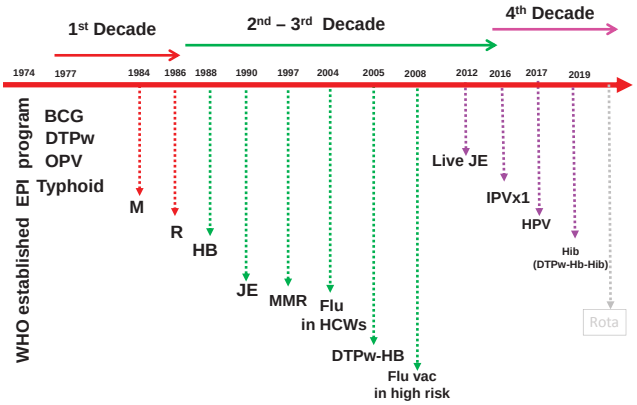
Progress of vaccines for children introduction into NIP



Immunization in Thai Children
เรามีสองมาตรฐาน

	Public	Private	สีแดง=วัคซีนที่ผู้ปกครองต้องจ่ายเอง
Birth	BCG, HBV	BCG, HBV	
	-----(1 M HBV for HBsAg+ mother only)----		
2, 4 M	DTP-HB-Hib, OPV/IPV, Rota 1,2	DTaP-IPV-Hib-HBV, PCV1, Rota1,2	
6 M	DTP-HB-Hib, OPV, (Rota3)	DTaP-IPV-Hib-HBV, PCV, (Rota3)	
	Influenza x2	Influenza x2	
9-12 M	MMR1	Live JE1	
12-18 M	Live JE1	MMR1 or MMRV1 at 12 M VZV1, HAV, PCV	
18 M	DTP, OPV	DTaP-IPV-Hib, Live JE2	
2-2 ½ Y	MMR2, Live JE2	MMR2, VZV2 (or MMRV2), (HAV2 inactivated)	
4-6 Y	DTP, OPV	Tdap-IPV	
10-12 Y	dT, HPVx2 (ป.5)	Tdap-IPV, HPVx2	
6M – 18Y	Influenza yearly to 2 yo	Influenza yearly up to adolescents	

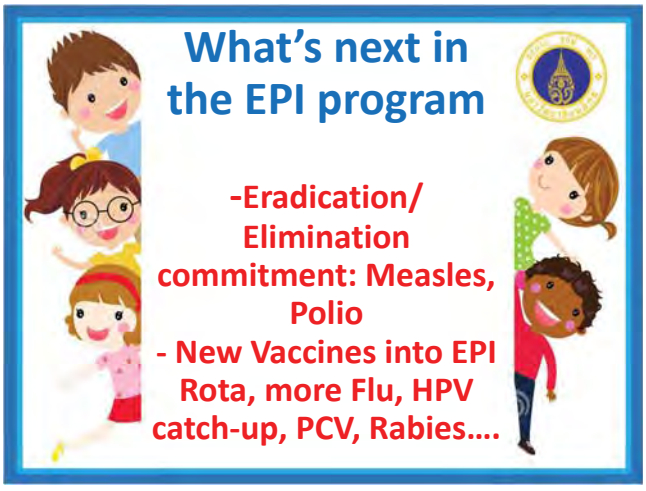
Immunization in Thai Children
เรามีสองมาตรฐาน

	Public	Private	สีแดง=วัคซีนที่ผู้ปกครองต้องจ่ายเอง
Birth	BCG, HBV	BCG, HBV	
	-----(1 M HBV for HBsAg+ mother only)----		
2, 4 M	DTP-HB-Hib, OPV/IPV, Rota 1,2	D… …1,2	
6 M	DTP-HB-Hib, OPV, (Rota3)	DTa… …ta3)	
	Influenza x2	Influenza x2	
9-12 M	MMR1	Live JE1	
12-18 M	Live JE1	M…	
18 M	DTP, OPV	DTaP-IPV-Hib, Live JE2	
2-2 ½ Y	MMR2, Live JE2	MMR2, VZV2 (or MMRV2), (HAV2 inactivated)	
4-6 Y	DTP, OPV	Td…	
10-12 Y	dT, HPVx2 (ป.5)	…	
6M – 18Y	Influenza yearly to 2 yo	Influenza yearly up to adolescents	

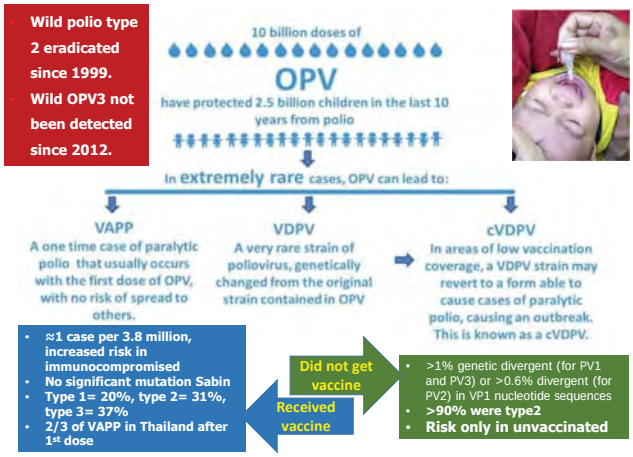
AcelDTP Hexa, PCV

MMRV, VZV, HAV

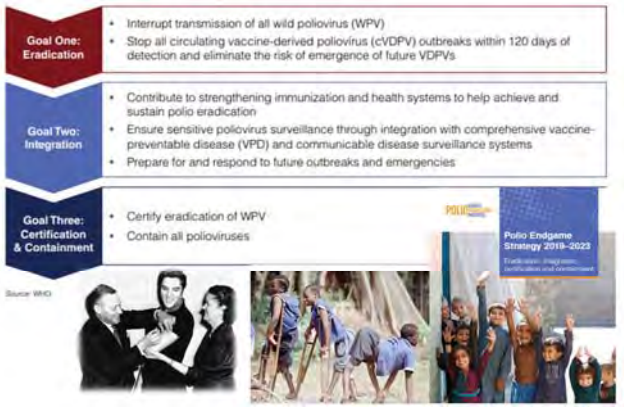
Tdap HPV catch-up



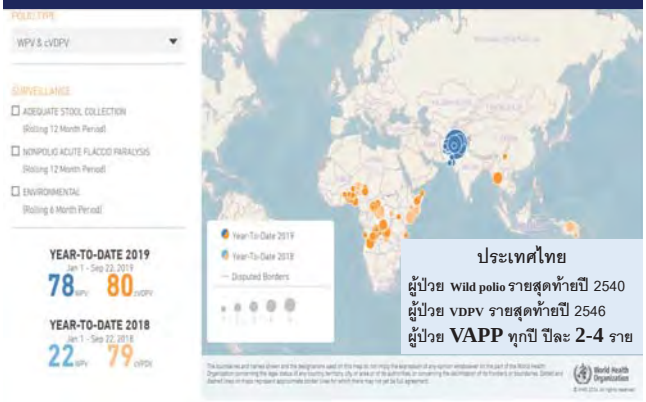
Polio Eradication



Goal of Polio Endgame Strategy 2019-2023



Global Situation of Poliomyelitis



ที่มา : http://polioeradication.org/polio-today/polio-now/

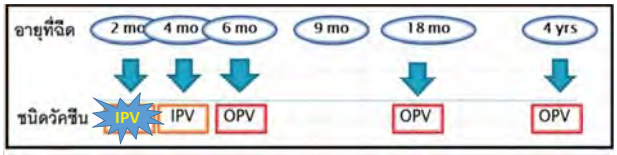
AFP following vaccination received Media attention
Luckily, all were VAPP

ลูกสาว 5 เดือนอาจพิการตลอดชีวิต หลังไป ฉีดวัคซีน เข็มแรกที่โรงพยาบาล ขาซ้ายกลับขยับไม่ได้ ผ่านมา 3 เดือนยังไม่มีท่าทีว่าจะดีขึ้น พ่อแม่ร้องปวิณาช่วย

VDPV Type 2 in Philippines

VDPV Type 1 in Myanmar

Ideal IPV introduction to EPI, Thailand
For polio endgame ต้องเพิ่ม IPV ที่ 2 เดือน



เราควรให้ 2 โด๊ส เพื่อป้องกัน VAPP (ซึ่งมักเกิดหลังได้รับโด๊สแรก) และเพื่อปิด immunity gap of OPV2 ป้องกัน VDPV ตั้งแต่อายุ 2 เดือน

แต่ด้วยความจำกัดของงบประมาณ จึงให้ได้เพียง 1 โด๊ส

WHO: If 1 dose of IPV is used, it should be given from14 weeks of age (when maternal antibodies have diminished and immunogenicity is significantly higher) co-administered with an OPV dose

การเฝ้าระวังผู้ป่วย AFP ในประเทศไทย

Acute Flaccid Paralysis (AFP)

ผู้ป่วยที่มีอาการอ่อนแรงของแขน, ขา หรือทั้งขาและแขน

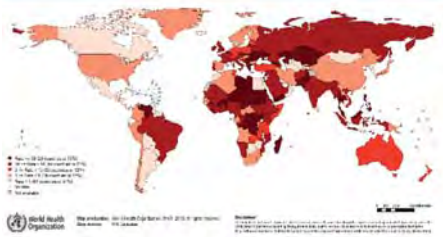
ข้างใดข้างหนึ่ง หรือ ทั้งสองข้าง ซึ่งอาการเกิดขึ้นอย่างรวดเร็ว

ยกเว้นผู้ป่วยที่มีอาการบาดเจ็บรุนแรง (Trauma) ซึ่งนำไปสู่อาการอัมพาต กล้ามเนื้ออ่อนแรง

Measles Incidence Rate per Million (12M period)
Low immunization rate is the root cause

