

Silver Highlights in Pediatric Infectious Disease in the Philippines



Ma. Liza Antoinette M. Gonzales, MD, Msc
Fellow, PPS and PIDSP

25th PIDSP Annual Convention
“Forging Ahead in Pediatric Infectious Diseases”
February 22, 2018





Objectives

- ◆ **Discuss infectious diseases affecting children that made the news in the region and in the Philippines in 2017**
- ◆ **Discuss issues and challenges**
- ◆ **Present possible strategies for prevention and control for 2018 and beyond**

Global HIV/AIDS estimates for adults and children | 2016



36.7 MILLION

people worldwide are currently living with HIV/AIDS.

2.1 MILLION CHILDREN

worldwide are living with HIV. Most of these children were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.



The vast majority of people living with HIV are in low- to middle-income countries, particularly in Sub-Saharan Africa.



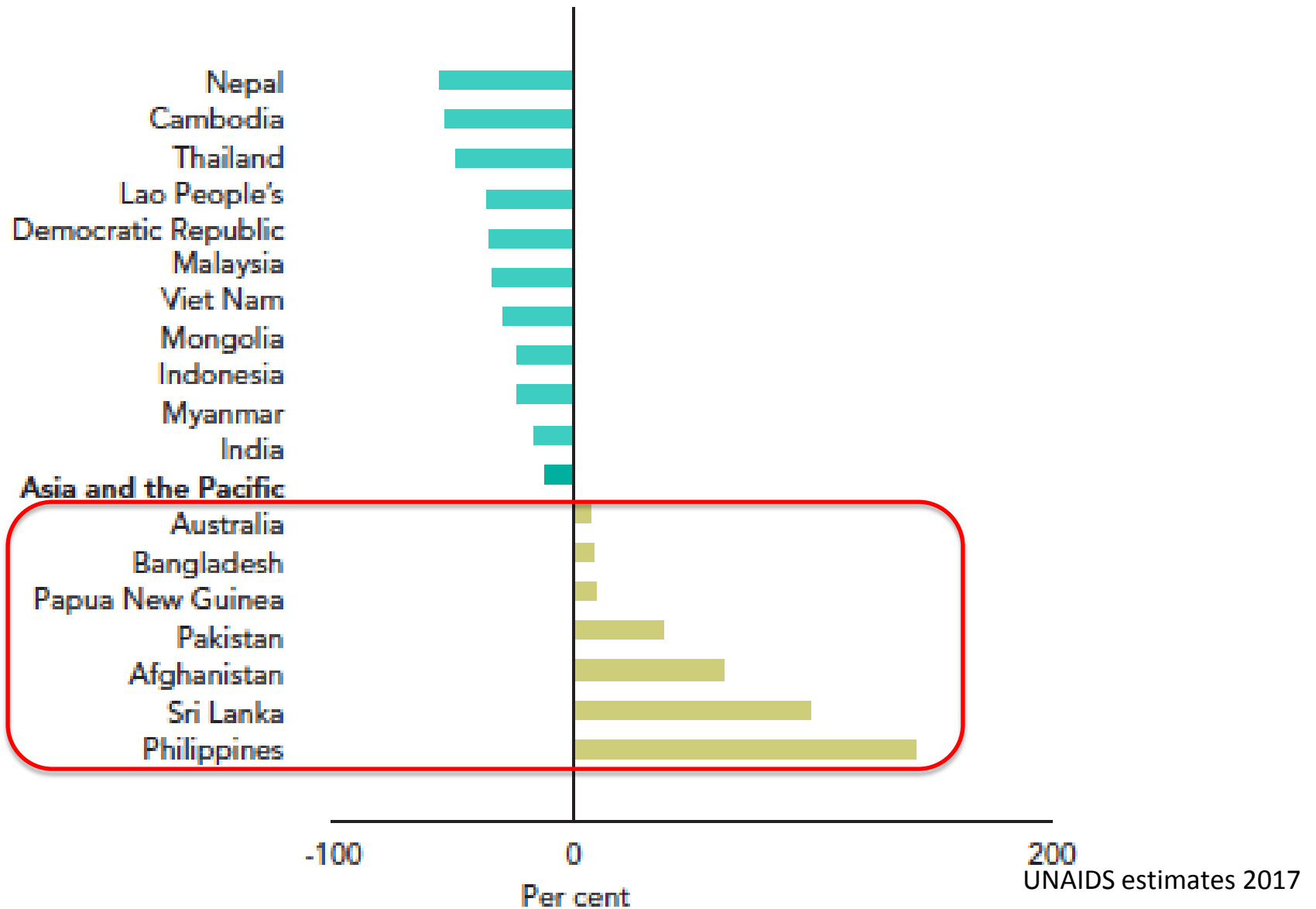
THE GLOBAL HIV/AIDS EPIDEMIC

About 5000 new HIV infections in adults and children a day

HIV

...one of the world's most serious health and development challenges

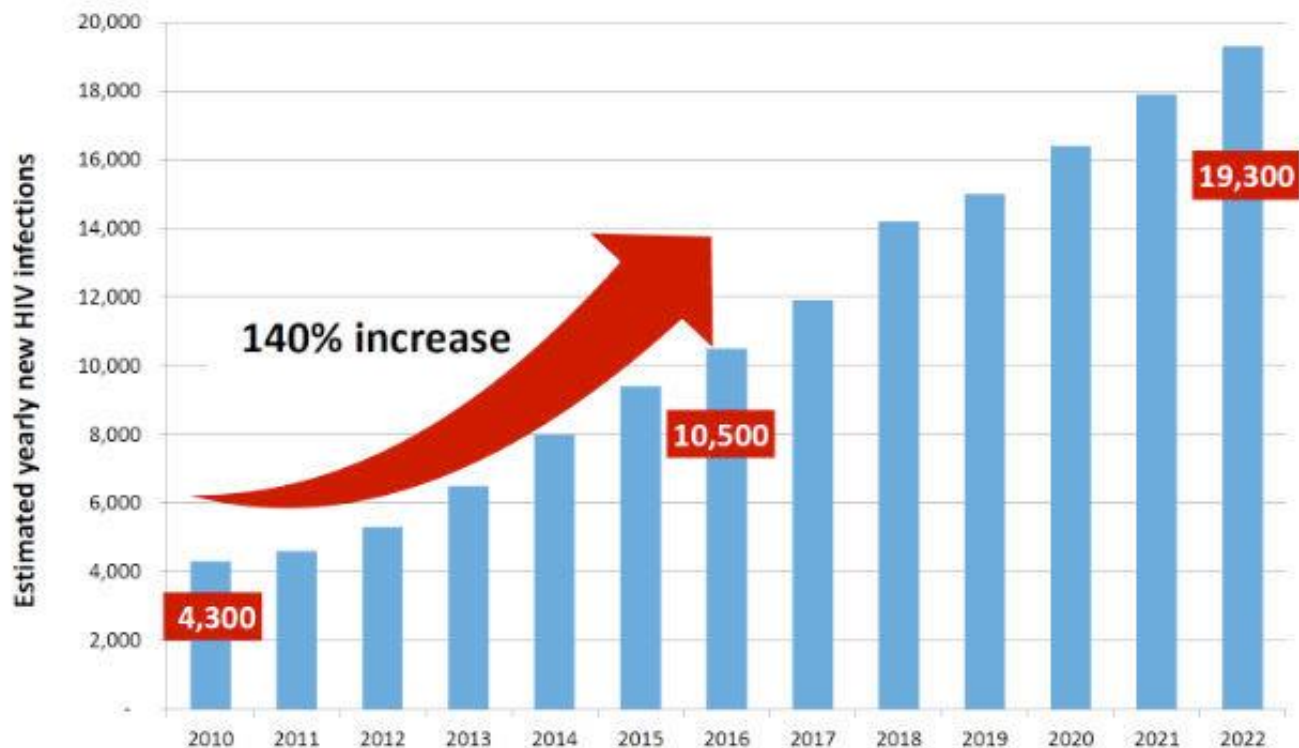
Percent Change in HIV New Infections, by Country Asia and the Pacific 2010 to 2016



The Philippine HIV Epidemic

Fast and Furious

**140% increase in yearly new HIV infections
from 2010 to 2016**



Source: Philippine Spectrum Projections, May 2017



No. Newly Diagnosed HIV Cases per day in the Philippines

1

4

9

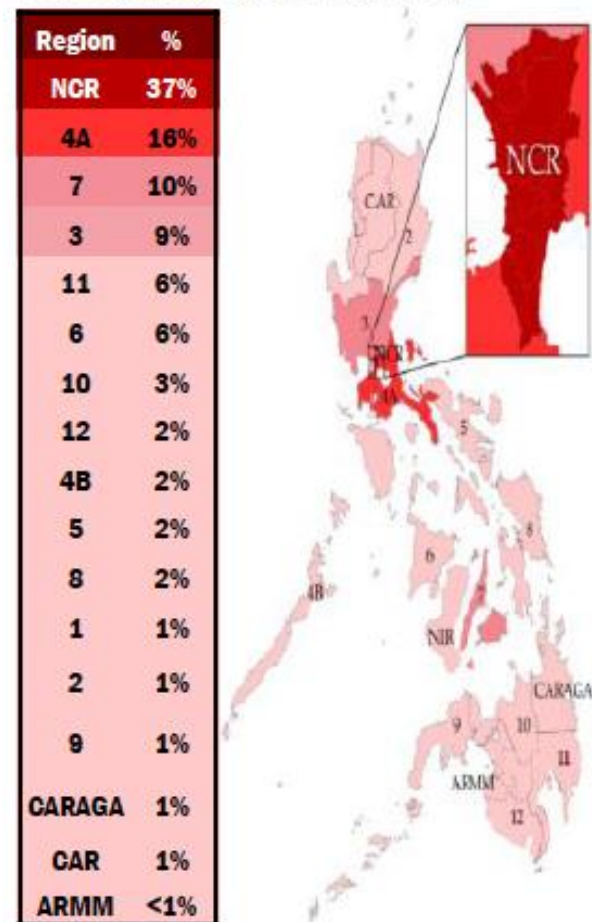
17

26

31

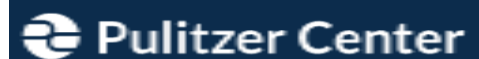
Demographic Data	Cumulative Jan 1984 – Sept 2017
Total Reported Cases	47,921
Asymptomatic	43,235 (90%)
AIDS	4,686 (10%)
Male	44,694 (93%)
Female	3,216 (7%)
Age Range (Median)	1-82 (28)
<15 yrs	139 (0.29%)
15-24 yrs	13,282 (27.7%)
25-34 yrs	24,578
35-49 yrs	8,571
≥ 50 yrs	1,277
Total PLHIV on ART	23,307
Reported Deaths	2,343 (4.89%)

