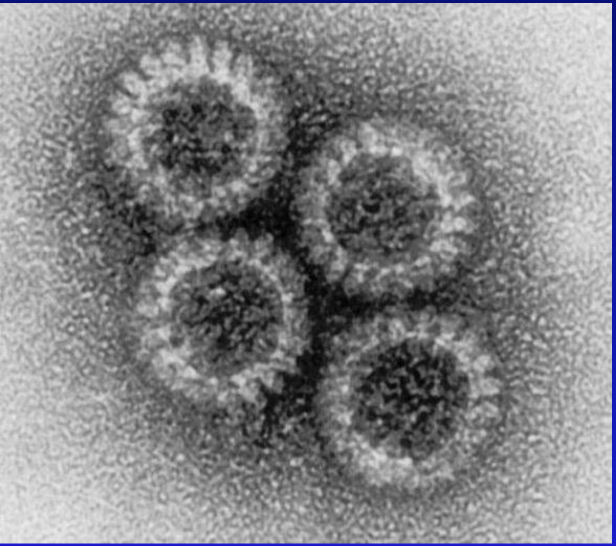
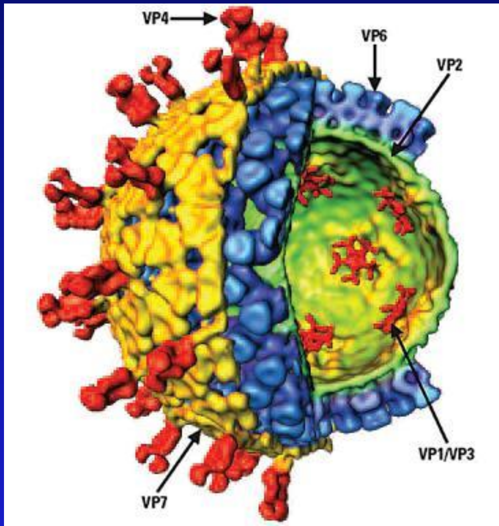
Rota Vaccine Introduction
in the Thai National Program





16th Annual Scientific Meeting of CEID 11 June 2019

School of Public Health, Prince of Wales Hospital

Shatin, New Territories, Hong Kong SAR

CHARUNG MUANGCHANA M.D., M.P.H., Ph.D.

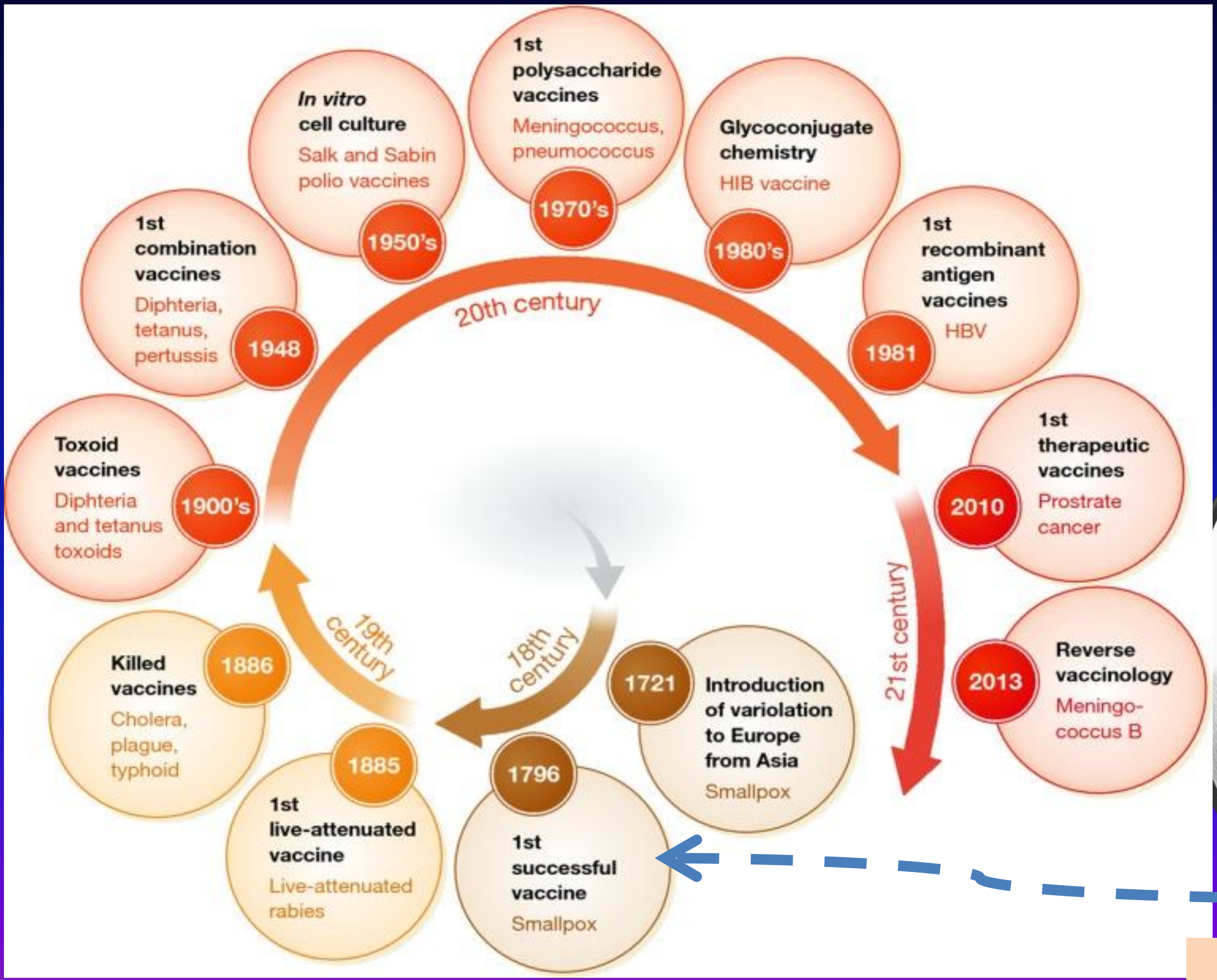
Former Director of the National Vaccine Institute (NVI), Thailand

Outline

- Advance of vaccine development & its contribution
- Clinical and public health burden of diarrheal diseases and rotavirus gastroenteritis
- Rotavirus vaccine recommendation by WHO

and implementing situation, including Thailand

Major milestones in the historical path of the development of vaccinology and vaccine design



Isabel Delany, Rino Rappuoli, and Ennio De Gregorio 2014

Edward Jenner 1749-1823(Smallpox Vaccine-1796)

29 diseases are currently preventable by vaccination

Cervical cancer[1]
Diphtheria[1]
Haemophilus influenzae type b[1]
Hepatitis A[1]
Hepatitis B[1]
Herpes zoster[1]
Human papillomavirus[1]
Influenza[1]
Measles[1]
Meningococcal[1]
Mumps[1]
H1N1 flu[1]
Pertussis[1]
Poliomyelitis[1]
Pneumococcal[1]
Rotavirus[1]
Rubella[1]
Smallpox and vaccinia[1]
Tetanus[1]
Tuberculosis[1]
Varicella[1]

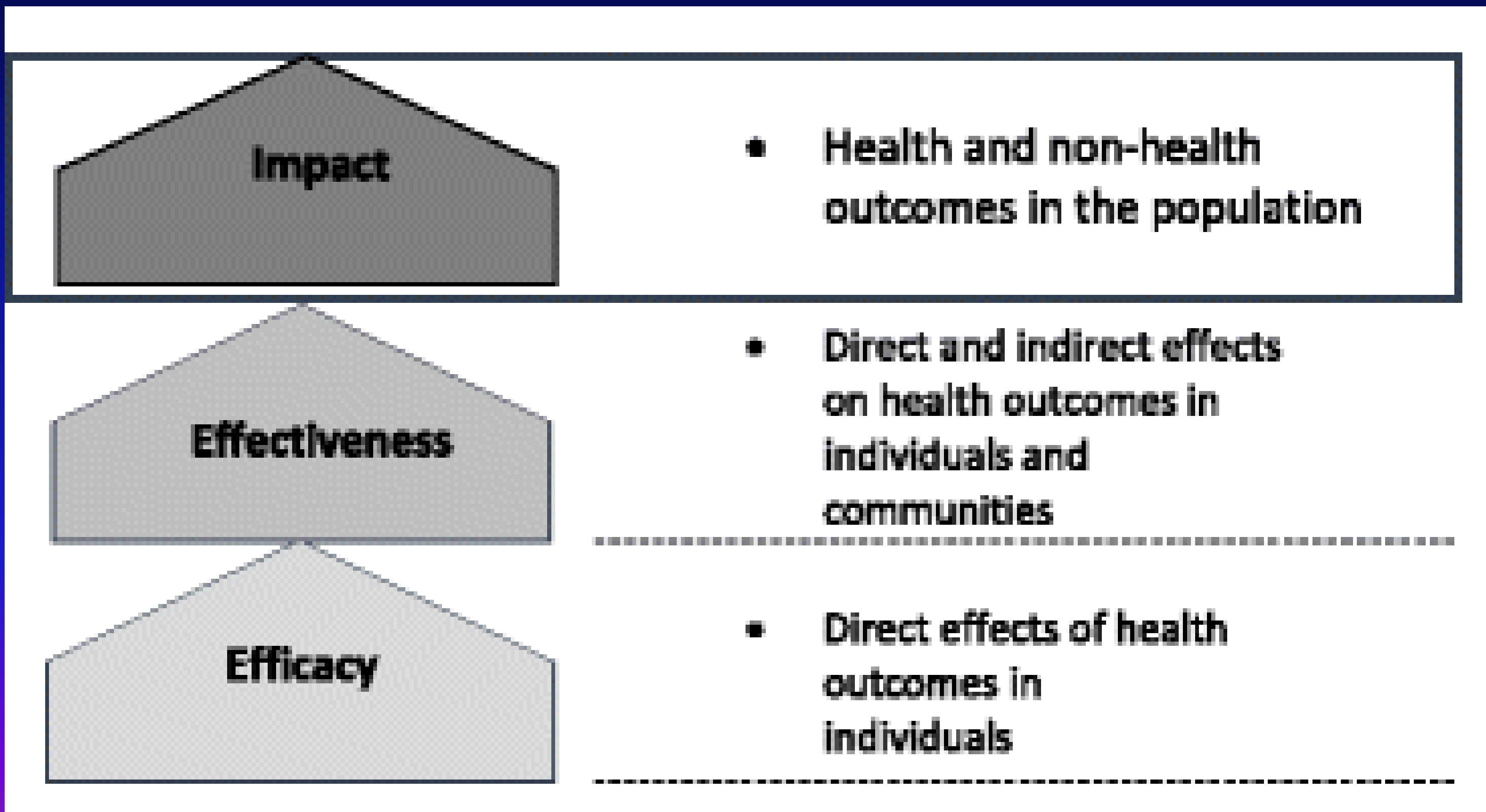
‘Vaccines are one of the greatest achievements of biomedical science and public health’

Anthrax[1]
Cholera[2]
Japanese encephalitis[1]
Monkeypox[1]
Tick-borne encephalitis[3]
Typhoid fever[1]
Rabies[1]
Yellow fever[1]

1. Centers for Disease Control and Prevention (CDC). Vaccines and preventable diseases. Available at: www.cdc.gov/vaccines/vpd-vac/default.htm (accessed August 2013); 2. Roush *et al. MMWR* 1999;48:243–8; 3.CDC. Special pathogens branch. Available at: www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/TBE.htm (accessed August 2013)