Top 10**		
Country	Cases	Rate
Ukraine	63948	1439.02
India	63364	47.85
Madagascar	59407	2386.35
Pakistan	30747	159.14
Philippines	19401	187.78
Yemen	11746	425.82
Brazil	10262	49.42
Nigeria	5847	31.44
Venezuela (Bolivarian Republic of)	5668	179.55
Thailand	5579	81.02

Other countries with high incidence rates***		
Country	Cases	Rate
Georgia	3176	809.09
Liberia	3194	692.27
Albania	1476	504.38
Serbia	4176	473.46
Israel	3377	412.24
Montenegro	201	319.75
Kyrgyzstan	1509	253.37

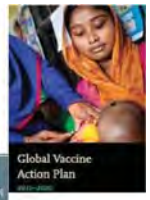


Measles cases from countries with known discrepancies between case-based and aggregate surveillance, as reported by country			
Country	Year	Cases	Data Source
DR Congo	2018	67072	SITUATION EPIDEMIOLOGIQUE DE LA ROUGEOLE EN RDC, Week of 05/03/2019
	2019	17646	
Somalia	2018	9135	Somali EPI/POL Weekly Update Week 09
	2019	720	

Notes: Based on data received 2019-03 and covering the period between 2018-02 and 2019-01 - Incidence: Number of cases / population* * 100,000 - * World population prospects, 2017 revision - ** Countries with the highest number of cases for the period - *** Countries with the highest incidence rates (excluding those already listed in the table above)

WHO Measles Elimination Target
Postpone from 2020 to 2024

Target: Absence of indigenous measles transmission in 2020>>>2024



Measles continues to spread within the USA and internationally in isolated, under-resourced and conflict-riven areas.

Prior to the introduction of the measles vaccine in 1963, an estimated 3 to 4 million people in the USA contracted measles

Vaccine Hesitancy is the Most Problematic around the world and in Deep South of Thailand


Perspective

Vaccination over Parental Objection — Should Adolescents Be Allowed to Consent to Receiving Vaccines?

Donahue Hagan Klein & Weisberg, LLC

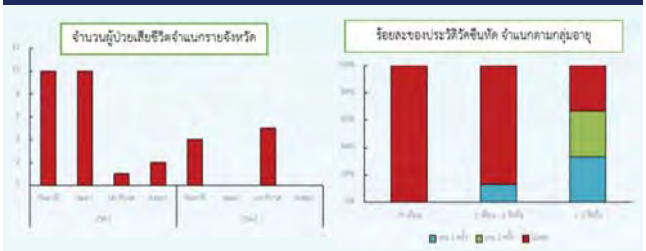
"because this matter does not concern the children's attendance at school. ... Rather, this is a matter of ensuring the health and safety of children in the care and custody of the Division.

เราจะจัดการกับการไม่ยอมรับวัคซีนอย่างไร
- ต่างประเทศใช้กฎหมายบังคับ..... การไม่รับวัคซีนเป็นอันตรายต่อเด็กคนอื่นซึ่งรัฐต้องคุ้มครอง


New Jersey Court Allows Vaccination Over Parents' Objection

The current measles epidemic across the U.S. has brought the issue of vaccination to the forefront. Many states allow parents to refuse to vaccinate their children for religious or other reasons. While New Jersey law allows an exemption from mandatory immunization for medical or religious reasons, that right is not absolute. A recent New Jersey Appellate Division case dealt with...

Death Case in Southern Provinces, 2018-2019



มีปัจจัยที่ทำให้ผู้ป่วยเสียชีวิต
- ภาวะทุพโภชนาการ
- มารับการรักษาที่โรงพยาบาลล่าช้า
- ผู้ปกครองปฏิเสธกระบวนการรักษาที่สำคัญ
- ได้รับวิตามินเอขนาดสูงล่าช้า
- ได้รับยาปฏิชีวนะล่าช้า

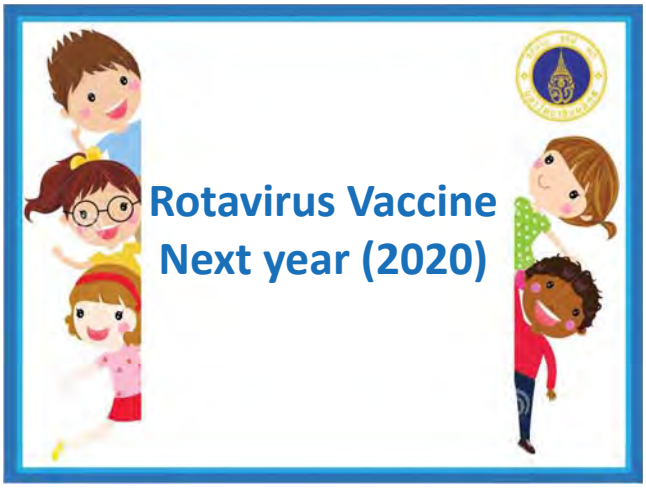
สำนักระบาด

ข้อเสนอแผนเร่งรัดการกำจัดโรคหัด 2562-2563

1.เพิ่มและรักษาระดับความครอบคลุมการได้รับวัคซีน
2.เร่งรัดการเฝ้าระวังโรคและการตรวจยืนยันทางห้องปฏิบัติการ
3.เสริมสร้างความเข้มแข็งของการสอบสวนและควบคุมโรค
4.รณรงค์ให้วัคซีนโรคหัด
5.ตอบโต้การระบาดอย่างเต็มที่

การรณรงค์วัคซีนหัดเพื่อการกำจัดโรคหัดของประเทศไทย

กลุ่มเป้าหมาย	เด็ก	ผู้ใหญ่อายุ 20-40 ปี (เกิด 2010-2045)
จำนวนกลุ่มเป้าหมาย	5.23 แสนคน	1.14 ล้านคน
รายละเอียด	• เด็กอายุ 1-12 ปี • ได้รับวัคซีนไม่ครบถ้วนตามเกณฑ์	• ทหาร • ผู้ต้องขังในเรือนจำ • พนักงานโรงงาน • พนักงานสถานประกอบการท่องเที่ยว • เจ้าหน้าที่สาธารณสุข
ชนิดวัคซีน	เด็กอายุ 1-7 ปี (MMR) เด็กอายุ 7-12 ปี (MR)	MR
ปีที่ดำเนินงาน	2562-2563	2563



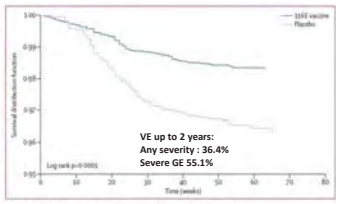
The Available Pre-Q Rotavirus Vaccines

Rotavirus vaccines	Rotarix (GSK)	Rotataq (MSD)	Rotavac (Bharat Biotech)
Licensure	Several countries, 2006	Several countries, 2006	India, 2014
2Y VE stratum B/D	72%/61%	78%/38%	NA/54%
Strains	Monovalent, human derived G1P8	Pentavalent, WC3 G6P5 bovine, reassortants G1-4, P8	Monovalent, human-bovine neonatal derived G9P11
No. of doses	2	3	3
Age 1st-last dose	6 weeks	6 weeks	6 weeks
Dosage	10^6 of live attenuated human G1P[8]	2.0-2.8 x 10^6 infectious units per reassortant	10^5 FFU of live rotavirus

http://www.who.int/immunization/research/forums_and_initiatives/gvirf/Gagandeep_Kang_2018.pdf assess on Apr 19

ROTAVAC มาแรง

Bharat Biotech has supplied approximately 30 million doses of ROTAVAC to the Indian government to date



Bharat Biotech's diarrhoea vaccine ROTAVAC gets WHO pre-qualification

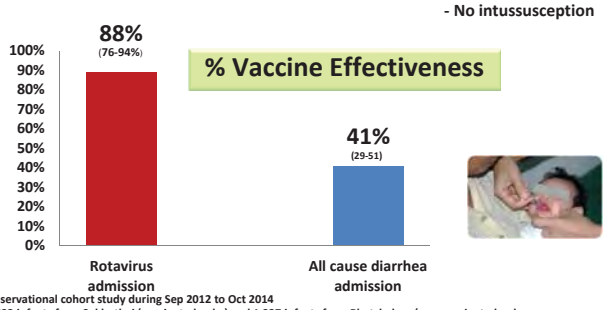
But need -20°C, and multidose-package

New Delhi, January 24, 2016—PATH applauds Indian vaccine manufacturer Bharat Biotech for receiving prequalification from the World Health Organization (WHO) for their oral rotavirus vaccine, ROTAVAC. As a partner in the development of ROTAVAC...

Double-blind, placebo-controlled trial (N=4354:2187) 3-dose 4 weeks apart from 6 wo: Bhandari N. The Lancet 2014;383:2136-43

First HRV vaccination in Sukhothai under the pilot programme by MOPH, Thailand

Coverage: 96.5%
Co-administer with OPV
- NO SAE
- No intussusception



- Observational cohort study during Sep 2012 to Oct 2014
- 2,893 infants from Sukhothai (vaccinated only) and 1,937 infants from Phetchabun (non-vaccinated only)
- Case rotavirus admission 10/55 and case All cause diarrhea admission 203/232 in Sukhothai/Phetchabun respectively.

Tharmaphornpilas P, et al. Vaccine 2017:35(5);796-801.

Is it possible for adults to contract rotavirus?