Figure 2. Percentage of Newly Diagnosed Cases per Region (September 2017)

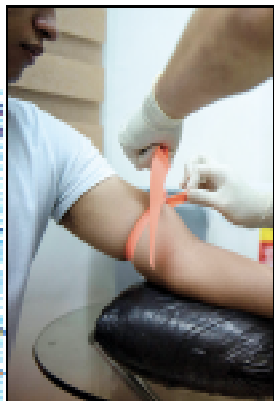


HIV in the Philippines: State of Emergency

‘While most countries around the world have managed to control the rate of HIV infections, the Philippines is starting to feel the impact of a rising epidemic...’



Losing the fight against HIV in the Philippines



Getty Images/NOTEL/CELESTINE/REUTERS/628460376

The Philippines is facing an unprecedented HIV crisis. New infections have doubled in the past 6 years to more than 10 000 new cases last year alone. Undoubtedly, stigma remains one of the major reasons for the spread of HIV in the Philippines, as Risa Hontiveros, Filipina Senator and Vice-Chairperson of the Senate Committee on Health, said on Aug 2, urging the Government to declare the HIV epidemic a national emergency.

This growing rate of infection stands in stark contrast to the absence of comprehensive public and health

purchase condoms further hinder protection of young at-risk populations.

The rate of new infections is most likely underestimated. President Rodrigo Duterte's harsh punitive policies on drug use will have discouraged people who inject drugs (PWID), another key at-risk population, from accessing HIV prevention and care. Harm-reduction policies, such as needle exchanges, have largely been stopped for fear of censure, worsening risky behaviour.

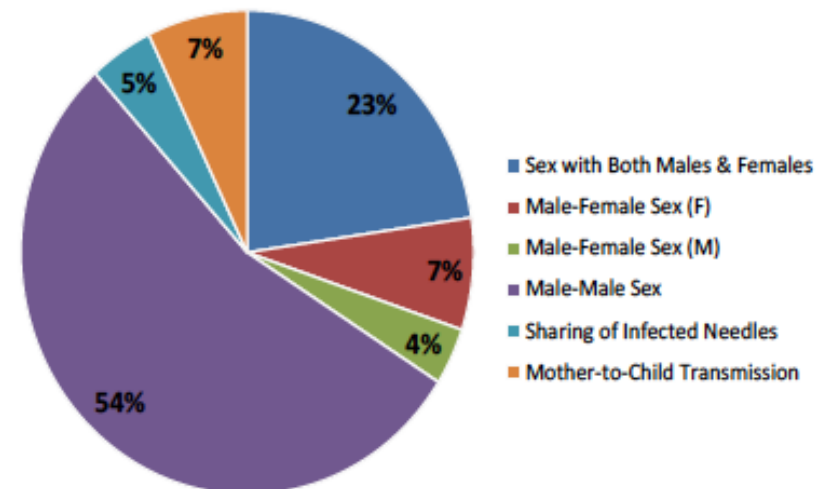
The country has a small window of opportunity to curb



HIV/AIDS in Children (<10 years old) and Adolescents (10-19 years old) Philippines, Jan 1984-Sept 2017

- 1873 HIV cases in ≤19 years old:
 - **128 children:** 125 (98%) infected through MTCT
 - **1745 adolescents** (93% males):
 - 94% infected through sexual contact (majority MSM)
 - 85 (5%) through needle sharing
 - 8 (<1%) through MTCT

Figure 8. Modes of Transmission Among Children and Adolescents, January 1984 - September 2017 (N=1,873*)

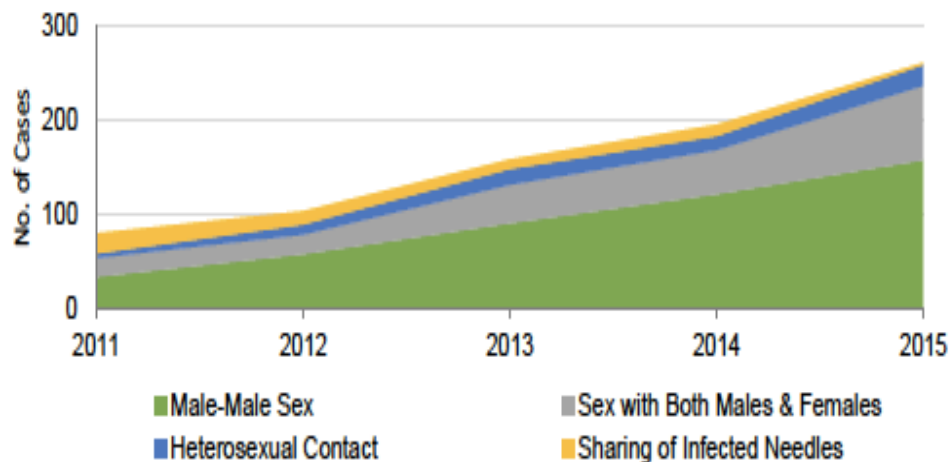




The Growing HIV Epidemic among Adolescents in the Philippines

sg.news.yahoo.com

Figure 1. Number of newly diagnosed HIV cases among adolescents by mode of transmission, 2011-2015 HIV/AIDS & ART Registry of the Philippines (HARP)



Philippines only country in Asia where teen pregnancy rising

MANILA, Philippines (AP) — The Philippines is the only Asia-Pacific country where the rate of teen pregnancies rose over the last two decades and the slow decline of its overall fertility rate may deprive the country of the faster economic growth expected in places that have more working-age people than younger and older dependents, the U.N. Population Fund said Thursday.

Girls aged 15 to 19 make up 10 percent of the country's population of 100 million and one out of 10 of them have already given birth, UNFPA country representative Klaus Beck said. That fertility rate in that age group is 57 births for every 1,000 girls as of 2013 — higher than rates found by surveys every five years from 1998.

He emphasized the urgency of fully implementing a reproductive health law, investing in quality education and health services for teenage girls, and increasing jobs for youth.

The cost of not finishing high school education over the lifetime of young people would be equivalent to about 1 percent of the country gross domestic product, he added.

Associated Press 7 July 2016

Why are HIV-infected children vulnerable?

- ◆ **HIV/AIDS is rapidly fatal in children**
- ◆ **Children have higher viral burden , develop faster depletion of infected CD4 lymphocytes, more rapid progression than adults**
- ◆ **Early diagnosis (virological test) needed for timely initiation of ART to reduce poor outcomes**
- ◆ **Children need special care to make sure that they are growing and developing optimally**





World Health
Organization

GUIDELINES



CONSOLIDATED GUIDELINES ON
**THE USE OF
ANTIRETROVIRAL DRUGS
FOR TREATING AND
PREVENTING HIV INFECTION**

**“TREAT-ALL”
recommendation:**

- All populations and age groups are eligible for treatment, including pregnant women and children

RECOMMENDATIONS FOR A
PUBLIC HEALTH APPROACH

**SECOND EDITION
2016**



Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

ADMINISTRATIVE ORDER
No. 2017- _____

Revised Policies and Guidelines on the Use of Antiretroviral Therapy (ART) among People living with Human immunodeficiency virus (HIV) and HIV-exposed infants

This guideline is developed to ensure safe and effective use of ART in a scale up program. It is a local adaption of the 2016 WHO recommendations on the use of antiretroviral drugs for treating and preventing HIV infection.

OBJECTIVE: To provide standards for the use of ARV among PLHIV and infants exposed to HIV in the Philippines.

- Early use of ART keeps Filipinos living with HIV alive and healthier... helps reduce the risk of transmitting the virus to their sexual and drug-sharing partners.
- Strategic approaches such as “test early”, “treat early”, and “treat all” : all populations and age groups are now eligible for treatment, including pregnant women and children.