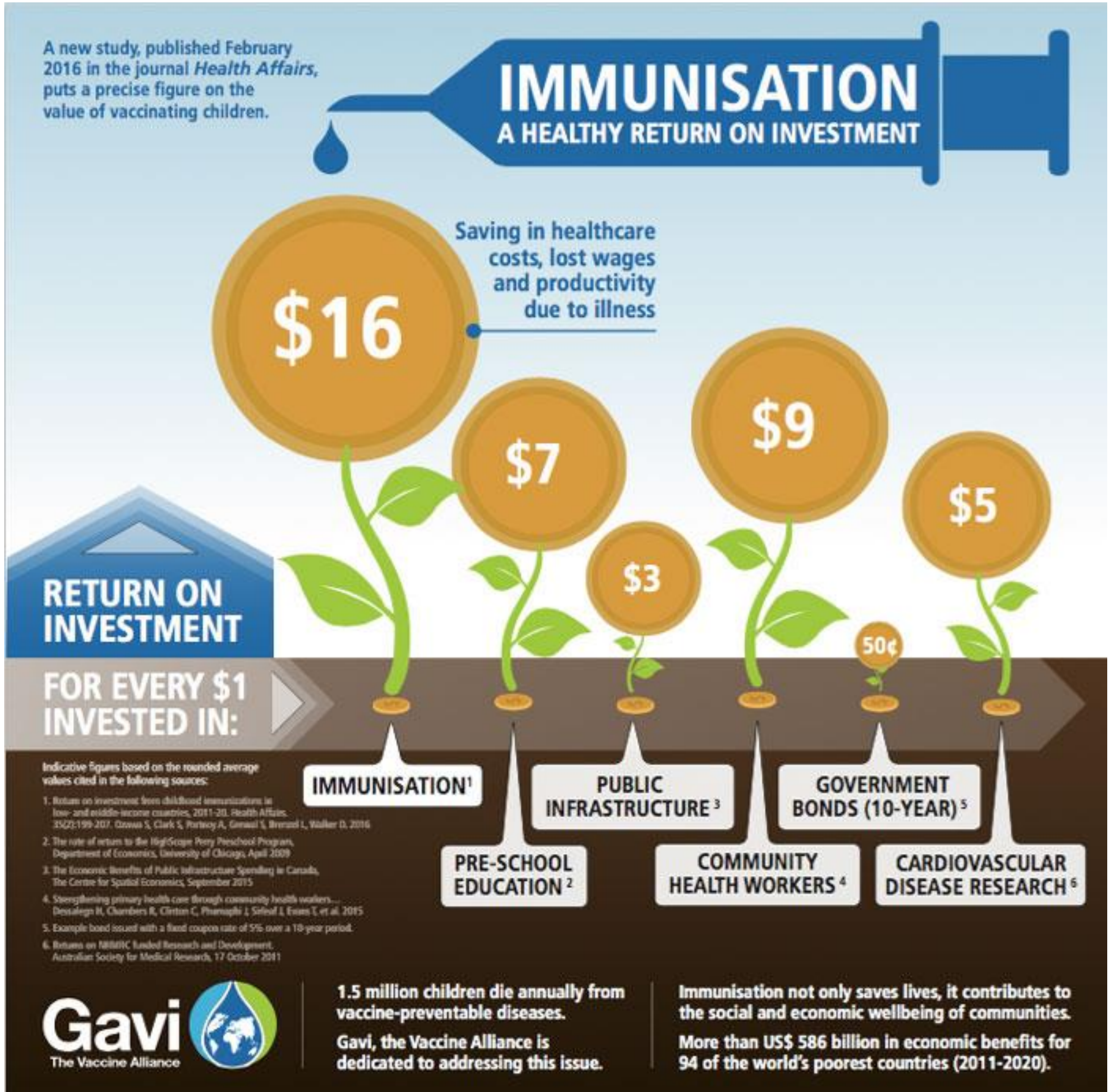
GlaxoSmithKline Vaccines

Public Health Value of Vaccines Beyond Efficacy



A. Wilder-Smith 2017

- **Immunization is one of the most cost-effective ways to save lives, improve health and ensure long-term prosperity**



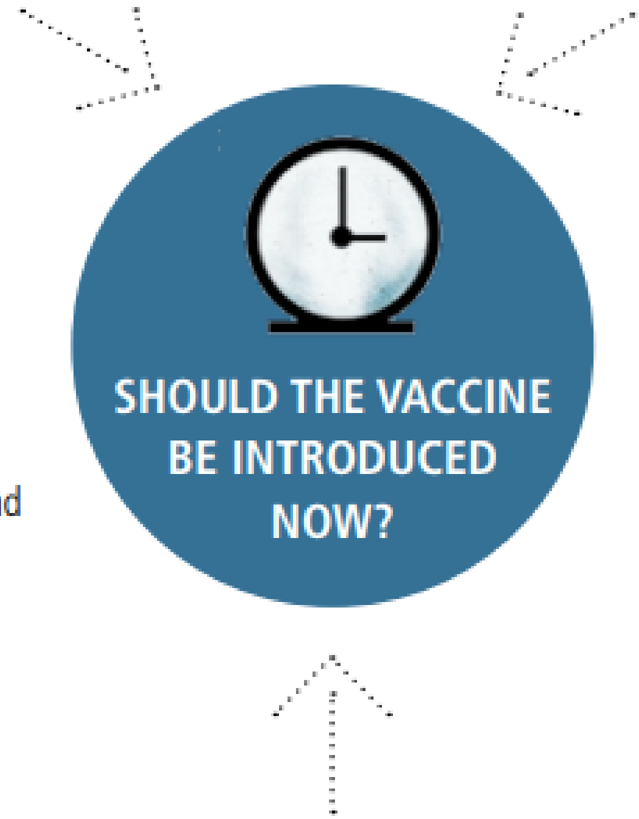
Key issues to consider when deciding on the introduction of a vaccine

THE DISEASE

- Public health and political priorities, alignment with global and regional recommendations
- Disease burden
- Status of other disease prevention and control measures

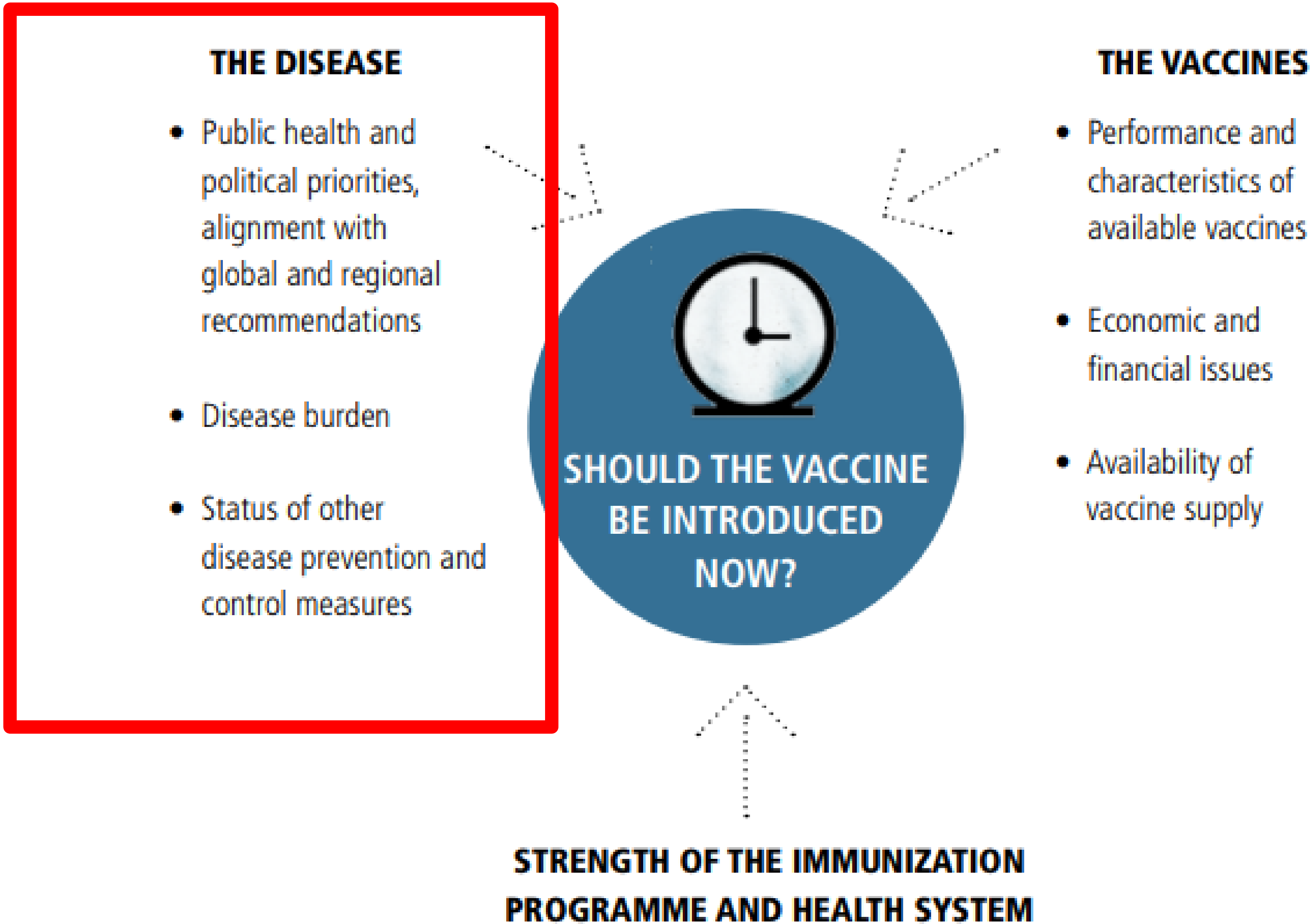
THE VACCINES

- Performance and characteristics of available vaccines
- Economic and financial issues
- Availability of vaccine supply



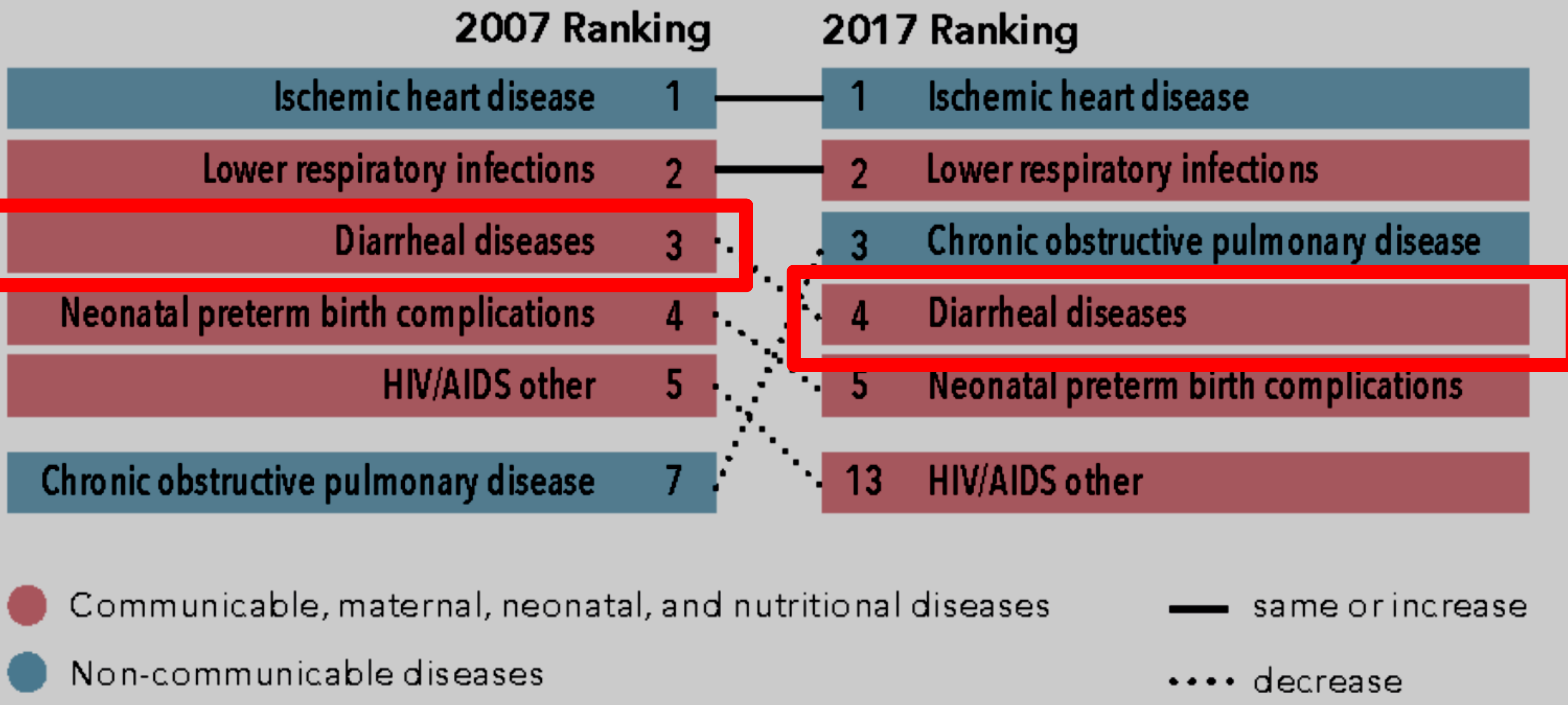
STRENGTH OF THE IMMUNIZATION PROGRAMME AND HEALTH SYSTEM

Key issues to consider when deciding on the introduction of a vaccine



World Health Organization 2014

Top five causes of early death and disability globally, 2007 and 2017**



**This figure measures the top five causes of early death and disability globally by disability-adjusted life years, or DALYS. It shows that the burden from non-communicable diseases is increasing in importance glob
of communicable, maternal, neonatal, and nutritional dis

http://www.healthdata.org/

Diarrheal Disease—Still a Leading Child Killer

- Diarrheal deaths have dropped significantly since 2000, falling from 1.2 million to <u>526,000</u> in 2015 – a decline of 57%
- Yet children continue to experience an average of <u>three episodes of diarrhea per year</u>
- A case of severe diarrhea, especially during important developmental stages, can have a lasting <u>effect on a child's growth</u>
- Diarrhea can also make children <u>more susceptible to death from other causes</u> like pneumonia

1.Kotloff, K.L., et al., *Burden and aetiology of diarrhoeal disease in infants and young children in developing countries* 2013

2.UNICEF, *One is too many: Ending child deaths from pneumonia and diarrhoea.* 2016.

