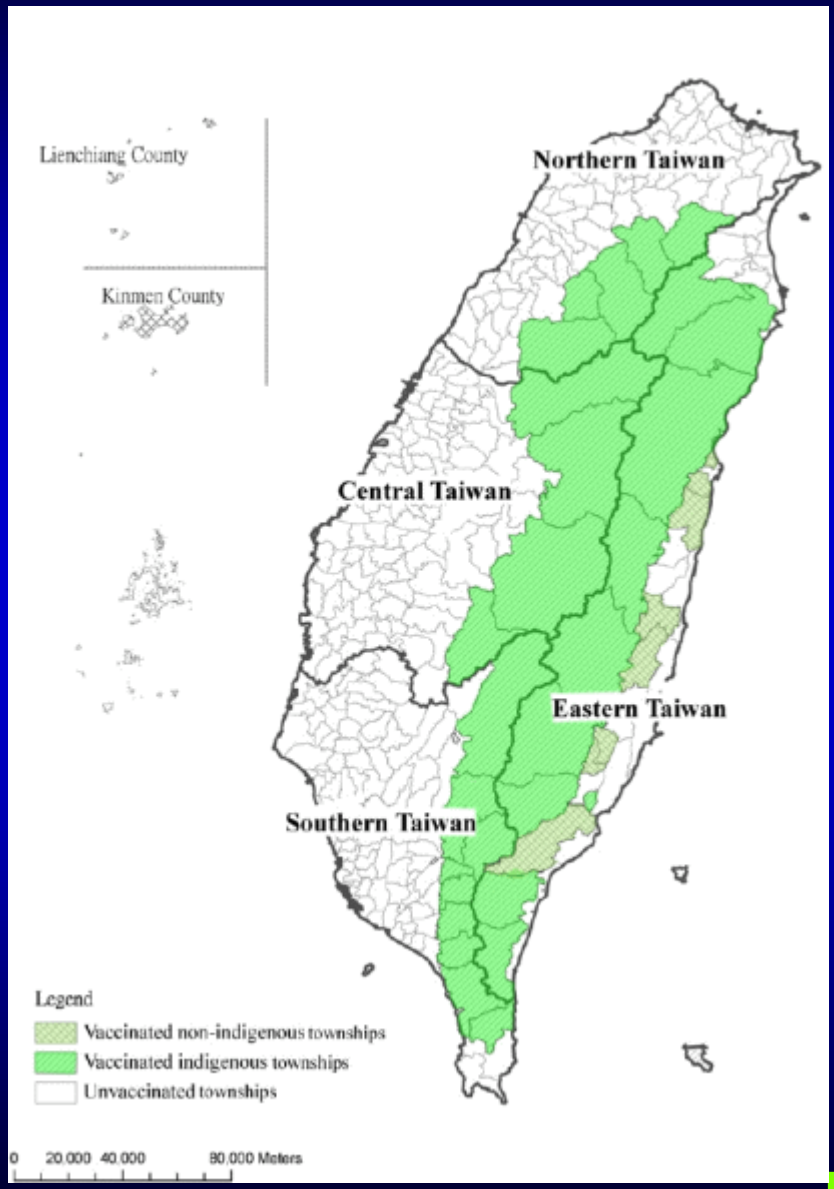
HAV vaccination strategy

CDC, Taiwan

- **1995**: Routine HAV vaccination in children at 12 to 23 months of age in **aboriginal areas**
- **2%** of pediatric population in Taiwan

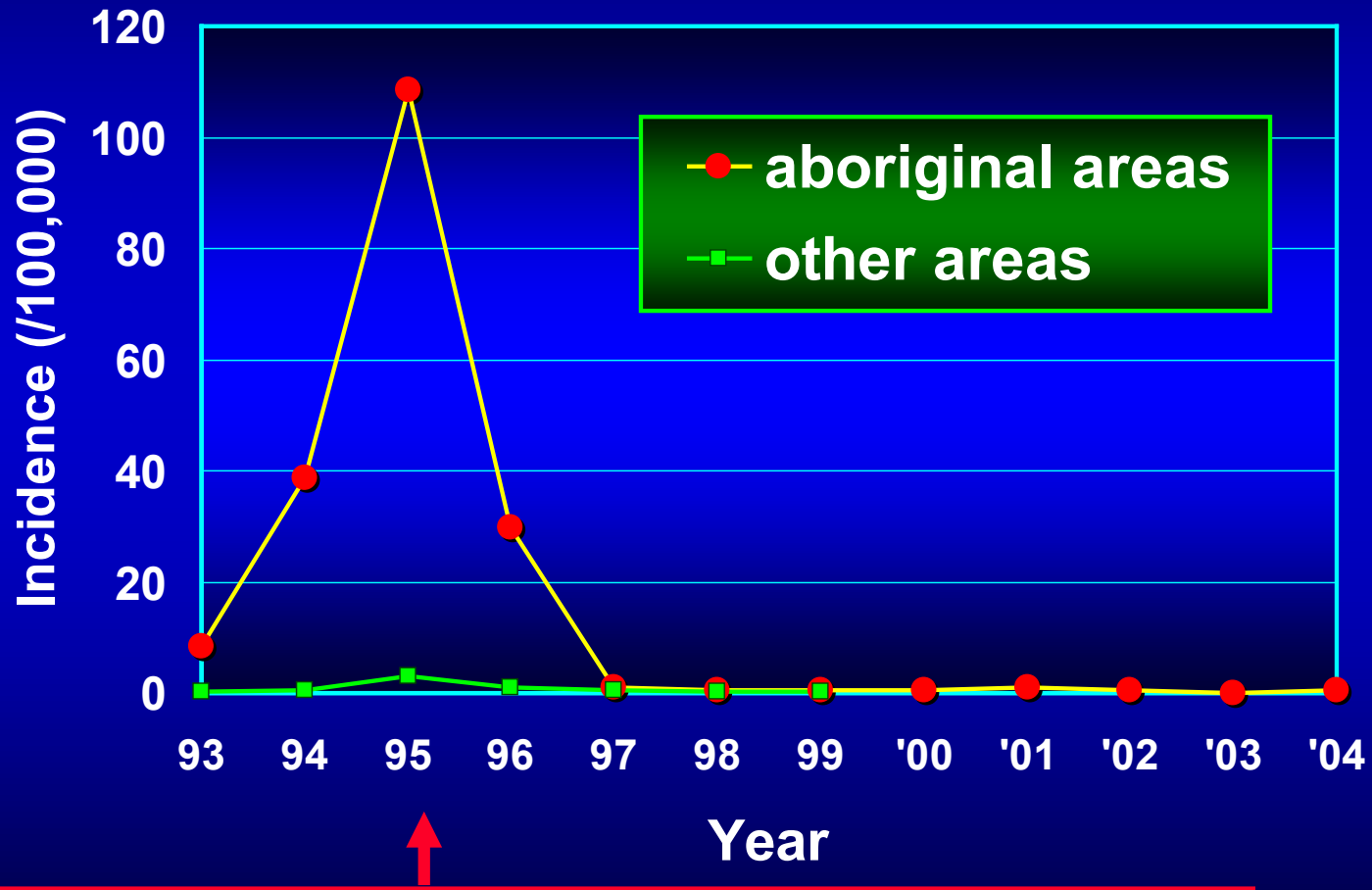


G.Q. Tsou TP. Vaccine 2011;29:2956.