ROTAVIRUS INFECTION IN CHILDREN AND ADULTS WITH ACUTE GASTROENTERITIS IN THAILAND

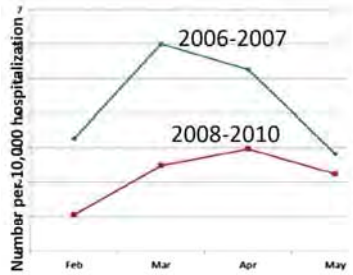
Leera Kittigul[1], Thitiluck Swangsri[1], Kannika Pombubpa[1], Nopporn Howteerakul[2], Pornphan Diraphat[1] and Chakrit Hirunpetcharat[1]

Distribution by age of patients with acute gastroenteritis caused by rotavirus

Age group (years)	Number (n = 260)	Rotavirus infection		
		Number (n = 110)	Percent of each age group	Percent of 260 cases
<2	70	36	51	14
2-4	36	23	64	9
5-17	23	15	65	6
18-59	70	22	31	8
≥60	61	14	23	5

Southeast Asian J trop Med public health. Vol 45 No. 4 July 2014

Vaccinating children is associated with "indirect protection" of adults in US



Prevalence of rotavirus among stools sent for bacterial stool culture from adults

Protection Against Gastroenteritis in US Households With Children Who Received Rotavirus Vaccine

significantly lower rates of hospitalization with a rotavirus gastroenteritis or unspecified gastroenteritis discharge code occurred in vaccinated households among persons 20–29 years and females 20–29 years (2008/2009), and males 30–39 years (2009/2010). Lower emergency department gastroenteritis rates occurred in vaccinated households among females 20–29 years (2009/2010) and individuals 5–19 years (2010/2011). These data suggest rotavirus vaccination of infants provides indirect protection against moderate-to-severe rotavirus disease in young parents and older siblings.

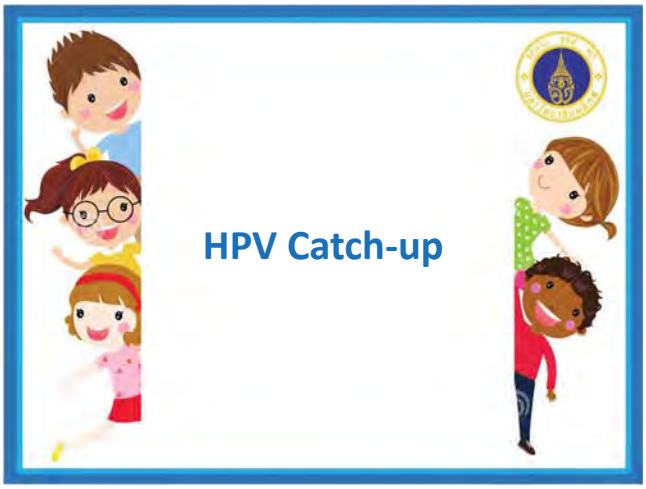
โรต้า เป้นวัคซีนเพื่อครอบครัว หยอดในเด็กเพื่อป้องกันผู้ใหญ่

Anderson E J et al. Clin Infect Dis. 2013;56:755-760

Types of seasonal influenza vaccine: Trivalent vs Quadrivaalent

Type of vaccines
Inactivated, Live-attenuated, Cell culture

Trivalent (TIV)	Tetravalent (QIV)
A-H1N1	A/H1N1
A-H3N2	A/H3N2
B-Yamagata OR B-Victoria	B-Yamagata AND B-Victoria
WHO 2018/19 (Northern hemisphere) A/Michigan/45/2015 (H1N1)pdm09 A/Singapore/INFIMH-16-0019/2016 (H3N2) B/Colorado/06/2017 (Victoria lineage) B/Phuket/3073/2013 (Yamakata lineage)	WHO 2019 (Southern hemisphere) A/Michigan/45/2015 (H1N1)pdm09 A/Switzerland/8060/2017 (H3N2) B/Colorado/06/2017 (B/Victoria/2/87 lineage) B/Phuket/3073/2013 (B/Yamagata/16/88 lineage)
Northern 2019-2020: A/Brisbane/02/2018 (H1N1)pdm09-like virus; A/Kansas/14/2017 (H3N2)-like virus; * B/Colorado/06/2017-like virus (Victoria lineage); B/Phuket/3073/2013-like virus (Yamagata lineage).	Southern 2020: A/Brisbane/02/2018 (H1N1)pdm09-like virus; A/South Australia/34/2019 (H3N2)-like virus; * B/Washington/02/2019-like virus (Victoria lineage); B/Phuket/3073/2013-like virus (Yamagata lineage).



The most recent vaccine to EPI
HPV vaccine in 5thgrade girls, no catch-up
Cost around 10 million U$ per year
Either HPV2 or HPV4 are good

Target: grade 5 female students
Schedule: 2 doses (0, 6 months)


ปัญหาคือ เด็กที่โตกว่า ป 5 เสี่ยงกว่า แต่ไม่ได้รับวัคซีน
เด็กผู้ชายก็เสี่ยงมาก แต่ไม่ได้วัคซีน

ต้องสร้างวัฒนธรรมการให้เด็กวัยรุ่นและผู้ใหญ่ตอนต้นไปรับวัคซีนอย่างทั่วถึง

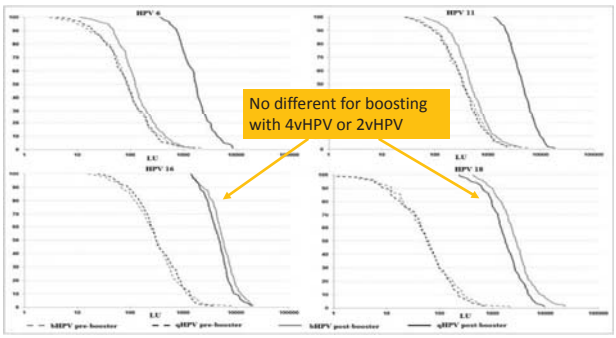
แม้จะไม่ฟรี แต่ต้องหาทางให้สามารถเข้าถึงได้ (ราคาไม่แพงเกินไป)

Post hoc analysis of the Costa Rica Vaccine Trial and PATRICIA on Dose-stratified VE against incidence of HPV infection, Kreimer 2015

ฉีด 1 เข็มก็อาจจะพอ

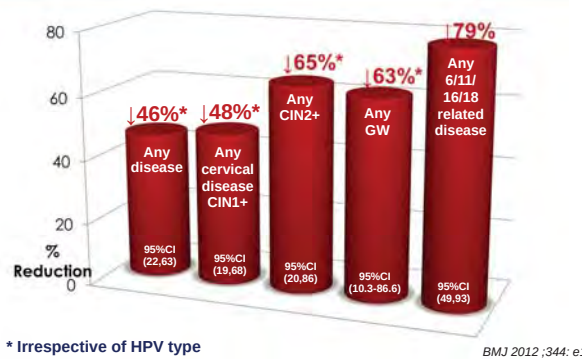
Doses, no.	Arm	Women, no.	Events, no.	Person years	Rate per 100 PY (95%CI)	Vaccine Efficacy
Incident one-time detection of HPV16/18						
3 (standard regimen)	HPV	11110	529	43140	1·23 (1·12 to 1·34)	77·0% (74·7 to 79·1%)
	Control	11217	2172	40682	5·34 (5·12 to 5·57)	
2	HPV	611	22	2538	0·87 (0·56 to 1·29)	76·0% (62·0 to 85·3%)
	Control	574	82	2271	3·61 (2·89 to 4·46)	
1	HPV	292	8	1220	0·66 (0·30 to 1·25)	83·7% (70·7 to 91·7%)
	Control	251	45	982	4·58 (3·38 to 6·08)	
Incident detection of HPV16/18 that persisted ≥12 months						
3	HPV	11104	84	43775	0·19 (0·15 to 0·24)	87·0% (83·7 to 89·7%)
	Control	11203	627	42589	1·47 (1·36 to 1·59)	
2	HPV	611	3	2576	0·12 (0·03 to 0·32)	89·6% (68·9 to 97·5%)
	Control	574	26	2324	1·12 (0·75 to 1·62)	
1	HPV	292	1	1234	0·08 (0·00 to 0·40)	95·1% (73·2 to 99·8%)
	Control	249	17	1021	1·67 (1·00 to 2·61)	

The effect of a booster dose of 4vHPV 2vHPV vaccine when administered to girls previously vaccinated with two doses of 4vHPV vaccine: Both can boost
ฉีดสลับยี่ห้อได้



Gilca V. Hum Vaccin Immunother. 2015 Mar; 11(3): 732–738.

Impact of 4vHPV on the Incidence of New HPV Disease After Treatment for Cervical Disease



*** Irrespective of HPV type**

BMJ 2012 ;344: e1401

แพทย์ประจำบ้านอายุก็ไม่น้อย (> 26 ปี) ถามว่า

หนู/ผม ควรฉีดวัคซีน HPV ไหม?

ก. ถ้ายังสดอยู่ก็น่าจะฉีด

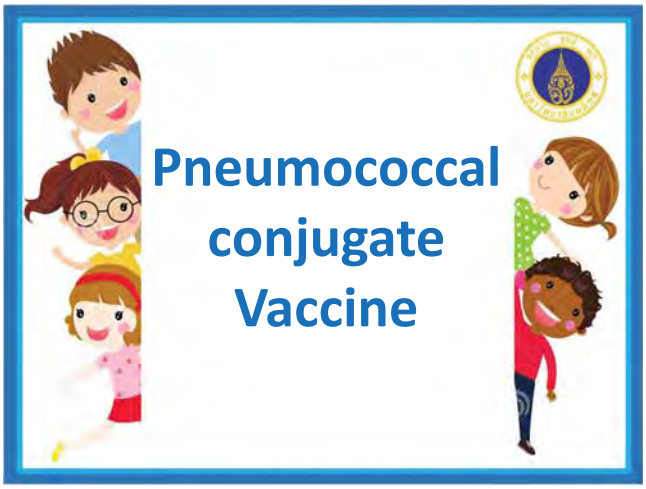
ข. ถ้ายังมีโอกาสเสี่ยงก็ควรฉีด แม้ไม่สด

แพทย์ประจำบ้านอายุก็ไม่น้อย (> 26 ปี) ถามว่า

หนู/ผม ควรฉีดวัคซีน HPV ไหม?