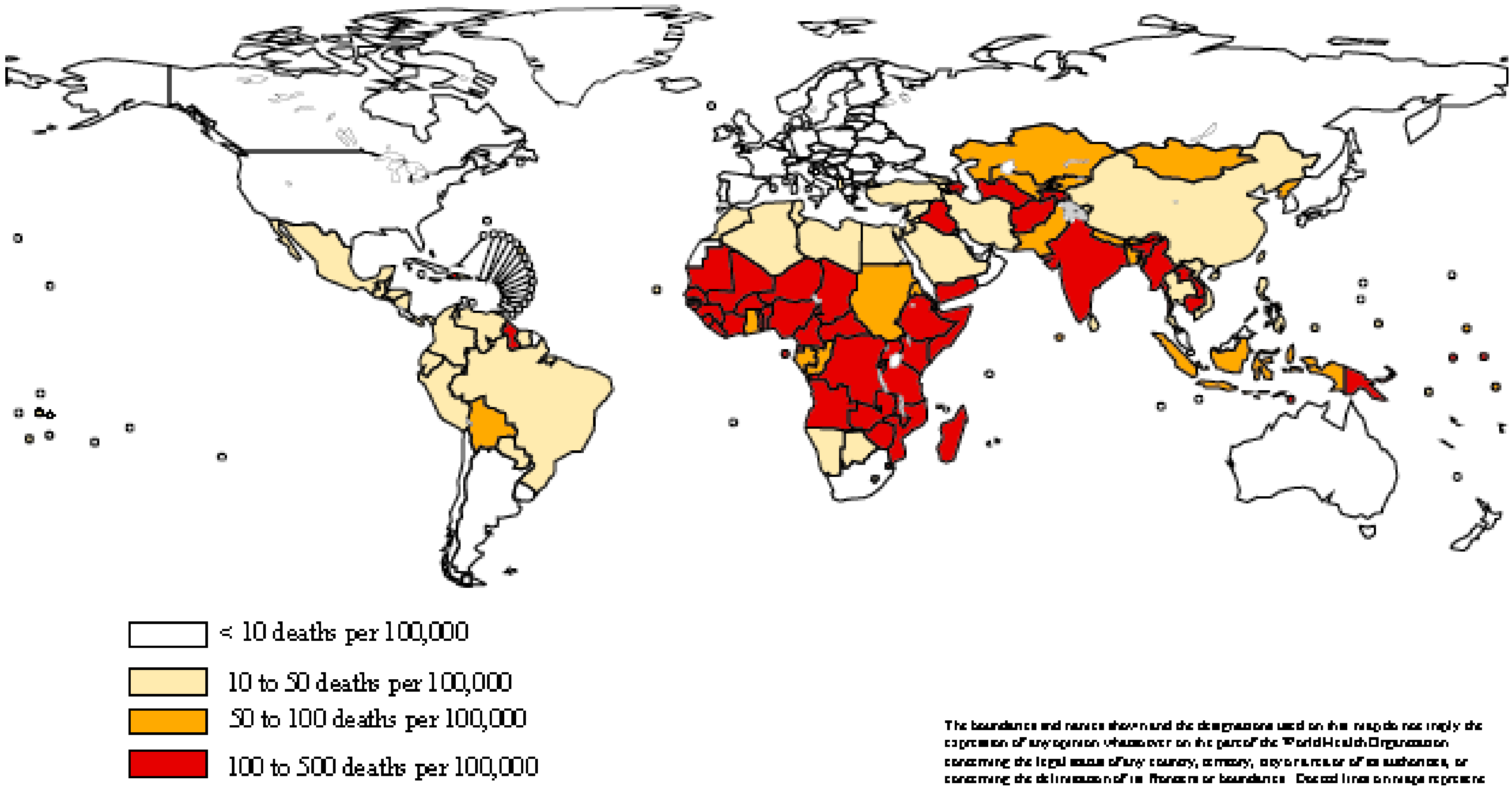
3.Walker, C.L., et al., *Global burden of childhood pneumonia and diarrhoea.* 2013

Number of diarrheal deaths estimated for each pathogen in children 0-59 m of age in the world, 2011

Pathogen	Medians restricted to add 100%		
	Median	No. Deaths (×1000)	95% CI (×1000)
Viruses			
Rotavirus	27·8%	197	110–295
Calicivirus	9·9%	71	39–113
Astrovirus	2·1%	15	9–26
Adenovirus	3·1%	22	12–37
Bacteria			
EPEC	11·1%	79	31–146
ETEC	6·0%	42	20–76
Shigella spp	3·9%	28	12–53
Campylobacter spp	3·2%	22	11–50
Salmonella spp	2·5%	18	10–30
Vibrio cholerae O1	1·3%	9	0–37
Parasites			
Cryptosporidum spp	2·0%	14	3–31
Giardia lamblia	2·3%	16	0–66
Entamoeba histolytica	0·2%	1	0–19
Episodes with unknown etiology	24·5%	176	56–304
Total	100·0%	712	491–1 049

Lanata, Claudio F et al. "Global causes of diarrheal disease mortality in children <5 years of age: a systematic review." PloS one vol. 8,9 e72788. 4 Sep. 2013, doi:10.1371/journal.pone.0072788

Rotavirus mortality rate per 100,000 population less than 5 years of age: 2004



Annual Global Disease Burden of Rotavirus Gastroenteritis

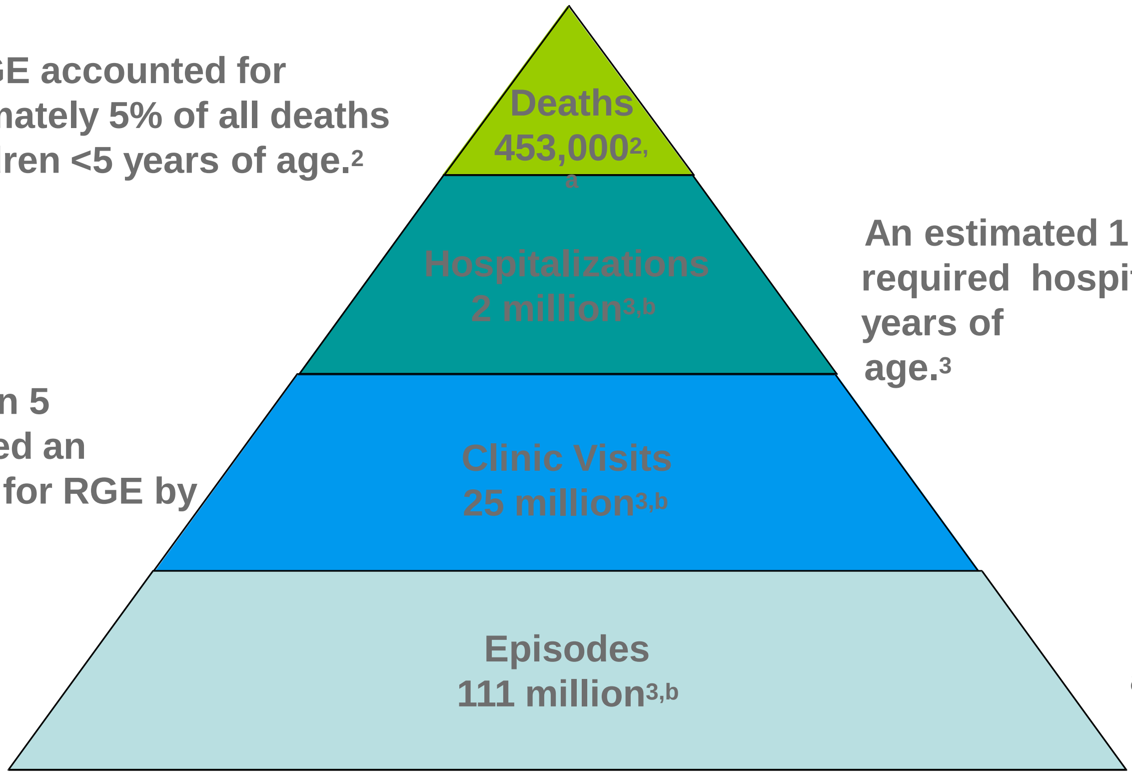
RGE is the most common cause of severe gastroenteritis in infants and young children <5 years of age worldwide.[1]

RGE accounted for approximately 5% of all deaths in children <5 years of age.[2]

An estimated 1 in 65 children required hospitalization for RGE by 5 years of age.[3]

An estimated 1 in 5 children required an outpatient visit for RGE by 5 years of age.[3]

Nearly every child is affected by 5 years of age.[3]



Annual RGE-Related Events

RGE=rotavirus gastroenteritis.

[a]2008 estimate based on literature published 2001–2011. [b]Based on literature published 1986–2000.

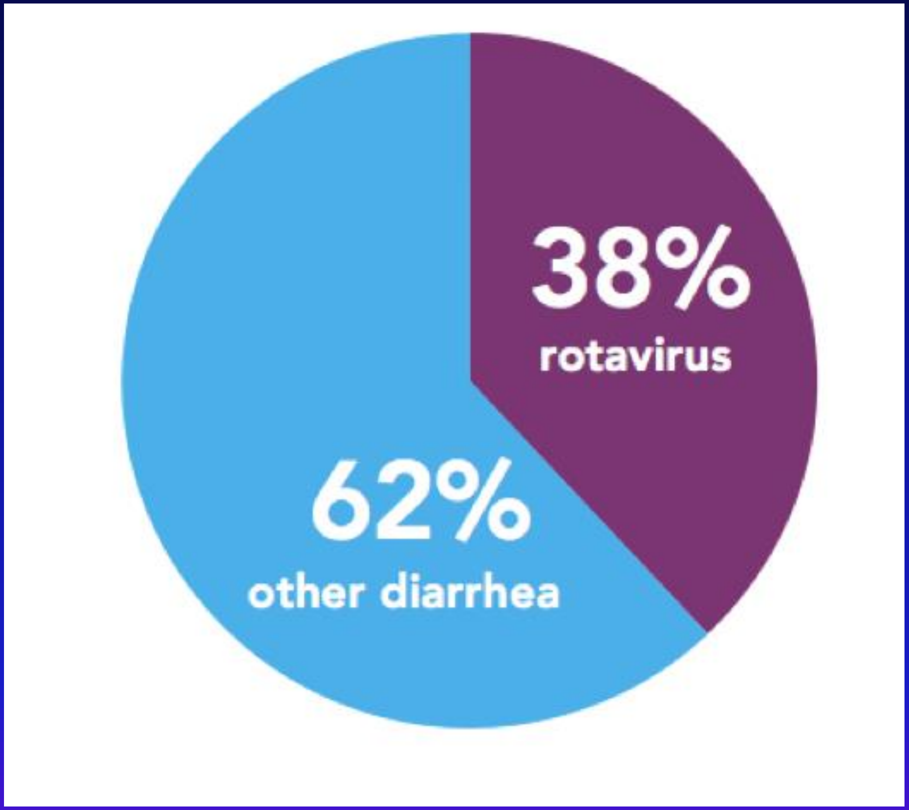
1. Glass RI et al. *Lancet*. 2006;368:323–332. **2.** Tate JE et al. *Lancet Infect Dis.* 2012;12:136–141. **3.** Parashar UD et al. *Emerg Infect Dis.* 2003;9:565–572.