台大醫院 NTUH

Incidence of hepatitis A

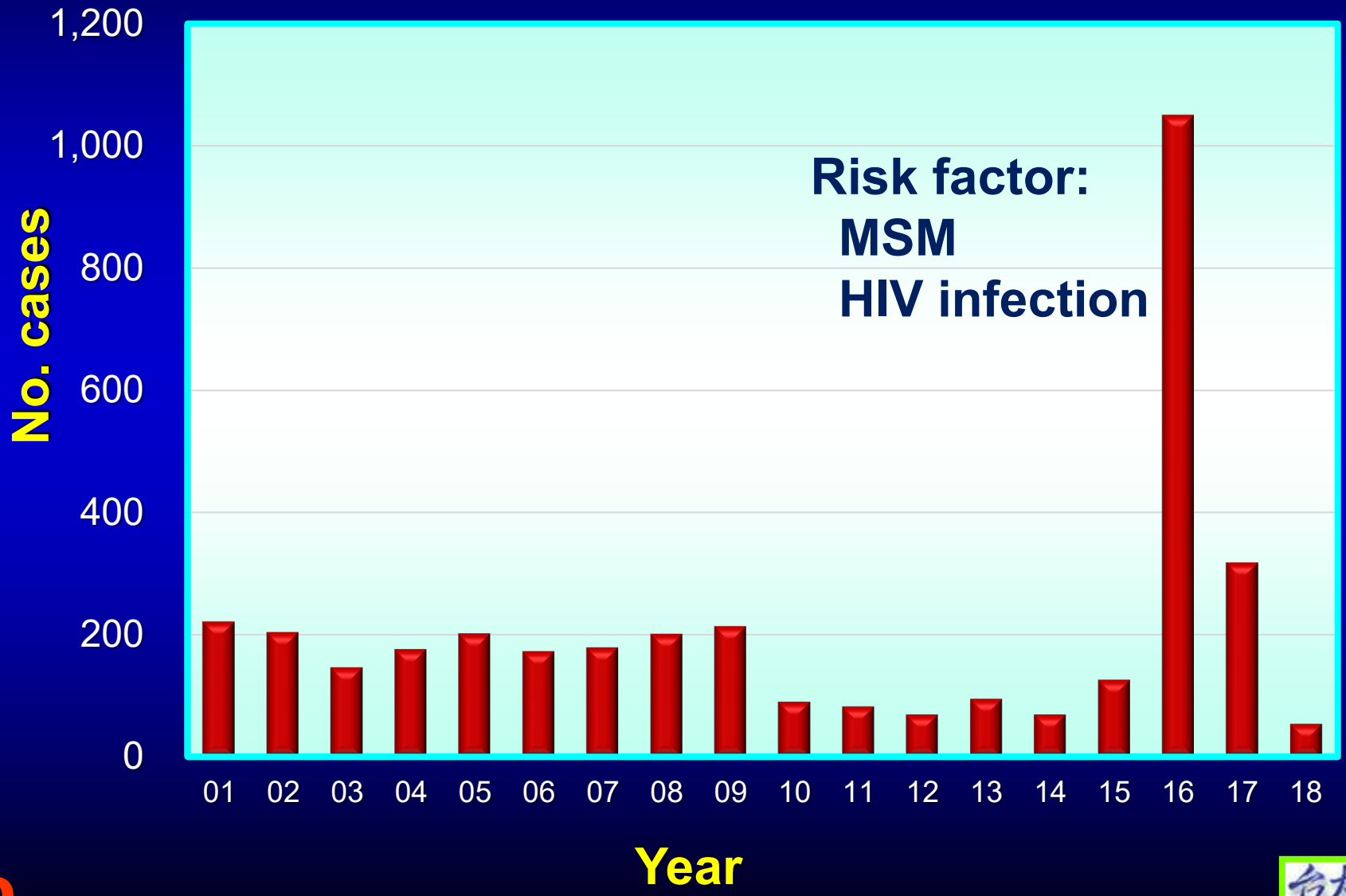
CDC Taiwan



G.Q.

Acute hepatitis A in Taiwan

CDC, Taiwan



G.Q.

Recommendations for use of hepatitis A vaccine 2006, ACIP, USA

- **Children**: 12-23 months
- **Traveling** to or working in countries that have high or intermediate endemicity of infection
- **MSM**
- Users of injection and noninjection **drugs**
- **Occupational risk** for infection
- **Clotting-factor disorders**
- **Chronic liver disease**

G.Q.

WHO position paper on hepatitis A vaccines 2012

- Both inactivated and live attenuated hepatitis A vaccines are highly immunogenic and immunization will generate long-lasting, possibly life-long, protection against hepatitis A in children as well as in adults.
- **WHO recommends that vaccination against HAV be integrated into the national immunization schedule for children aged ≥ 1 year if indicated** on the basis of incidence of acute hepatitis A, change in the endemicity from high to intermediate, and consideration of cost-effectiveness.

G.Q.

WHO. Wkly Epidemiol Rec 2012;87(28/29):261.

Hepatitis B

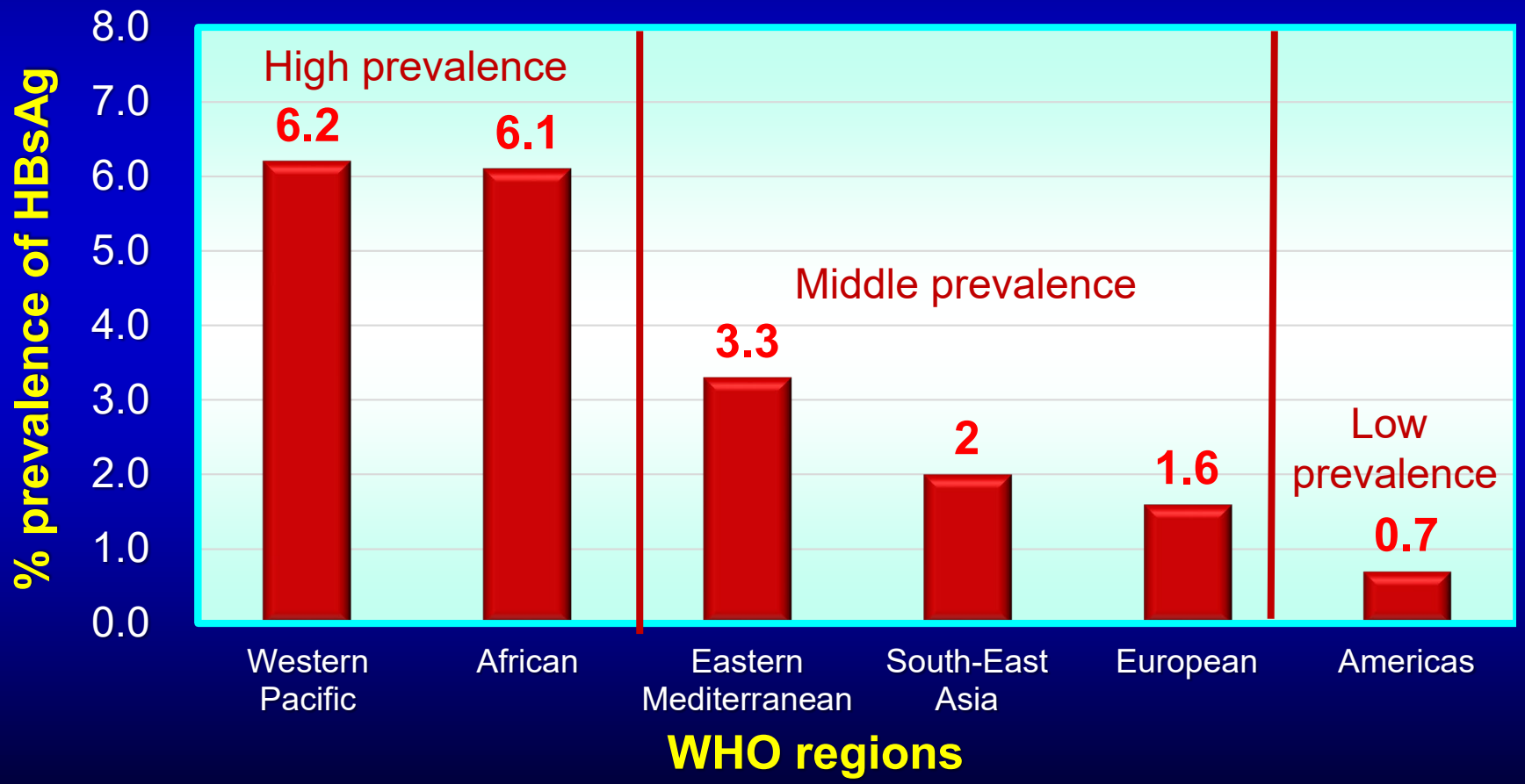
HEPATITIS B

- **Chronic infection(+)**
- **Transmission: parenteral**
  - Unsafe injection
  - Blood transfusion
  - Illegal drug use
  - Sexual transmission
  - Occupational exposure
  - Perinatal transmission: up to 90% of infants born to HBeAg(+) carrier mothers.
- **Antiviral agents(+) with limited effect**
- **Very effective vaccines(+)**

G.Q.

Prevalence of HBV infection (HBsAg) in the general population by WHO region WHO, 2015

Globally, in 2015, an estimated 257 million people were living with chronic HBV infection.



Global Hepatitis Report, 2017
(http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/)

G.Q.

Hepatitis B Virus

Taiwan

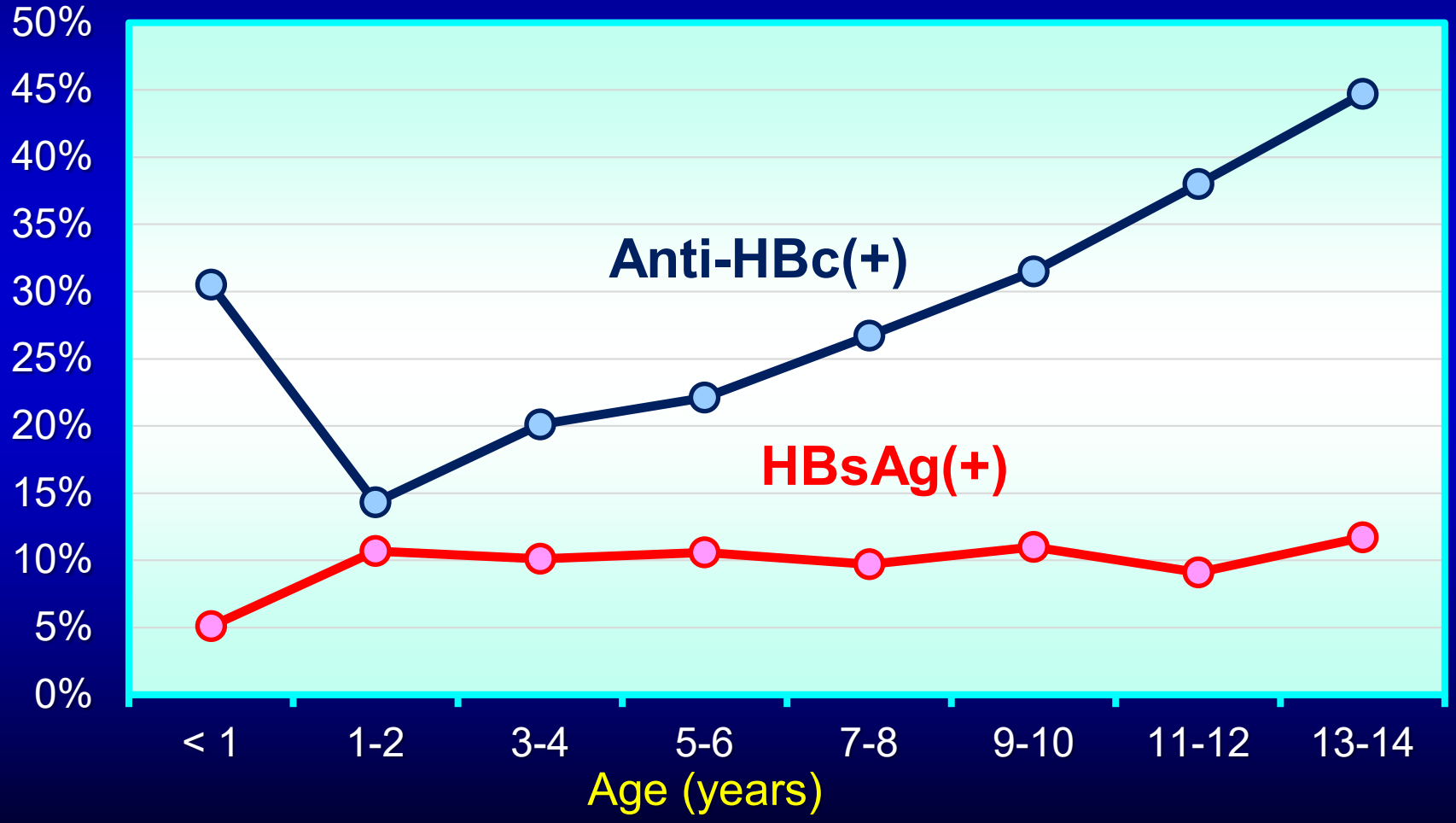
- HBsAg carriers: **10-20%** before vaccination
- Transmission:
  - **Vertical: 40-50% of carriers**
    - HBeAg(+) mother: **90%** carrier children
    - HBeAg(-) mother: **10%** carrier children
  - **Horizontal:**
    - Unsafe injection
    - Living with highly infectious family members