Significant Developments in the Prevention and Control of HIV

- ◆ **Point-of-care diagnostic tests for rapid diagnosis**
- ◆ **Early initiation of ART for prevention and treatment of HIV**
- ◆ **New and more effective ARV drugs and regimens for prevention and treatment**
- ◆ **Consolidated guidelines on the use of ARV drugs**



Strategies for the Prevention and Control of HIV

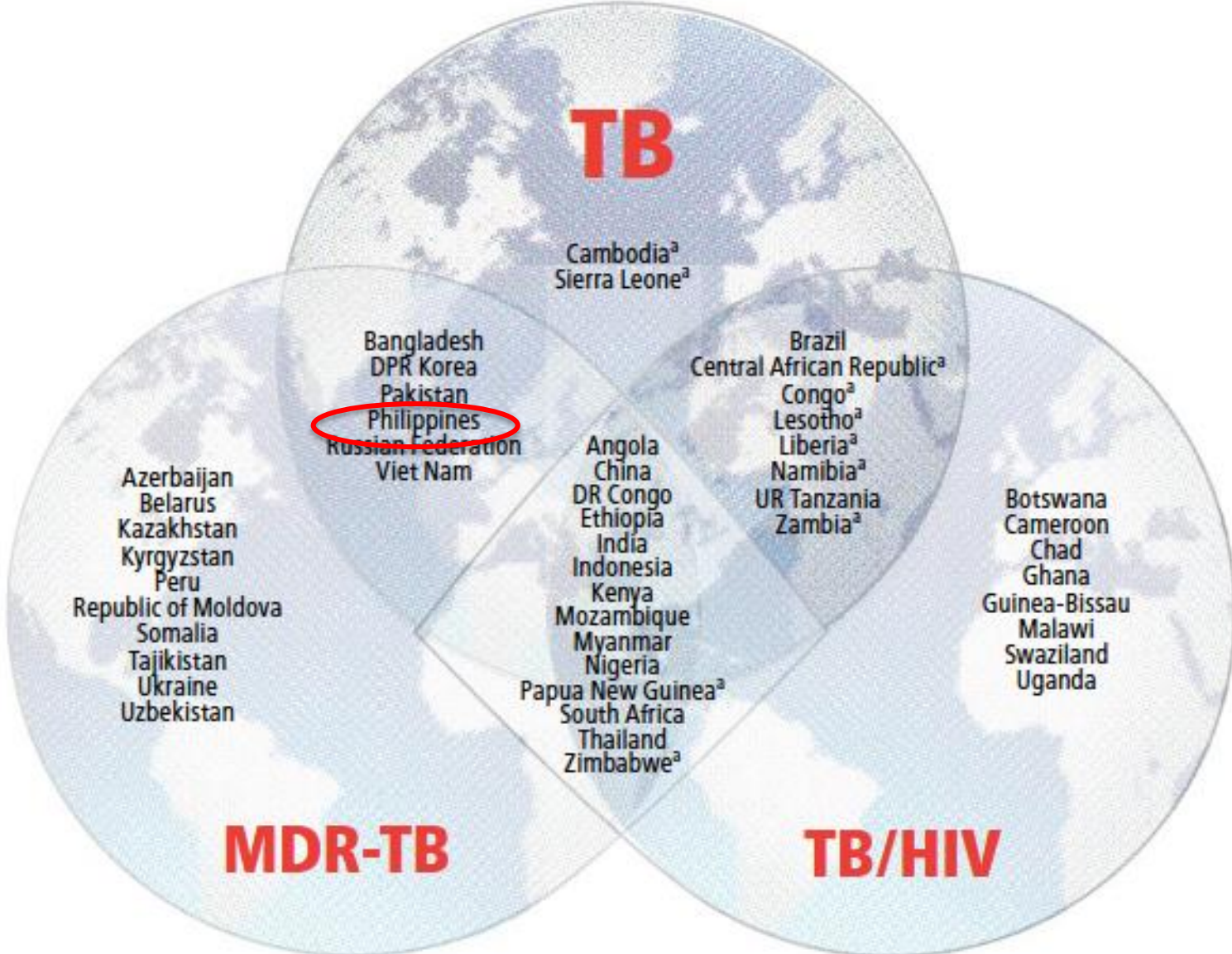
- ◆ **Routine screening for HIV risk and testing those at high risk**
- ◆ **Newer diagnostic tests, e.g. rapid viral load tests**
- ◆ **Universal access to ARV drugs**
- ◆ **Comprehensive child- or adolescent-friendly health services and continuous monitoring to ensure adherence and compliance**
- ◆ **Concerted and greater efforts to address stigma and discrimination**



The Continuing Scourge of Tuberculosis

- ◆ **TB is the leading cause of death from a single infectious agent worldwide**
- ◆ **Heaviest burden of TB is on the world's most poor and vulnerable**
- ◆ **Global TB burden, 2016:**
 - ✧ **10.4 M million TB cases**
 - ✧ **1.67 M deaths**
- ◆ **Drug Resistant TB: 600,000 cases of Rif-resistant TB, including 490,000 MDR-TB**

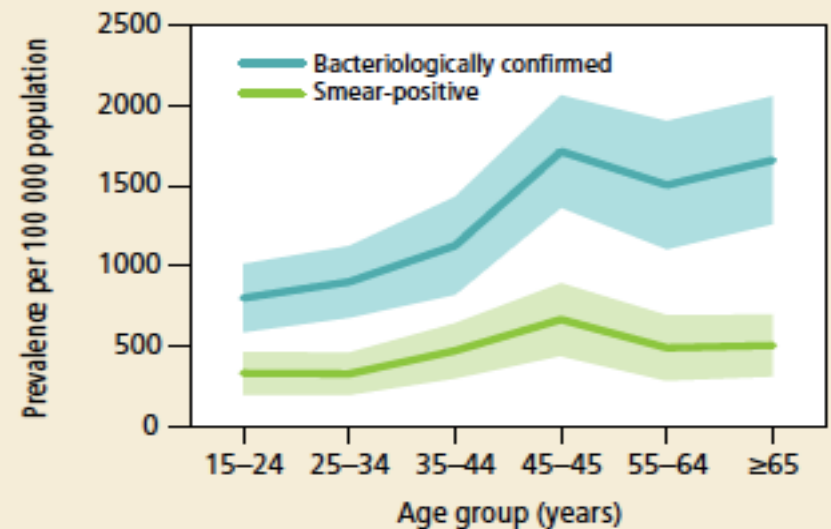
Countries in the three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020, and their areas of overlap



2016 National TB Prevalence Survey in the Philippines

- ◆ Nationwide, population-based, cross-sectional TB prevalence survey from Mar-Dec 2016
- ◆ Out of the 61,466 eligible individuals ≥ 15 years old, 46,689 (76%) participated in the survey
- ◆ 466 bacteriologically-confirmed PTB (15% by MTB culture, 51% by Xpert MTB/RIF, 34% by both)
- ◆ Prevalence for smear(+): 434/100,000
- ◆ Prevalence for bacteriologically confirmed TB: 1159/100,000

Prevalence of smear and bacteriologically confirmed pulmonary TB



Comparison of the National TB Prevalence Surveys

Indicator	1983	1997	2007	2016
<i>NTPS</i>	<i>1st</i>	<i>2nd</i>	<i>3rd</i>	<i>4th</i>
Prevalence of smear(+)	6.6/1000	3.1/1000	2.0/1000	4.34/1000
Prevalence of culture (+)	8.6/1000	8.1/1000	4.7/1000	11.59/1000

Key Findings of the 2016 NTPS

- ◆ **TB burden remains high among Filipino adults, higher than previously estimated**
 - ✧ **Around 1 M Filipinos are expected to have TB, and may or may not know it**
 - ✧ **Around 760,000 Filipinos aged ≥ 15 years are estimated to have PTB**
 - ✧ **No evidence of a decline in PTB prevalence rates compared to the 2007 NTPS**



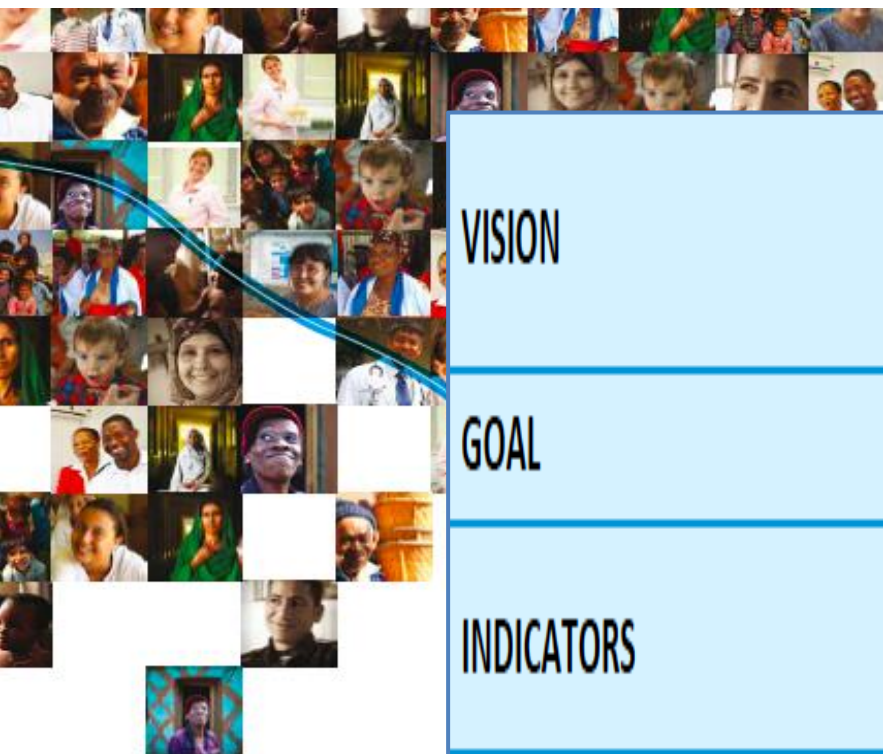
Key Findings of the 2016 NTPS

- ◆ **Current modes of screening by symptoms and diagnosis by sputum microscopy are not sufficient for early diagnosis of TB**
- ◆ **Under-reporting of TB cases to the national TB registry is likely**
- ◆ **Health care-seeking behavior for symptoms suggestive of TB remains inappropriate**



Recommendations from the 2016 Philippine National TB Prevalence Survey

- ◆ **Systematic screening for TB among high-risk, vulnerable groups (men, older age group, poor, slum dwellers, smokers, DM)**
- ◆ **Enhance diagnostic tools to find missing cases: CXR, Xpert MTB/RIF**
- ◆ **Develop innovative behavioral interventions and enablers to improve health care seeking and adherence to treatment**
- ◆ **Reinvigorate and transform public-private partnerships**