Median proportions of pathogens isolated in stool samples from diarrheal episodes seen in IPD services, in 208 studies in children 0-59 m of age in the world, 2011

Pathogen	Single pathogen (n=208 studies)					Studies that sought 5–13 pathogens (n=27 studies)				
	N studies	N samples positive	N samples examined	Median %	Age adjusted median % (95%CI)*	N studies	N samples positive	N samples examined	Median %	Age adjusted median % (95%CI)
Viruses										
Rotavirus	180	59 226	161 126	39·4%	39·4% (37·1–43·1)	24	8 384	43 719	19·7%	20·2% (15·7–26·3)
Calicivirus	12	639	4 412	15·6%	15·6% (10·5–21·2)	7	2 681	39 195	8·2%	8·2% (4·8–12·7)
Astrovirus	1	28	708	4·0%	4·0% (NA)	10	577	39 597	2·3%	2.3% (1·1–3·5)
Adenovirus	1	17	866	2·0%	2·0% (NA)	10	942	39 615	3·6%	3·6% (1·7–5·8)
Bacteria										
EPEC	0	-	-	-	-	9	605	2 961	15·8%	15·8% (7·9–29·2)
ETEC	1	43	314	13·7%	13·7% (NA)	16	355	5 461	8·1%	8·2% (5·1–11·9)
Shigella spp	2	118	668	17·1%	24·5% (NA)	24	520	43 947	6·0%	7·2% (3·2–7·9)
Campylobacter spp	1	64	2 163	3·0%	3·0% (NA)	23	596	43 882	4·8%	4·8% (3·1–9·3)
Salmonella spp	0	-	-	-	-	24	853	44 060	3·2%	3·2% (2·7–3·5)
Vibrio cholerae O1	2	134	1 441	10·5%	10·5% (NA)	11	227	36 025	0·2%	0·2% (0·0–6·1)
Parasites										
Cryptosporidium spp	7	192	5 451	2·8%	2·8% (2·0–6·1)	17	290	40 493	2·6%	2·6% (0·4–7·0)
Giardia lamblia	1	46	291	15·8%	15·8% (NA)	14	425	39 762	2·8%	2·8% (0·4–10·5)
Entamoeba histolytica	0	-	-	-	-	12	150	39 067	0·3%	0·3% (0·0–3·8)

Lanata, Claudio F et al. "Global causes of diarrheal disease mortality in children <5 years of age: a systematic review." 2013

Global diarrhea hospitalizations for children under 5



Lanata, C.F., et al., *Global causes of diarrheal disease mortality in children <5 years of age: a systematic review.* 2013.

Parashar, U.D., et al., *Rotavirus and severe childhood diarrhea.* 2006

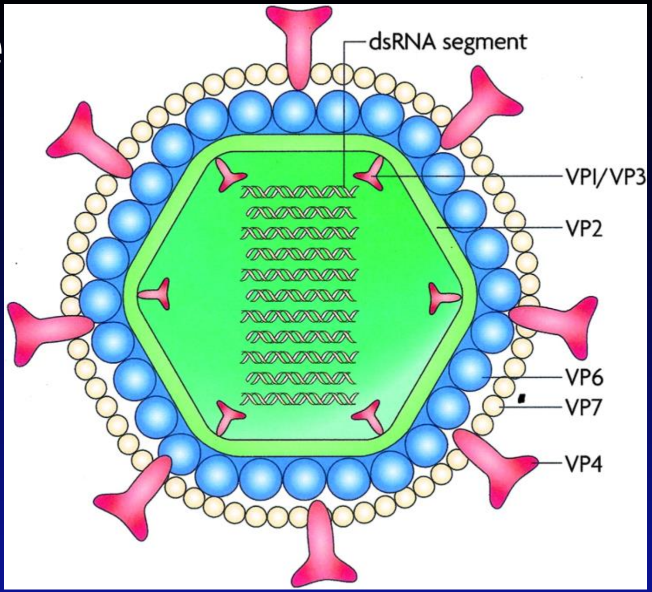
Median age-adjusted proportions of causes of diarrhea, constrained to fit 100%, in 286 inpatient studies of children <5 years of age published between 1990–2011, by WHO region

Pathogen	AFRO (n=22)		AMRO (n=53)		EMRO (n=19)		EURO (n=50)		SEARO (n=64)		WPRO (n=78)	
	N	Median	N	Median	N	Median	N	Median	N	Median	N	Median
Viruses												
Rotavirus	18	26·8	47	23·4	16	31·3	44	25·9	42	25·5	75	32·6
Calicivirus	1	15·9	6	13·6	1	10·2	11	9·8	6	8·4	11	10·3
Astrovirus	1	6·6	5	3·1	0	–	7	0·9	3	2·1	10	2·8
Adenovirus	1	3·7	4	2·4	0	–	10	2·7	4	5·1	11	3·4
Bacteria												
EPEC	1	10·3	6	10·8	2	13·0	0	–	2	8·9	0	–
ETEC	1	5·0	10	7·4	3	5·0	0	–	7	4·3	0	–
Shigella spp	2	4·1	15	5·7	2	11·9	5	0·1	10	3·5	2	0·2
Campylobacter spp	2	2·3	9	6·1	1	7·9	6	2·1	9	3·5	5	1·9
Salmonella spp	2	3·2	12	2·1	2	6·0	6	5·2	8	2·6	4	3·2
Vibrio cholerae O1	2	0·4	4	0·0	1	0·0	0	–	11	4·5	1	0·04
Parasites												
Cryptosporidium spp	2	2·5	12	3·1	0	–	1	0·0	9	2·1	1	0·3
Giardia lamblia	1	1·8	10	4·7	0	–	1	0·0	4	5·2	1	0·5
Entamoeba histolytica	1	0·3	8	0·02	0	–	1	0·0	4	1·7	1	0·2

Rotavirus gastroenteritis(RVGE)

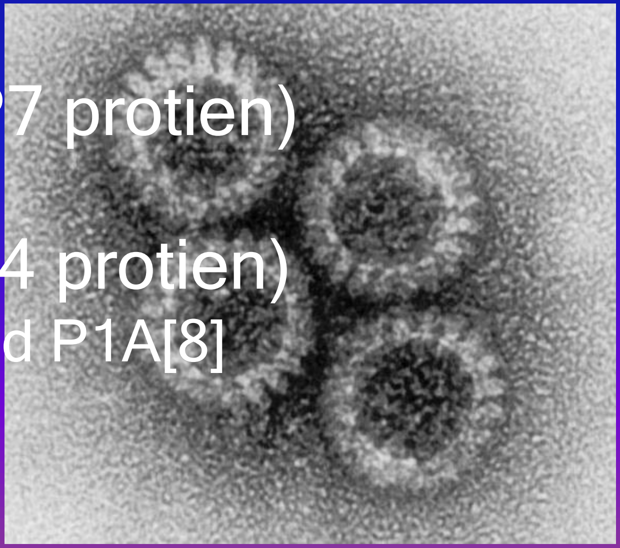
- RVs are highly contagious
- RVs damage the enterocyte lining of the small intestine villi resulting in reduced absorptive capacity and diarrhea
- Clinical manifestations of RVGEs: watery diarrhea, fever, vomiting, resulting in dehydration with shock, electrolyte imbalance, and death

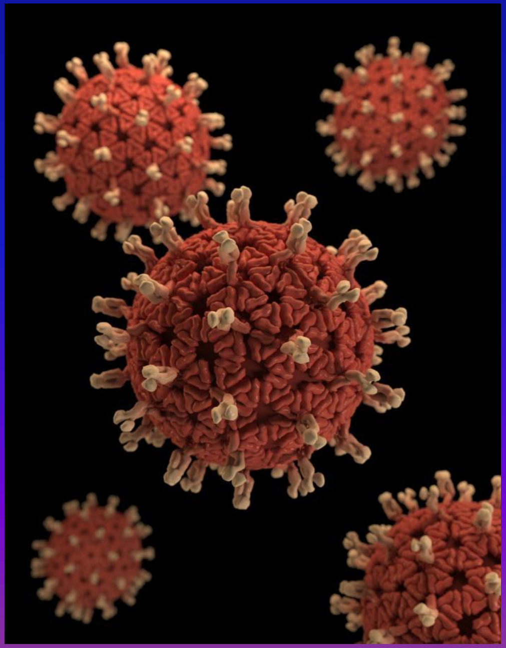
- Rotavirus is in family Reoviridae
  - Non-envoloped ds-RNA virus
  - 3 layers capsid



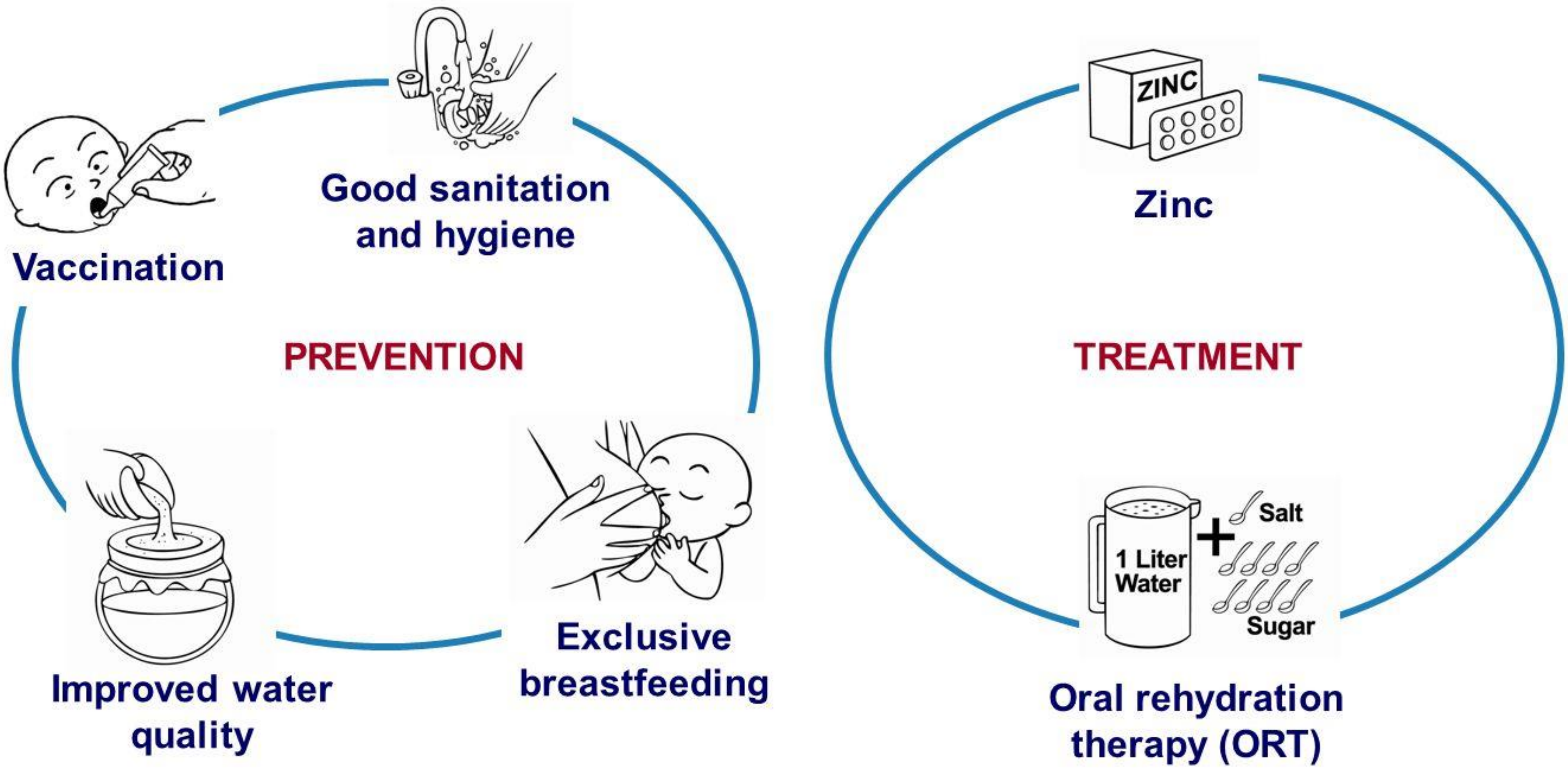
- Serogroups
  - 7 serogroups (group A-G)
    - A, B,C,G	cause disease in human animal
    - D, E, F	cause disease in animal only