G.Q.

Seroepidemiology of HBV infection in Taipei

1984, pre-vaccination program

Age of infection↓ chronic infection↑



G.Q.

Hsu HY et al., J Med Virol 1986; 18:301

Hepatitis B Vaccine and HBIG

Beasley RP, 1983

- Infants born to HBeAg(+) carrier mothers

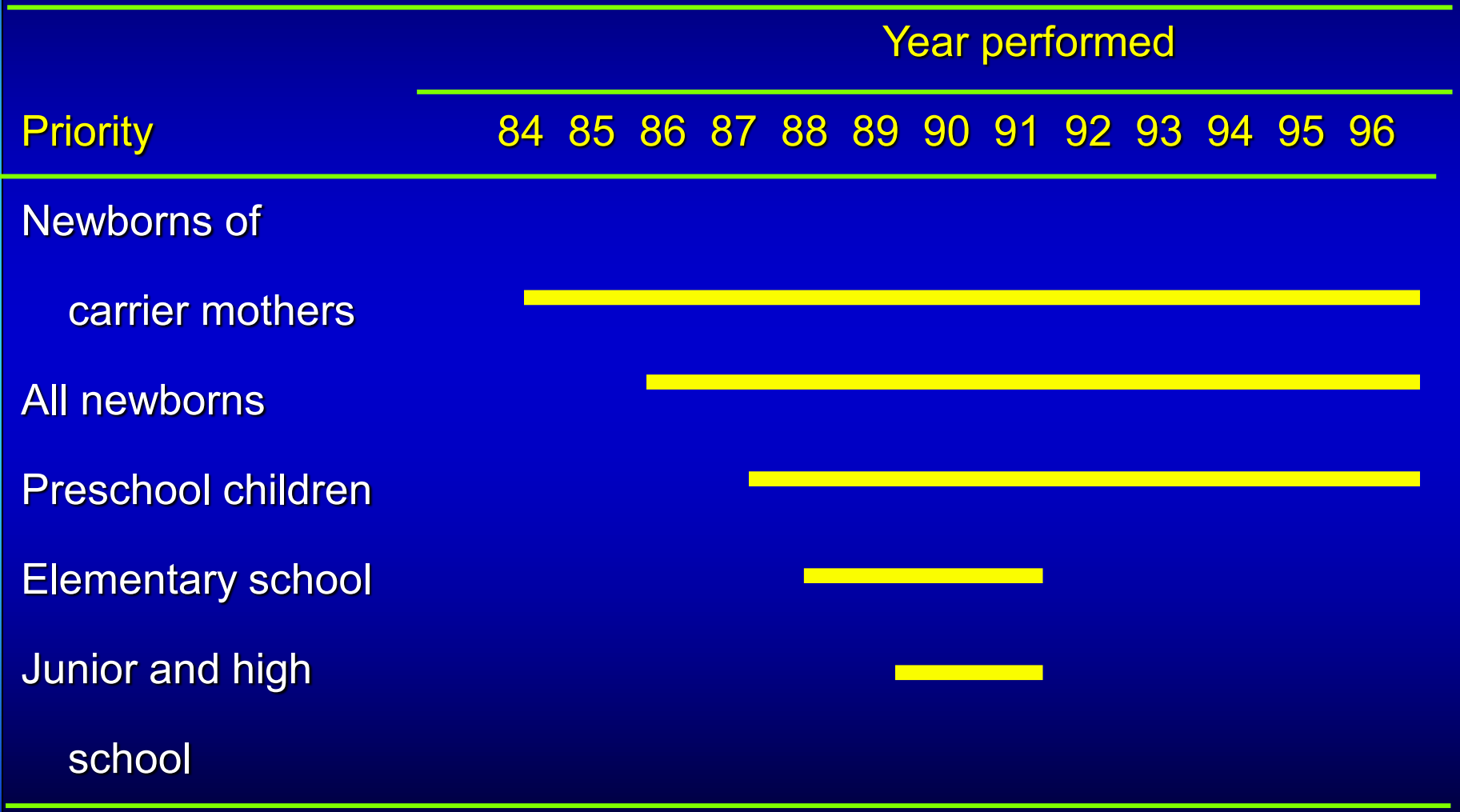
Vaccine	HBIG	No.	% carrier	Efficacy
-	-	61	**92**	-
-	at birth	67	54	**42%**
0-1-6 mo	-	57	33	**62%**
0-1-6 mo	at birth	50	6	**93%**

Vaccine: plasma-derived hepatitis B vaccine
HBIG: hepatitis B immune globulin

G.Q.

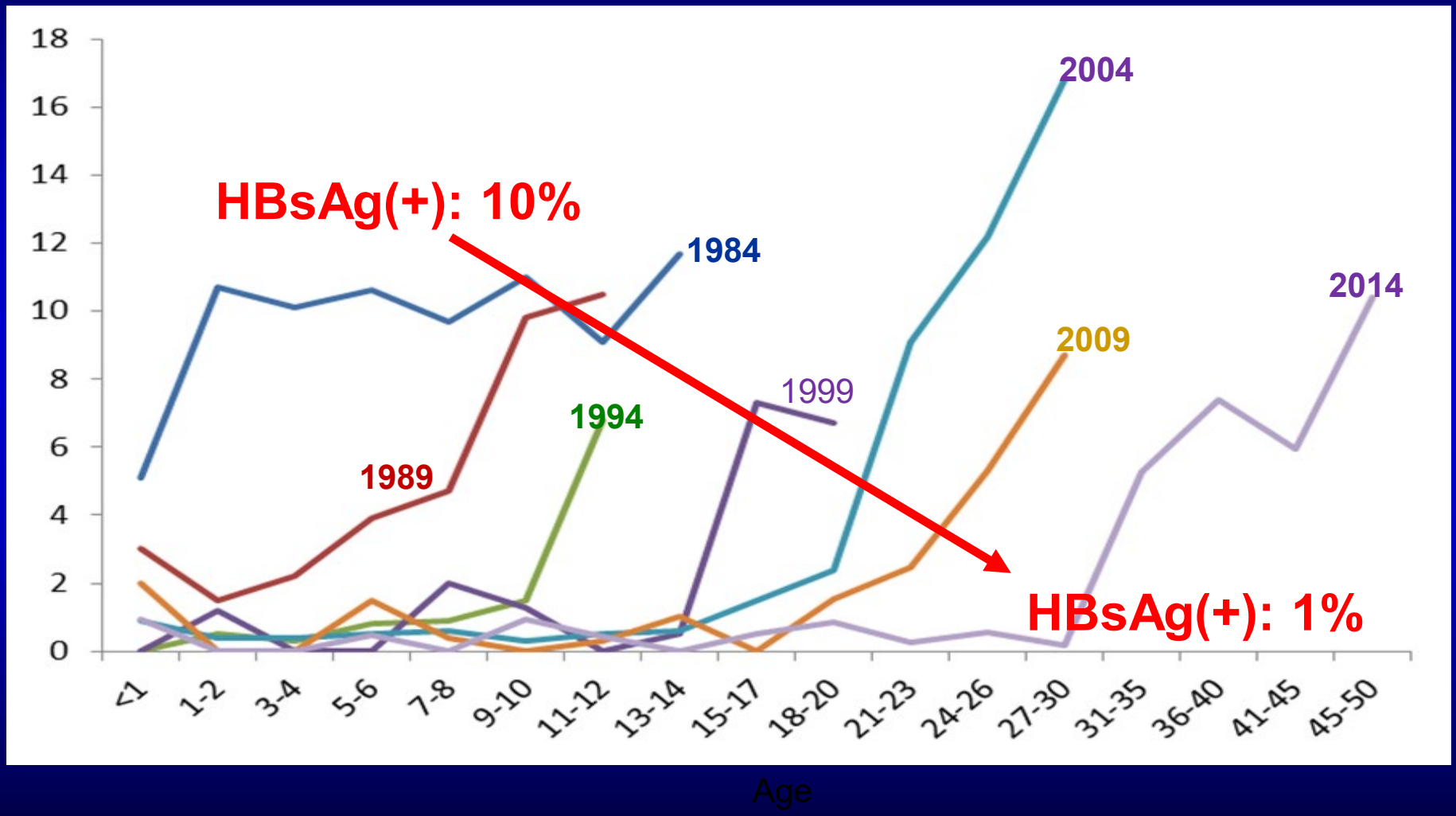
Beasley RP, Lancet 1983;ii:1099 Beasley RP, Hepatology 1983;3:135

Universal HB vaccination program
Started in 1984, Taiwan



G.Q.

