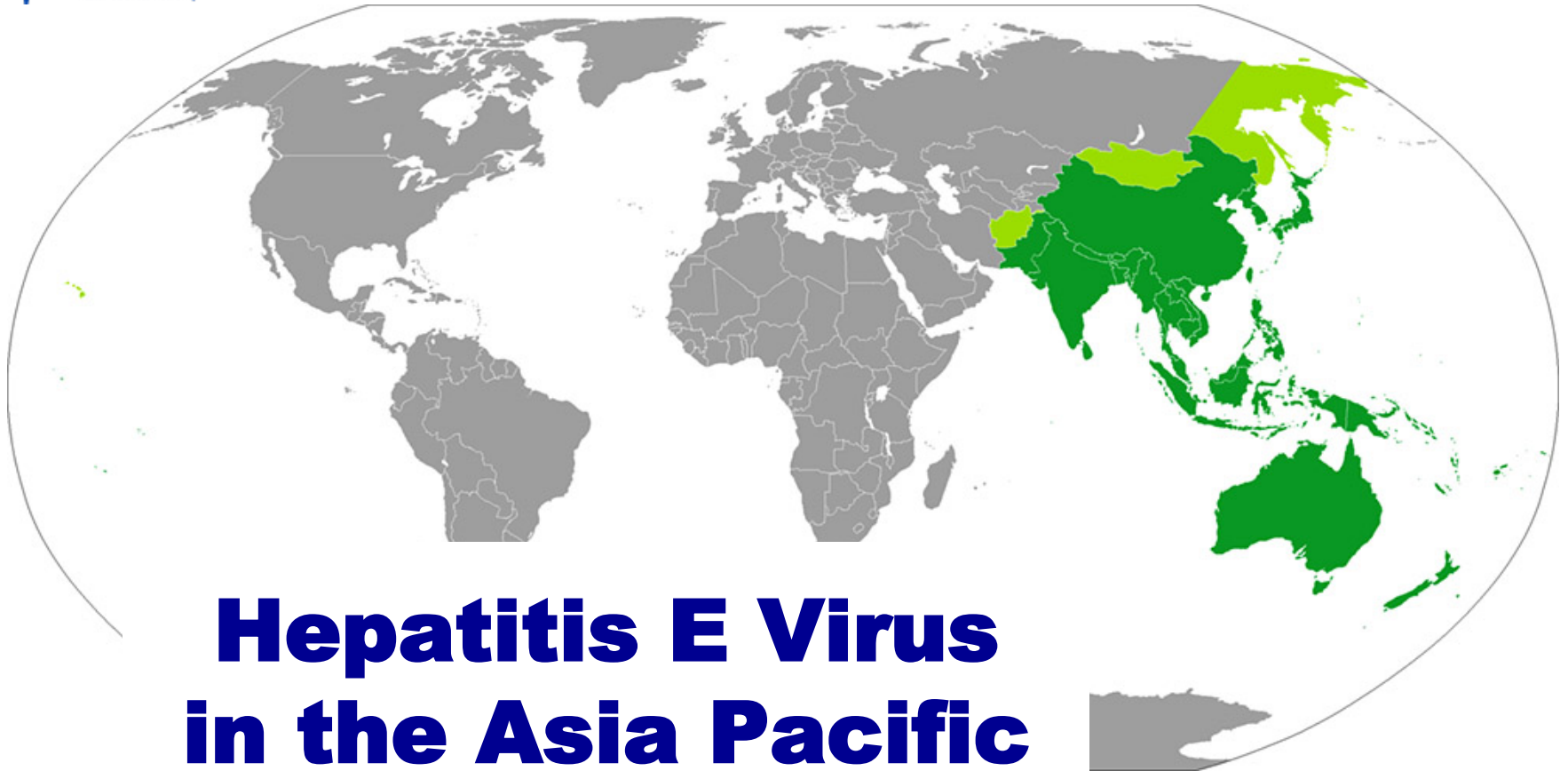
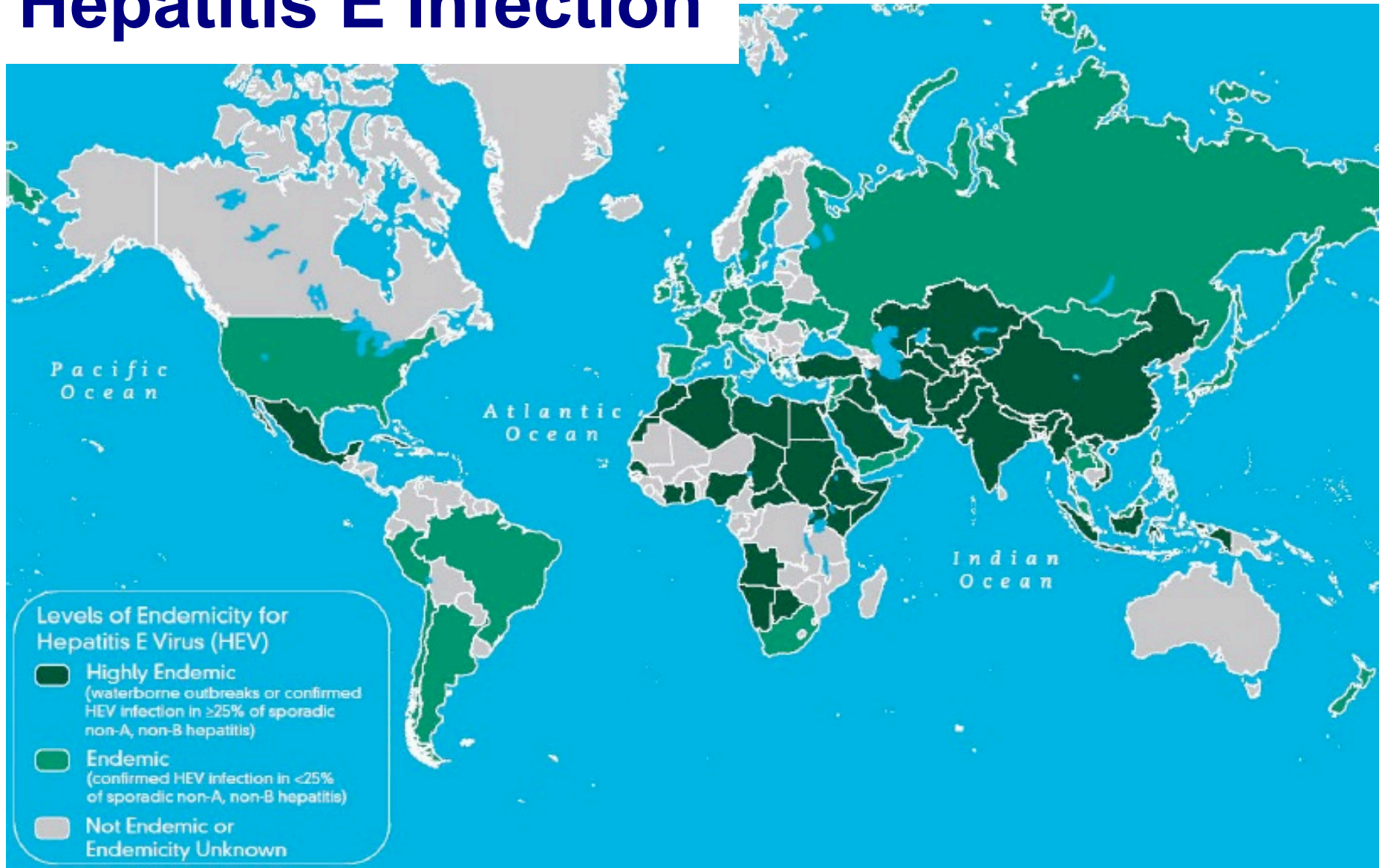




Hepatitis E Virus in the Asia Pacific

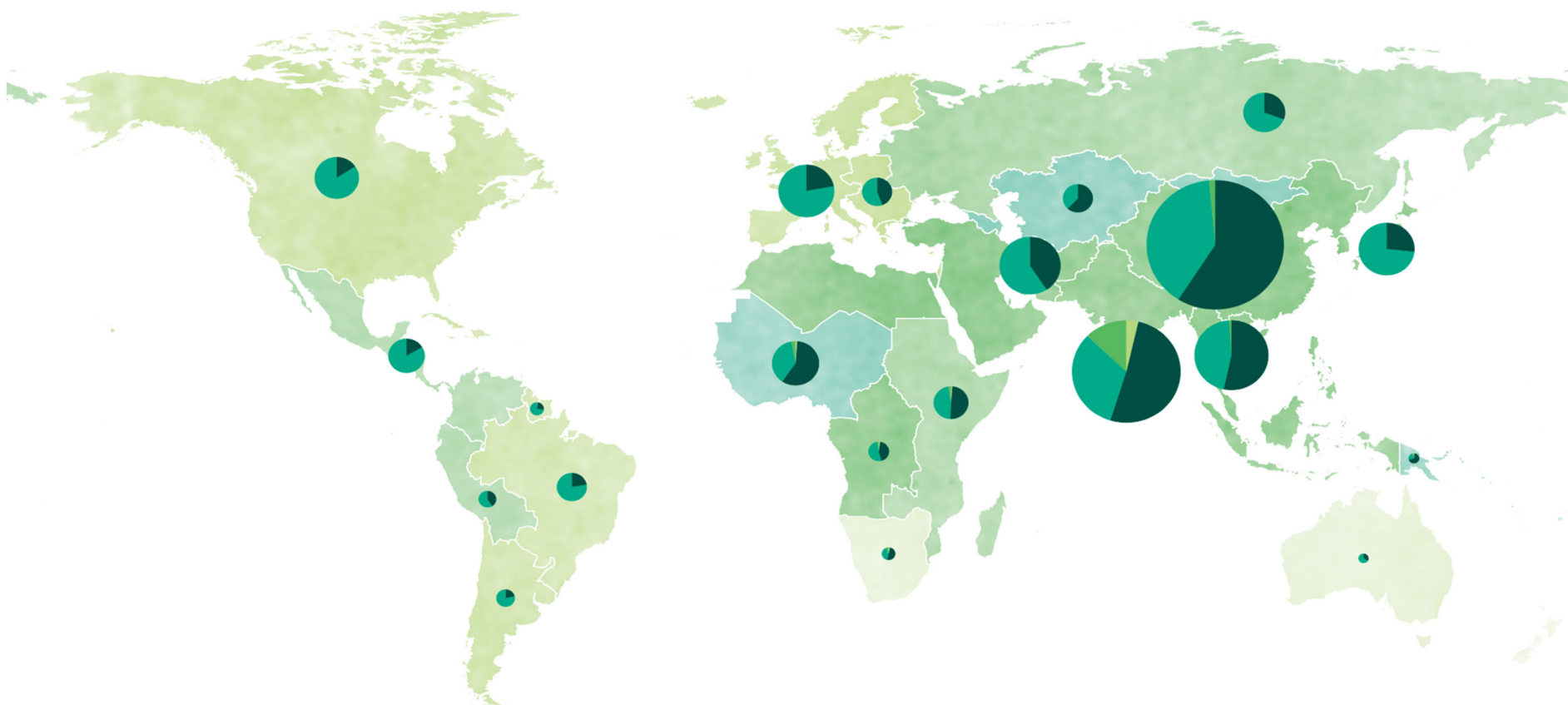
Diana Teo
Health Sciences Authority
Singapore