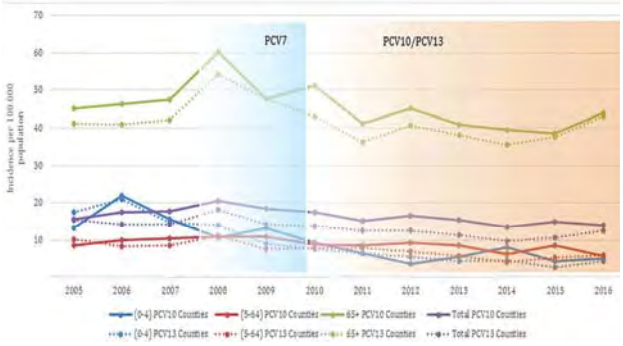
ก. ถ้ายังสดอยู่ก็น่าจะฉีด

ข. ถ้ายังมีโอกาสเสี่ยงก็ควรฉีด แม้ไม่สด



Comparison of the Impact of Pneumococcal Conjugate Vaccine 10 or Pneumococcal Conjugate Vaccine 13 on Invasive Pneumococcal Disease in Equivalent Populations: Incidence of IPD

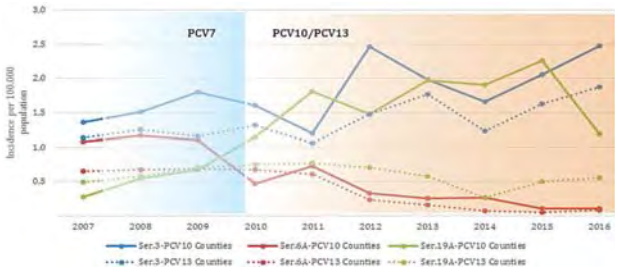
Both PCV10 and PCV13 county had similar IPD rate



Naucler P. CID 2017;65:1780-9.

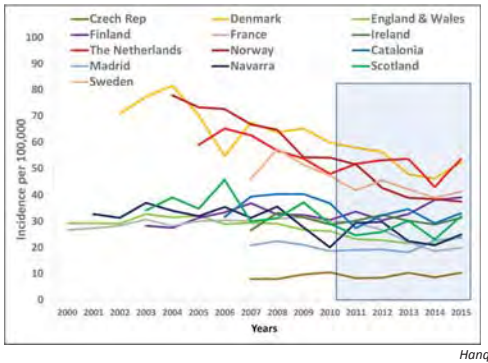
Comparison of the Impact of Pneumococcal Conjugate Vaccine 10 or Pneumococcal Conjugate Vaccine 13 on Invasive Pneumococcal Disease in Equivalent Populations: Incidence of IPD

- 19A incidence was higher in PCV10 counties, but the overall impact in incidence was not different, suggesting that the number is low
- There was no effect against serotype 3, with lower trend in PC13 counties
- **All counties, both PCV10 and PCV13, had NVT increased 2.4 times**



Naucler P. CID 2017;65:1780-9.

Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination



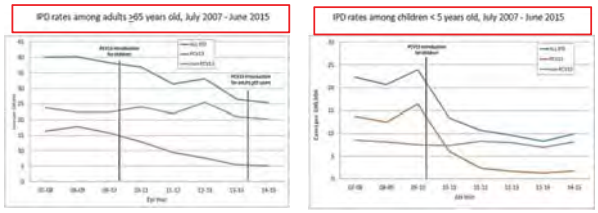
Overall incidence of invasive pneumococcal disease per site and years in persons aged ≥65 years over the period 2000–2015: SpIDnet/IMOVE+ multicentre study.

Hanquet G. Thorax 2018.

Direct and Indirect Impact of PCV13 Use on Invasive Pneumococcal Disease (IPD) Among Children and Adults

OXFORD UNIVERSITY PRESS

An estimated **230,000 IPD cases and 16,500 deaths were prevented** among all ages through PCV13 use in the US.



- PCV13 use among children reduced IPD incidence among children and adults. ***To date, we found no evidence of significant replacement disease with non-PCV13 types***.

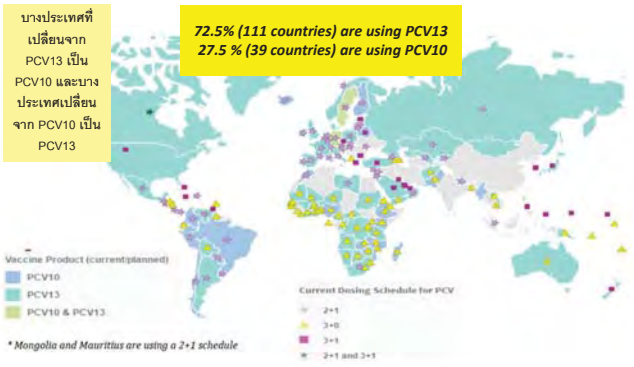
Open Forum Infect Dis. 2016;3(suppl_1). doi:10.1093/ofid/ofw194.79

Global introduction of PCVs 2018

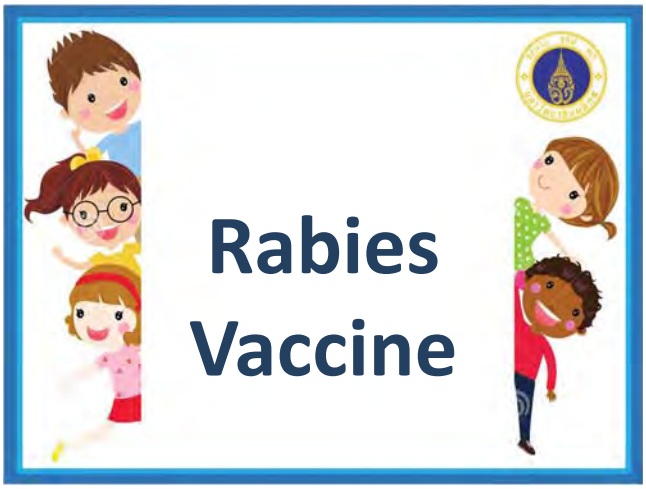
ภาพรวมทั้งสองวัคซีน อาจไม่ต่างกันมาก ต้องประเมินความคุ้ม

บางประเทศที่เปลี่ยนจาก PCV13 เป็น PCV10 และบางประเทศเปลี่ยนจาก PCV10 เป็น PCV13

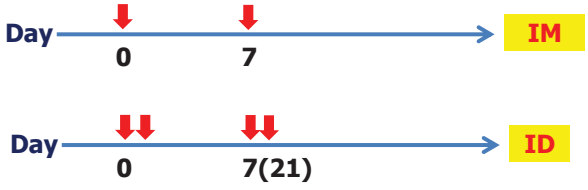
72.5% (111 countries) are using PCV13
27.5 % (39 countries) are using PCV10



IVAC, The Johns Hopkins Bloomberg School of Public Health, Jun3 2018

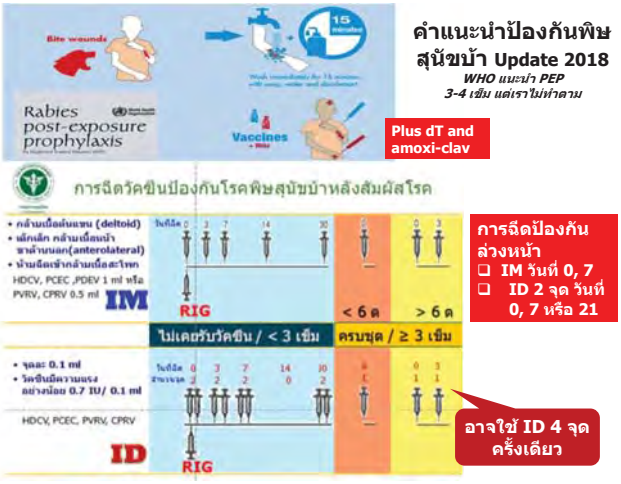


Pre-exposure prophylaxis (ใหม่)



ถ้าเป็น immunosuppress host หรือเสี่ยงสัมผัสโรคตลอดเวลา ต้องฉีด 3 ครั้ง 0, 7, 21-28

Rabies vaccines: WHO position paper – April 2018



คำแนะนำป้องกันพิษสุนัขบ้า Update 2018

WHO แนะนำ PEP 3-4 เข็ม แต่เราไม่ทำตาม

We need to control stray dogs or give rabies PrEP?

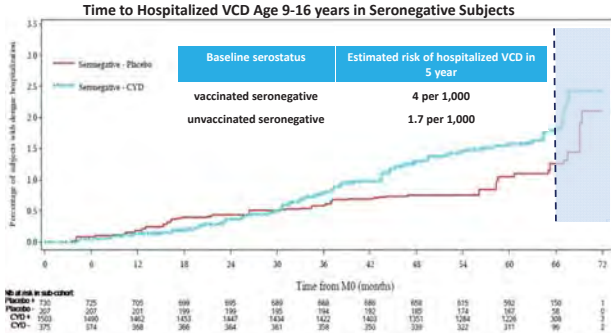
- **WHO: Pre-exposure vaccination should be offered :**
  - **(i) where access to postexposure prophylaxis is limited or delayed;**
  - **(ii) where the risk of exposure is high and may go unrecognized**
  - **(iii) where controlling rabies in the animal reservoir is difficult.**
- **Pre-exposure prophylaxis should not distract from canine vaccination efforts, provision of postexposure**

It was found that costs of both strategies, PREP of children or PEP of exposed, become equal when the dog bite incidence is 2–30%; depending on which PEP regimens are used.

Chulasugandha P, et al. Vaccine. 2006 Feb 27;24(9):1478-82.

DENGUE Vaccine: The Bad Dream
Become adult vaccine!