THE
END TB
STRATEGY

VISION	<h2 style="color: red;">A World free of TB</h2> <p>– zero deaths, disease and suffering due to tuberculosis</p>			
GOAL	<h2 style="color: red;">End the global TB epidemic</h2>			
INDICATORS	MILESTONES		TARGETS	
	2020	2025	SDG 2030	END TB 2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	80% (<20/100 000)	90% (<10/100 000)
TB-affected families facing catastrophic costs due to TB (%)	Zero	Zero	Zero	Zero

Challenges in TB in Children



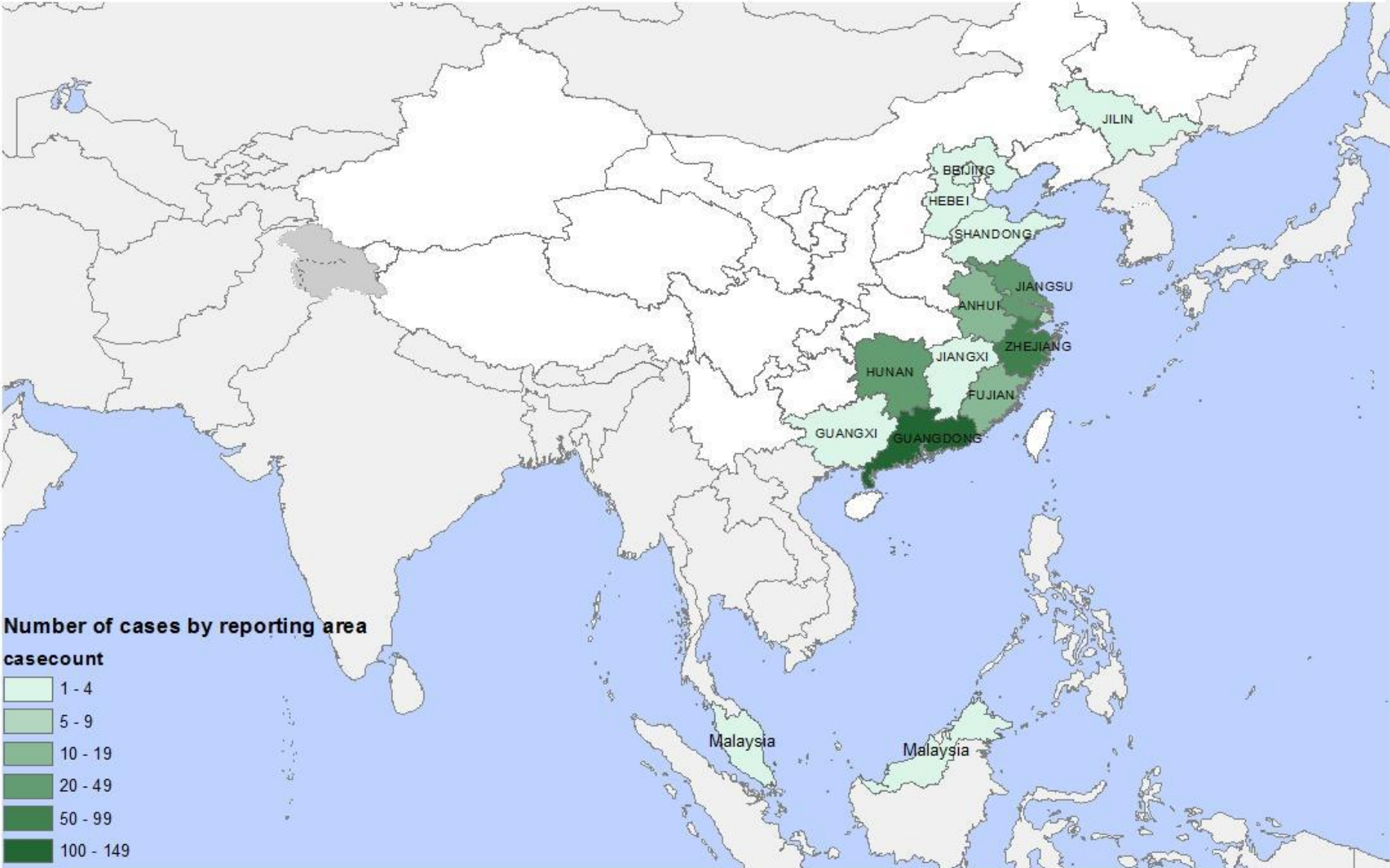
- ◆ **Improve recognition and reporting of TB in infants and children**
- ◆ **Develop rapid diagnostic tests to detect TB disease and resistance, and to accurately measure LTBI progression to active disease.**
- ◆ **New drugs and drug regimens to treat drug-susceptible or drug-resistant TB**
- ◆ **Scaling up of Isoniazid Preventive therapy for children and develop shorter regimens for TB preventive treatment**
- ◆ **Increase BCG vaccination coverage (In the Phil, 76% in 2016)**
- ◆ **Develop more effective vaccine that provides protection against all forms of TB in all age groups.**



Avian Influenza (“Bird Flu”)

- ◆ Infectious viral disease of birds caused by type A strain
- ◆ Occasionally transmitted to humans through direct or indirect contact with poultry
- ◆ Cause disease ranging from mild illness to death
- ◆ Majority of human cases of avian influenza have been sporadic, or resulted in localized outbreaks
- ◆ Currently, novel influenza A viruses associated with severe disease in humans include:
 - ✦ **A(H5N1) virus** -highly pathogenic avian influenza, first reported in HK in 1997; re-emerged 2003, spread from Asia to Europe and Africa; last case reported Egypt 26 Sept 2017
 - ✦ **A(H7N9) virus** – first reported in China in 2013; increase in human infections and many deaths since 2016; additional cases detected in HK, Taiwan, Malaysia, and Canada.

Areas reporting confirmed human cases for influenza A(H7N9) to WHO from 2013-06-01 *

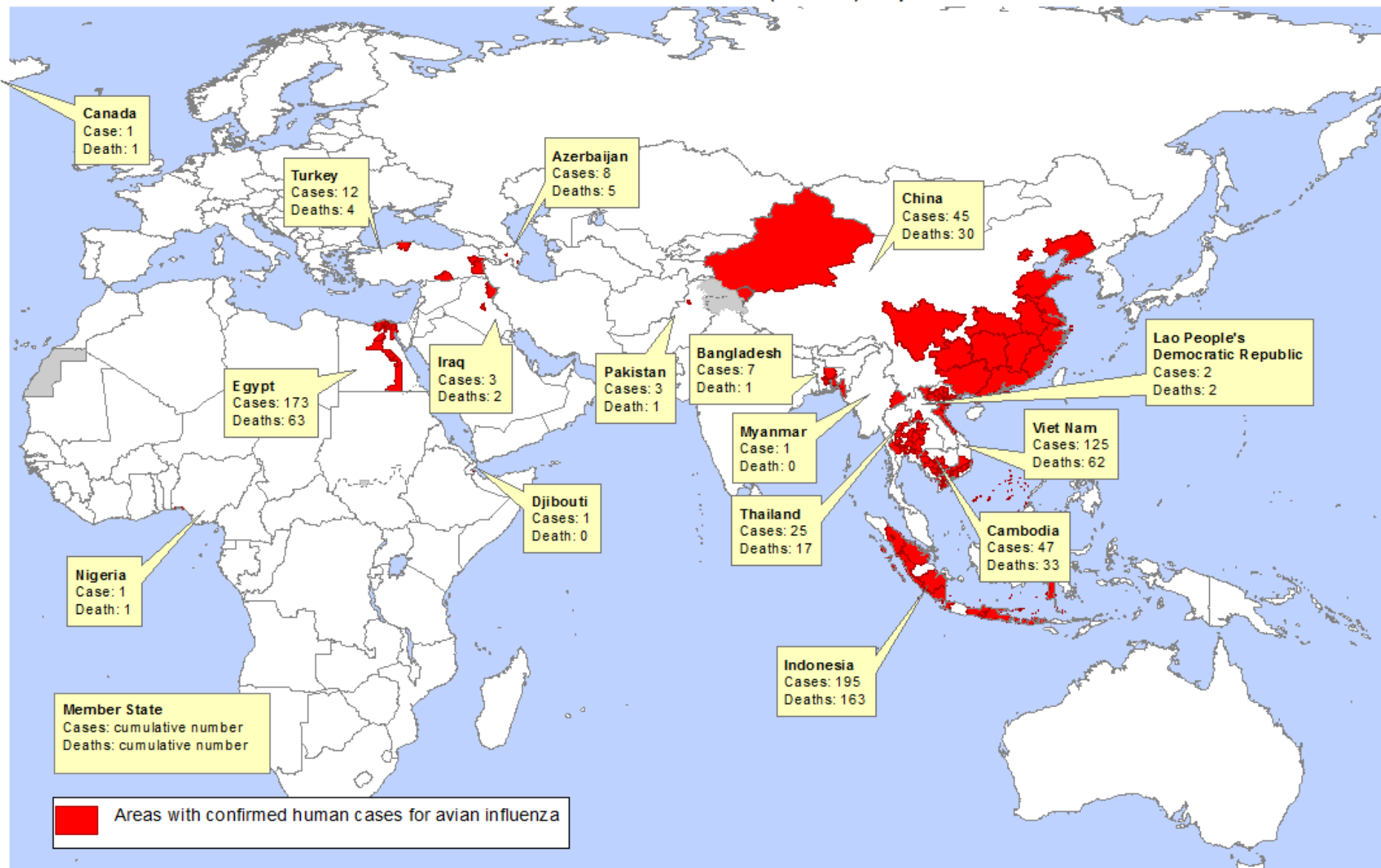


*All dates refer to onset of illness
 Data as of 14/07/2014
 Source: WHO

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
 © WHO 2013. All rights reserved.



Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013*



*All dates refer to onset of illness
Data as of 24 January 2014
Source: WHO/GIP

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not be full agreement.
© WHO 2013. All rights reserved.



Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2017

Country	2003-2009*		2010-2014**		2015		2016		2017		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	56	37
Canada	0	0	1	1	0	0	0	0	0	0	1	1
China	38	25	9	5	6	1	0	0	0	0	53	31
Djibouti	1	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	120	50	136	39	10	3	3	1	359	120
Indonesia	162	134	35	31	2	2	0	0	1	1	200	168
Iraq	3	2	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	0	0	0	0	2	2
Myanmar	1	0	0	0	0	0	0	0	0	0	1	0
Nigeria	1	1	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	12	4
Viet Nam	112	57	15	7	0	0	0	0	0	0	127	64
Total	468	282	233	125	145	42	10	3	4	2	860	454

* 2003-2009 total figures. Breakdowns by year available on subsequent tables.

** 2010-2014 total figures. Breakdowns by year available on subsequent tables.

Total number of cases includes number of deaths.
WHO reports only laboratory cases.
All dates refer to onset of illness.

Source: WHO/GIP, data in HQ as of 7 December 2017

Until 2016, the disease has not been reported in the Philippines.

Impact of Avian Influenza Outbreaks



- ◆ **Outbreaks of avian influenza continue to be a global public health concern.**
- ◆ **Substantial negative economic impact on tourism, travel and trade, cause significant political and social disruption.**
- ◆ **In birds: mass killing and destruction of both domestic and wild birds have serious consequences on both livelihoods and international trade in many countries**
- ◆ **In humans: Avian influenza subtypes (e.g. H5N1, H7N9) transmitted from infected poultry to humans may cause serious illness and high mortality**
- ◆ **No evidence of sustained human to-human spread of these viruses at this time**
- ◆ **Close monitoring for sustained human-to-human transmission is critical due to the pandemic potential of these viruses**



***Bird Flu Alert* : 2017 Central Luzon H5N6 outbreak**

- ◆ **Apr-Sept 2017: outbreak of H5N6 avian influenza affected poultry in at least 3 towns in 2 provinces in Central Luzon:**
 - ✧ **Pampanga (San Luis) - outbreak confirmed Aug 11**
 - ✧ **Nueva Ecija (Jaen, San Isidro) - confirmed Aug 18**
- ◆ **This is the FIRST AVIAN FLU OUTBREAK recorded in the Philippines.**
- ◆ **37,000 birds died from H5N6 (August 11); 600,000+ birds culled (September 4)**
- ◆ **Animal to human transmission was monitored but no human cases or deaths due to H5N6 was documented**
- ◆ **September 2017: outbreak officially declared over**
- ◆ **Estimated loss in the country's poultry industry ₱ 2.3 B**



Philippine government response to prevent the spread of the Disease

- ◆ **Quarantine and culling of infected wild and domesticated birds**
- ◆ **Temporary trade ban against transporting birds and poultry products**
- ◆ **Greater bio-security measure in farms in the country**
- ◆ **Community education on prevention of transmission: infection control measures, postexposure prophylaxis, advice for travelers.**
- ◆ **DOH stepped-up the human flu like-illness surveillance**
- ◆ **Implementation of the 2010 Philippine Preparedness and Response Plan for Pandemic and Avian Influenza**



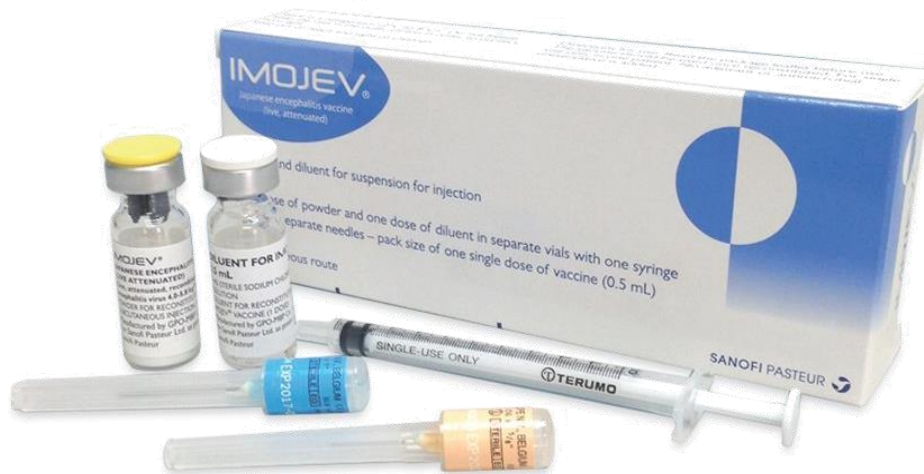
Avian Influenza Challenges and Strategies for Prevention and Control

- ◆ **Significant outbreaks of disease due to novel influenza viruses have revealed weaknesses in the public health infrastructure and disease surveillance systems of many countries and areas in the region.**
- ◆ **Lack of preparedness to respond to outbreaks: understaffed poorly trained health workforces, and lack of capacity for reliable laboratory diagnosis, investigation and control**
- ◆ **Potential of currently-circulating avian, swine and other zoonotic influenza viruses to result in a future pandemic is unknown**
- ◆ **Strengthened surveillance in both animal and human populations, thorough investigation of every zoonotic infection and pandemic preparedness planning is crucial**