Hepatitis E Infection

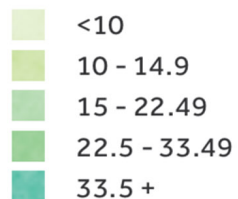


Endemic and epidemic in Southeast and Central Asia plus Japan, Middle East, North and West Africa, Mexico, Brazil

Figure 3. Regional distribution of viral hepatitis deaths



MORTALITY RATE (PER 100,000 PY)



PROPORTION ATTRIBUTABLE TO EACH VIRUS

The area of each pie is proportional to the number of hepatitis-attributable deaths in that region: each wedge represents the proportion of those deaths attributable to a given virus



From: Global health sector strategy on viral hepatitis 2016–2021 (2016), WHO

HEV in the WHO South East Asia Region

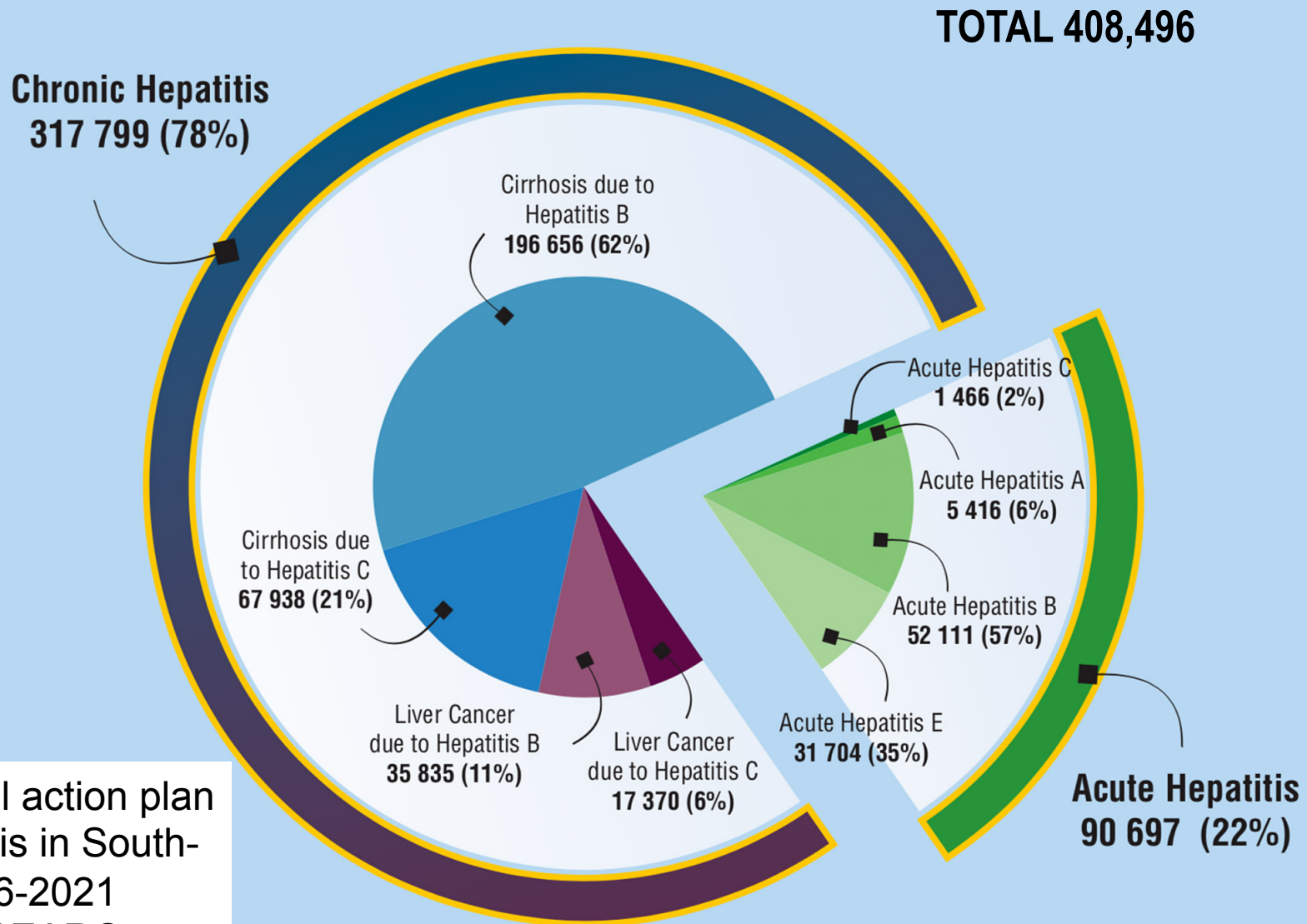
- Annual symptomatic cases of HEV estimated at 6 million, with 160,000 deaths, 2,700 stillborns
- >50% of global HEV deaths occur in the region
- HEV outbreaks have been documented in all countries of the region except DPR Korea
- Most outbreaks related to consumption of contaminated drinking water - overall attack rates ranging from 1-15%, disease rates highest in young adults
- Also accounts for large proportion of acute sporadic HEV infection - comparative studies in Bangladesh, India, Indonesia, Nepal, Thailand demonstrate 38-68% of all acute hepatitis is associated with HEV infection

From: Viral Hepatitis in the WHO South-East Asia Region, WHO SEARO, 2011

HEV in the WHO South East Asia Region

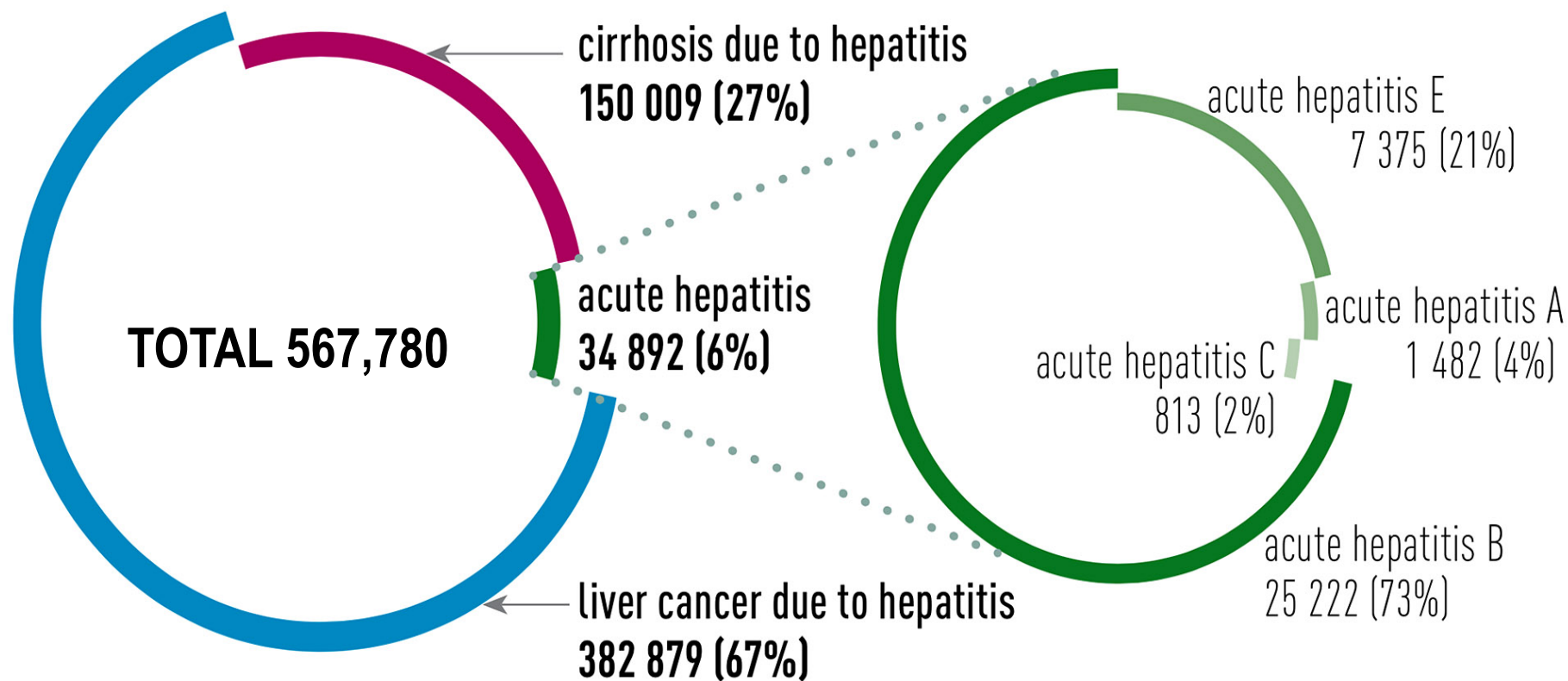
- Hyper-endemic in India, accounts for 60-70% of sporadic cases of acute viral hepatitis; acute disease common in age group of 15-45 years; accounts for 20-30% maternal and perinatal mortality
- Lack of surveillance data
 - Absence of routine reporting
 - Lack of laboratory facilities for suspected cases
 - Current available laboratory diagnostic kits for HEV produced by different institutions are not standardised
 - Panel of reference sera for quality control needed

**Fig. 3. Mortality due to viral hepatitis
in the South-East Asia Region, 2015**



From: Regional action plan
for viral hepatitis in South-
East Asia: 2016-2021
(2017), WHO SEARO

FIGURE 1. Mortality from viral hepatitis in the Western Pacific Region in 2013



Source: GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age/sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015 Jan 10; 385(9963):117–71.