- Serotypes
  - G-serotype (by VP7 protien)
    - G1 to G4 and G9
  - P-serotype (by VP4 protien)
    - P1B[4], P2A[6], and P1A[8]



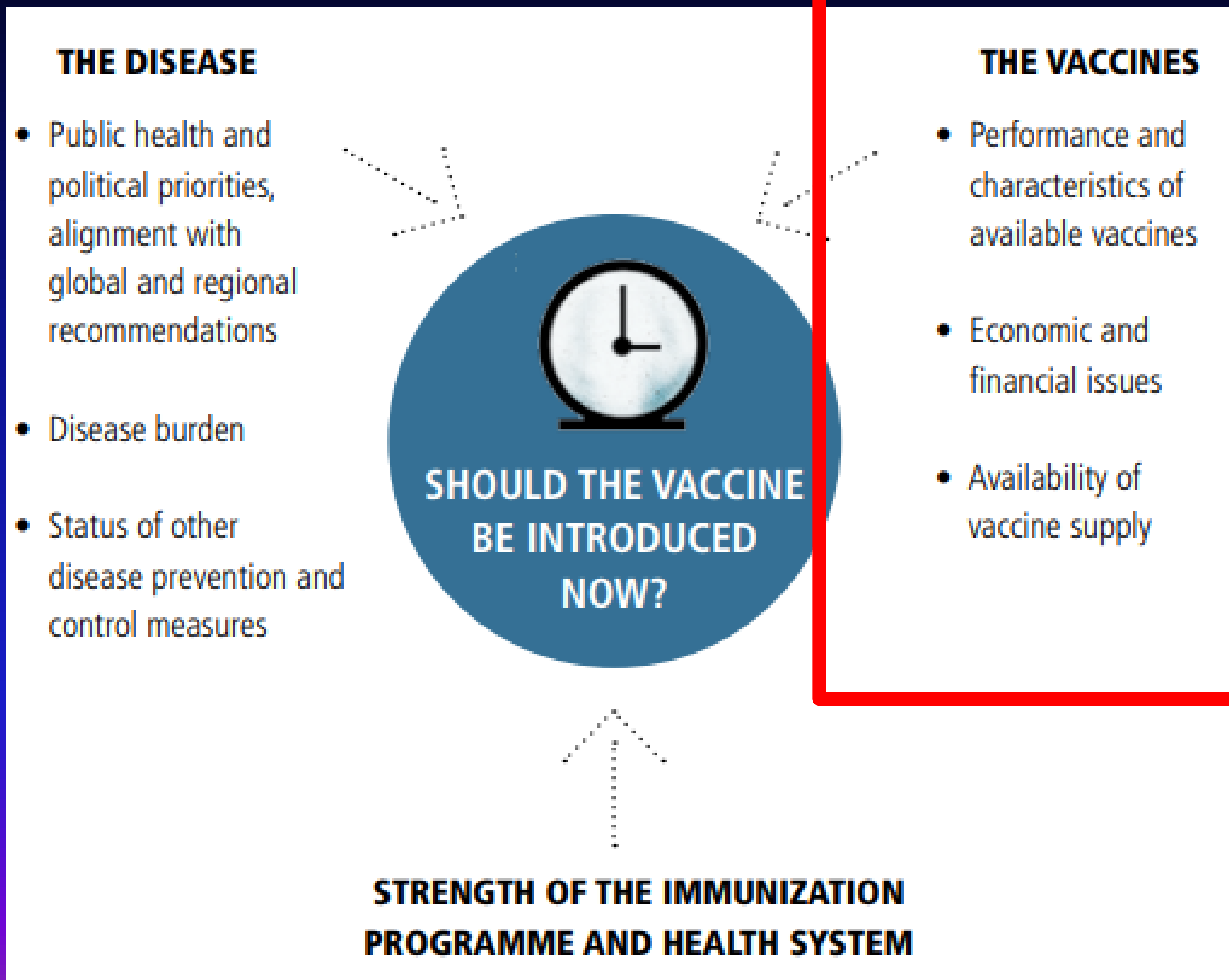


What can be done to prevent and treat rotavirus disease?



World Health Organization

Key issues to consider when deciding on the introduction of a vaccine



World Health Organization 2014

Globally-used products: Rotarix™ & RotaTeq®

VACCINE	Rotarix™	RotaTeq®
MANUFACTURER	GlaxoSmithKline	Merck & Co., Inc.
FORMULATION	Monovalent attenuated human rotavirus strain	Pentavalent, human-bovine reassortant vaccine
STRAINS PRESENT IN VACCINE	G1P[8]	G1, G2, G3, G4, and P[8]
PROTECTION AGAINST OTHER STRAINS	Yes, broad protection demonstrated	Yes, broad protection demonstrated
EFFICACY AGAINST SEVERE ROTAVIRUS DIARRHEA IN CHILDREN <1 YR (HIGH-INCOME COUNTRIES)	95.8-100%	85-96%
EFFICACY AGAINST SEVERE ROTAVIRUS DIARRHEA IN CHILDREN <1 YR (LOW- AND MIDDLE-INCOME COUNTRIES)	49-85%	51-64%

NEJM, 2010; Vesikari T, NEJM, 2006; Ruiz-Palacios, NEJM, 2006; Patel MM, NEJM, 2011; AMA, 2012; Cortese, PIDJ, 2010; Haber P, Pediatrics, 2008; Buttery JP, PIDJ, 2011; Vesikari T, Lancet, 2007; Chandran A, Biologics, 2010; Phua KB, Vaccine, 2009; Eberly MD, Vaccine, 2011; Patel M, J Infect Dis, 2009.

COUNCIL
Rotavirus Organization of Technical Allies

The Available Rotavirus Vaccines

Rotavirus vaccines	Rotarix (GSK)	Rotataq (MSD)	Rotavac (Bharat Biotech)	Rotasil (Serum)	Rotavin (Polyvac)	LLR (Lanzhou)	Rotashield (Wyeth, Biovirx)
Licensure	Several countries, 2006	Several countries, 2006	India, 2014	India, 2017	Vietnam, 2012	China, 2000	Several countries, 1998
Pre-qual	Yes	Yes	Yes	No	No	No	No
Strains	Monovalent, human derived G1P8	Pentavalent, WC3 G6P5 bovine, reassortants G1-4, P8	Monovalent, human-bovine neonatal derived G9P11	Pentavalent, UK Bovine G6P5, reassortants G1-4, G9	Monovalent, human G1P8	Monovalent, human G10P12	Tetravalent, RRV G3P3 rhesus backbone, reassortants G1, 2, 4
No. of doses	2	3	3	3	2	1 per year for 3 yr	3 (2 neonatal)
Age first dose	6 weeks	6 weeks	6 weeks	6 weeks	6 weeks	2-36 mon	6 weeks
Dosage	10^6 of live attenuated human G1P[8] particles	2.0-2.8 x 10^6 infectious units per reassortant	10^5 FFU of live rotavirus	$10^{5.6}$ Infectious unit per reassortant	$10^{6.3}$ of live attenuated human G1P[8] particles	> 5.5 log $CCID_{50}$	1 x 10^5 plaque-forming units (pfu) of each component

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

Rotavirus vaccines are cost-effective

Recent studies show that national rotavirus vaccination programs will be highly cost-effective and also reduce healthcare costs due to rotavirus-related illness.[1-7]

COUNTRY	NUMBER OF CASES AVERTED	DEATHS AVERTED	HEALTHCARE COSTS AVERTED	DATE RANGE
Iran	35.1 million	266	US$280 million	2014-2023
Kenya	1.2 million	61,000	US$30 million	2014-2033
Senegal	2 million	8,500	US$8 million	2014-2033
Uganda	4 million	70,000	US$10 million	2016-2035
Malawi	1 million	4,313	US$8 million	2014-2033
Afghanistan	1 million	12,000	US$1.35 million	2017-2027
Bangladesh	3.9 million	3900	US$7 million	2017-2027

In the US, in just four years, rotavirus vaccination saved nearly US$1 billion by preventing hospitalizations, emergency visits and doctors' visits among children under age 5.[5]

ROTA COUNCIL
Rotavirus Organization of Technical Allies

[1]Sigei C, Vaccine, 2015; [2]Javanbakht M, Vaccine, 2015 ; [3]Diop A, Vaccine, 2015 ; [4]Bar-Zeev N, Clin Infect Dis. 2016; [5] Leshem E, Pediatrics, 2014; [6]Palwasha A., Vaccine, 2017; [7]Pecenka C, Vaccine, 2017

WHO's position papers on rotavirus vaccine

WHO's position papers on rotavirus vaccine: 2007, 2009 & 2013

Years	Recommendations
2007	the inclusion of rotavirus vaccination into the national immunization programs of regions and countries where vaccine efficacy data suggest a significant public health impact and where appropriate infrastructure and financing mechanisms are available to sustain vaccine utilization
2009	rotavirus vaccine for infants should be included in all national immunization programs. In countries where diarrheal deaths account for ≥10% of mortality among children aged <5 years, the introduction of the vaccine is strongly recommended
2013	Rotavirus vaccines should be included in all national immunization programs and considered a priority, particularly in countries with high RVGE-associated fatality rates, such as in south and south-eastern Asia and sub-Saharan Africa