The Tale of Two Vaccines

Japanese Encephalitis Vaccine



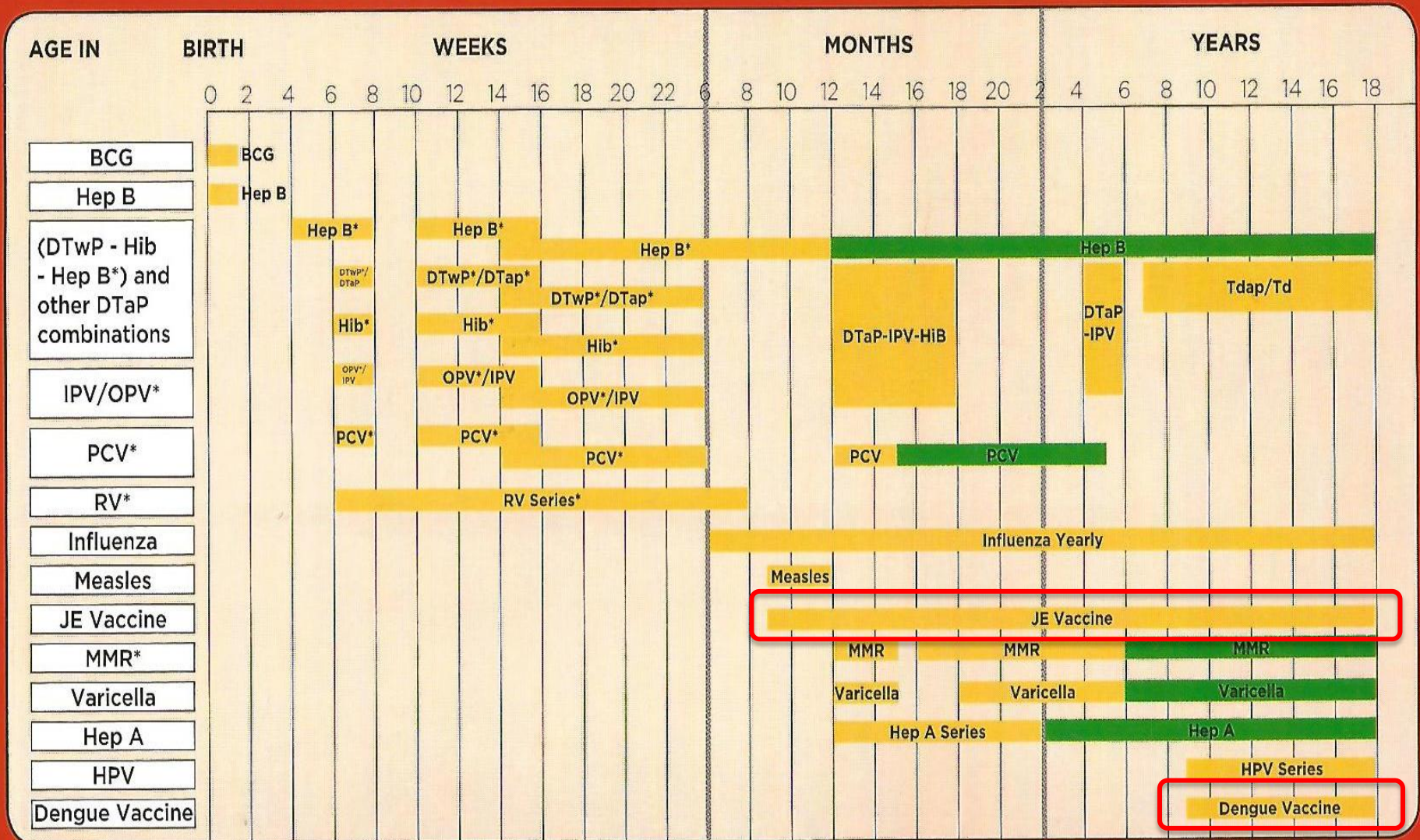
Stock out

Dengue Vaccine



Pull out

Childhood Immunization Schedule 2017



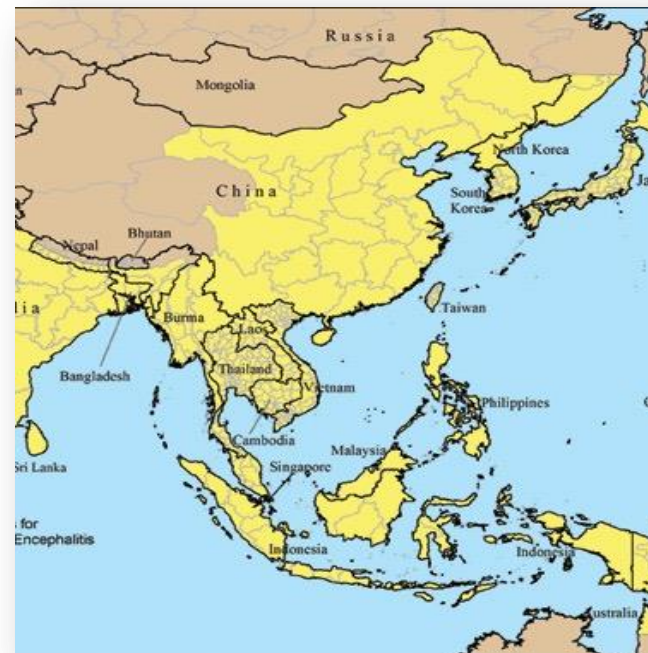
Range of Recommended Age

Catch Up Immunization

*Primary doses are given at least 4 weeks apart

Japanese Encephalitis

- ◆ JE virus (JEV) found in nearly every country in Asia
- ◆ Most common cause of viral encephalitis in Asia
- ◆ Approx. 67,900 JE cases occur annually in JE-endemic countries (incid 1.8 per 100,000 overall)
- ↗ JE occurs in all ages but primarily affects children below 15 years of age
- ↗ 20–30% of cases are fatal; long-term neurologic sequelae occur in 30–50% of survivors



Japanese encephalitis in the Philippines

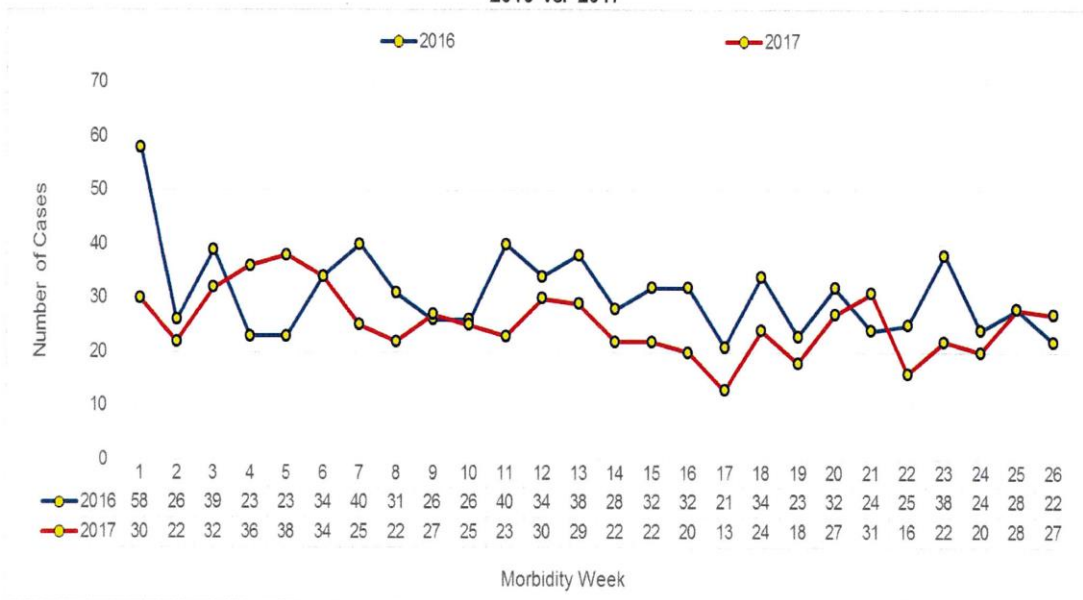
- ◆ **JEV is endemic in the Philippines**
- ◆ **Extensive geographic range: cases reported in 68 out of 81 provinces and major cities**
- ◆ **68% percent of the cases were in children < 15 years old**
- ◆ **Transmission probably occurs year-round due to all-year round rainfall , reaching peak levels in June and July due to higher mosquito population**
- ◆ **JEV was the causative agent in 7-18% of cases of clinical meningitis and encephalitis combined, and 16- 40% of clinical encephalitis**



Morbidity Week 31: January 1 – August 5, 2017

**Epidemiology Bureau
 Public Health Surveillance Division**

Figure 1. Reported AMES Cases by Morbidity Week, Philippines
 2016 vs. 2017*



*data as of August 5, 2017

Figure 6. Lab confirmed JE Cases by Age Group and Sex
 Philippines, January 1 – August 5, 2017 (n=57)

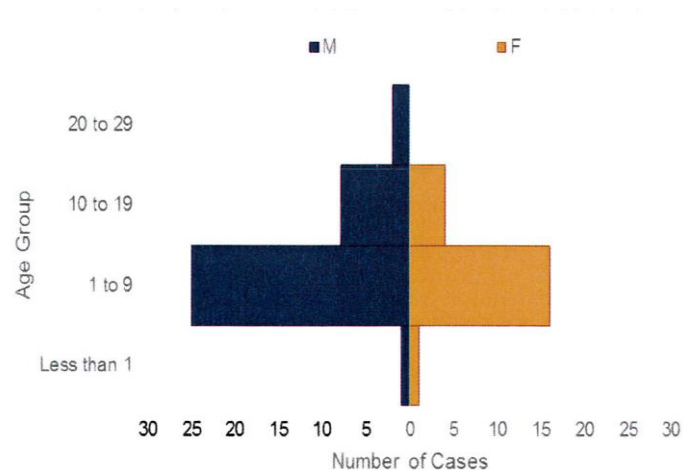


Table 2. Confirmed JE Cases 2016 vs. 2017
 Philippines, January 1 to August 5, 2017 (n=57)

Laboratory Confirmed JE cases (Morbidity Week 1-31)	2017		2016		Percent difference
	Cases	Deaths	Cases	Deaths	
AMES surveillance	38	0	143	11	↓73.43
AES surveillance	19	0	62	2	↓69.35
Total	57	0	205	13	↓72.20



Increased reporting of JE cases in the Philippines

- ◆ **August 18-29, 2017: Isolated cases reported in several provinces in the Philippines, majority in central Luzon: Pampanga, Zambales, Pangasinan, Nueva Ecija**
- ◆ **The increased reporting was attributed to increased surveillance with laboratory confirmation and increased public awareness**
- ◆ **DOH confirmed that there was no increase in laboratory confirmed cases of JE and the number of suspected Acute meningitis-encephalitis cases reported from Jan to Aug 2017 (actually 20% decrease compared to the same period the previous year)**
- ◆ **Undue public alarm compounded by stock-out of the JE vaccine in both private and government health facilities promoted the unscrupulous sale of vaccines by disreputable dealers**

DOH, doctors say 'no need to panic' over Japanese encephalitis

The Food and Drug Administration warns parents against buying the Japanese encephalitis vaccine online. Only Sanofi Pasteur is accredited to distribute the vaccine in the country.

DOH warns against Japanese Encephalitis, other mosquito-borne diseases this rainy season

Metro Manila (CNN Philippines, September 6) —The Health Department is reminding the public to step up preventive measures to avoid mosquito-borne diseases - including the lesser-known Japanese encephalitis (JE) - this rainy season.

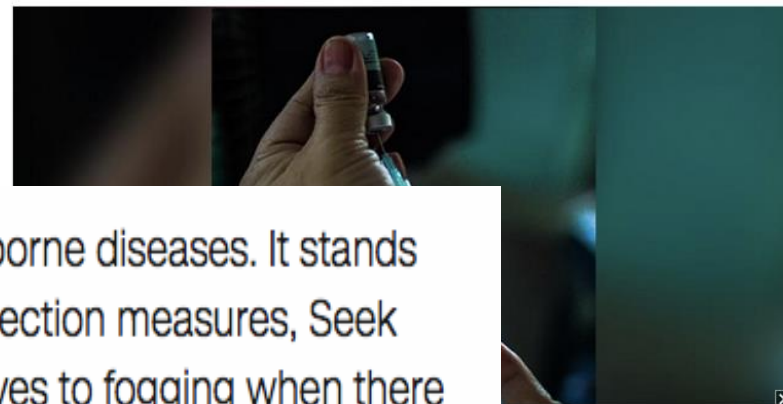
In a press release on Wednesday, the Department of Health warned cases of mosquito-borne diseases such as dengue, chikungunya, and Japanese encephalitis typically rise during the rainy season.

"I urge the public to take JE preventive measures following the 4-S against dengue and other mosquito-borne diseases. This includes getting rid of standing water, maintaining

The 4S campaign is the department's way to curb mosquito-borne diseases. It stands for "Search & destroy mosquito breeding places, use Self-protection measures, Seek early consultation for fever lasting more than 2 days, and Say yes to fogging when there is an impending outbreak," according to the DOH website.

DOH warns consumers vs fake Japanese encephalitis vaccines

© Monday, September 11, 2017





Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY



DOH URGES PUBLIC TO PROTECT THEMSELVES FROM MOSQUITO BITES TO PREVENT JAPANESE ENCEPHALITIS AND CAUTIONS AGAINST USE OF VACCINES DURING THIS PERIOD

Press Release

September 06, 2017

The Department of Health (DOH) today calls on local executives and families to **intensify** mosquito prevention and control measures at home and in the community, and to protect themselves from being bitten by mosquitoes, **particularly in high-risk areas**. As the country moves further into the rainy

As of 26 Aug 2017, the DOH- Epidemiology Bureau recorded a 44% decrease of lab-confirmed JE cases compared to the same period last year... heightened awareness resulted to an increased health seeking behavior and increased reporting....

the people resulted to an increased health seeking behavior thus increased reporting in Pampanga as

Studies showed that there is no known benefit of the vaccine when given during the peak season...