From: Regional action plan for viral hepatitis in the Western Pacific:
2016-2021 (2016), WHO

Hepatitis E Infection

Characteristics	Genotype 1	Genotype 2	Genotype 3	Genotype 4
Geographic Location	Africa & Asia	Mexico, W Africa	Developed Countries	China, Taiwan, Japan
Transmission route	Water-borne faecal-oral Person to person	Water borne faecal-oral	Food-borne Person to person	Food-borne
Zoonotic transmission	No	No	Yes	Yes
Groups at high risk for infection	Young adults	Young adults	Older adults (>40 yr) & males; Immuno-compromised persons	Young adults
Mortality rate	0.5-3%	0.5-3%	Not determined	0.5-3%
Chronic	No	No	Yes	No
Occurrence of outbreaks	Common	Smaller scale outbreaks	Uncommon	Uncommon

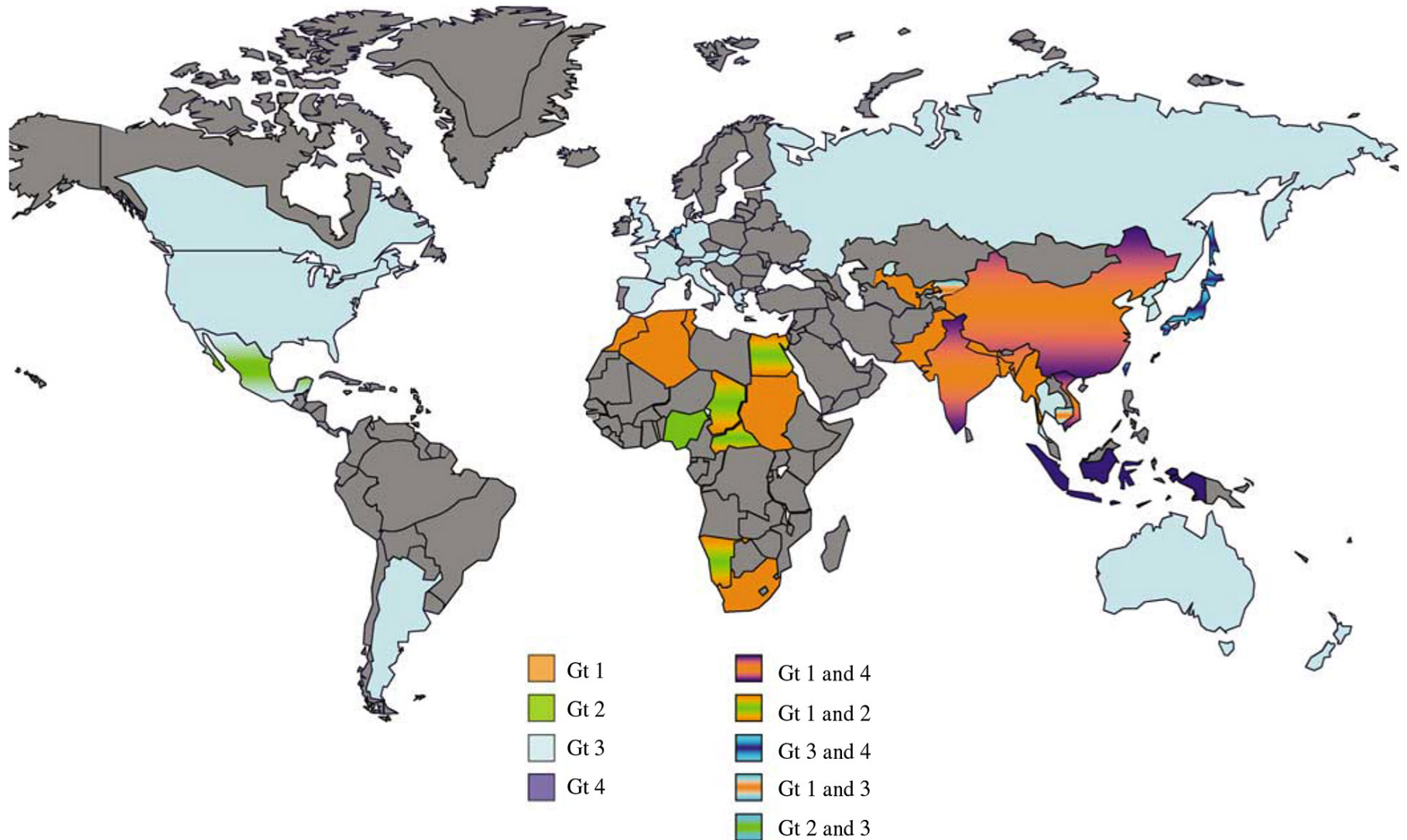


Figure 3 Geographical distribution of HEV isolates according to genotypes (Gt). HEV Gt 1 and 2: epidemic strains causing human infection. HEV Gt 3 and 4: zoonotic strains isolated from humans and a variety of animals, particularly pigs. In some countries, different genotypes co-circulate in distinct ecological niches: Gt 1 and 4 in China, India, and Vietnam; Gt 1 and 2 in several African countries, including Namibia, Chad, and Sudan; Gt 3 and 4 in Japan; Gt 1 and 3 in Cambodia; Gt 2 and 3 in Mexico.

From: Pelosi & Clarke (2008) Hepatitis E: a complex and global disease, *Emerging Health Threats Journal*, 1:1, 7069,



SITUATION IN ASIA PACIFIC

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Pakistan*

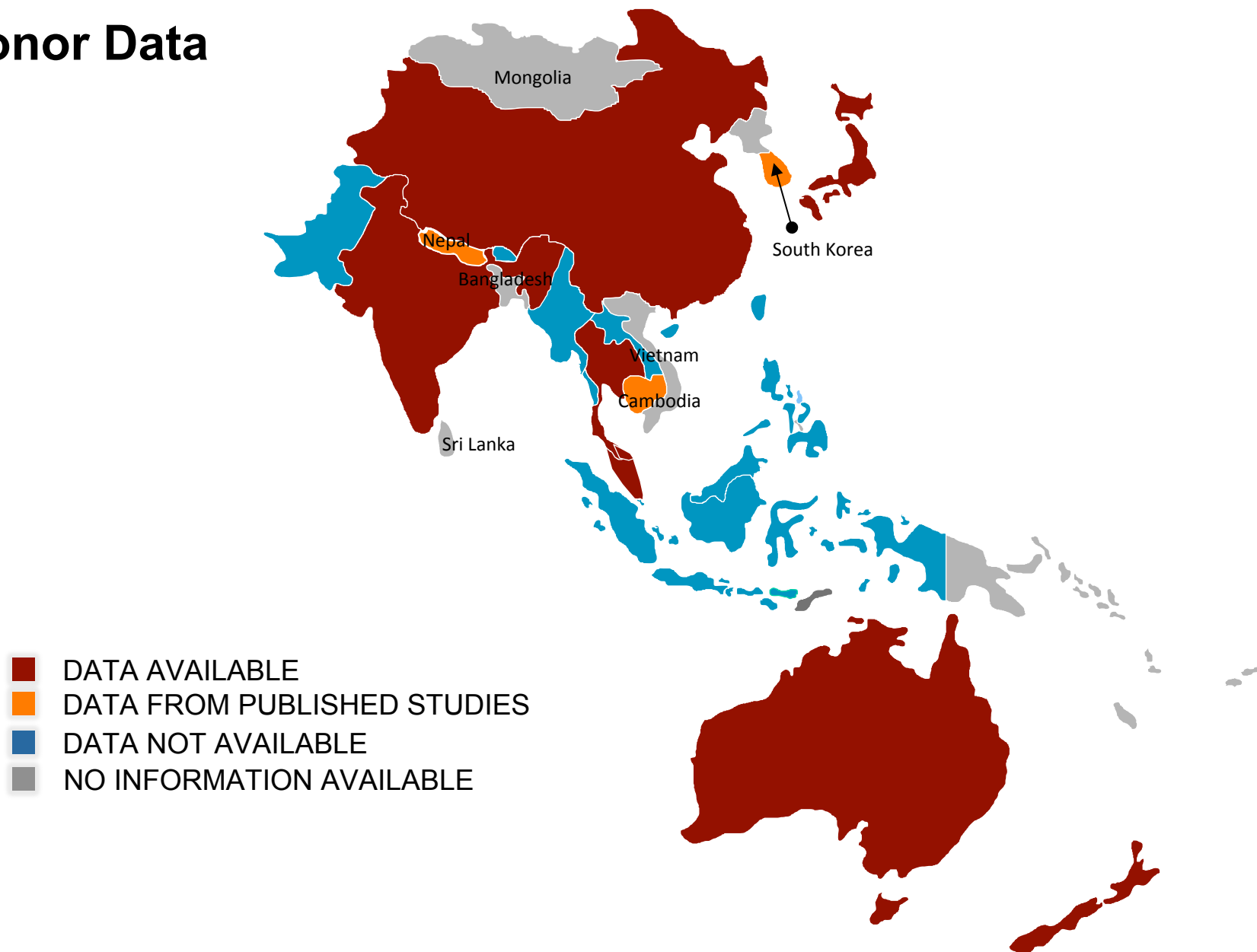
HEV in Asia Pacific

Geographic Location of Respondents



HEV in Asia Pacific

Donor Data



Prevalence of HEV in Blood Donors

Geographic Location	Available Data	Source
Cambodia	(2016) Study of donors (n=301), 28.2% anti-HEV IgG positive, 1.0% anti-HEV IgM positive, 0.3% HEV-RNA positive; Genotype 3 clustered with Cambodian riverine HEV-3 isolate	Nouhin, 2016
Malaysia	(1999) Study of donors in Pahang (n=100), 2% anti-HEV IgG positive	Seow, 1999
Singapore	(2017) Study of donors at BSG using ID-NAT with 7.9 IU/mL sensitivity (n=12,541), 0.15% HEV-RNA positive; 8/19 genotyped - Genotype 3	BSG
Thailand	(1996) Study of adult population incl donors, 9-22% anti-HEV IgG positive (2000) Study of blood donors in 4 northern provinces (n=636), 8.7% anti-HEV IgG positive	Poovorawan, 1996 Jutavijittum, 2000