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

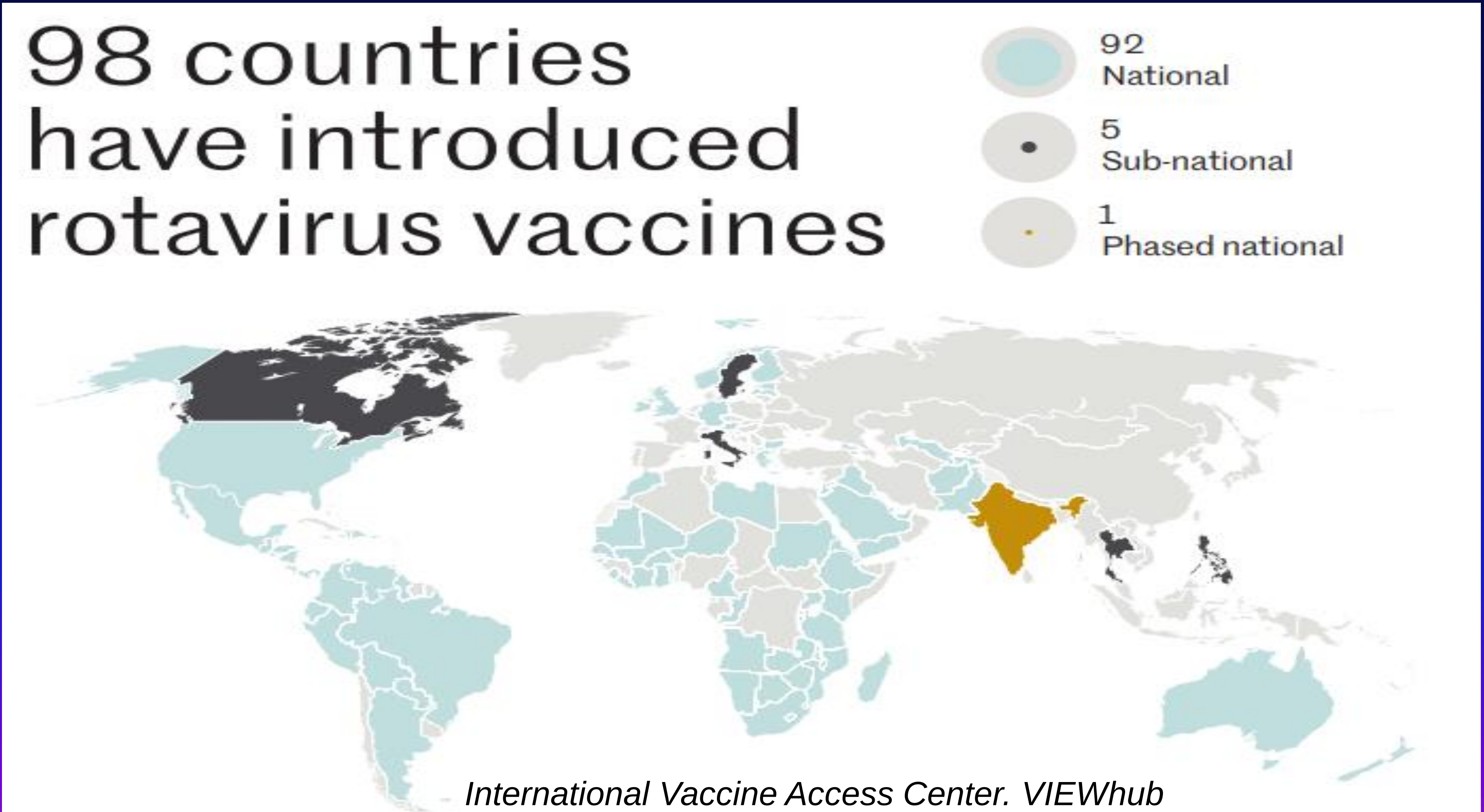
Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for all children								
BCG [1]		As soon as possible after birth	1					Birth dose and HIV; Universal vs selective vaccination; Co-administration; Vaccination of older age groups; Pregnancy
Hepatitis B [2]	**Option 1**	As soon as possible after birth (<24h)	3	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2			Premature and low birth weight Co-administration and combination vaccine High risk groups
	Option 2	As soon as possible after birth (<24h)	4	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2	4 weeks (min),with DTPCV3		
Polio [3]	**bOPV + IPV**	6 weeks (see footnote for birth dose)	4 (IPV dose to be given with bOPV dose from 14 weeks)	4 weeks (min) with DTPCV2	4 weeks (min) with DTPCV3			bOPV birth dose Transmission and importation risk criteria
	IPV / bOPV Sequential	8 weeks (IPV 1st)	1-2 IPV 2 bOPV	4-8 weeks	4-8 weeks	4-8 weeks		
	IPV	8 weeks	3	4-8 weeks	4-8 weeks		(see footnote)	IPV booster needed for early schedule (i.e. first dose given <8 weeks)
DTP-containing vaccine [4]		6 weeks (min)	3	4 weeks (min) - 8 weeks	4 weeks (min) - 8 weeks		3 Boosters 12-23 months (DTP-containing vaccine); 4-7 years (Td/DT containing vaccine), see footnotes; and 9-15 yrs (Td)	Delayed/ interrupted schedule Combination vaccine; Maternal immunization
***Haemophilus influenzae* type b** [5]	**Option 1**	6 weeks (min) 59 months (max)	3	4 weeks (min) with DTPCV2	4 weeks (min) with DTPCV3		(see footnote)	Single dose if >12 months of age Not recommended for children > 5 yrs Delayed/ interrupted schedule Co-administration and combination vaccine
	Option 2		2-3	8 weeks (min) if only 2 doses 4 weeks (min) if 3 doses	4 weeks (min) if 3 doses		At least 6 months (min) after last dose	
Pneumococcal (Conjugate) [6]	**Option 1 3p+0**	6 weeks (min)	3	4 weeks (min)	4 weeks			Schedule options Vaccine options HIV+ and preterm neonate booster
	Option 2 2p+1	6 weeks (min)	2	8 weeks (min)			9-18 months	
Rotavirus [7]		6 weeks (min) with DTP1	2 or 3 depending on product	4 weeks (min) with DTPCV2	For three dose series – 4 week (min) with DTPCV3			Vaccine Options Not recommended if >24 months old
Measles [8]		9 or 12 months (6 months min, see footnote)	2	4 weeks (min) (see footnote)				Combination vaccine; HIV early vaccination; Pregnancy
Rubella [9]		9 or 12 months with measles containing vaccine	1					Achieve and sustain 80% coverage Co-administration and combination vaccine; Pregnancy
HPV [10]		As soon as possible from 9 years of age (females only)	2	6 months (min 5 months)				Target 9-14 year old girls; Multi-age cohort vaccination; Pregnancy Older age ≥ 15 years 3 doses HIV and immunocompromised

Refer to http://www.who.int/immunization/documents/positionpapers/ for table & position paper updates.

This table summarizes the WHO vaccination recommendations for children.The ages/intervals cited are for the development of country specific schedules and are not for health workers.

National schedules should be based on local epidemiologic, programmatic, resource & policy considerations. While vaccines are universally recommended, some children may have contraindications to particular vaccines.

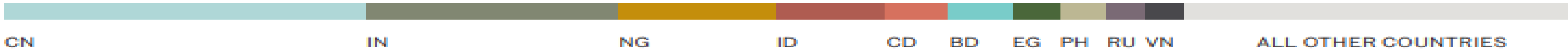
Number of countries introduced rotavirus vaccine, Oct 2018



International Vaccine Access Center. VIEWhub

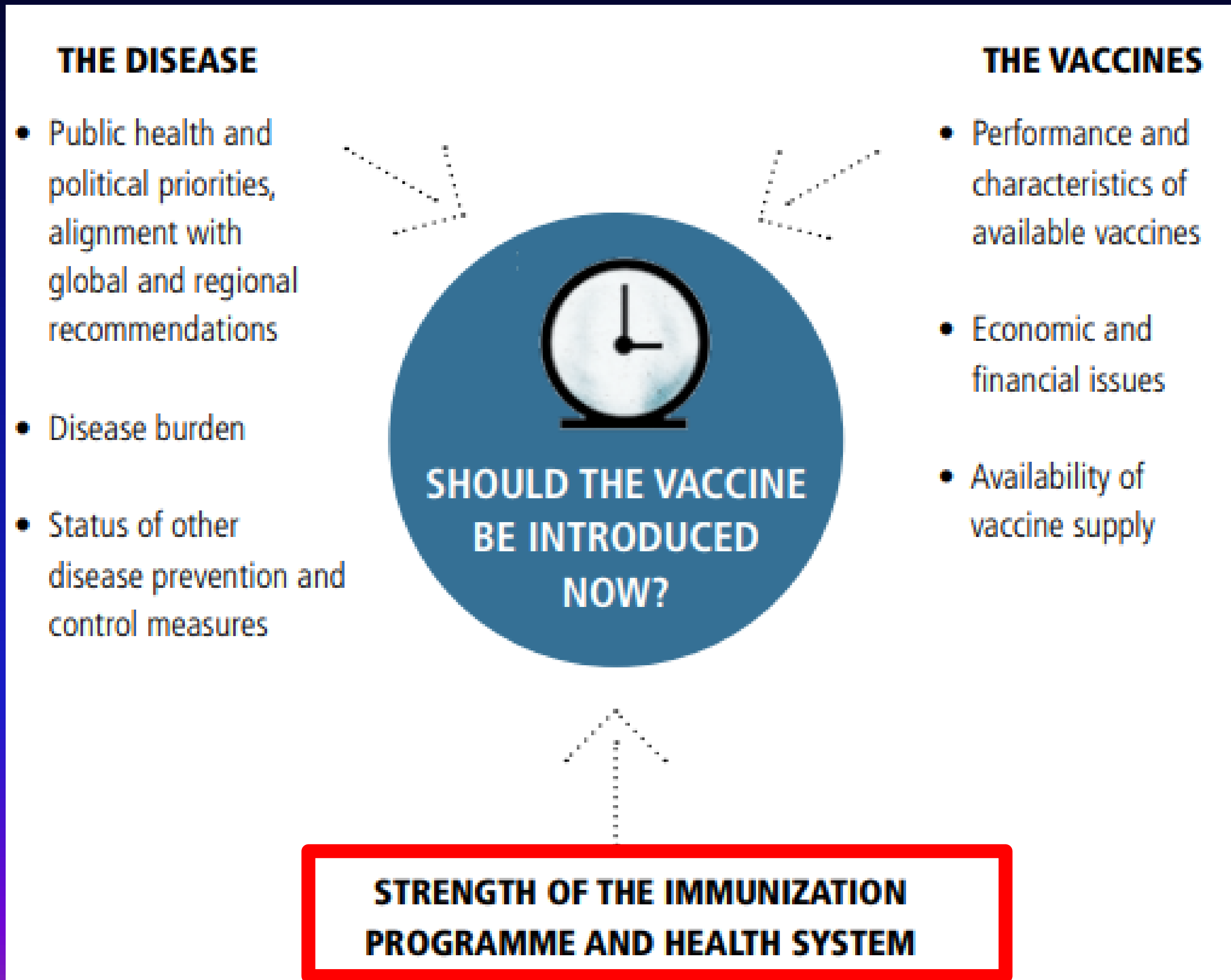
Worldwide, 71 million children lack access to rotavirus vaccine & most of them live in just 10 countries

75% of all children without access live in 10 countries[1]
(53,749,809 children)



% of children without access	Country (Number of children without access)	% of children without access	Country (Number of children without access)
23%	China (16,181,955)	4%	Bangladesh (2,976,098)
16%	India (11,490,478)	3%	Egypt (2,422,840)
10%	Nigeria (6,912,789)	3%	Philippines (2,348,562)
7%	Indonesia (4,778,241)	2%	Russia (1,768,080)
4%	DR Congo (3,209,000)	2%	Vietnam (1,532,753)

Key issues to consider when deciding on the introduction of a vaccine



World Health Organization 2014

Selected Thailand Demographics

Population 67 millions

Birth cohort 733,014

Infant mortality 15.0/1,000 live births

Total fertility 1.66

Pop growth rate 0.5%

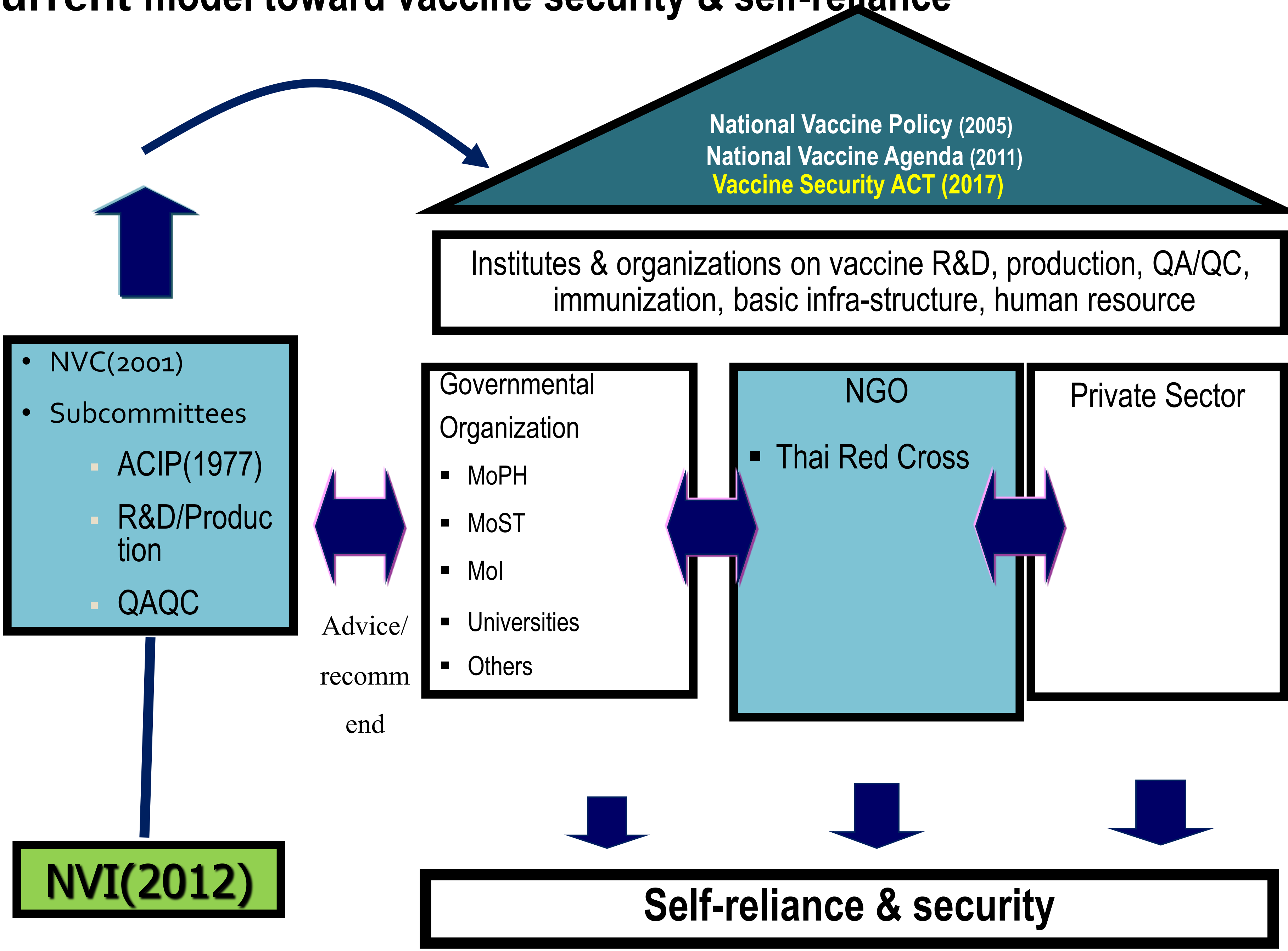
Urban pop 34%

GDP per capita 6,000 USD

Ethnic groups Thai 75% Chinese

Religions Buddhist 94.6% Muslim 4.6%

Current model toward vaccine security & self-reliance



Products

Products	2016	2017	2018	2019	2020	2021

Vaccine Management

การบริหารจัดการวัคซีนและการให้บริการ

- ระบบการจัดหา สำรองและกระจายวัคซีนที่มีประสิทธิภาพทั้งในภาวะปกติ และภาวะฉุกเฉิน
- ระบบการให้บริการวัคซีนที่เหมาะสมและจำเพาะกับสภาพพื้นที่/สังคม