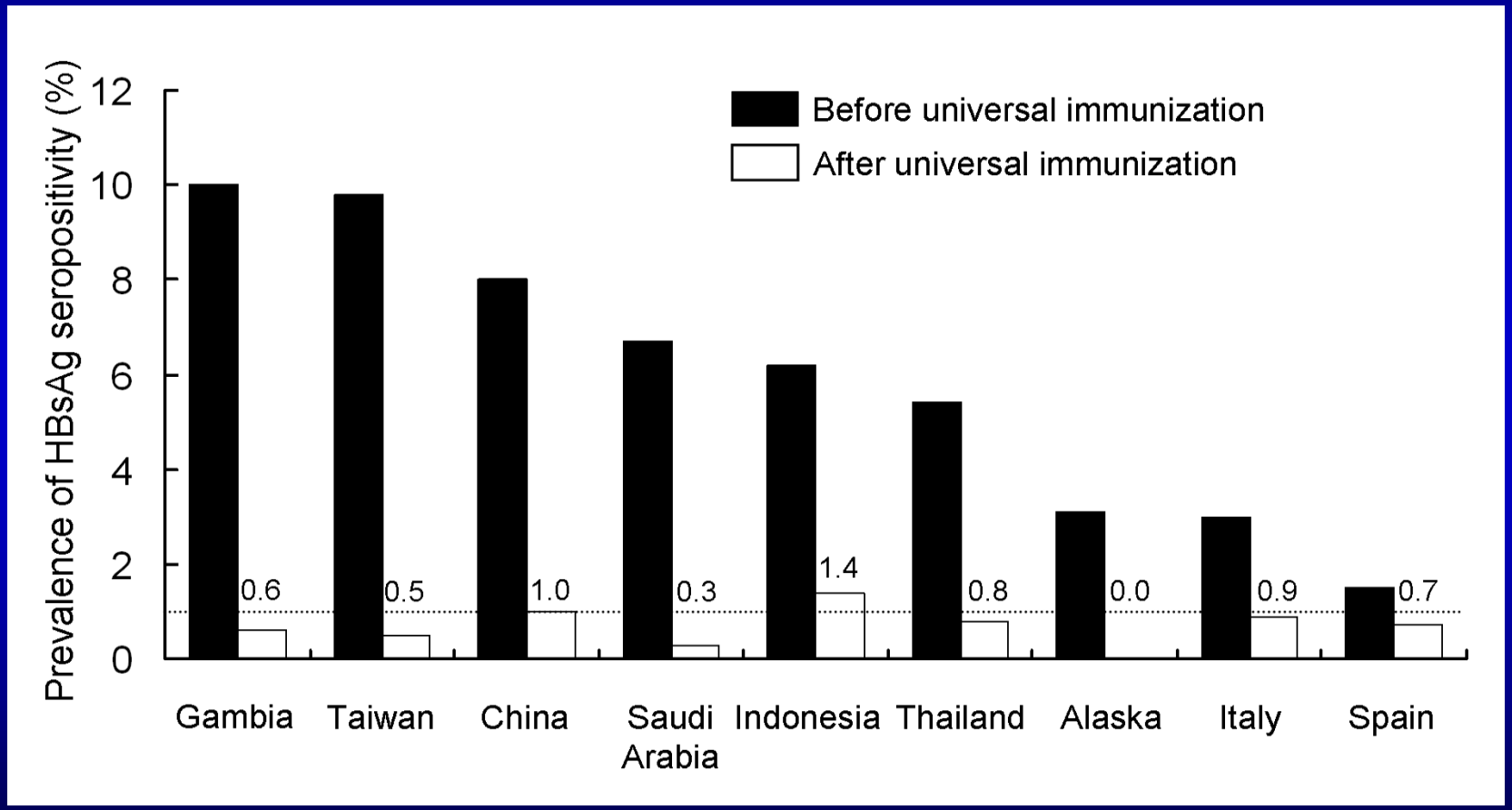
30-year follow-up of universal hepatitis B vaccination program Taipei, 1984-2014



Chen HL et al. JAMA 1996;276:906-8; Ni YH, et al. Ann Intern Med 2001;135:796-800;J Hepatol 2012; 57: 730-5; Clin Gastroenterol Hepatol. 2016 ;14:1324-30.

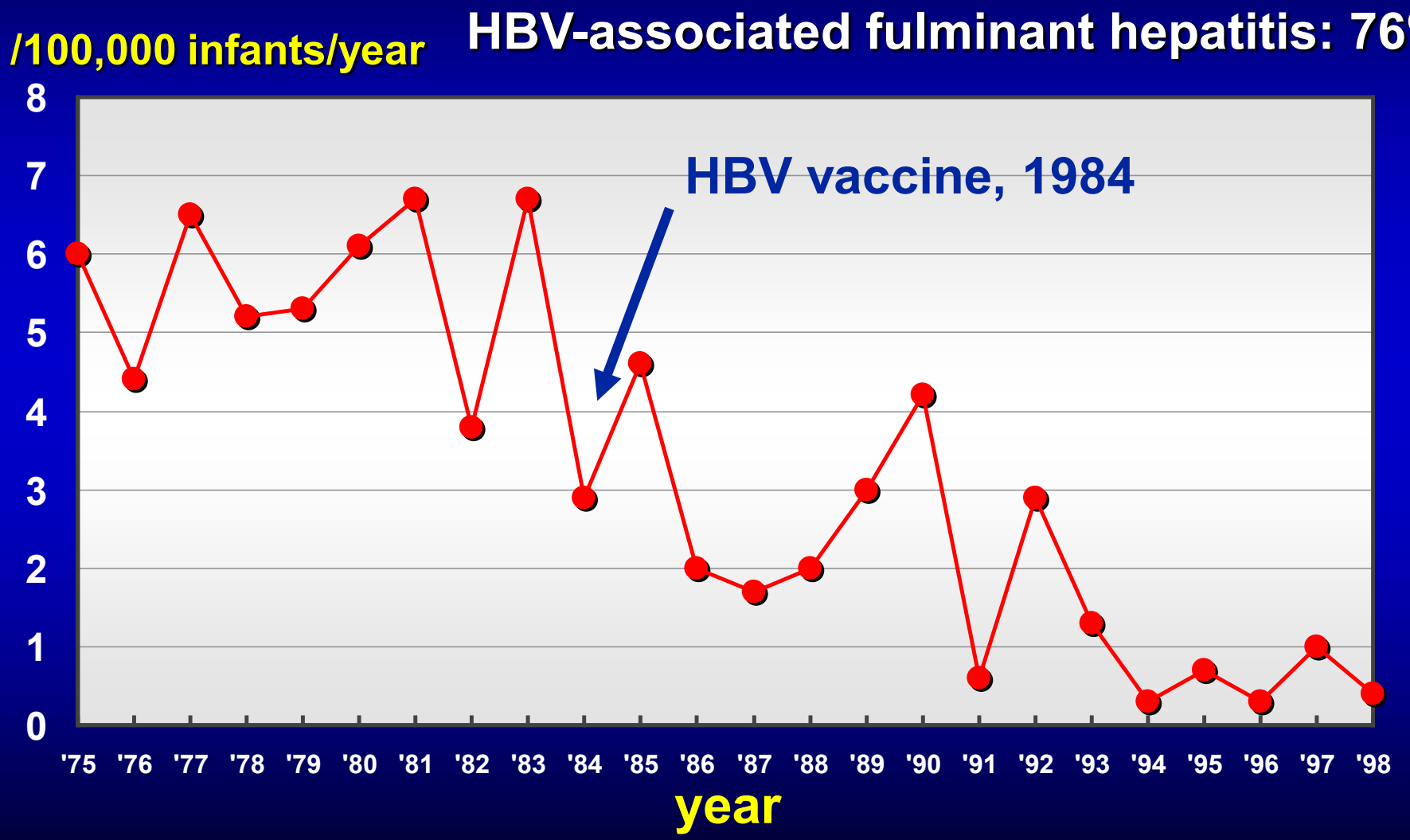
G.Q.

Global epidemiology of chronic hepatitis B in children before and after universal infant immunization programs



G.Q. Chen ST, Chang MH. In Jonas M ed., Viral Hepatitis in Children: Unique Features and Opportunities., 2010.

Annual mortality from fulminant hepatitis in infants 1975 - 1998



G.Q. Kao JH. J Pediatr 2001;139:349.