Prevalence of HEV in Blood Donors

Geographic Location	Available Data	Source
Mainland China	(2007) Study of donors in Shaoxing (n=3,701), 29.19% anti-HEV IgG , 1.35% anti-HEV IgM, 0.16% HEV RNA positive; Genotype 1	Sang, 2007
	(2010) Study of donors (n=44,816), anti-HEV IgG 32.6% , anti-HEV IgM 0.94% , 30/420 IgM+ RNA positive 0.02-0.14% – Genotype 1 and 4	Guo, 2010
	(2014) Study of donors across regions (n=10,741), 27.42% anti-HEV IgG , 1.02% anti-HEV IgM, 0.06% HEV antigen positive; 4/8 HEV antigen positive were HEV RNA positive – Genotype 4	Ren, 2014
	(2016) Meta-analysis of HEV in donors (n=486-20,389), pooled rates 30% anti-HEV IgG , 1.09% anti-HEV IgM; HEV-RNA positive cases were Genotype 1 (19/33) and Genotype 4 (14/33); higher anti-HEV rates in Southwest region and in donors aged ≥ 30 yrs	Zhang, 2016

Prevalence of HEV in Blood Donors

Geographic Location	Available Data	Source
Japan	<p>(2010) Study of donors across Japan (n=12,600), 3.4% anti-HEV IgG positive; prevalence higher in Eastern Japan (5.6%) than Western Japan (1.8%), and in men (3.9%) than women (2.9%)</p> <p>(2015-2017) Rate of HEV-RNA in Hokkaido using ID-NAT with 7.9 IU/mL sensitivity (n=764,762), 0.044% HEV-RNA positive – Genotype 3 (84.5%), Genotype 4 (15.5%)</p> <p>(2016) Rate of HEV-RNA in Tokyo using ID-NAT with 7.9 IU/mL sensitivity (n=15,039), 0.073% HEV-RNA positive – all Genotype 3</p>	<p>Takeda (JRC), 2010</p> <p>JRC</p>
Korea	(1995) Study of donors (n=96), 17.7% anti-HEV IgG positive	Choi, 2003

Prevalence of HEV in Blood Donors

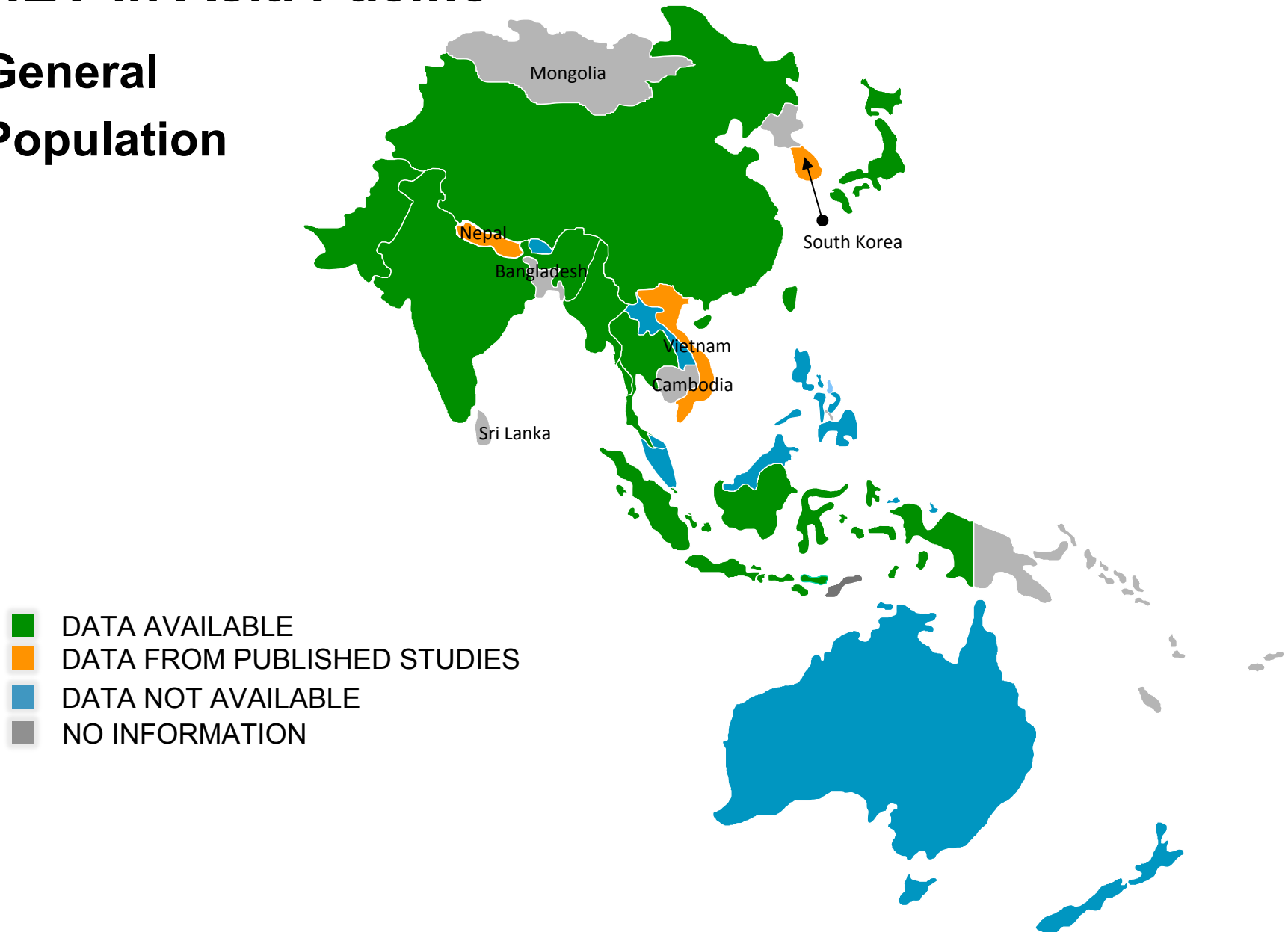
Geographic Location	Available Data	Source
Australia	(2013) Study of donors (n=3,237), 5.99% anti-HEV IgG positive	Shrestha, 2014
	(2016) Study of whole blood donations (n=74,131), 0.0013% or 1:74,131 HEV-RNA positive; estimated viral load 180 IU/ml	Hoad, 2017
New Zealand	(2014) Study of blood donors (n=1,013), 7.8% anti-HEV positive (2014) Study of blood donors using minipool of 8 by PCR (n=5000), 0 HEV-RNA detected, sensitivity of test 0.31 IU/uL	Hewitt, 2018

Prevalence of HEV in Blood Donors

Geographic Location	Available Data	Source
India	(1998) Study of donors in Pune (n=200), 18.6% anti-HEV IgG positive, 1.5% HEV-RNA (RT-PCR)	Arankelle, 1998
	(2000) Study in Pune using donors as controls (n=412), 37.4% anti-HEV IgG positive	Arankelle, 2000
	(2011) Study of donors in Delhi (n=262), 13.7% anti-HEV IgG positive	Bajpai, 2011
	(2014) Study of donors in Pune (n=460), 4.78% anti-HEV IgM positive	Gajjar, 2014
	(2015) Study of donors in Faridkot (n=551), 10.7% anti-HEV IgG positive	Kukar, 2015
Nepal	(2016) Study of donors post-earthquake (n=1,845), 41.9% anti-HEV IgG , 3.0% anti-HEV IgM, 0.054% or 1:922 HEV antigen positive	Shrestha, 2016

HEV in Asia Pacific

General Population



HEV Seroprevalence in General Population

Geographic Location	Available Data	Source
Cambodia	General population in northwestern Cambodia (n=868), 18.4% anti-HEV IgG , 0.23% (2/868) HEV-RNA positive – Genotype 3 and 4	Yamada, 2015
Indonesia	Healthy individuals in Bali (n= 276), 20% anti-HEV IgG ; in Lombok (n=446), 4% anti-HEV IgG ; in Surabaya (n=393), 0.5% anti-HEV IgG	Wibawa, 2004
	General population in northeastern Indonesia (n=581), 5.9% anti-HEV positive	Achwan, 2007
	Local residents (excl swine workers) in Java (n=142), 3.5% anti-HEV (IgG, IgM, IgA) positive; in Bali (n=135), 8.1% anti-HEV positive; no HEV-RNA detected	Dewiyani, 2013)
Laos	Persons with no h/o jaundice or liver disease (n=186), 17% anti-HEV IgG positive	Bounlu, 1998

HEV Seroprevalence in General Population

Geographic Location	Available Data	Source
Myanmar	General population of healthy and w liver disease (n=371), 213 healthy & 190 w liver disease), 32% (117/371) anti-HEV IgG positive (3% for age < 20 years, 30% or more for age ≥ 20 years)	Nakai, 2001
Singapore	Adult hospital patients w no liver disease (n= 124), 10.5% anti-HEV IgG positive	Chow, 1996
Thailand	Healthy Hmong persons in northern Thailand (n=139), 6.5% anti-HEV positive Young men in Thailand (n=7,760), 14% anti-HEV IgG positive, lowest in south 2 similar sized demographically different provinces w different swine farm densities, Lopburi (n=416), 37.3% anti-HEV IgG ; Narathiwat (n=305), 8.9% anti-HEV IgG HEV genotype 3 usually found in Thailand	Louisirirotchanaku I, 2002 Gonwong, 2014 Sanguanmoo, 2015 Suwannakarn, 2010