JE prevention should focus on identification and destruction of mosquito breeding sites and environmental cleanliness.

mosquito breeding sites and environmental cleanliness.



POSITION PAPER ON JAPANESE ENCEPHALITIS VACCINES

Pediatric Infectious Disease Society of the Philippines

a specialty society of the
Philippine Pediatric Society



SUMMARY STATEMENT

The Philippine Pediatric Society (PPS) and the Pediatric Infectious Disease Society of the Philippines (PIDSP) recognize that Japanese encephalitis is an important public health problem in the Philippines. Although relatively few cases are reported, the severity of the disease, its high case-fatality rates and the complications of JE present a significant burden to the community. JE vaccination has been incorporated in the recommendations for childhood immunization by the PPS/PIDSP/PFV since 2016. In the recent months there have been increased demand for the vaccine due to alleged increase in the number of JE cases.

The unfortunate situation of misinformation, especially through social media, has forced health care providers to seek guidance regarding the best possible use of scarce vaccine supply. Thus, the PPS and PIDSP, through this position paper, propose these recommendations:

- **Sustained surveillance**
- **Timely communication of accurate information and guidance**
- **Prevention methods and personal protection together with timely JE vaccination**
- **Prioritize JE vaccination to children <15 yrs and those living in high risk areas**



JEV: Challenges and Strategies for Prevention and Control

- ◆ **Continued and improved surveillance to quantify burden of disease**
- ◆ **Incorporation of JE vaccination into routine immunization programs in areas where: JE constitutes a public health problem or environment is suitable for JEV transmission.**
- ◆ **The Philippine government has developed plans to:**
 - ✧ **expand sentinel JE surveillance with laboratory confirmation to collect systematic data from all regions of the country and to provide a baseline for measuring vaccine impact.**
 - ✧ **introduce JE vaccination among young children in 2018**



Dengue

- ◆ **Dengue - the most important, most rapidly spreading mosquito-borne viral disease in the world**
- ◆ **Annually, > 390M cases from more than 120 countries worldwide; estimated 270M in Asia**
- ◆ **Caused by 4 dengue virus serotypes (DEN-1, DEN-2, DEN-3, DEN-4)**
- ◆ **Severe dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries.**

Dengue in the Philippines

- ◆ Dengue – all year round disease in the Philippines
- ◆ Peak incidence during the wet season
- ◆ All four DENV serotypes are present
- ◆ Epidemics of DF and DHF occur every 3-4 years; local outbreaks occur every year
- ◆ Highest dengue cases in children 5-9 yrs old, followed by 10-14 yrs old
- ◆ Overall dengue CFR 0.30 – 0.56%

Year	Cases	Deaths	CFR (%)
2012	187,031	921	0.49
2013	204,906	660	0.32
2014	121,580	465	0.38
2015	200,415	598	0.30
2016	220,518	1092	0.50
2017	131,827	732	0.56





Dengue Prevention and Control

Dengue control involves a comprehensive and integrated approach.

- ◆ **Vector control**
- ◆ **Monitoring and surveillance**
- ◆ **Emergency preparedness**
- ◆ **Capacity building and training**
- ◆ **Dengue vaccination**



Challenge of any Candidate Dengue Vaccine

- ◆ Infection with dengue virus provides long-term protection against the particular serotype that caused disease but only short-lived immunity to the other 3 serotypes
- ◆ A safe, effective and affordable dengue vaccine represents a major advance for disease control and an important tool for reaching WHO goal: reduction in dengue morbidity by 25%, mortality by 50% by 2020.

Challenge of any Candidate Dengue Vaccine

- ◆ **Ideally any candidate dengue vaccine should:**
 - ✧ **produce balanced protective, immunity against all four serotypes**
 - ✧ **Induce long-lived protective immunity**
 - ✧ **reduce symptomatic virologically confirmed dengue, particularly severe dengue.**

Dengue Vaccines

Table 1. Dengue fever vaccines in clinical testing, listing the number of genes, structural and nonstructural, which are included in the final construct

Type of vaccine	Genes (N)		Stage of development
	Structural	Nonstructural	
Live attenuated virus (molecular mutant)	DENV1–4 (two each)	DENV1,3,4 (eight each)	Phase III tetravalent (Butantan, U.S. National Institutes of Health)
Yellow fever chimera	DENV1–4 (two each)	Yellow fever (eight each)	Completed phase III (Sanofi Pasteur)
Dengue 2 chimera	DENV1–4 (two each)	DENV2 (eight each)	Phase III tetravalent (Takeda)



- **First Licensed Dengue Vaccine: CYD-TDV (Dengvaxia, Sanofi Pasteur)**
- **Live attenuated recombinant chimeric tetravalent dengue vaccine, administered in 3 doses (months 0, 6,12)**
- **Product of 20 years development**
- **2 large-scale, multicentre, Phase-III clinical trials, one conducted in 2–14 year-olds in 5 countries in Asia, the other in 9–16 year-olds in 5 countries in Latin America.**
- **Currently licensed in 19 endemic countries in individuals aged 9-45 in Asia or 9-60 year olds in Latin America**

CYD-TDV Vaccine Efficacy in the 25-month Active Surveillance Phase

Outcome	Study Population	CYD14	CYD15	Pooled	Pooled ≥ 9 years
VCD-DENV1-4	All	54.8% (46.8-61.7)	64.7% (58.7-69.8)	60.3% (55.7-64.5)	65.6% (60.7-69.9)
	2-5 years	33.7% (11.7-50.0)	NA	NA	NA
	6-11 years	59.5% (48.9-68.0)	61.7% (52.3-69.3)**	Not published	Not published
	12-16 years	74.4% (59.2-84.3)*	67.6% (59.3-74.3)	Not published	Not published
	Seropositive	74.3% (53.2-86.3)	83.7% (62.2-93.7)	78.2% (65.4-86.3)	81.9% (67.2-90.0)
	Seronegative	35.5% (-27.0-66.6)	43.2% (-61.6-80.0)	38.1% (-3.4-62.9)	52.5% (5.9-76.1)

- ◆ **60.3% Overall Vaccine efficacy against VCD, any serotype**
- ◆ **Sub-group analysis showed greater efficacy:**
 - ✦ **Serotypes DENV 3 & 4 than DENV 1 & 2**
 - ✦ **Older children (≥ 9 yrs old)**
 - ✦ **Hospitalized dengue (72.7%) and severe dengue (79.1%)**
 - ✦ **Seropositive participants (78.2%) compared to those who were seronegative (38.1%)**
- ◆ **Acute adverse events were similarly infrequent in the vaccine and control groups.**

CYD-TDV Vaccine Safety beyond 2 Years of Follow-up

- ◆ **In CYD14 (Asian study), Year 3 of surveillance:**
 - ✧ **increased risk of hospitalized and severe dengue in vaccine recipients 2–5 years old**
 - ✧ **no consistent increase observed in risk of hospitalization or severe dengue in vaccinated individuals aged 9–16**
- ◆ **The biologic mechanism not fully understood but could be related to negative serostatus and/or age: waning protection, lower vaccine-induced immune response in younger children, temporal clustering**
- ◆ **This trend could also indicate the potential for immune enhancement of disease in younger flavivirus-naïve subjects (ADE).**

**◆ Key RECOMMENDATION:**

- ✧ **Countries should consider implementation of CYD-TDV in national or subnational territories where at least 70% in the age group targeted for vaccination are seropositive for dengue.**
- ✧ **Dengue vaccine introduction should be a part of a comprehensive dengue control strategy together with a communication strategy, sustained vector control, evidence-based clinical care for dengue patients, and robust dengue surveillance**
- ✧ **Countries which want to introduce the dengue vaccine should have the following:**
 - ◆ **a comprehensive dengue control strategy**
 - ◆ **strong capacity in place to monitor and manage any adverse events following vaccination**
 - ◆ **a dengue surveillance system able to detect and report hospitalized and severe dengue cases.**

DOH ADVISORY



DENGUE SCHOOL-BASED IMMUNIZATION

(Regions III, IV-A and NCR)



- ◆ in April 2016 , the Philippines became the first country to roll out a dengue school-based vaccination program
- ◆ 3.5 billion pesos (\$69 million) worth of Dengvaxia purchased to be used for one million children in parts of the Philippines hard-hit by dengue.
- ◆ Congressional inquiry on the on the school-based dengue vaccination program started Nov-Dec 2016
- ◆ Approx. 830,000 children, aged 9 and older, had been inoculated with Dengvaxia since April 2016.



Sanofi updates information on dengue vaccine

- ◆ **New analysis of long-term Dengvaxia® data found differences in vaccine performance based on prior dengue infection**
- ◆ **Dengvaxia provides persistent protective benefit against dengue fever in those who had prior infection.**
- ◆ **But for those not previously infected by dengue virus, more cases of severe disease could occur following vaccination upon a subsequent dengue infection.**
- ◆ **Updated Recommendation:**
 - ✧ **For individuals who have not been previously infected by dengue virus, vaccination should not be recommended**
 - ✧ **Healthcare professionals assess the likelihood of prior dengue infection in an individual before vaccinating.**

A timeline of events

WHO advises Dengvaxia be used only in people previously infected with dengue



NOV. 30, 2017
Sanofi Pasteur global announcement on new risk data on Dengvaxia

DEC. 1, 2017
DOH suspends dengue vaccination program; review and consultation is ongoing with experts, key stakeholders, and the WHO.