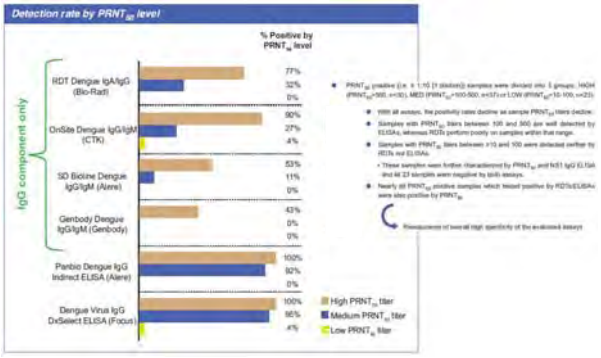
Time to Hospitalized VCD Age 9-16 years in Seronegative Subjects



Baseline serostatus	Estimated risk of hospitalized VCD in 5 year
vaccinated seronegative	4 per 1,000
unvaccinated seronegative	1.7 per 1,000

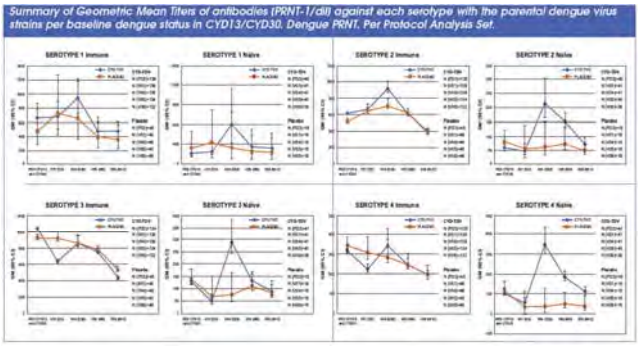
Unpublished data

EVALUATION OF RAPID DIAGNOSTIC TESTS AND CONVENTIONAL ENZYME-LINKED IMMUNOSORBENT ASSAYS TO DETERMINE PRIOR DENGUE INFECTION



Matthew Bonaparte1, Lingyi Zheng1, Sanjay Garg1, Bruno Guy2, Carlos DiazGranados1, Stephen Savarino1, Yasemin Ataman-Önal2
1Sanofi Pasteur, Swiftwater, PA, USA; 2Sanofi Pasteur, Marcy l'Etoile, FranceXVIII Congreso Latinoamericano de Pediatria – 5-8

Immunogenicity 28 days and 1 year after a Dengue Vaccine Booster in Healthy Adolescents and Adults in Latin America after 4 to 5 Years of a Primary 3-Dose Schedule



Diana Coronel. 67th Annual Meeting of the American Sosiety of Tropical Medicine & Hygiene (ASTMH), 28 October - 1 November 2018, New Orleans, LA, USA. Abstract No. LB3190

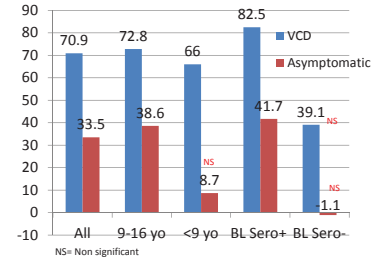
CYD Tetravalent Dengue Vaccine Reduces Symptomatic and Asymptomatic Dengue Virus Infections in Healthy Children Aged 2–16 Years in Asia and Latin America (N=3,736)

Efficacy against asymptomatic infection reduce transmission

80% of all dengue infections are asymptomatic[1]

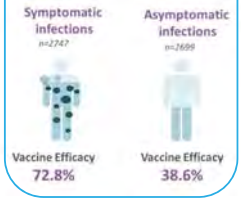
Asymptomatic individuals are significantly more infectious to mosquitoes than people with symptomatic infections. *Duong V et al. PNAS 2015; 112(47):14688–14693.*

The annual incidence of asymptomatic vs symptomatic = 14.8% vs 3.4% (4.4 times)



NS= Non significant

Efficacy against symptomatic and asymptomatic infections in 9–16 Yo

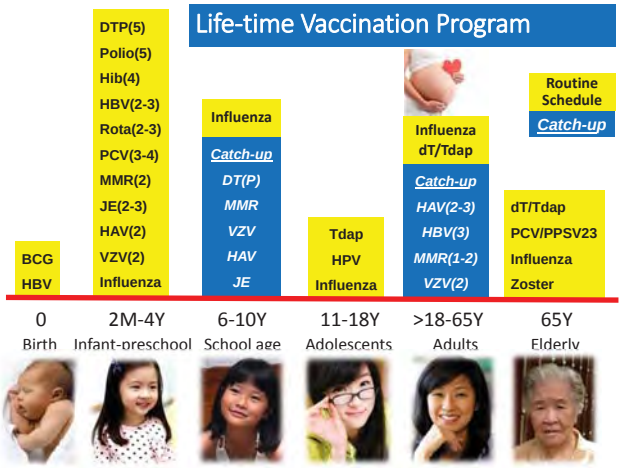


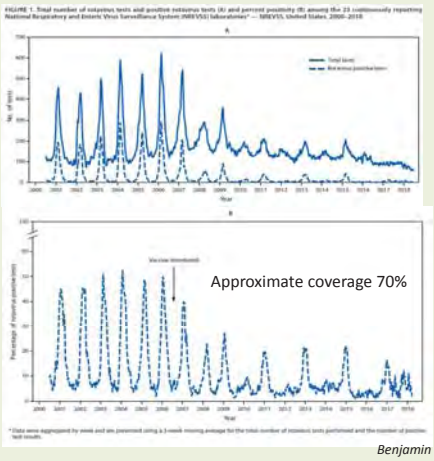
Olivera-Botello G. JID 2016;214:994-1000.

Formalin Inactivated Enterovirus71 Vaccine: Newly approved

It is still completely unclear if the vaccine can cross protect all strains

Organizations	EV71 strain	Dosage (μg)	Population target	Sample size	Status	References
Sinovac Biotech Co., Ltd. (China)	C4a (FY7VP5 strain)	1	6-35 month children	10,245 VE= 88%	Phase 3 completed, approved	NCT01507857
Beijing Vigoo Biological Co., Ltd. (China)	C4a (H07 strain)	0.8	6-35 month children	10,077 VE= 82%	Phase 3 completed	NCT01508247
CAMS (China)	C4a (H07 strain)	0.25	6-71 month children	12,000 VE= 97%	Phase 3 completed, approved	NCT01569581
NHRI (Taiwan)	B4	5 and 10	Adults	60	Phase 1 completed	NCT01268787
Inviragen (Singapore)	B2	0.6 and 3	Adults	36	Phase 1 completed	NCT01376479



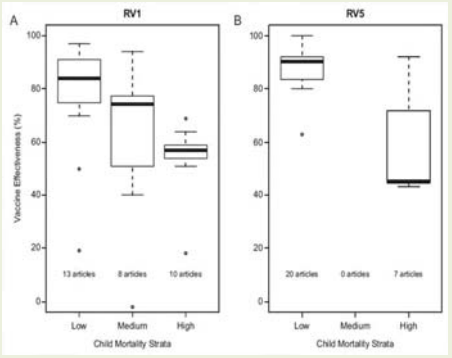


ผลจากการใช้วัคซีนในอเมริกา

Trends in the Laboratory Detection of Rotavirus Before and After Implementation of Routine Rotavirus Vaccination — United States, 2000–2018

Benjamin D. MMWR 2019;68:539-43.

Effectiveness of Rotavirus Vaccination: A Systematic Review of the First Decade of Global Postlicensure Data, 2006-2016



A, RV1 publication characteristics and summary vaccine effectiveness (VE, %) by mortality strata. *Cases and controls are not reported separately for RV1 and RV5. †Nondiarrhea controls are community controls and were used for analyses when rotavirus (RV) test–negative controls did not exist. ‡Q = 117.9, I2 = 86%. ▫Q = 22.6, I2 = 67%. ▫Q = 5.7, I2 = 0%. B, RV5 publication characteristics and summary VE by mortality strata. *Cases and controls are not reported separately for RV1 and RV5. †Nondiarrhea controls are community controls and were used for analyses when RV test–negative controls did not exist. ‡Q = 55.0, I2 = 64%. ▫Q = 6.9, I2 = 6.9.

Jonesteller CL. Cid 2017;65:840-50.

Efficacy of a monovalent human-bovine (116E) rotavirus vaccine (ROTAVAC) in Indian infants: a randomised, double-blind, placebo-controlled trial (N=4354:2187) 3-dose 4 weeks apart from 6 wo

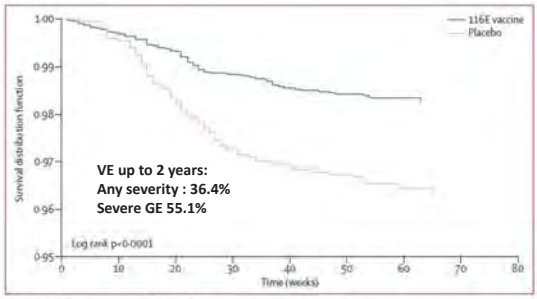
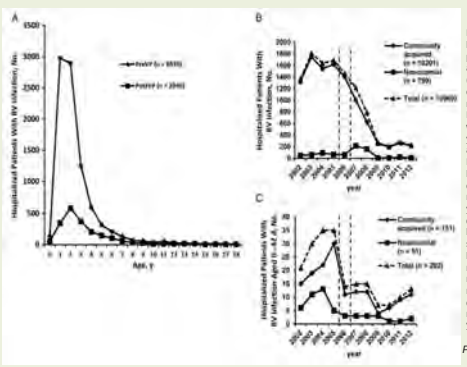


Figure 2: Kaplan-Meier survival curves for severe rotavirus gastroenteritis
Per-protocol population. Time 0 represents 15 days after receipt of the third dose of vaccine or placebo

Bhandari N. The Lancet 2014;383:2136-43.