Mass HBV vaccination and hepatocellular carcinoma in children aged 6-14 years

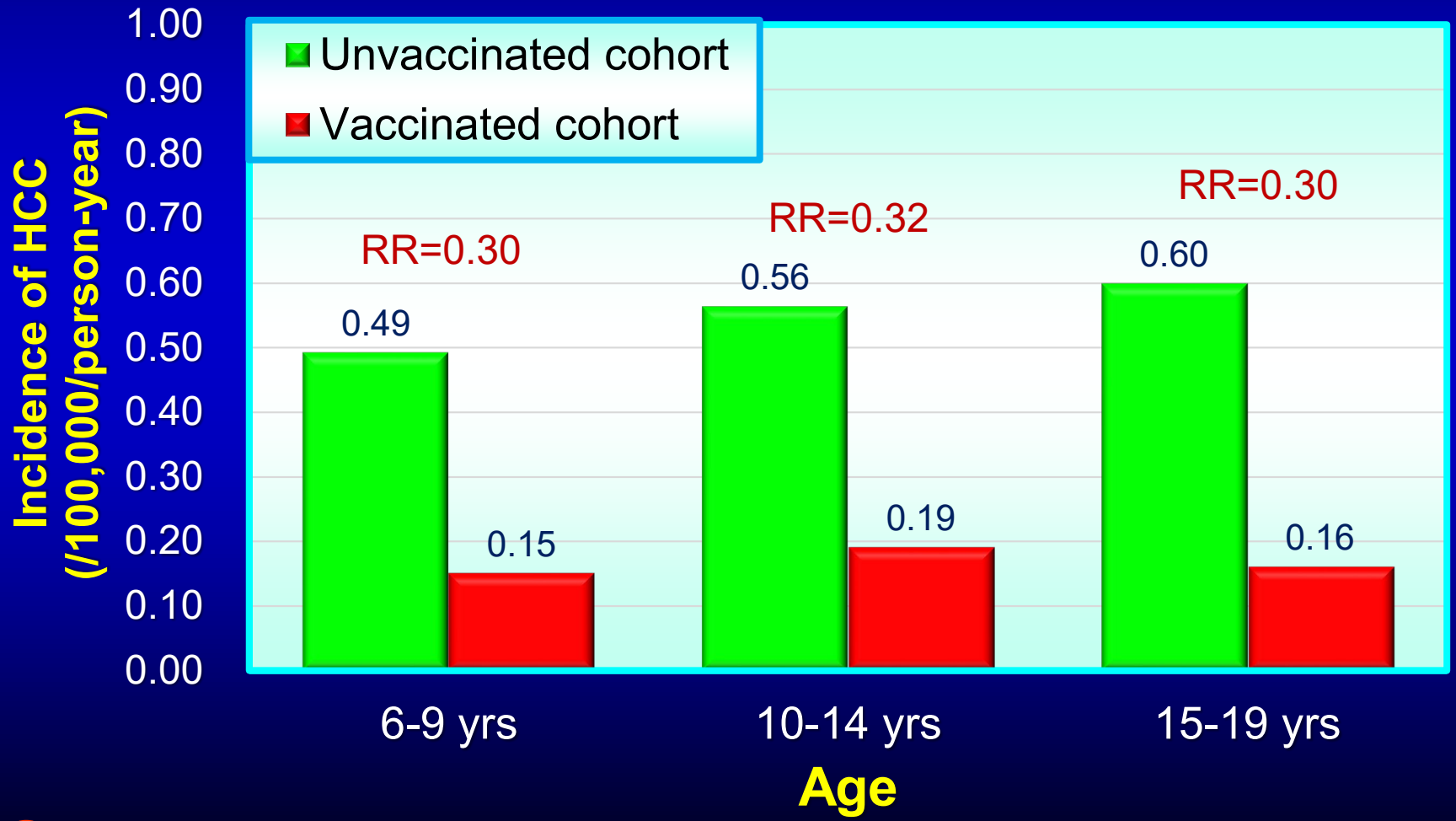
1981-1994

G.Q.

Chang MH. N Engl J Med 1997;336(26):1855.

Incidence of hepatocellular carcinoma in children aged 6-19 years 1983-2004

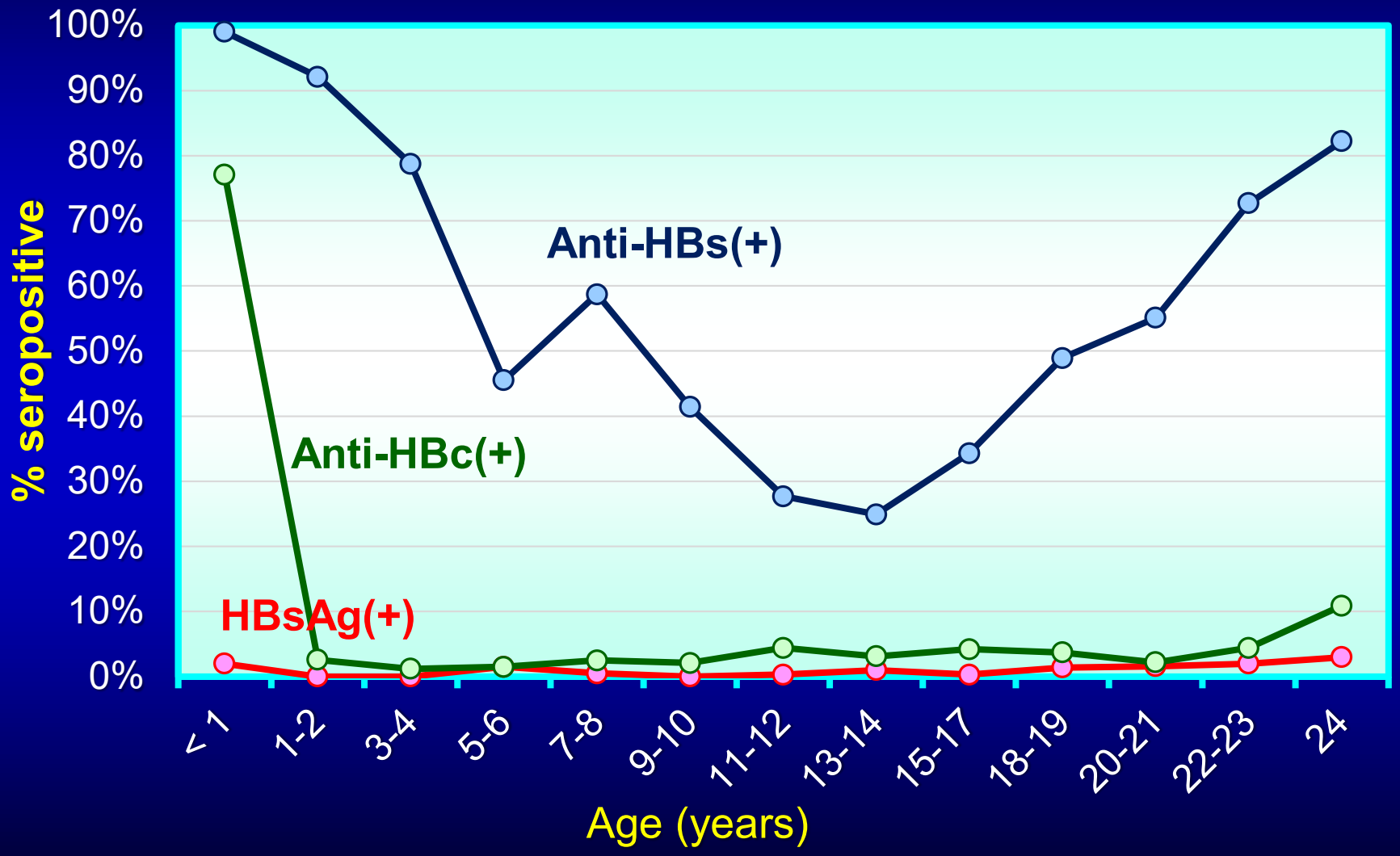
Relative risk: **0.31** after HBV vaccination program (1984)



G.Q.

Chang MH. J Natl Cancer Inst 2009;101:1348.