HEV Seroprevalence in General Population

Geographic Location	Available Data	Source
Vietnam	<p>Controls (n=187), 14% anti-HEV IgG positive</p> <p>Healthy persons in community, randomly selected (n=646), 9% anti-HEV IgG positive, rate increased with age</p> <p>Hospital attending population in Southern Vietnam (proxy for general pop) (n=1,726), 5.9% anti-HEV positive</p>	<p>Corwin, 1996</p> <p>Hau, 1999</p> <p>Berto, 2018</p>
Taiwan	<p>Healthy subjects > 20 yrs (n=384), 10.7% anti-HEV IgG positive</p> <p>Healthy subjects (n=400), 8.9% anti-HEV IgG positive</p> <p>Health examination attendees in rural Taiwan (n=314), 11.5% anti-HEV positive</p>	<p>Lee, 1994</p> <p>Lee, 2005</p> <p>Lee, 2013</p>

HEV Seroprevalence in General Population

Geographic Location	Available Data	Source
Mainland China	Healthy persons (n=936), 18.8% anti-HEV IgG positive	Wong, 2004
	Healthy persons in 8 rural areas in Guangxi province (n=7,284), 43% (25-66%) anti-HEV positive	Li, 2006
	Healthy persons aged 8-49 yrs (n=426), 31% anti-HEV IgG positive	Toole, 2006
	Healthy persons of different ages (n=12,052), 17.2% anti-HEV IgG positive; 7.92% in aged < 10y, 21.48% in >= 60 yrs	Dong, 2007
	Cross-section of general population 2005-2006 (n=15,852), 23.46% anti-HEV (total) positive; varied across geographic region and province	Jia, 2014

HEV Seroprevalence in General Population

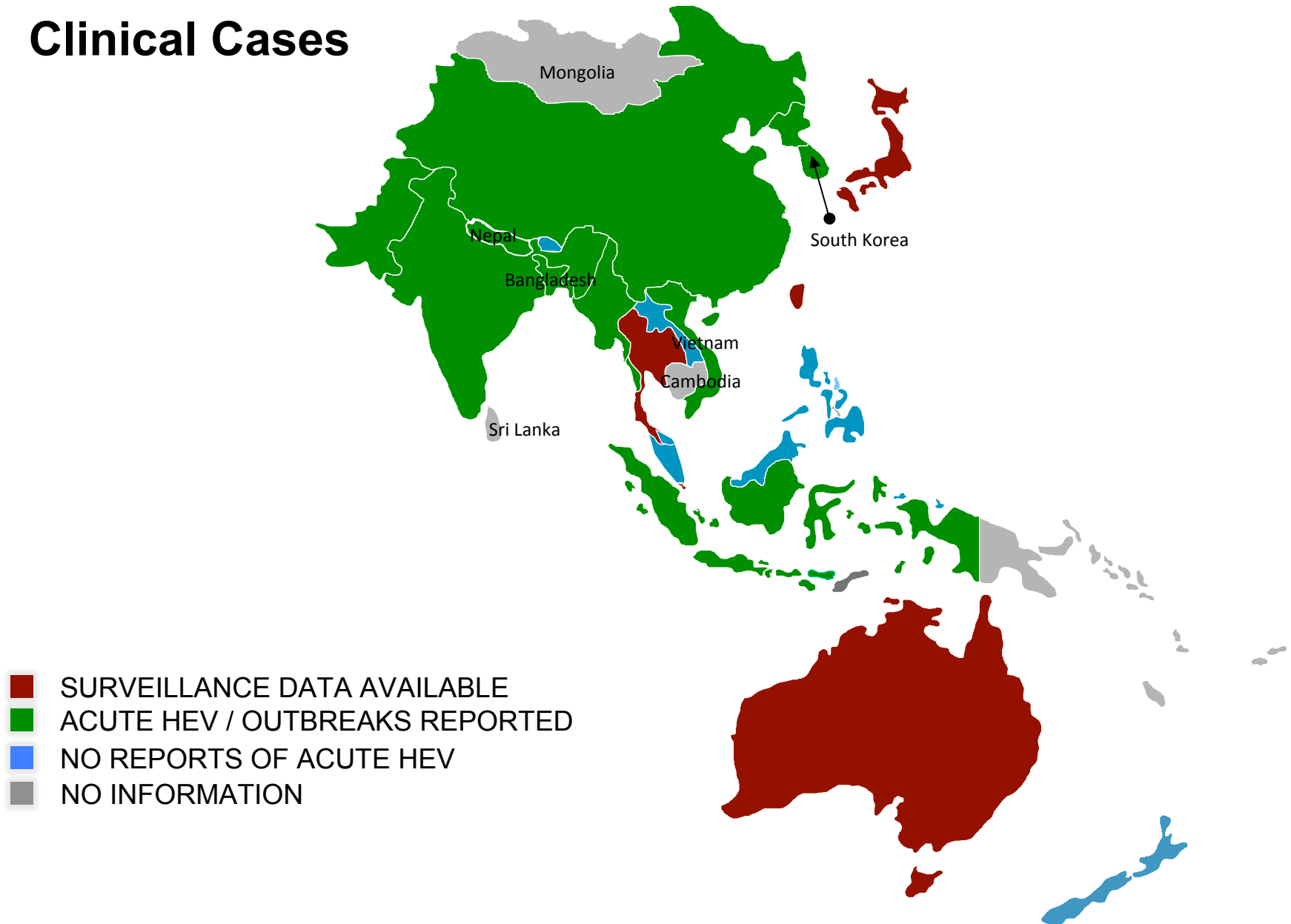
Geographic Location	Available Data	Source
Hong Kong	Archived hospital samples submitted for virological investigations 2008-2009, hepatitis-related samples removed (n=450), 28.7% anti-HEV IgG positive; 8% in 1-10 yrs, 56% in >80 yrs	Chiu, 2013
Japan	Healthy individuals undergoing health check 2002-2007, using in-house ELISA (n=22,027), 5.3% anti-HEV IgG positive; 2.7% in < 50 yrs, 6.6% in >=50 yrs; 0.014% (3/22,014) positive for HEV-RNA in MP49/50 – Genotype 3	Takahashi, 2010
Korea	Blood samples collected from population (n=497), 9.4% anti-HEV IgG positive Health individuals from community health centres and medical colleges (n=361), 11.9% anti-HEV IgG positive	Yun, 2011 Ahn, 2005

HEV Seroprevalence in General Population

Geographic Location	Available Data	Source
India	Healthy persons (n=600), 4% anti-HEV positive, rate increasing with age Systematic review by WHO in October 2014, 14.5% anti-HEV IgG in healthy individuals, 11.3% in medical students 5.3%-16.7% in different age groups in general population in various studies	Daniel, 2004 Survey response
Nepal	Healthy individuals (n=757), 16-31% anti-HEV IgG positive	Clayson, 1997
Pakistan	Adults (18-45 yrs) (n=100), 16% anti-HEV IgG	Qureshi, 2000

HEV in Asia Pacific

Clinical Cases



HEV in Asia Pacific

Clinical Cases

SINGAPORE

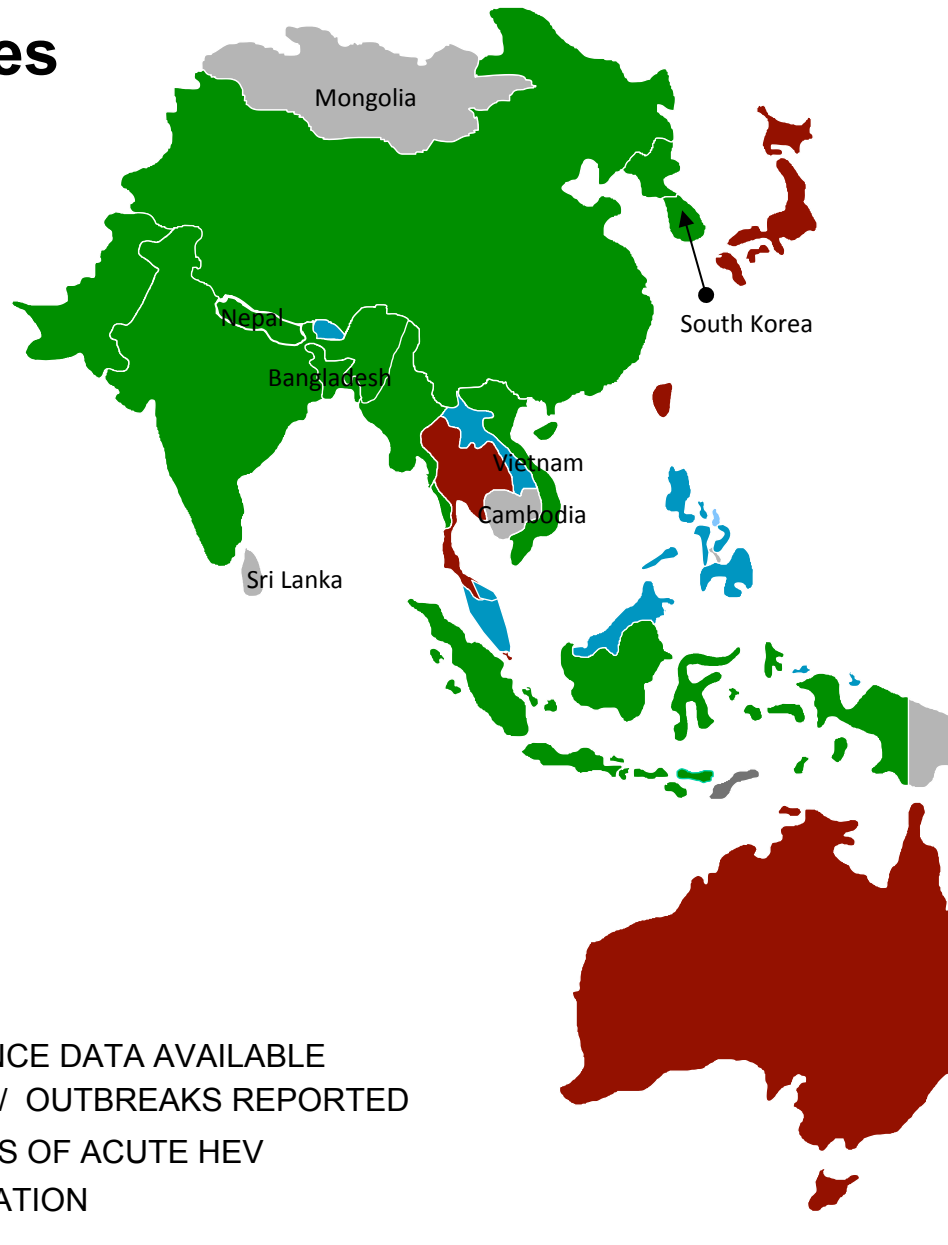
(2017) 76 cases;
(2016) 83 cases;
1.3/100,000 pop