Universal Mass Vaccination Against Rotavirus: Indirect Effects on Rotavirus Infections in Neonates and Unvaccinated Young Infants Not Eligible for Vaccination

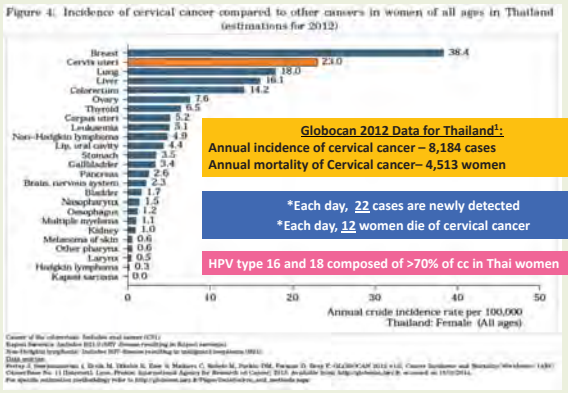


Rotavirus (RV)–associated hospitalizations in the prevaccination period (PreVP) and postvaccination period (PostVP) by age and community-acquired versus nosocomial infection. A, Numbers of hospitalized patients with RV are shown by age in years. Total numbers of patients are shown for the PreVP and PostVP. B, Total numbers of hospitalized patients with community-acquired or nosocomial RV infections by year of diagnosis. First (left) dotted vertical line indicates licensing of RV vaccination; second (right) dotted vertical line, introduction of universal mass vaccination. C, Total numbers of hospitalized neonates and infants ≤42 days old with community-acquired or nosocomial RV infections, by year of diagnosis

Prelog M. JID 2016;214:546-55.

HPV gets in first after several years!

Cervical Cancer is the second most common cancer in women in Thailand

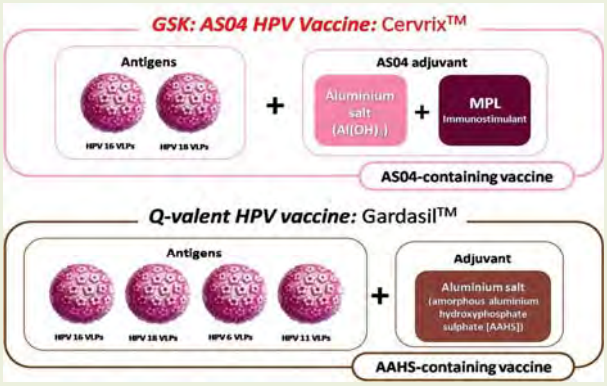


Globocan 2012 Data for Thailand[1]:
Annual incidence of cervical cancer – 8,184 cases
Annual mortality of Cervical cancer– 4,513 women

*Each day, 22 cases are newly detected
*Each day, 12 women die of cervical cancer

HPV type 16 and 18 composed of >70% of cc in Thai women

มีวัคซีน HPV ให้เลือก 2 ชนิด

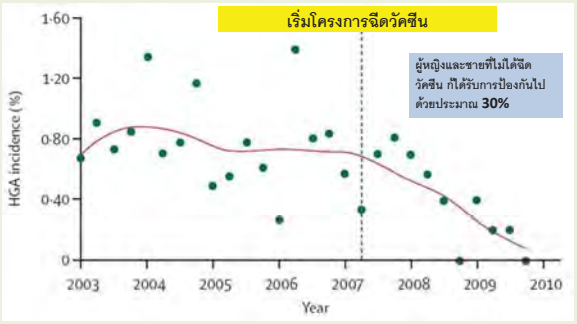


Those who can pay will go for 9HPV

2vHPV	4vHPV	9vHPV
2vHPV Serotype	4vHPV Serotype	Increased 15% Coverage
• 16	• 6	• 6
• 18	• 11	• 11
	• 16	• 16
	• 18	• 18
		• 31
		• 33
		• 45
		• 52
		• 58

การลดลงของ CIN2+ และ AIS ในผู้หญิงต่ำกว่า 18 ปี ในออสเตรเลีย

Trends in HG-CIN in women < 18 yr of age in Victoria, Australia, before and after introduction of GARDASIL© *



* Green dots represent the number of new diagnoses within a 3-month period per 100 women tested. Red line represents Lowess smoothing trend.

HG-CIN = CIN 2+ & AIS

Brotherton JM, et al. Lancet,2011;377:2085-92

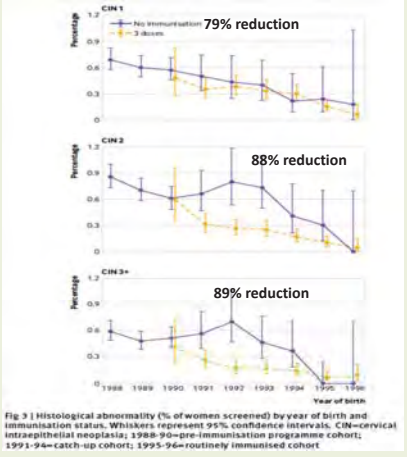


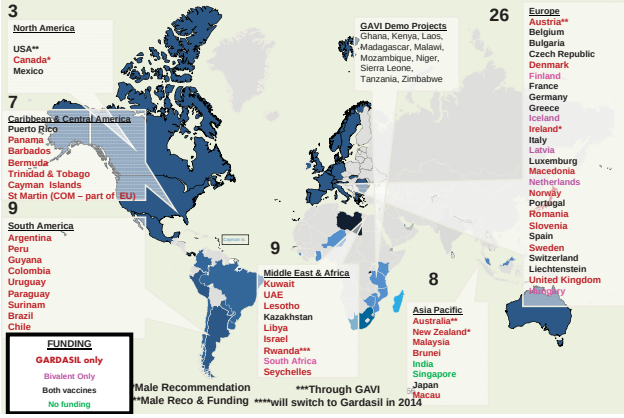
Fig 3 | Histological abnormality (% of women screened) by year of birth and immunisation status. Whiskers represent 95% confidence intervals. CIN=cervical intraepithelial neoplasia; 1988-90=pre-immunisation programme cohort; 1991-94=catch-up cohort; 1995-96=routinely immunised cohort

การลดลงของ CIN1-3 ในสก๊อตแลนด์ หลังจากใช้ Bivalent Vaccine

Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study

Palmer T. BMJ 2019.

การใช้วัคซีน HPV ทั่วโลกใน National Immunization Program



Pneumococcal Conjugate (PCV) and Polysaccharide (PPSV) Vaccines

Pneumococcal conjugate vaccines

PCV 10	Protein Carriers: Protein D, †Diphtheria toxoid, ‡Tetanus toxoid	4	6B	9V	14	18C‡	19F†	23F	1	5	7F	(Cross protection: 6B for 6A, 19F for 19#)		
PCV 13	Protein Carrier: CRM_{197}	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A

Pneumococcal polysaccharide vaccine

PSV 23	2	9N	11A	15B	20	33F	4	6B	9V	14	1	5	3	
	8	10A	12F	17F	22F		18C	19F	23F		7F		19A	

Klugman K, et al. Vaccine 2011;295:C43-48.

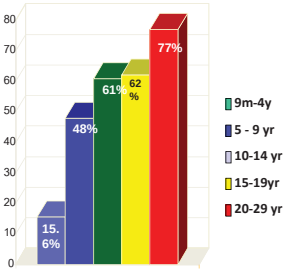
PCV Implementation

Year	Country	Product	Status
2013	Lao PDR	PCV13	Introduced in October
2015	Cambodia	PCV13	Introduced in January
2016	Myanmar	PCV10	Introduced in July

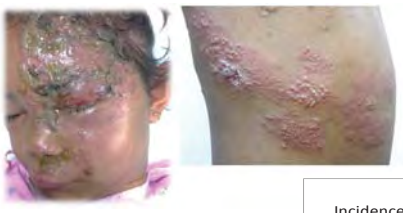
Source: International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. VIEW-hub Global Vaccine Introduction and Implementation Report, June 2016.

วัคซีนป้องกันอีสุกอีใส

- ประมาณหนึ่งในสี่ของผู้ใหญ่ ยังไม่มีภูมิต้านทาน
- อีสุกอีใสในผู้ใหญ่ มีโอกาสพบภาวะแทรกซ้อนได้มากกว่าเด็ก25เท่า
  - Pregnancy, immunocompromised
- วัคซีนงูสวัด ป้องกันโรคและ post herpetic neuralgia ได้
- ทำให้เกิดcongenital infection:
  - 0.4-2% in 1st-2nd trimester (Peak13-20 wk)



Lolekha S. Am J Trop Med Hyg 2001; 64(3,4):131-3.