- รูปแบบการให้บริการวัคซีนตลอดช่วงชีวิต เช่น วัยรุ่น วัยผู้ใหญ่ และผู้สูงอายุ เป็นต้น
- ประชาชนทุกกลุ่มเป้าหมายรับรู้และตระหนักถึงความสำคัญของวัคซีนในการป้องกันโรค

New vaccine introduction

	2016	2017	2018	2019	2020	2021
New vaccine introduction		HPV	Hib	Rota	Pneumo.	DTP-HB-Hib-IPV

Research & Production

Products	2016	2017	2018	2019	2020	2021
(1) Dengue vaccine (LAV/DNA/VLP)-1	ผลิต GMP Pilot plant	ทดสอบใน pre-clinic				
(2)Dengue vaccine-2 (Chimeric)	ผลิต GMP Pilot plant	Clinic ph. I		Clinic ph. II		Clinic ph. III
(3) LAIV	Pilot study/ ผลิต Seed	Pre-clinic	Clinic Ph. I-II	Registered		
(4) IIV	Clinic Ph. II	Pilot plant production	Clinic Ph.III	ยื่นข้อมูลขึ้น ท/บ	Registered	
(5) dT/DTP/DTP-HB	สังเคราะห์ Ag	Bulk D,T,P	Stab. study/ Pre-clinic	Clinic Ph. I/II	Clinic Ph. III	Registered
(6) aP	Clinic Ph. III	Registered				
(7) Live chimeric JE	MOU & สร้างโรงงาน		Machine optimization & Validation	Clinic Ph. I-II	Clinic Ph. III	Registered
(8) BCG	ออกแบบ & สร้างโรงงาน		Machine optimization & Validation	Clinic Ph. I-II	Clinic Ph. III	WHO-PQ

Infra-structures/Human resource

การพัฒนาบุคลากร (HRD)

- บุคลากรสาขาที่จำเป็นและขาดแคลนในวงจรวัคซีนได้รับการพัฒนาอย่างเพียงพอและมีคุณภาพ
- การบริหารเพื่อการแลกเปลี่ยนทรัพยากรบุคคลในสาขาที่จำเป็นและขาดแคลนระหว่างรัฐและเอกชน
- มาตรการสร้างแรงจูงใจบุคลากรในสาขาที่ขาดแคลน

โครงสร้าง พ.ฐ. (Infra structure)

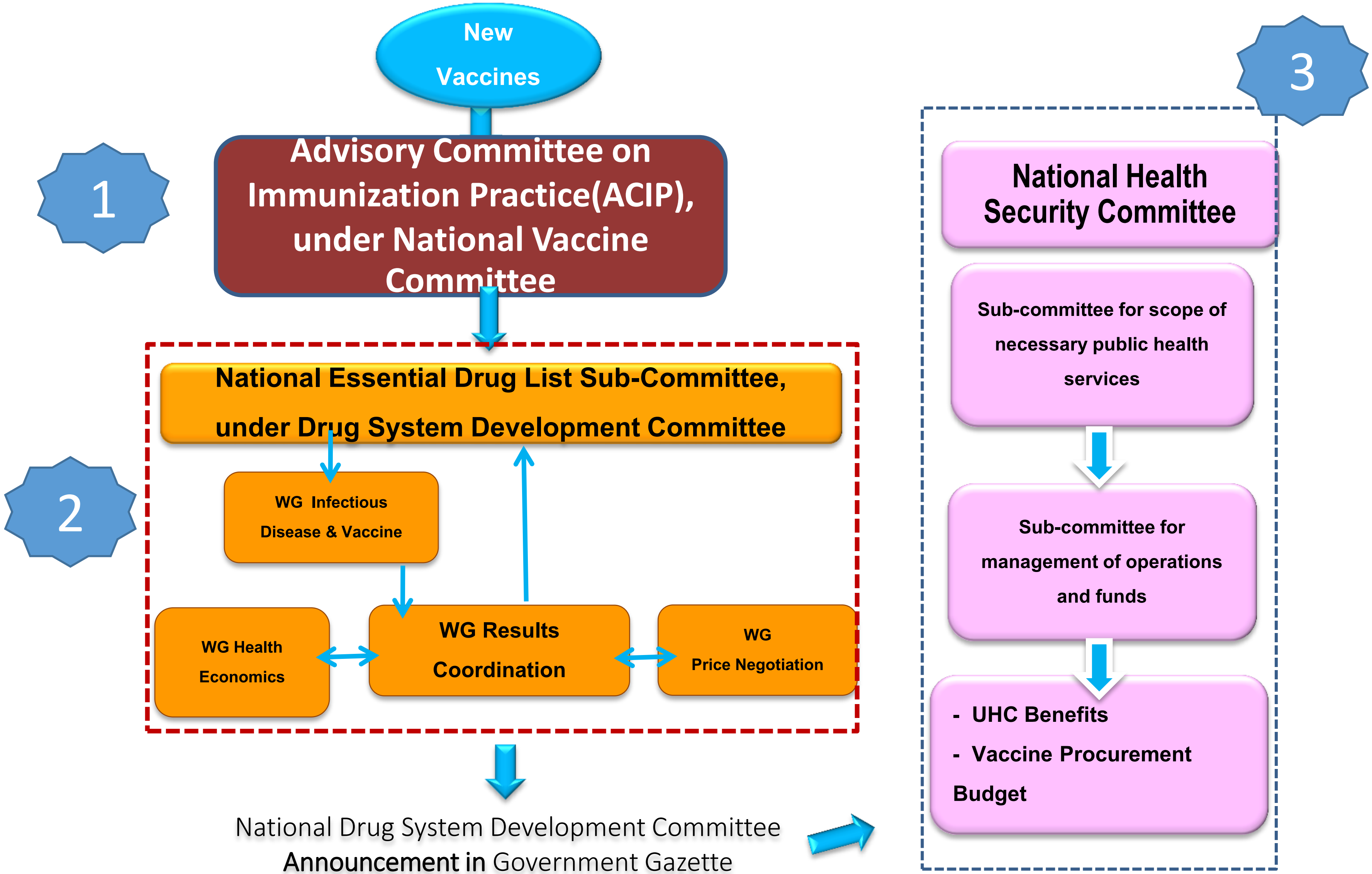
Animal testing lab., Non infectious (OECD GLP) → ห้องปฏิบัติการมาตรฐาน GLP → GMP pilot plant → Industrial GMP plants (JE,BCG) → Animal testing lab., Infectious (OECD GLP)

หน่วยงาน เครือข่าย (NVI+Networks)

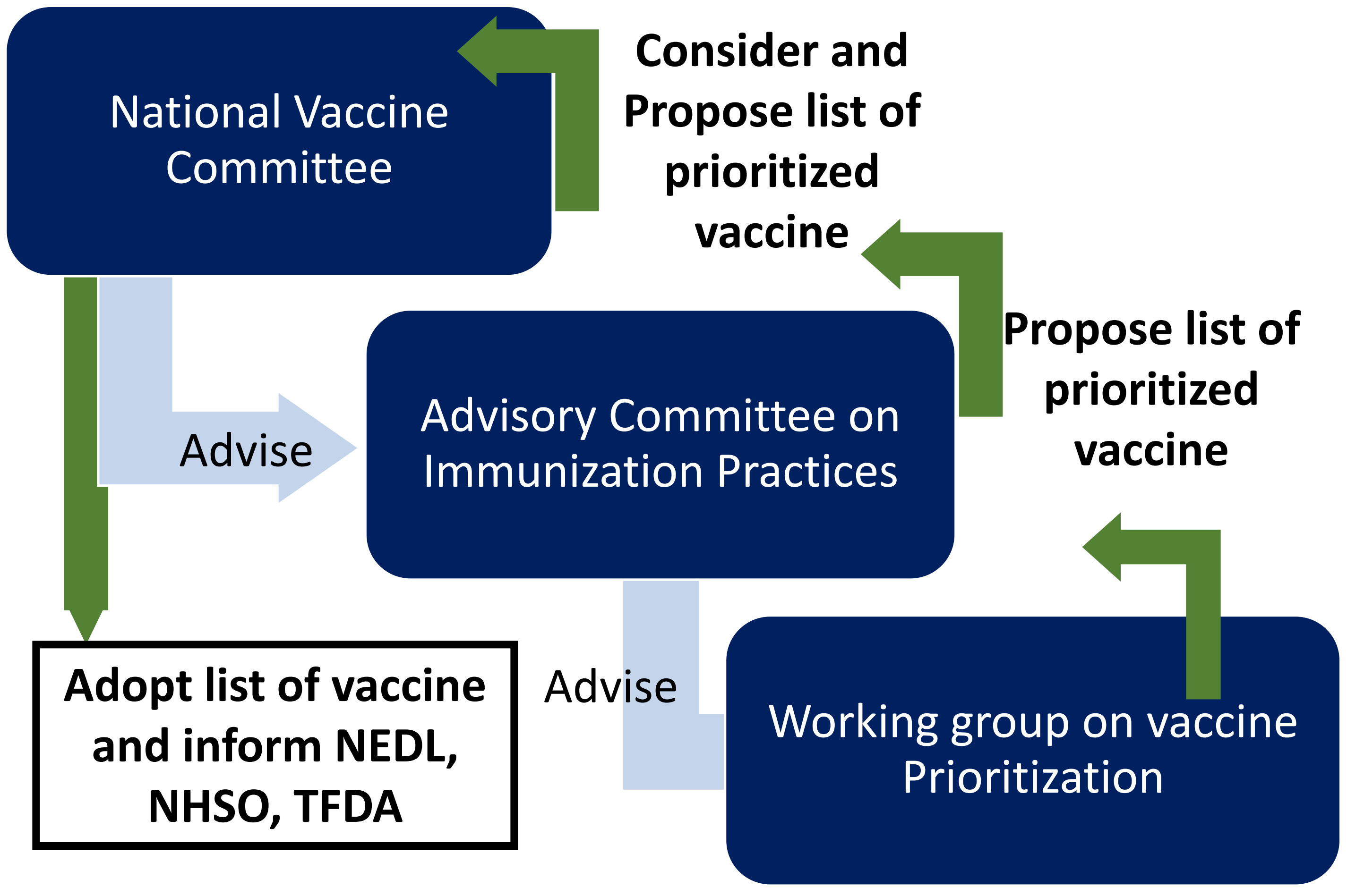
องค์กรภาคีเครือข่ายวัคซีนมีศักยภาพ ความพร้อม และร่วมมือวิจัย ผลิต ควบคุมกำกับ และสร้างเสริมภูมิคุ้มกันโรค ทั้งระดับประเทศและนานาชาติ

- NVI มีสมรรถนะสูงในการขับเคลื่อนนโยบาย
- Vaccine knowledge center
- Project manager/Co-ordinator ของวัคซีนรายชนิด

Process of new vaccine introduction in Thailand



Vaccine Prioritization



Scoring for Measurable Criterion

Criterion	5	4	3	2	1
Size of pop. affected	≥ 10,000	1,000 - 9,999	10 - 999	10 - 99	0 - 9
Case fatality rate	51-100	21-50	11-20	1-10	0-0.9
Efficacy/Effectiveness	>90	81-90	71-80	61-70	≤60
Safety	<0.01%	0.01–0.09%	0.1–0.9%	1–9%	≥10%
Estimated budget	< 300 MB	300–499 MB	500-799 MB	800–1,599MB	>1,600 MB
Vaccine production in country	At least 1 upstream manufacturing	At least 2 down stream manufacturing	One down stream manufacturing	At least 2 import vaccines	One Import vaccine