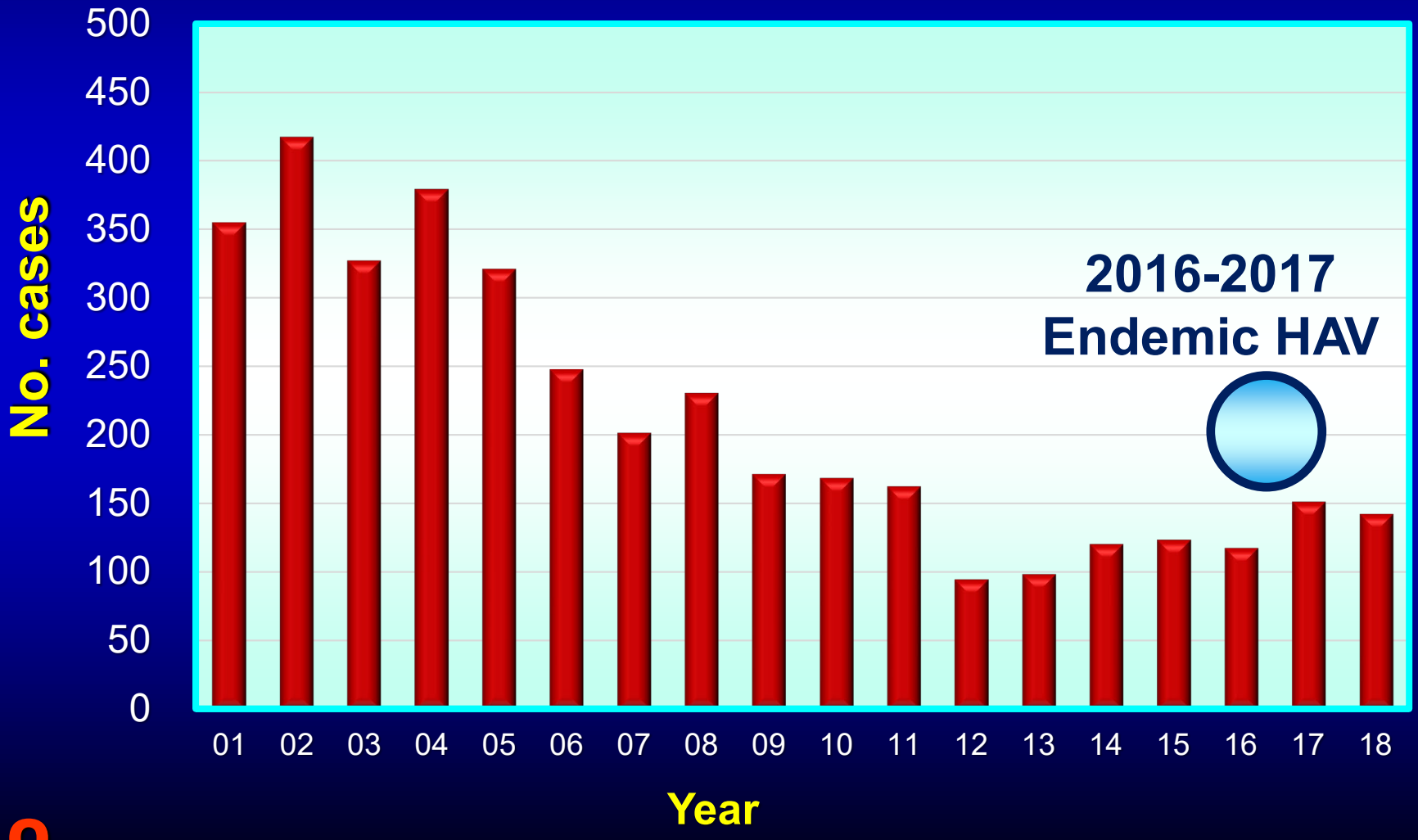
Seroepidemiology 25 years after universal vaccination in Taipei



G.Q. Ni YH. J Hepatol 2012;57(4):730.

Acute hepatitis B in Taiwan

CDC, Taiwan



G.Q.

WHO position paper on hepatitis B vaccines 2017

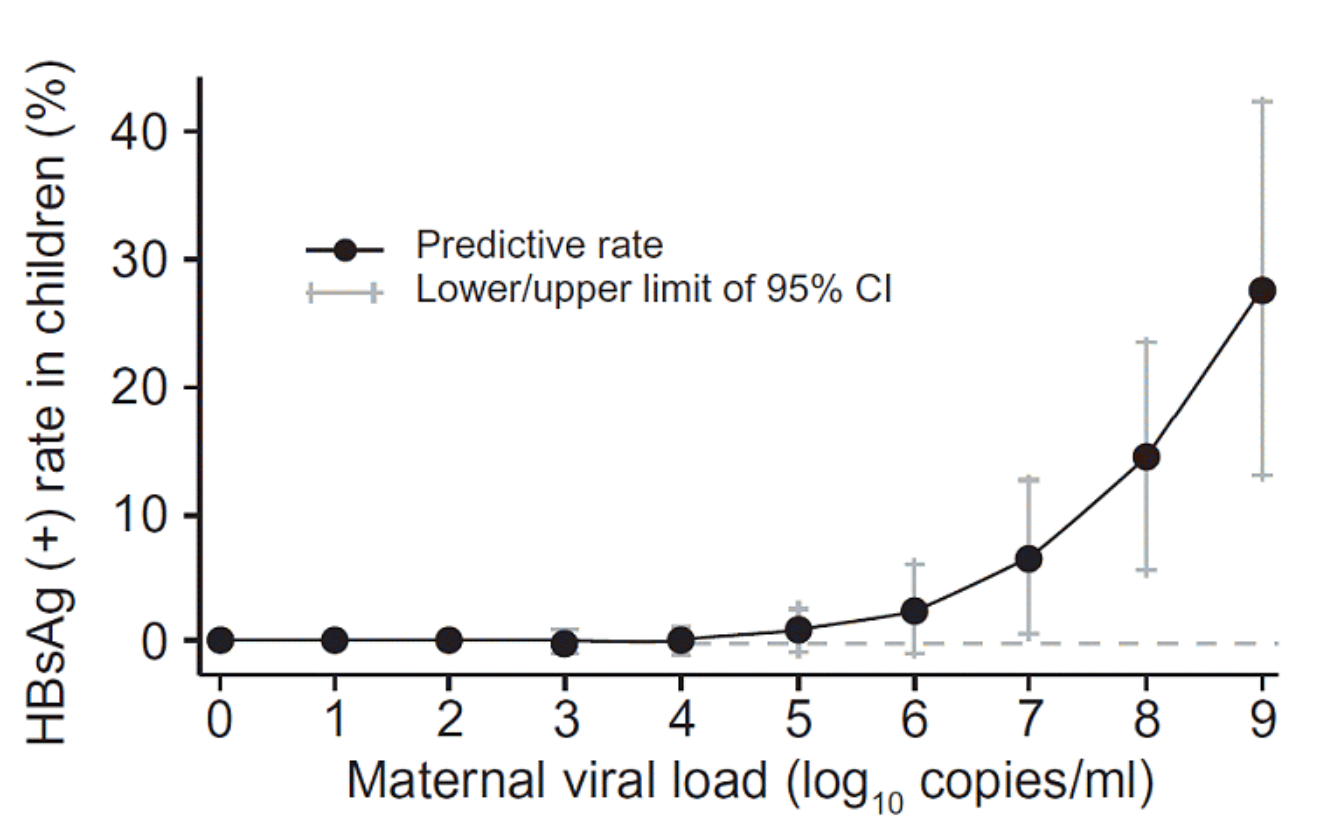
- WHO recognizes the importance of hepatocellular carcinoma and other HBV-related diseases as global public health problems and reiterates its recommendation that **hepatitis B vaccines should be included in national immunization programmes**.
- **Hepatitis B vaccination is recommended for all children worldwide.** Reaching all children **with at least 3 doses** of hepatitis B vaccine should be the standard for all national immunization programmes.
- All national programmes should include a **monovalent hepatitis B vaccine birth dose**.

G.Q. WHO. Vaccine 20197;37(2):223.

Predictive rates of HBV infection at various maternal viral load levels

N=303, 2007-2011, Taiwan

Immunoprophylaxis failure at birth: **10%**

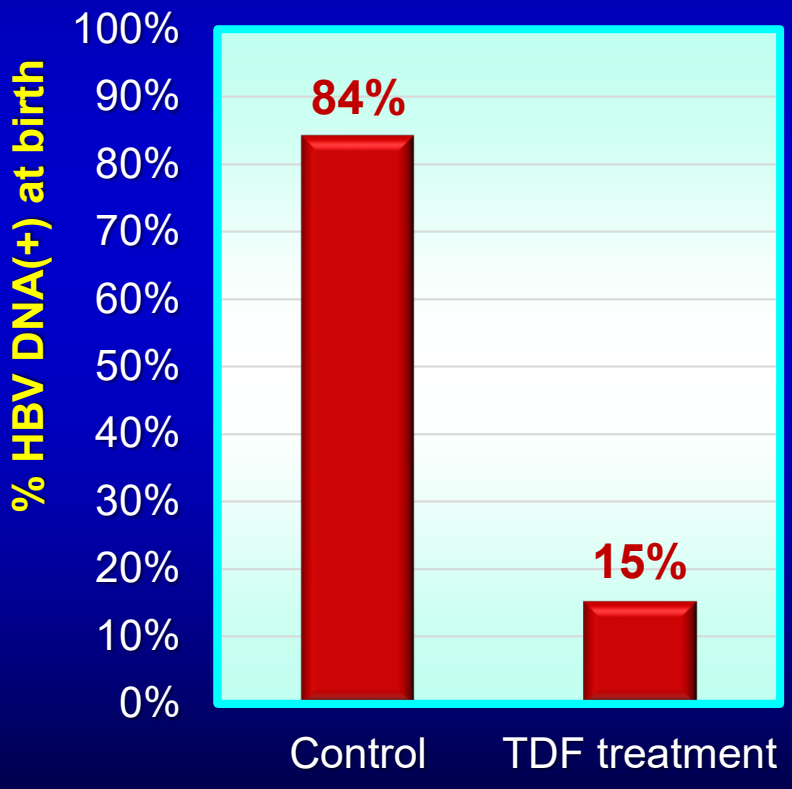


G.Q. Wen WH. J Hepatol 2013;59(1):24.