MACAU

(2017) 4 cases;
(2016) 26 case;
Average rate
1.64/100,000 pop

THAILAND

(2016) 38 cases;
(2015) 46 cases;
0.06/100,000 pop



JAPAN

(2017) 298 cases;
4 TT-HEV
(2016) 356 cases;
3 TT-HEV ;
0.28/100,000 pop

TAIWAN

(2017) 13 cases;
Crude IR
0.05/100,000 pop

AUSTRALIA

(2017) 47 cases;
(2016) 43 cases;
0.18/100,000 pop
(2017)

- SURVEILLANCE DATA AVAILABLE
- ACUTE HEV / OUTBREAKS REPORTED
- NO REPORTS OF ACUTE HEV
- NO INFORMATION

Clinical Surveillance Data

Geographic Location	Data	Source
Australia	(2017) 47 cases notified (2016) 43 cases notified	http://www9.health.gov.au/cda/source/rpt_3.cfm
Japan	(2017) 298 cases reported (2016) 356 cases reported	National Institute of Infectious Disease
Macau	(2017) 4 cases reported (2016) 26 case reported Average rate 1.64/100,000 pop	Centre for Disease Control and Prevention, Macau
Singapore	(2017) 76 cases notified (2016) 83 cases notified 1.3/100,000 pop; (2016) 56 indigenous - 22 PCR+ – 45.5% Gt 3, 9.1% Gt 1	http://www.moh.gov.sg
Taiwan	(2017) 13 cases reported; crude incidence rate 0.05/100,000 pop	Centers for Disease Control, Taiwan
Thailand	(2016) 38 cases reported; (2015) 46 cases reported	http://203.157.15.110/boeeng/

Donor and Population Prevalence

Geographi c Location	Donor HEV-RNA	Donor Anti-HEV	Population Anti-HEV	Clinical HEV /100,000 pop
Cambodia	0.3%	28.2%	18.4%	na
Indonesia	na	na	0.5-20%	Yes
Laos	na	na	17%	No
Malaysia	na	2%	na	No
Myanmar	na	na	32%	Yes
Philippines	na	na	na	No
Singapore	0.15%	na	10.5%	1.3
Thailand	na	8.7-22%	8.9-37.3%	0.06
Vietnam	na	na	5.9-14%	Yes

Donor and Population Prevalence

Geographic Location	Donor HEV-RNA	Donor Anti-HEV	Population Anti-HEV	Clinical HEV /100,000 pop
Mainland China	0.16%	27-42%	17.2-43%	Yes
Hong Kong	na	na	28.7%	Yes
Japan	0.044-0.073%	1.8-5.6%	5.3%	0.28
Korea	na	17.7%	9.40-11.9%	Yes
Macau	na	na	na	1.64
Taiwan	na	na	8.9-11.5%	0.05

Donor and Population Prevalence

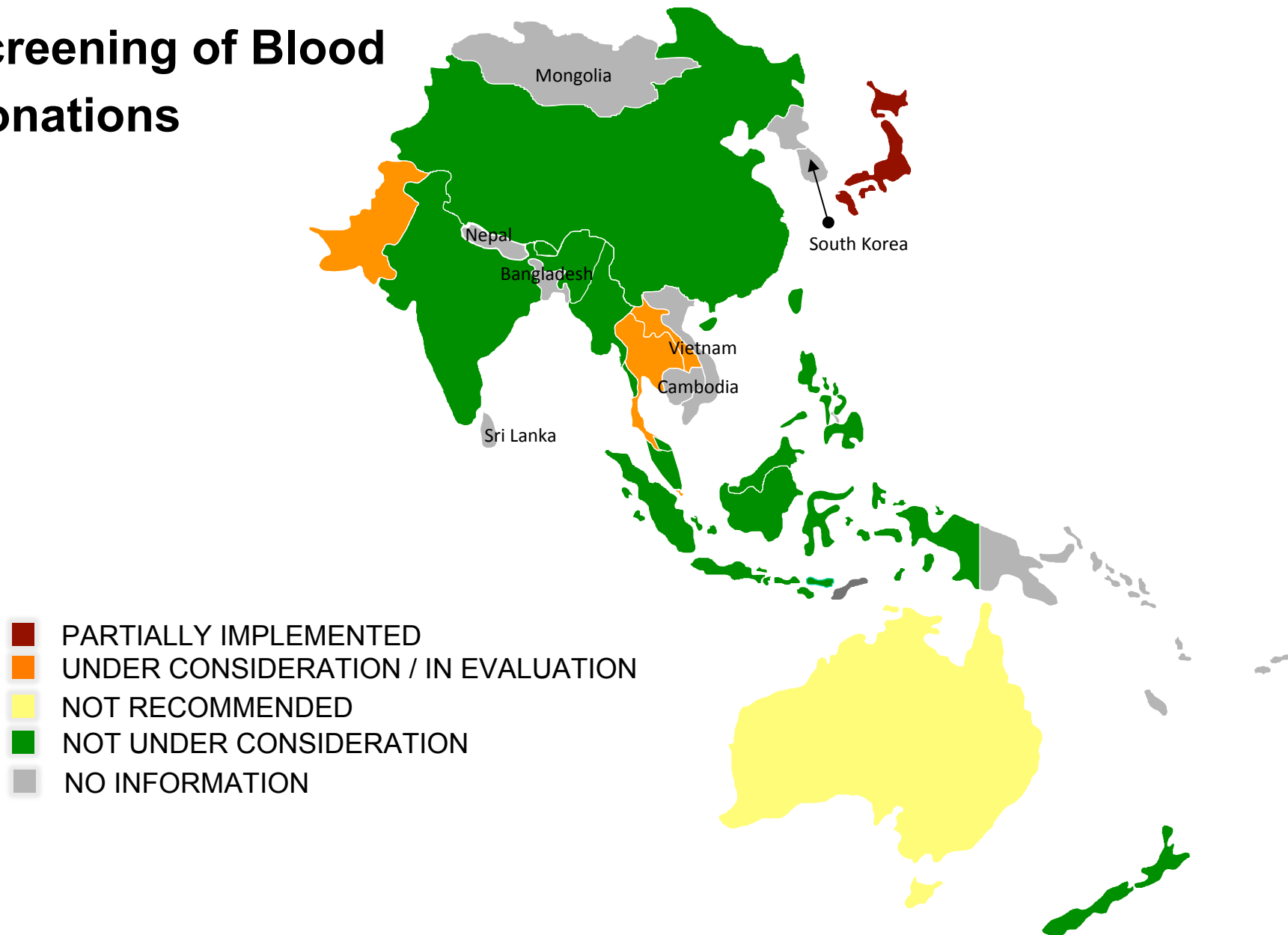
Geographic Location	Donor HEV-RNA	Donor Anti-HEV	Population Anti-HEV	Clinical HEV /100,000 pop
Australia	0.0013%	5.99%	na	0.18
New Zealand	0	7.8%	na	No
Bhutan	na	na	na	No
India	1.5%	4.78-37.4%	4-16.7%	Yes
Nepal	0.054% (HEV Ag)	41.9%	16-31%	Yes
Pakistan	na	na	16%	Yes