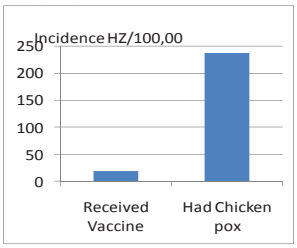
Herpes Zoster

ป้องกันได้ด้วยวัคซีนอีสุกอีใส

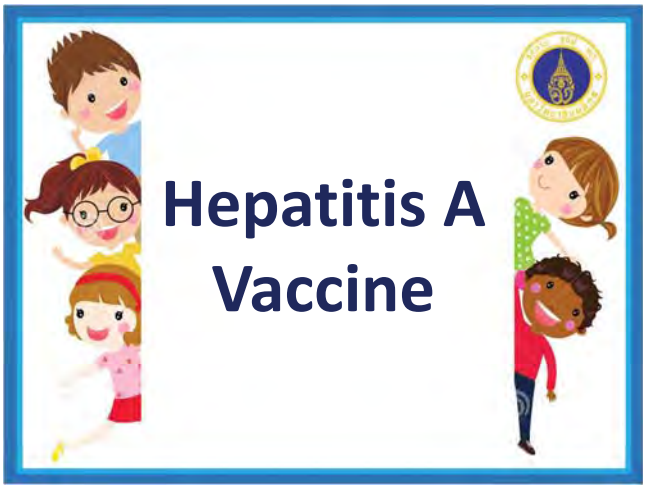
Rate/1,000/yr	
< 10 yo	0.74
20-50 yo	2.5
>80 yo	80

Hope-Simpson 1965

Vaccination reduce zoster from 15% to 2%

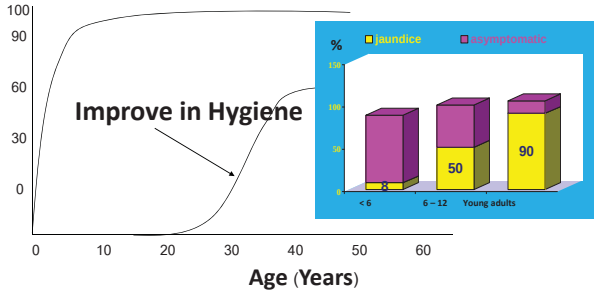


VZV vaccine prevents Zoster by 92%



Hepatitis A: Prevalence Changes with Improvement in Hygiene *But symptomatic infection increased with age*

Prevalence of Anti-HAV (%)



Hepatitis A Vaccine

ฉีดเข้ากล้าม 2 เข็ม ที่ 0, 6-12 เดือน ในเด็กอายุตั้งแต่ 1 ปี ขึ้นไป

วัคซีน	ขนาดในเด็ก	อายุที่แนะนำ	ขนาดในผู้ใหญ่	อายุที่แนะนำ
Havrix™	0.5 มล.(720 u)	1-18 ปี	1 มล. (1440 u)	≥19 ปี
Vaqta™	0.5 มล. (25 u)	1-17 ปี	1 มล. (50 u)	≥18 ปี
Avaxim™	0.5 มล. (80 u)	1-15 ปี	0.5 มล. (160 u)	≥16 ปี
Twinrix™ วัคซีนรวมตับอักเสบเอและบี	1 มล. (HA 720 u) (HB 20 มคก.)	1-15 ปี	1 มล. (HA 720 u) (HB 20 มคก.)	≥16 ปี 3 เข็ม 0, 1, 6 เดือน หรือ 4 เข็ม วันที่ 0, 7, 21-30 และ12 เดือน
Mevac™	0.5 มล	>18 ต	0.5 มล	ฉีดครั้งเดียว ห้ามในimmunocompromised

Vaccine

Volume 36, Issue 10, 28 February 2018, Pages 1279–1284

The impact of expanded program on immunization with live attenuated and inactivated Hepatitis A vaccines in China, 2004–2016

Vaccine Type	Vaccine Coverage	Dose	HepA incidence decline
Live Attenuated Vaccine - Region	98.7%	1	78%
Inactivated Vaccine - Region	99.6%	2	82%
p-value			NS (in all age group)

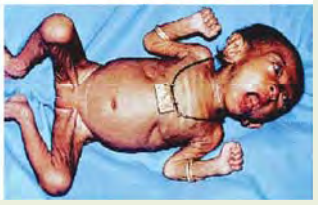
In summary, the study suggests that the EPI, with high coverage for both I-HepA and L-HepA, had positive impact on HepA incidence in China, not only on targeted population, but also showing herd protection for all age groups. Sustained surveillance of coverage and incidence were required to ensure the ongoing significant impact of HepA vaccine.

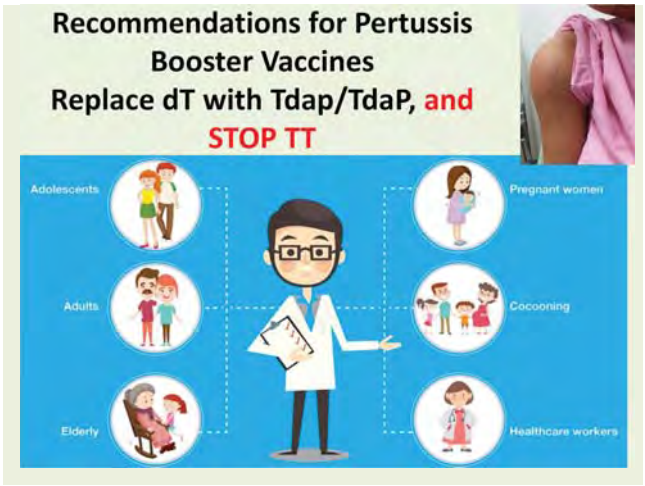
- The incidence declined in L-HepA and I-HepA regions without significant difference.
- Dramatic decline were seen in all age groups in both L-HepA and I-HepA regions.

Maternal and adult family members vaccination save infants

- ไอกรน ในผู้ใหญ่พบมาก แต่วินิจฉัยไม่ค่อยได้
- ไอกรนในผู้ใหญ่ทำให้ไอมาก นาน เสียคุณภาพชีวิต
- ไอกรนในเด็กเล็ก อาจทำให้หยุดหายใจ วิกฤต เสียชีวิต
- เด็กทารกหากยังได้รับวัคซีนไม่ครบ 3 เข็ม จะยังเสี่ยง
- ไอกรนในเด็กเล็กมักได้รับเชื้อจากสมาชิกในบ้าน

Bisgard K. PIDJ 2004;23:985–9





Impact of the US Maternal Tetanus, Diphtheria, and Acellular Pertussis Vaccination Program on Preventing Pertussis in Infants <2 Months of Age: A Case-Control

การให้วัคซีนในแม่ในช่วงตั้งครรภ์ ป้องกันทารกได้ดีที่สุด

Table 4. Effectiveness of Maternal Tdap Vaccination at Preventing Infant Pertussis Hospitalizations, by Timing of Vaccination

Vaccination Status	Cases, No. (%)		Controls, No. (%)		Multivariable VE*, % (95% CI)
Total	157	(%)	336	(%)	
Unvaccinated	76	(48.4)	109	(32.4)	Reference
Before pregnancy	16	(10.2)	46	(13.7)	76.2 (37.2–91.0)
First or second trimester	2	(1.3)	20	(6.0)	91.4 (24.8–99.0)
Third trimester	6	(3.8)	47	(14.0)	90.5 (65.2–97.4)
After pregnancy	57	(36.3)	114	(33.9)	32.5 (–23.5 to 63.1)

Abbreviations: CI, confidence interval; VE, vaccine effectiveness.

*The following variables were included in the final model: household size >2 persons, maternal education, household member with pertussis diagnosis, and infant age (weeks).

Skoff TH. CID 2017;65:1977-83.

ควรใช้Tdap/TdaP ในกรณีดังนี้

- วัยรุ่นทุกคนควรฉีดเมื่ออายุ 10-12 ปี (หลังจากนั้นให้เป็น dT ทุก 10 ปี)
- ผู้ใหญ่ทุกคนควรฉีด dT ทุก 10-20 ปี หรือเมื่อมีบาดแผล และควรใช้ Tdap แทน dT 1 ครั้ง
  - ควรพิจารณาให้ aP ถ้าต้องการป้องกันไอกรน แต่ได้ Tdap/dT มา <10 ปี เพื่อหลีกเลี่ยง Arthus reaction จากการฉีด dT บ่อย
- *หญิงตั้งครรภ์ทุกราย ควรฉีด Tdap อย่างน้อย 1 ครั้ง ในช่วงไตรมาสที่ 2-3 (ครรภ์ 27-36 สัปดาห์) ควรให้ Tdap ทุกครรภ์*
- *ควรฉีดให้ผู้ใหญ่ทุกคนในบ้านที่มีเด็กอ่อน("cocooning")*

- ไม่ต้องกังวลเรื่องการเว้นระยะกับ dT or TT
- There is not enough data to confirm the safety of repeating Tdap

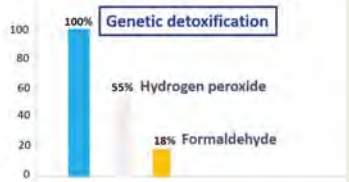
Genetic inactivation of Pertussis Toxin (PT)

Substitution of amino-acids (R9K/E129G) to obtain a recombinant PT (rPT)

rPT is a PT devoid of toxicity while maintaining the immunological and functional properties of the native PT.[1]

Chemically-detoxified PT introduces dramatic changes on the toxin surface epitopes.

Remaining epitope binding (% of native PT)[2]

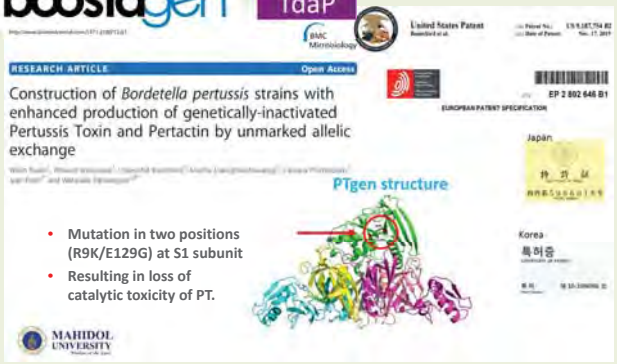


Chemical treatment used to inactivate PT can destroy up to 80% of surface epitopes.

1. Seubert A, et al. Expert Rev Vaccines 2014.
2. Ibsen PH. Vaccine 1996.

pertagen® aP
boostagen® TdaP

Recombinant DNA Technology



RESEARCH ARTICLE Open Access

Construction of *Bordetella pertussis* strains with enhanced production of genetically-inactivated Pertussis Toxin and Pertactin by unmarked allelic exchange

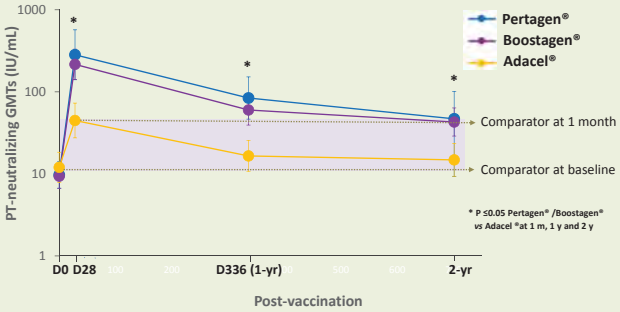
PTgen structure

- Mutation in two positions (R9K/E129G) at S1 subunit
- Resulting in loss of catalytic toxicity of PT.