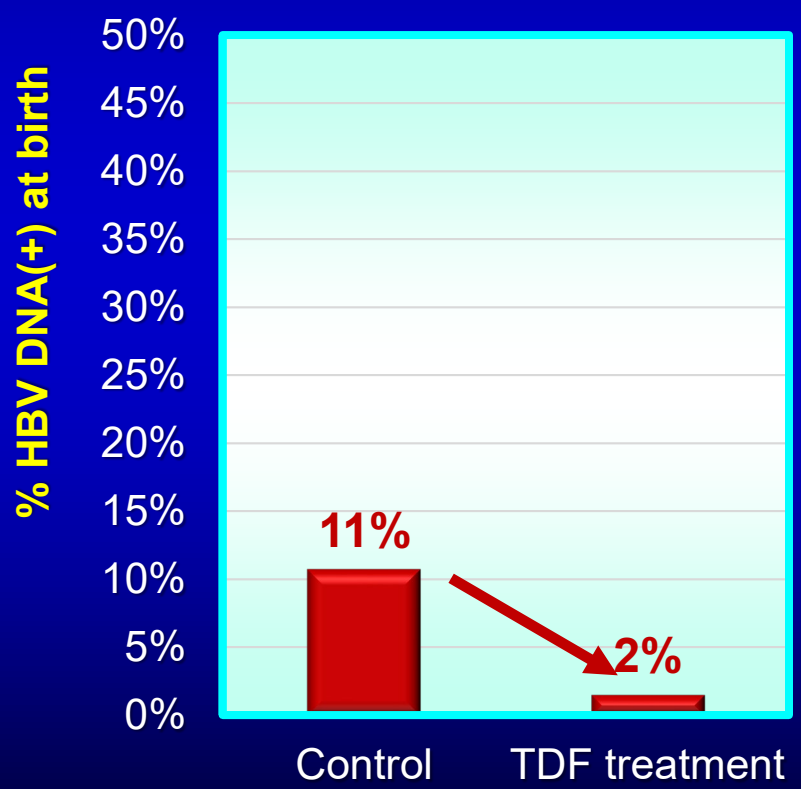
Maternal tenofovir for interrupting mother-to-infant transmission of hepatitis B Virus

N=118, 2011-2013, Taiwan

Tenofovir:* ↓ HBV DNA at birth



Tenofovir:* ↓ HBsAg(+) at 6 mo



* Tenofovir: from 30-32 weeks of gestation until 1 month postpartum

G.Q. Chen HL. Hepatology 2015;62(2):375.

Hepatitis C

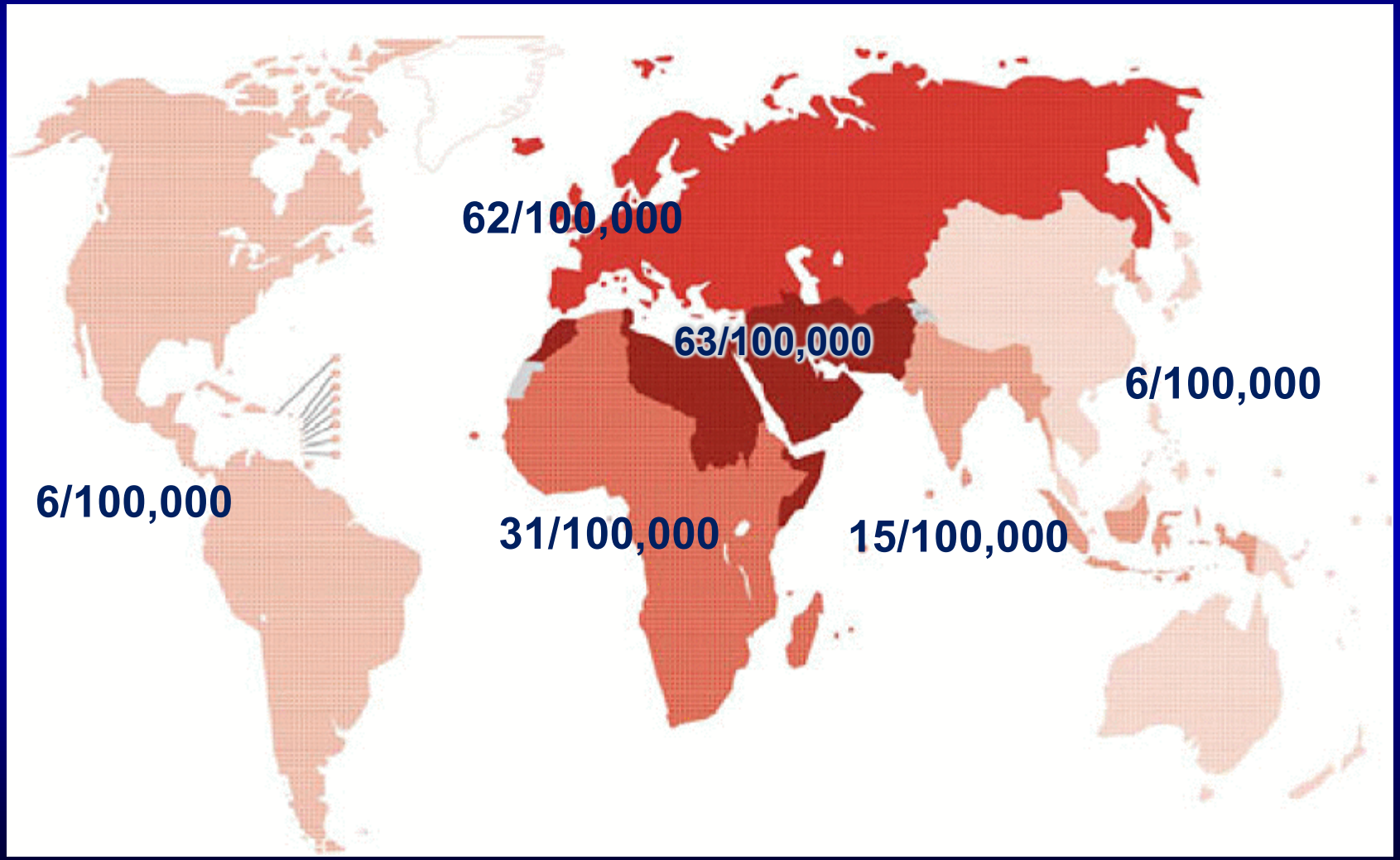
HEPATITIS C

- **Chronic infection(+)**
- **Transmission: parenteral**
  - Unsafe injection
  - Blood transfusion
  - Illegal drug use
  - Sexual transmission
  - Occupational exposure
  - Perinatal transmission: up to 5% of infants born to viremic mothers.
- **Antiviral therapy: very effective**
- **No effective vaccine**

G.Q.

Incidence of HCV infection in the general population WHO, 2015

1.75 million new infections



G.Q.

WHO. Global Hepatitis Report, 2017
(http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/)

Hepatitis C vaccine

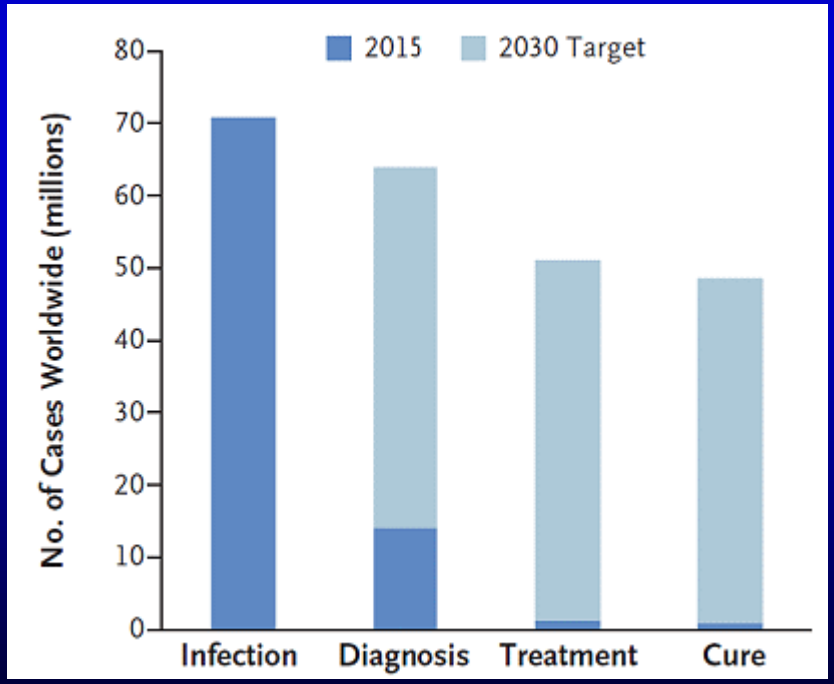
- **Barriers to HCV vaccine development**
  - Virus diversity
  - Limited models for testing vaccines
  - Incomplete understanding of protective immune responses
- **Vaccines in development**
  - Adjuvant envelope or core protein
  - Virus-vectored nonstructural antigen vaccines
  - Viral vectors encoding nonstructural proteins
- **A prophylactic vaccine is necessary for global control of HCV.**

G.Q.

Bailey JR. Gastroenterology 2019;156(2):418.

Hepatitis C: elimination by treatment

- **Treatment: cure rate > 95%**
  - Diagnosis and treatment: **very expensive**
- **2015:** only **20%** of the 71 million persons infected received a diagnosis, and only **7%** were successfully treated.



G.Q.

Thomas DL. N Engl J Med 2019;380(21):2041.