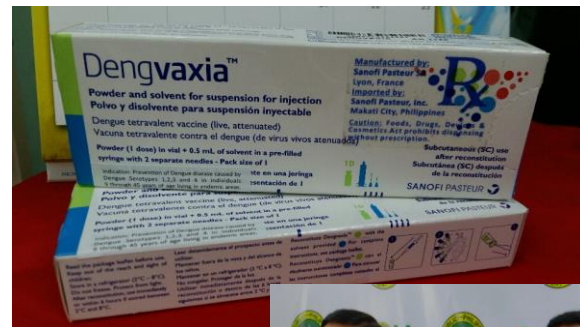
DEC. 5, 2017
Philippine FDA withdraws the approval of the vaccine

DEC. 7, 2017
WHO Global Advisory Committee on Vaccine Safety advises Dengvaxia be used only in people previously infected with dengue

DEC. 13, 2017
Start of Congress and Senate inquiry, criminal investigation



World Health Organization

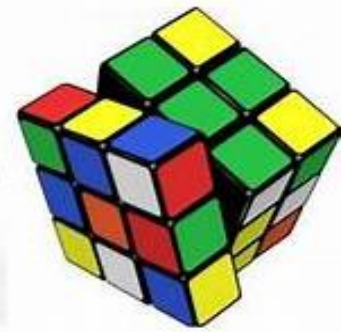


What are the risks in vaccinated individuals?

- ◆ It is not the vaccine itself that causes excess cases, but rather that the vaccine induces an immune status that increases the risk that subsequent infections are more pronounced.
- ✧ **5-year risk of severe dengue In vaccinated seronegative persons 4 per 1,000**
 - ✧ similar to the risk in unvaccinated seropositive persons (4.8 per 1,000 seropositive persons unvaccinated)
 - ✧ higher than unvaccinated seronegative persons (1.7 per 1,000 seronegative persons unvaccinated).
- ◆ No evidence that clinical severity of disease was greater in vaccinated seronegative persons compared to unvaccinated seropositive persons.
- ◆ Cases classified as severe dengue that occurred in initially seronegative vaccine recipients aged ≥ 9 yrs were categorized as DHF Grades I and II, did not lead to shock, severe bleeding or death, and all recovered.



What I know now about CYD-TDV Vaccine



◆ It is not the SILVER BULLET for dengue

- ◆
 - Depending on dengue serostatus at the time of vaccination, CYD-TDV may protect, be a wasteful intervention or harm the vaccinees
 - All individuals. regardless whether they have been vaccinated or

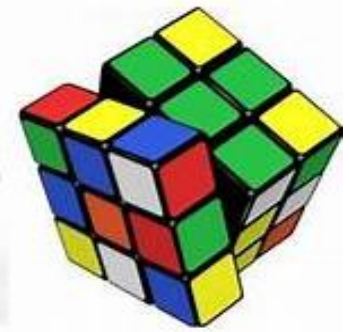
Following a consultation of the Global Advisory Committee on Vaccine Safety:

“The World Health Organization finds that the dengue vaccine CYD-TDV (Dengvaxia), *prevents disease in the majority of vaccine recipients* but it *should not be administered to people who have not previously been infected with dengue virus.*”

[http://www.who.int/medicines/news/2017/WHO advises Dengvaxia be used only in people previously infected with dengue.](http://www.who.int/medicines/news/2017/WHO%20advises%20Dengvaxia%20be%20used%20only%20in%20people%20previously%20infected%20with%20dengue) 13 Dec 2017



What do I know now about CYD-TDV Vaccine



- ◆ It is not the **SILVER BULLET** for dengue
- ◆ It is not a **“BAD” VACCINE**
- ◆ **Excitement and perils of being FIRST**

- Dengvaxia - first licensed dengue vaccine
- Philippines - first country where dengue vaccine was rolled out
- ◆ ➤ Deployment of a new vaccine should only be considered after a
 - Dengue vaccine efficacy is lower against DENV serotype 2 (also serotype 1)
 - Increased risk of Severe dengue in:
 - Age group 2-5 yrs old 2 years after vaccination
 - subsequent (2nd) infection in vaccinated seronegatives (simulate a secondary wild-type infection; ADE)



What do we need to do



- ◆ **Target the new vaccine to the right people at the right time**
 - ✧ **Vaccinate only those with serologic evidence or medical history or documentation of dengue illness**
- ◆ **Develop diagnostic tests to identify people most likely to benefit from the vaccine**
 - ✧ **Rapid diagnostic test that can be used at the time of vaccination, is affordable and provides reliable immediate results is urgently needed**
- ◆ **All individuals (vaccinated or not) should apply personal protective measures to avoid mosquito bites**
 - ✧ **Among populations where the vaccine has already been administered, enhance measures that reduce exposure to dengue infection to minimize illness for seronegative vaccinated people**

DOH Campaign against Mosquito-borne Infections

SUGPUIN ANG DENGUE!



 **STOP**
at 4 pm

 **LOOK**
sa loob at labas ng bahay para mag-
"Search and Destroy"
ng mga posibleng pamugaran ng lamok

 **LISTEN**
sa barangay officials para sa tamang paraan ng pagsugpo ng Dengue sa inyong lugar

Aksyon Barangay Kontra Dengue, PAGTIBAYIN!



Mag4S Laban sa Dengue

SEARCH and DESTROY

Para di maipunan ng tubig at pamugaran ng kiti-kiti:

- Palitan ang tubig at linisin ang flower vase minsan sa isang linggo.
- Takpan ng lupa o buhangin ang mga butas sa paligid ng inyong bahay.
- Takpan ang mga timba, drum o iba pang imbakan ng tubig.
- Tanggaliin at butasan ang mga gulong sa ibabaw ng inyong bubong o mga gulong sa inyong paligid.
- Itaob ang mga bote, lata at iba pang maaring pag-ipunan ng tubig at pangitugan ng lamok.
- Linisin at alisin ang tubig sa paminggalan.



SELF-PROTECTION MEASURES

- Iwasan ang maikling kasuotan upang di madaling makagat ng lamok.
- Maaari ding gumamit ng mosquito repellent sa araw.



SEEK EARLY CONSULTATION

- Kung may lagnat na ng 2 araw at may rashes sa balat, pumunta at komunsulta agad sa pinakamalapit na health center o ospital.



SAY NO TO INDISCRIMINATE FOGGING

- Yes to fogging only during outbreaks.



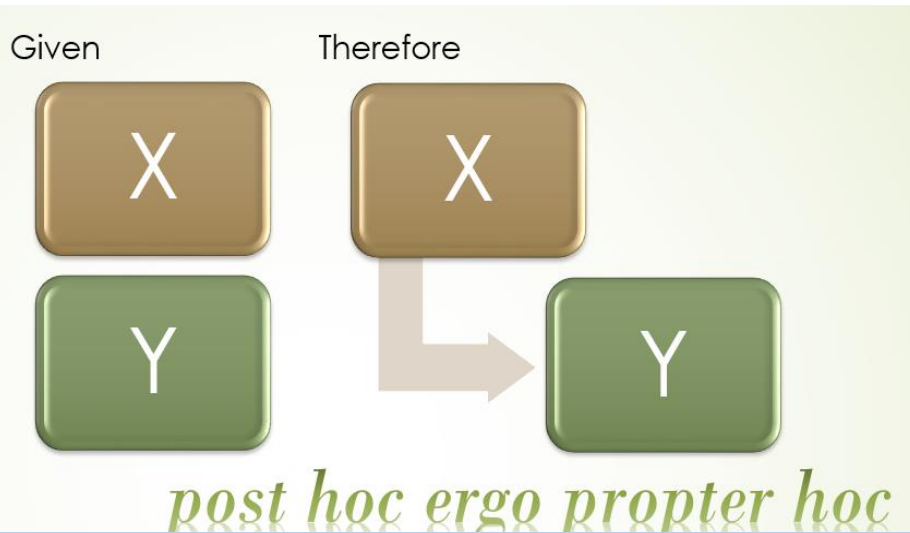


What do we need to do



- ◆ **Early medical consultation and prompt medical care for those presenting with dengue-like illness, *regardless of whether vaccinated or not***
- ◆ **Adhere to guidelines on dengue case management for appropriate medical care of all dengue patients**
- ◆ **Continue long-term surveillance for those vaccinated and comply with monitoring and reporting systems**
- ◆ **Organize a functional National Immunization Technical Advisory Group (NITAG)**

Patient/public education on a Fallacious argument: *Post hoc, ergo propter hoc*



"After this, therefore because of this"

Post Hoc Ergo Propter Hoc

The rooster crowed, the sun came up.
Therefore the rooster made the sun come up.





Silver Highlights in Pediatric Infectious Diseases

- ◆ **HIV : success and failures in controlling the epidemic**
- ◆ **TB : accomplishments amidst the continuing scourge**
- ◆ **Influenza (Avian) : Outbreak preparedness and response**
- ◆ **Japanese encephalitis : Public awareness and control measures**
- ◆ **Dengue : the unsolved problem**

Silver Lining in Pediatric Infectious Disease

Merriam-Webster dictionary definition of “*Silver lining*”

- ***a consoling or hopeful prospect***
- ***something good that can be found in a bad situation***
- ***gloomiest outlook contains some hopeful or consoling aspect***

Every cloud has a silver lining...



**...just wait for the sun to shine
through.**

Silver lining in Pediatric Infectious Disease

- ◆ There is continued research on new or improved vaccines against TB, HIV, Influenza, Dengue
- ◆ Continued research to develop rapid diagnostic methods for early detection of infection
- ◆ Greater public awareness leading to earlier consultation, early diagnosis and treatment for acute febrile illnesses
- ◆ Recognition of effective preventive measures for disease prevention and control
 - ✧ e.g. IPT for LTBI; screening and PMTCT strategies; isolation methods, Infection control guidelines to prevent disease transmission; outbreak preparedness and response
- ◆ Greater commitment to strengthen pharmacovigilance and health surveillance systems on infectious diseases, including vaccine-preventable diseases



Thank
you!