Blood Safety Measures



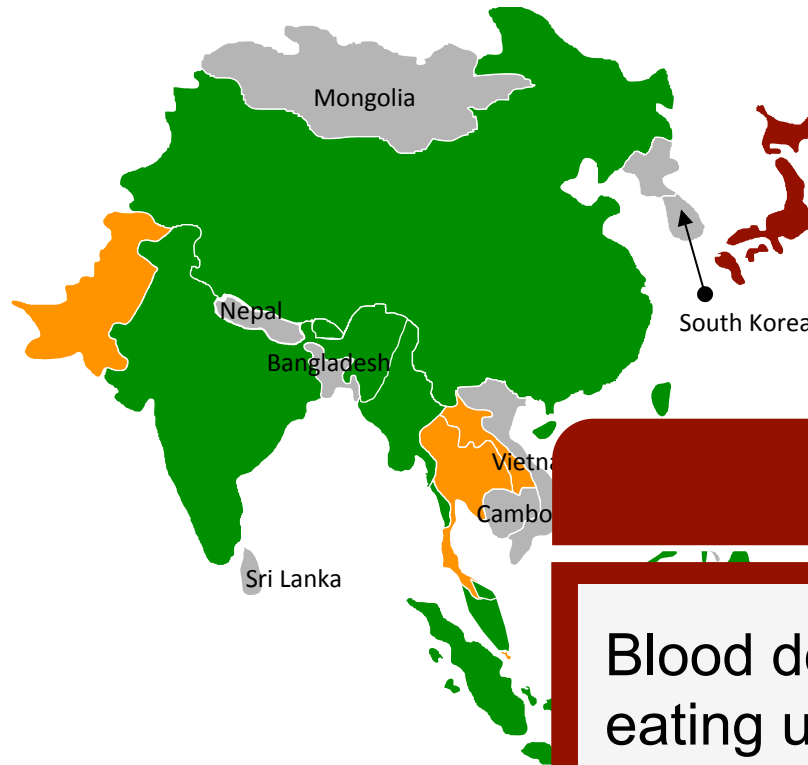
HEV in Asia Pacific

Screening of Blood Donations



HEV in Asia Pacific

Screening of Blood Donations



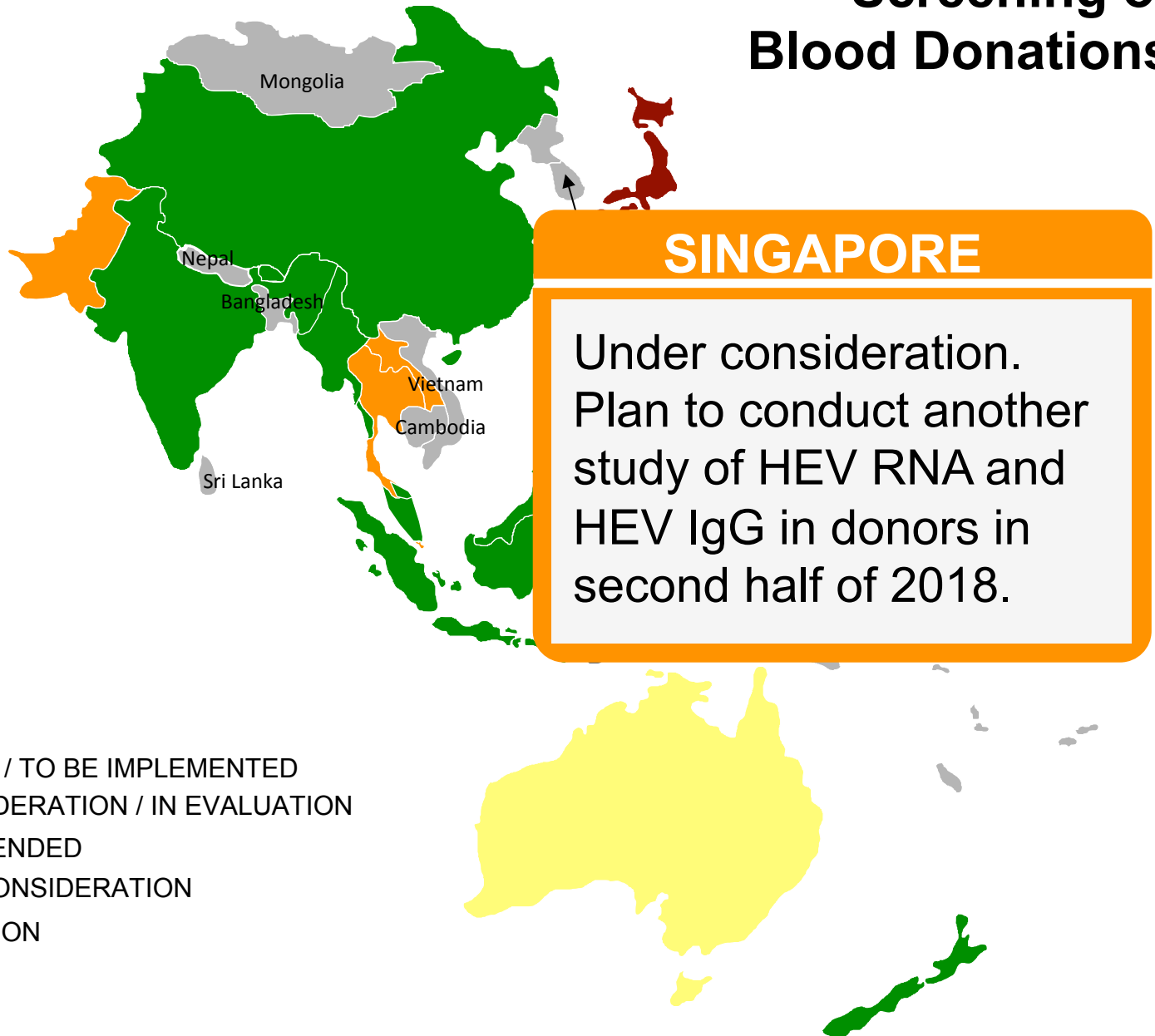
- IMPLEMENTED / TO BE IMPLEMENTED
- UNDER CONSIDERATION / IN EVALUATION
- NOT RECOMMENDED
- NOT UNDER CONSIDERATION
- NO INFORMATION

JAPAN

Blood donors advised to avoid eating undercooked pig, boar or deer meat during the 6 months prior to donation. Considering implementation of universal testing of donors for HEV RNA using ID-NAT.

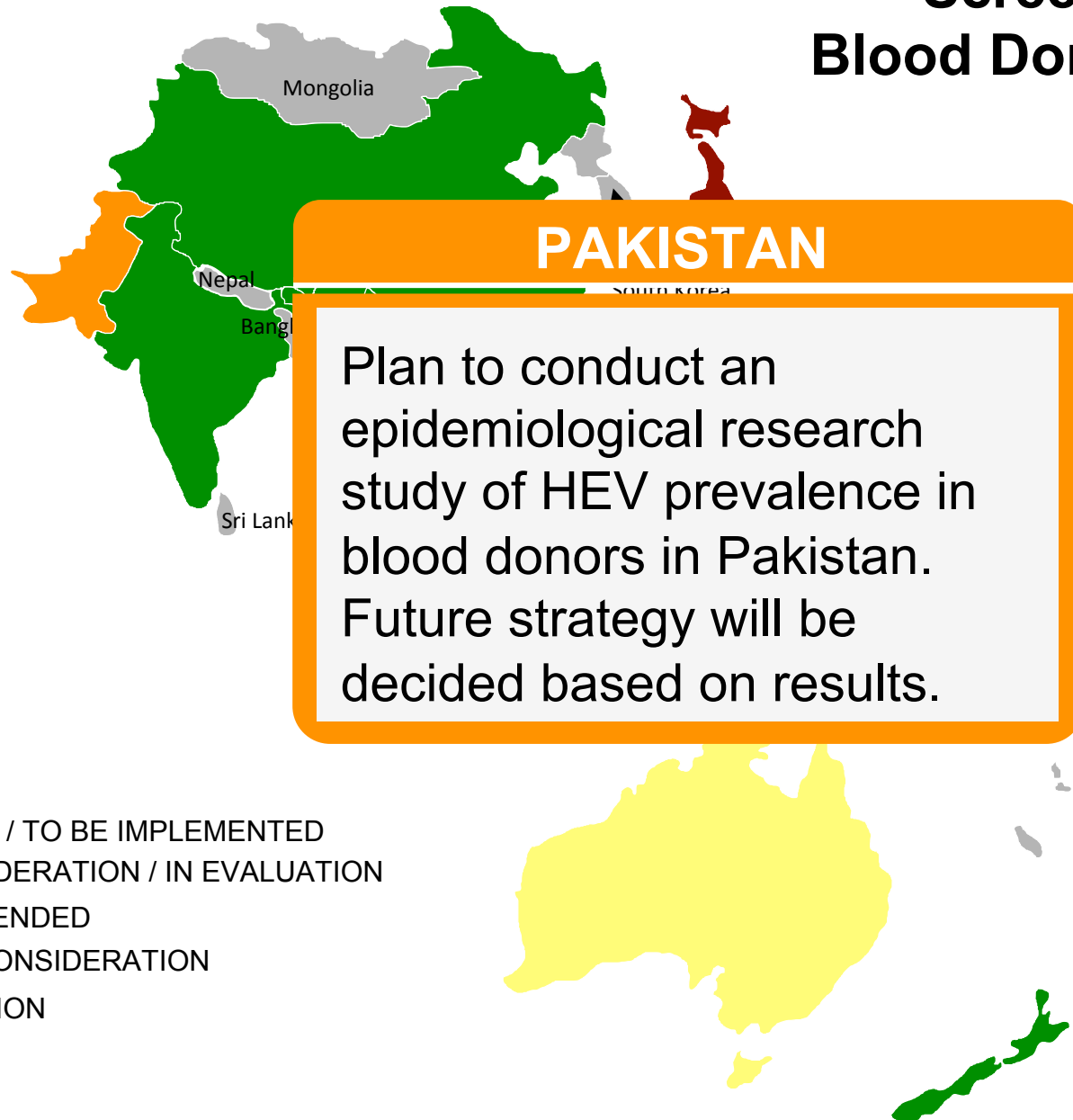
HEV in Asia Pacific

Screening of Blood Donations



HEV in Asia Pacific

Screening of Blood Donations



- IMPLEMENTED / TO BE IMPLEMENTED
- UNDER CONSIDERATION / IN EVALUATION
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HEV in Asia Pacific