Anti-HCV therapy funded by National Health Insurance 2018, Taiwan

- **Oral agents: 3-6 months, cure rate > 95%**
  - Daklinza + Sunvepra: genotype 1b, 24 weeks
  - Viekirax + Exviera: genotype 1b, no cirrhosis, or compensated cirrhosis, 12 weeks
  - Viekirax + Exviera + ribavirin: genotype 1a, no cirrhosis, 12 weeks
  - Viekirax + Exviera + ribavirin: genotype 1a, compensated cirrhosis, 24 weeks
  - Zepatier +/- ribavirin: genotype 1a, not resistant strain, 12 weeks
  - Zepatier + ribavirin: genotype 1a, resistant strain, 16 weeks
  - Zepatier +/- ribavirin: genotype 1b, 12 weeks
  - Zepatier: genotype 4, 12 weeks
  - Zepatier + ribavirin: genotype 4, 16 weeks
  - Harvoni +/- ribavirin: genotype 1, 4, 5, or 6, 12 weeks
  - Sovaldi + ribavirin: genotype 2, 12 weeks

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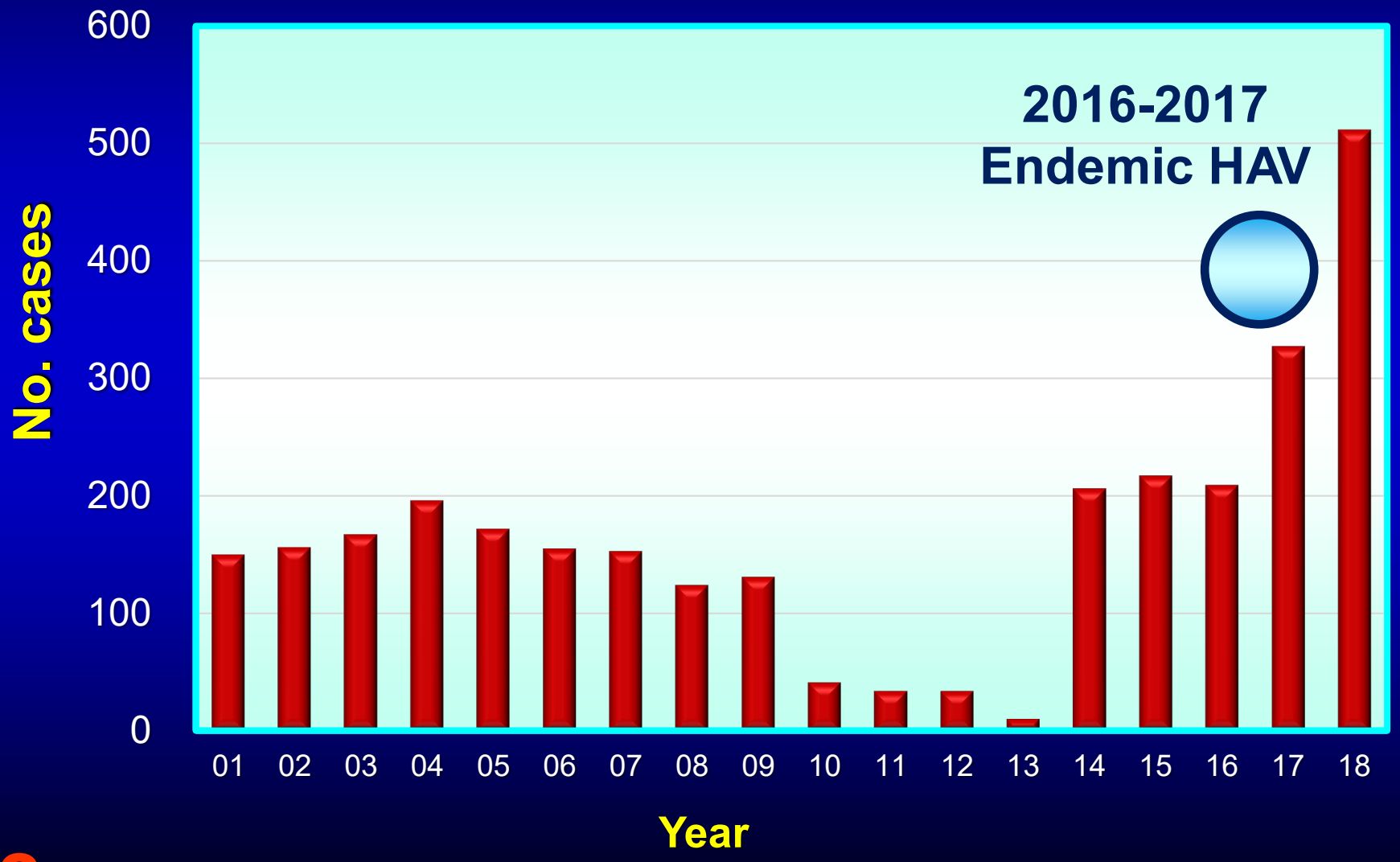
Acute hepatitis C in Taiwan

CDC, Taiwan



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Hepatitis D

HEPATITIS D

- A **defective** virus
- Infects only those already having **HBV infection**
- Transmission: **parenteral route**
- **Chronic infection(+)**
- Worsens the outcome of HBV infection
- **5%** of HBV-infected persons are co-infected with HDV
- No effective vaccine
- Prevention of HBV infection through vaccination also prevents HDV infection.

Global Hepatitis Report, 2017
(http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/)

G.Q.

HEPATITIS D

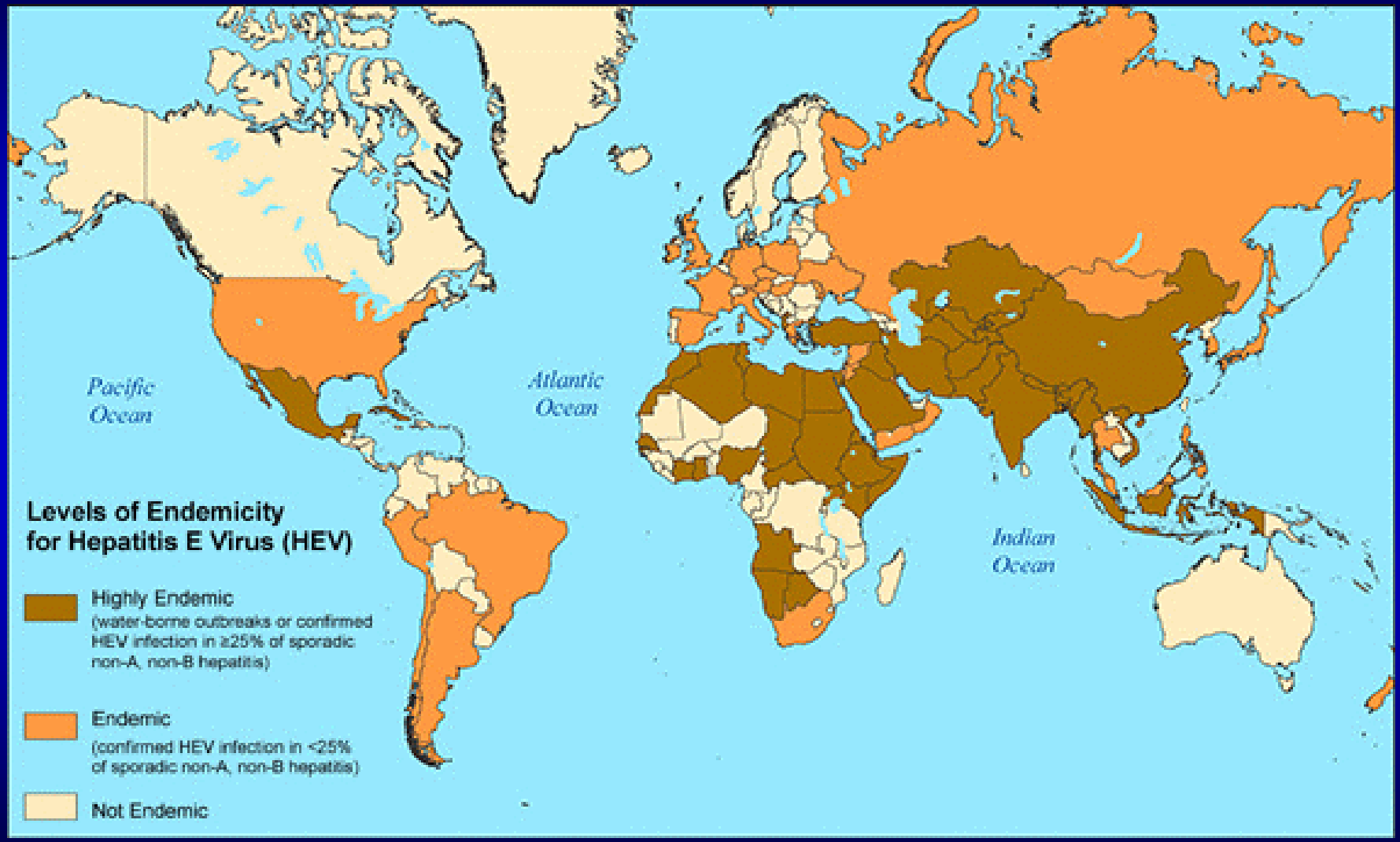
Hepatitis E

- **No chronic infection**
- Transmission: **fecal-oral route**
- Incidence: 3.3 million acute hepatitis E every year
- Illness usually self-limited, but some patients may progress to **acute liver failure**
- Higher case fatality in **pregnant women**
- **No available antiviral agent**
- **Vaccine(+)**

Global Hepatitis Report, 2017
(http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/)

G.Q.

Levels of endemicity fro hepatitis E



CDC, USA; Access: Sep. 9, 2019
(https://www.cdc.gov/hepatitis/hev/hevfaq.htm/)

G.Q.

台大醫院 NTUH

WHO position paper on hepatitis E vaccines 2015

- **WHO recognizes the importance of hepatitis E as a public health problem in many developing countries**, such as pregnant women and individuals living in camps for displaced persons and in outbreak situations.
- **Recombinant hepatitis E vaccine** (HEV 239 vaccine, Hecolin®) from China: The available data concerning this relatively new vaccine are **insufficient**.
- WHO **does not make recommendation** on the introduction of the vaccine for routine use in national programmes.

G.Q. WHO. Wkly Epidemiol Rec 2015;90(18):185.


Thanks!
Alishan