MAHIDOL UNIVERSITY

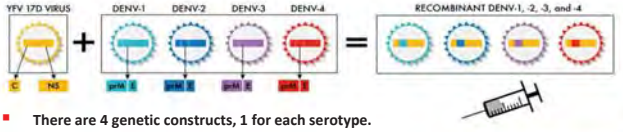
2-Year Antibody Persistence: PT Neutralizing Ab GMT

Pertagen®/Boostagen® at 2 years EQUAL to Adacel® at 1 month



New data - with kind provided by Prof. Punnee P., TropMed, Mahidol University

THE CURRENTLY AVAILABLE DENGUE VACCINE : Chimeric Yellow Fever 17D-Tetravalent Dengue Vaccine (CYD-TDV)



- There are 4 genetic constructs, 1 for each serotype.
- The envelope and precursor membrane genes from each serotype were combined with the genes encoding the capsid and non-structural proteins from the yellow fever (YFV 17D) vaccine strain.
- Freeze-dried and contains no adjuvant or preservatives.
- 3-dose schedule at 0, 6, 12 month

DENV-1 (strain PUO-359/TVP-1140, isolated in 1980 in Thailand)
DENV-2 (strain PUO-218, isolated in 1980 in Thailand)
DENV-3 (strain PaH881/88, isolated in 1988 in Thailand)
DENV-4 (strain 1228 (TVP-980), isolated in 1978 in Indonesia)

Guirakhoo, 2001, J Virol. / Guirakhoo, 2000, J Virol. / Guy, 2011, Vaccine.

SUMMARY: Efficacy Results in ≥9 years of age in CYD 14, CYD15 (Proposed age indication) at 25 months

25-month active phase* Pooled efficacy analyses‡1

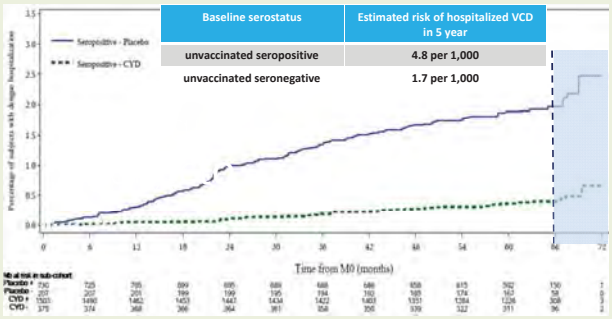
Reduction in symptomatic dengue	Reduction in hospitalized dengue	Reduction in severe dengue †
65.6% (95% CI: 60.7–69.9)	80.8% (95% CI: 70.1–87.7)	93.2% (95% CI: 77.3–98.0)

For each serotype:
- DENV-1: 58% (47.7–66.9)
- DENV-2: 47% (31.3–59.2)
- DENV-3: 73% (64.4–80.4)
- DENV-4: 83% (76.2–88.2)

*Data come from the 2 pivotal, phase III, large-scale efficacy trials CYD14 and CYD15, which were designed to fully assess efficacy; postdose 1; ‡*Full Analysis Set for Efficacy (FASE): all* subjects who received at least one injection. †dengue hemorrhagic fever, IDMC criteria or 92.9% according to World Health Organization 1997 criteria. CI=confidence interval; DENV=dengue virus.

Time to Hospitalized VCD Age 9-16 years in *Seropositive* Subjects

Baseline serostatus	Estimated risk of hospitalized VCD in 5 year
unvaccinated seropositive	4.8 per 1,000
unvaccinated seronegative	1.7 per 1,000



Unpublished data

An Inactivated Enterovirus 71 Vaccine (by CAMS) in Healthy Children: Phase III

Multivalent vaccines against HFMD is needed

Table 2. Efficacy of the Enterovirus 71 (EV71) Vaccine against Overall Hand, Foot, and Mouth Disease and EV71-Associated Hand, Foot, and Mouth Disease over an 11-Month Period, According to the Intention-to-Treat Analysis.

Cases of Hand, Foot, and Mouth Disease	Vaccine Group (N=6000)		Placebo Group (N=6000)		Vaccine Efficacy*	P Value
	Participants	Incidence no. of cases/1000 participants/yr	Participants	Incidence no. of cases/1000 participants/yr	% (95% CI)	
Clinically diagnosed and pathogenically confirmed cases						
Caused by EV71 — no.	4	0.7	151	25.2	97.4 (92.9 to 99.0)	<0.001
Age 6–23 mo — no./total no.	2/3500	0.6	94/3500	26.9	97.9 (91.4 to 99.5)	<0.001
Age 24–72 mo — no./total no.	2/2500	0.8	57/2500	22.8	96.5 (85.6 to 99.1)	<0.001
Caused by coxsackievirus A16 — no.	48	8.0	54	9.0	11.1 (-30.8 to 39.6)	0.55
Caused by other enterovirus — no.	106	17.7	128	21.3	17.2 (-6.0 to 35.8)	0.15
Clinically diagnosed cases — no.	202	33.7	392	65.3	48.5 (39.2 to 56.3)	<0.001

AE: fever (42% vs 35%) /local AE (5.9% vs 2.3%) were more common in vaccine group, but SAE/Gr3 AE were not different from placebo

Li R, et al. N Engl J Med 2014;370:829-37

Efficacy, Safety, and Immunogenicity of Sinovac's Enterovirus 71 Vaccine in China (N=10,007)

Table 2. Efficacy of the EV71 Vaccine against EV71-Associated HFMD or Herpangina during the 12-Month Surveillance Period in the Intention-to-Treat Population.*

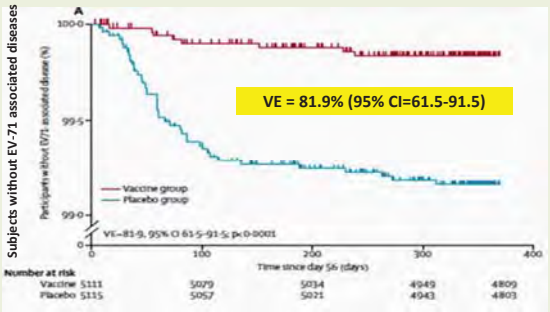
End Point	EV71 Vaccine		Placebo		Protective Efficacy
	No. of Cases	Incidence Density no. of cases/1000 person-yr	No. of Cases	Incidence Density no. of cases/1000 person-yr	% (95% CI)
At 6 Mo					
EV71-associated HFMD or herpangina	2	0.8	80	30.7§	97.5 (90.0 to 99.4)
HFMD	2	0.8	76	29.2§	97.4 (89.5 to 99.4)
Herpangina	0	0.0	4	1.5	100 (-49.0 to 100)
EV71-associated hospitalization¶	0	0.0	24	9.2§	100 (83.7 to 100)
EV71-associated HFMD with neurologic complications	0	0.0	8	3.1‖	100 (42.4 to 100)
All EV71-associated diseases	10	3.8	92	35.3§	89.3 (79.5 to 94.4)
At 1 Yr					
EV71-associated HFMD or herpangina	5	1.0	94	19.3§	94.8 (87.2 to 97.9)
HFMD	5	1.0	90	18.5§	94.6 (86.6 to 97.8)
Herpangina	0	0.0	4	0.8	100 (-48.4 to 100)
EV71-associated hospitalization¶	0	0.0	24	4.9§	100 (83.7 to 100)
EV71-associated HFMD with neurologic complications‖	0	0.0	8	1.6‖	100 (42.6 to 100)
All EV71-associated diseases	13	2.6	106	21.8§	88.0 (78.6 to 93.2)

* CI denotes confidence interval, EV71 enterovirus 71, and HFMD hand, foot, and mouth disease.
† In the vaccine group, there were 2651.3 person-years of follow-up at 6 months and 4979.2 person-years at 1 year.
‡ In the placebo group, there were 2607.1 person-years of follow-up at 6 months and 4873.0 person-years at 1 year.
§ P<0.001.
¶ All cases of EV71-associated hospitalization were in patients with HFMD.
‖ P<0.01.

Zhu F. N Engl J Med 2014; 370:818-828

Efficacy, safety, and immunology of an inactivated alum-adjuvant enterovirus 71 vaccine (by Beijing Vigoo) in children in China: A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

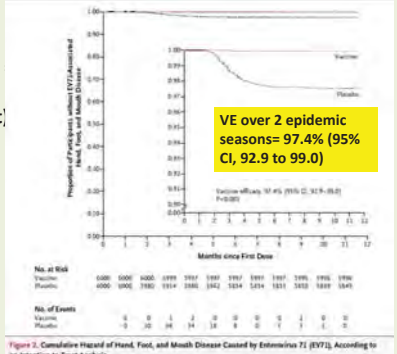
It is still completely unclear if the vaccine can cross protect all strains



Lancet. 2013 Jun 8;381(9882):2024-32. doi: 10.1016/S0140-6736(13)61049-1. Epub 2013 May 29.

An Inactivated Enterovirus 71 Vaccine (by CAMS) in Healthy Children: Phase III

- **The seroconversion rate 100% at 4 weeks after the 2 doses (4 wks apart)**
- **Weak cross-neutralization against EV71 C2 like or C1 subtype.**
- **No protection against other EV or CoxA16**



Li R, et al. N Engl J Med 2014;370:829-37