Screening of Blood Donations



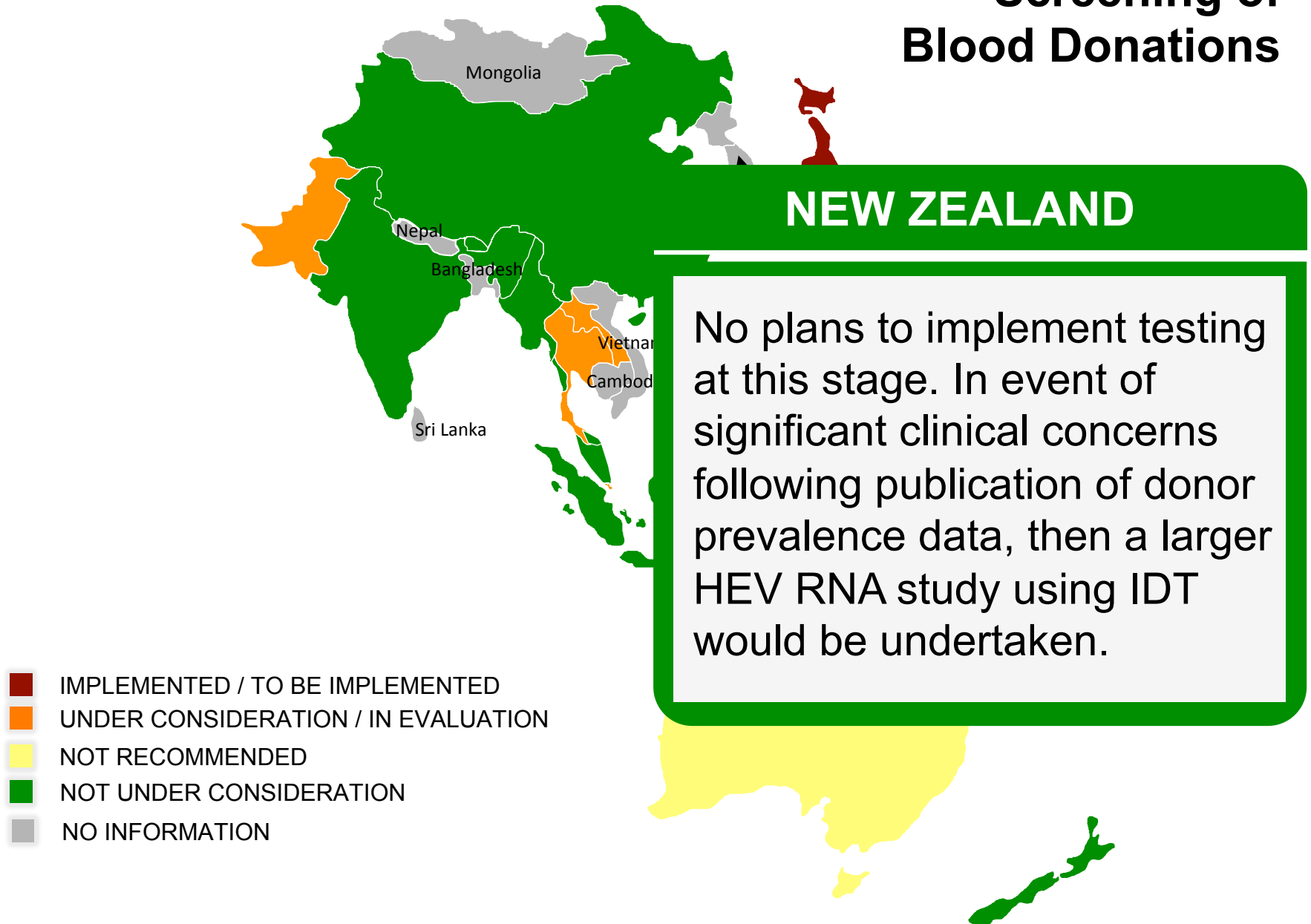
- IMPLEMENTED / TO BE IMPLEMENTED
- UNDER CONSIDERATION / IN EVALUATION
- NOT RECOMMENDED
- NOT UNDER CONSIDERATION
- NO INFORMATION

THAILAND

As HEV is becoming an important issue, considering plans to implement screening especially for components provided to immunocompromised patients.

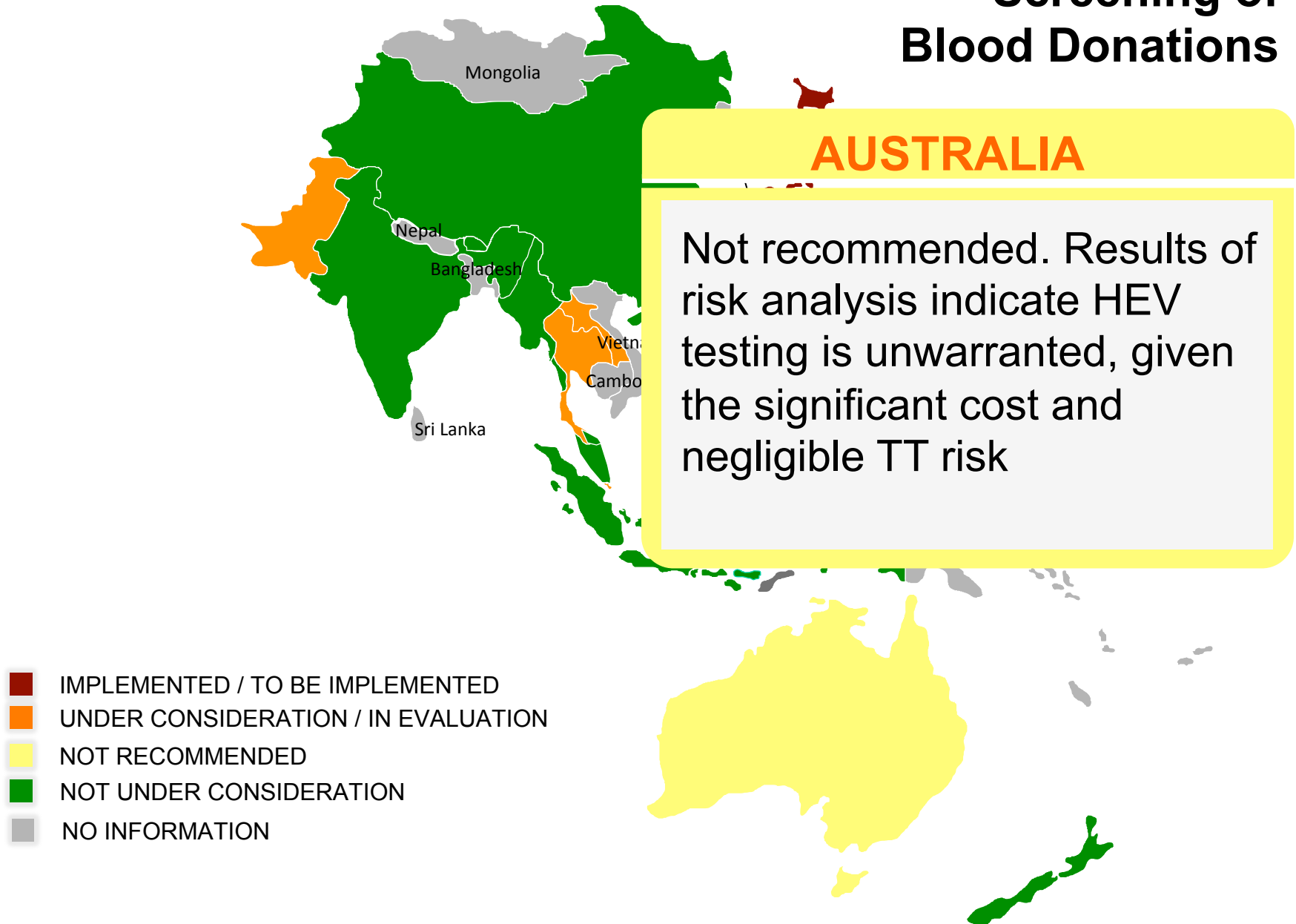
HEV in Asia Pacific

Screening of Blood Donations

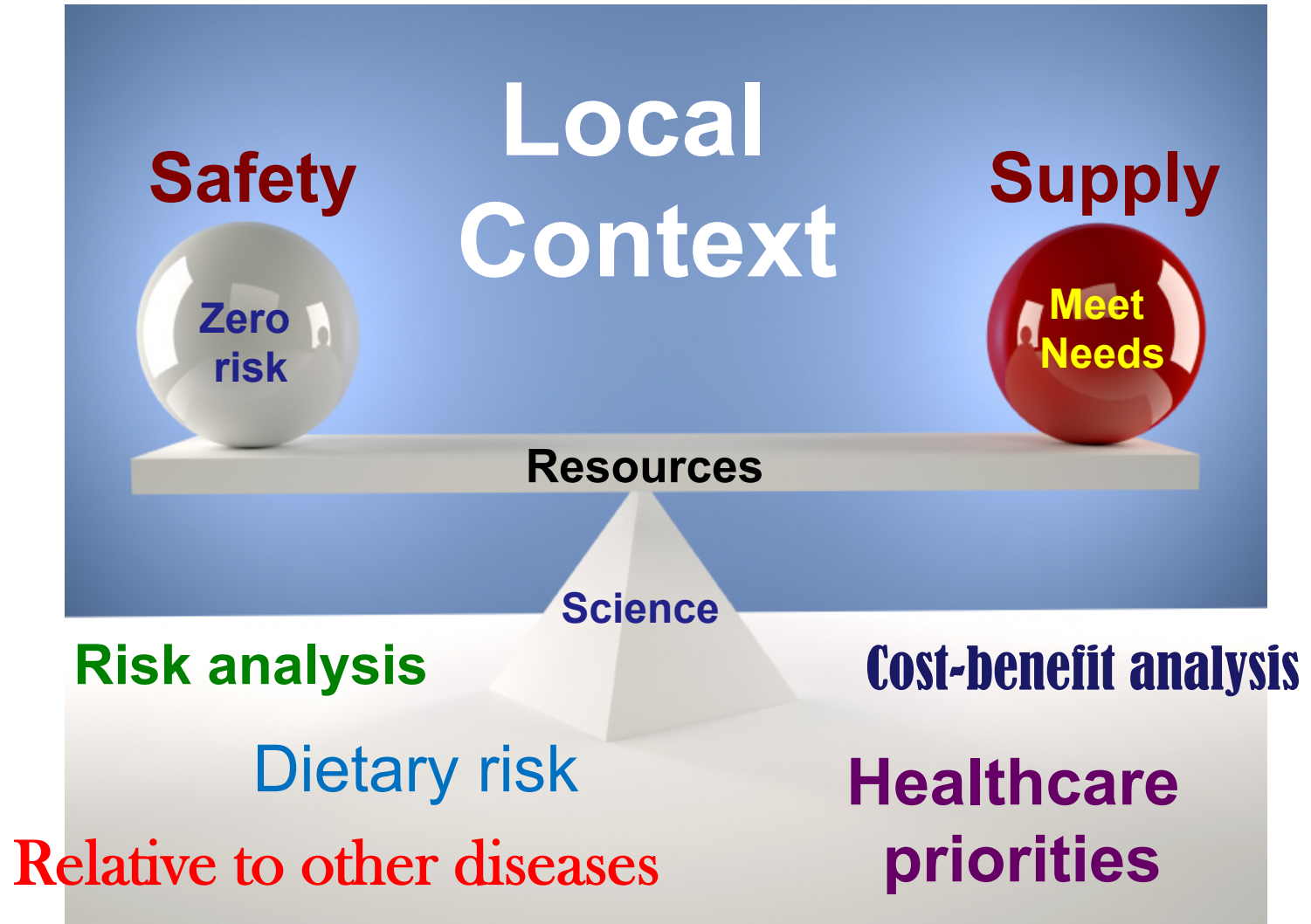


HEV in Asia Pacific

Screening of Blood Donations



Factors Influencing HEV Strategy



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Thank You