Vaccine Priorities by ACIP

Priority	Vaccines	Target population
Phase 1	Tdap	Pregnant woman
	Influenza	Pregnant woman (year round)
	DTwP-HB-Hib or DTwP-HB-Hib-IPV	Child < 5 years
	MR	Health care workers
Phase 2	DTaP-HB-Hib-IPV	Child < 5 years
	PCV	Child < 5 years
	Dengue	to be considered
	Varicella	Child < 5 years
	Hep A	Child < 5 years
	Rabies (pre-exposure)	Child < 5 years
Phase 3	Zoster	Elders

Consideration of vaccine introduction into Thai UC benefit package (EPI)

Criteria	1 ACIP	2 National Drug System Development Committee	3 NHSO
1. Disease Incidence & Severity	✓		
2. Disease Burden	✓		
3. Vaccine Safety & Efficacy	✓		
4. Cost-Effectiveness		✓	
5. Likelihood of introduction or pilot in 2-3 years	✓		
6. Budget Feasibility & Sustainability		✓	✓
7. Equality/Non-discrimination		✓	✓

8 years of the introduction activities of rota vaccine in Thailand

1

ACIP
2010

MoPH to conduct pilot of rotavirus vaccine in Sukhothai Province

June 8th

MoPH
2011

Pilot 2011-2013

-Results show vaccine cost-benefit of rotavirus vaccine

ACIP
21 Dec 2015

-Results of rotavirus pilot reported on effectiveness and cost-effectiveness on rotavirus vaccine in Sukhothai and Petchabun provinces

- ACIP support introduction of rotavirus vaccine

MoPH
19 May 2016

Collection of information for stakeholder presentation for new vaccine introduction

-NHSO Secretariat

-NVC Chairman

-National Essential Drugs Committee Chairman

Aim: Drive RV vaccine introduction in Thailand

Expand Pilot Project

2

National Essential Drugs List Sub-Committee 2018-2019

- NEDL evaluates Working Group evidence of health economics and vaccine price. Proposes to NHSO to evauate health budget and introduction to benefits package.

3

- NHSO provides resolution

1. Agree to to create budget plan for rotavirus vaccine for 2020, after consideration of readiness of procurement for sustainable introduction.
2. Agree to monitor vaccine target group to ensure long term sustainable vaccine access

Vaccine 30 (2012) 2839–2847

Contents lists available at SciVerse ScienceDirect

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

Economic analysis for evidence-based policy-making on a national immunization program: A case of rotavirus vaccine in Thailand

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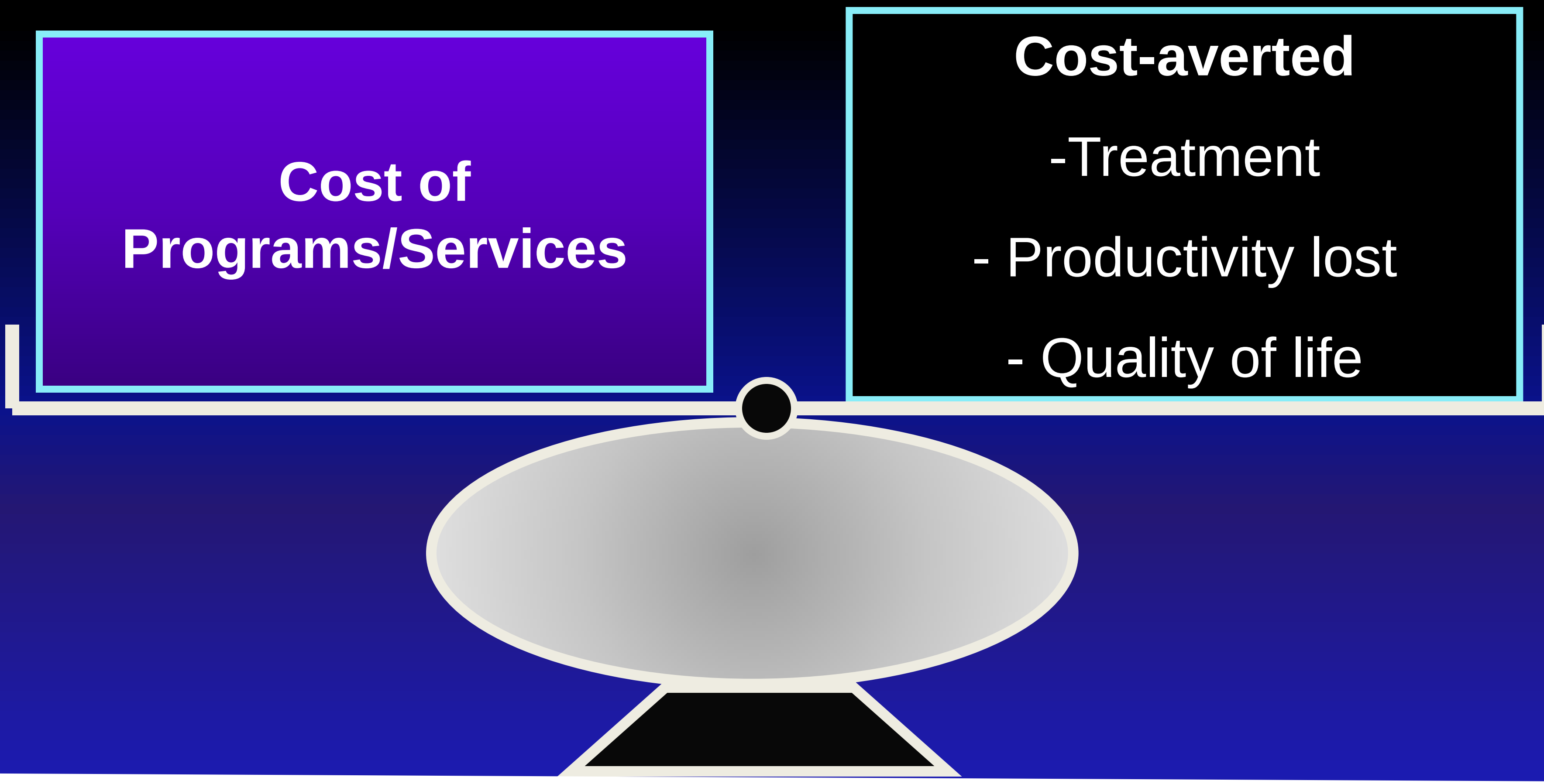
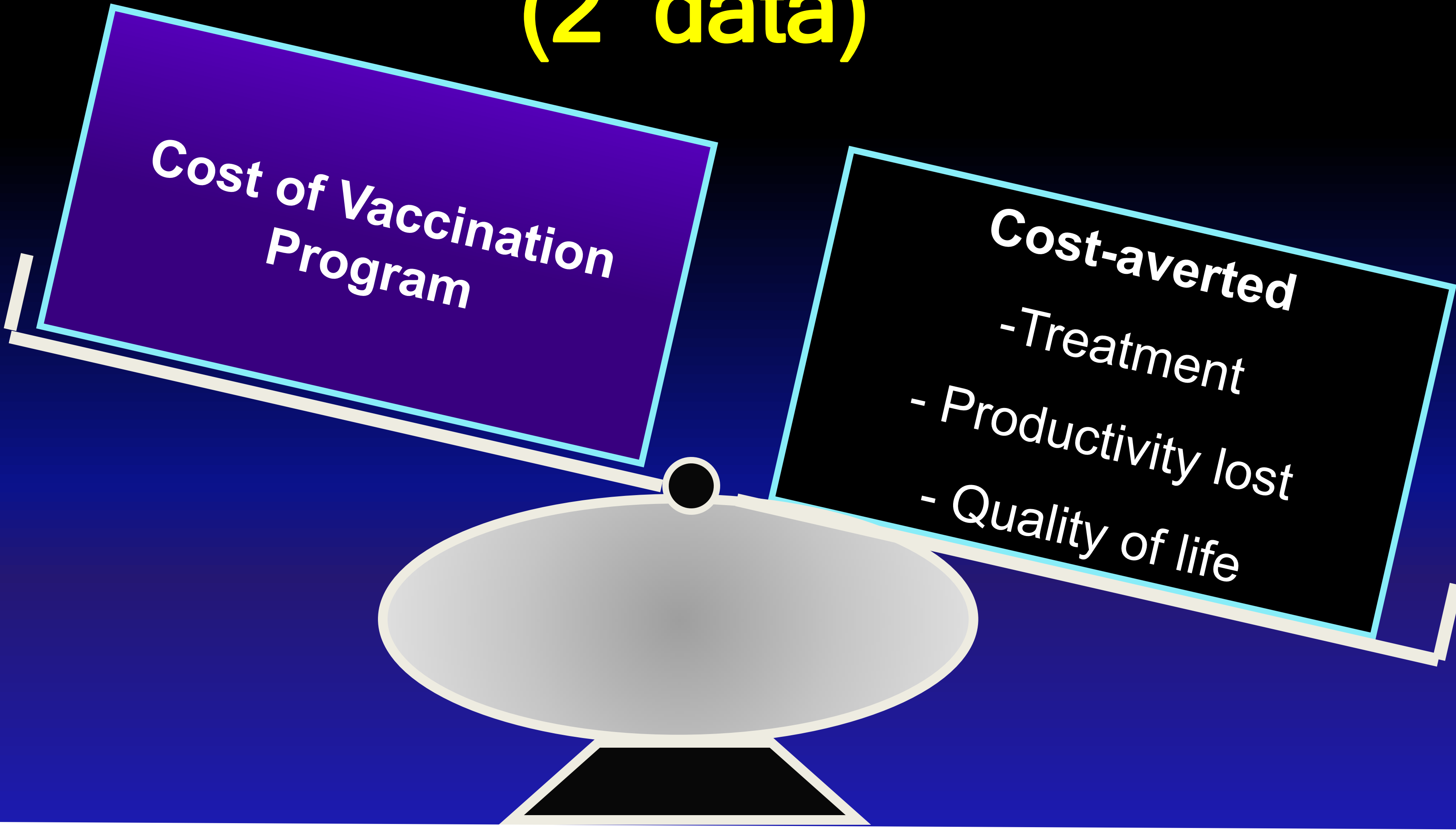
ABSTRACT

Severe diarrhea caused by rotavirus is a health problem worldwide, including Thailand. The World Health Organization has recommended incorporating rotavirus vaccination into national immunization programs. This policy has been implemented in several countries, but not in Thailand where the mortality rate is not high. This leads to the question of whether it would be cost-effective to implement such a policy. The Thai National Vaccine Committee, through the Immunization Practice Subcommittee, has conducted an economic analysis. Their study aimed to estimate the costs of rotavirus diarrhea and of a rotavirus vaccination program, and the cost-effectiveness of such a program including budget impact analysis. The study was designed as an economic evaluation, employing modeling technique in both provider and societal perspectives. A birth cohort of Thai children in 2009 was used in the analysis, with a 5-year time horizon. Costs were composed of cost of the illness and the vaccination program. Outcomes were measured in the form of lives saved and DALYs averted. Both costs and outcomes were discounted at 3%. The study found the discounted number of deaths to be 7.02 and 20.52 for vaccinated and unvaccinated cohorts, respectively (13.5 deaths averted). Discounted DALYs were 263.33 and 826.57 for vaccinated and unvaccinated cohorts, respectively (563.24 DALYs averted). Costs of rotavirus diarrhea in a societal perspective were US$6.6 million and US$21.0 million for vaccinated and unvaccinated cohorts, respectively. At base case, the costs per additional death averted were US$5.1 million and US$5.7 for 2-dose and 3-dose vaccines, respectively, in a societal perspective. Costs per additional DALYs averted were US$128,063 and US$142,144, respectively. In a societal perspective, with a cost-effectiveness threshold at 1 GDP per capita per DALYs averted, vaccine prices per dose were US$4.98 and US$3.32 for 2-dose and 3-dose vaccines, respectively; in a provider perspective, they were US$2.90 and US$1.93. One-way and probabilistic sensitivity analyses were included. The budget required for vaccine purchase was calculated for all scenarios.

Economic & Financial Issues (Public Health & Individual Perspective)



Economic & Financial Issues (2° data)



Pilot study for HRV vaccination by MOPH, Thailand(N=4,830), 2012-14

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

Sukhothai

Coverage: 96.5%

Co-administer with OPV

- NO SAE

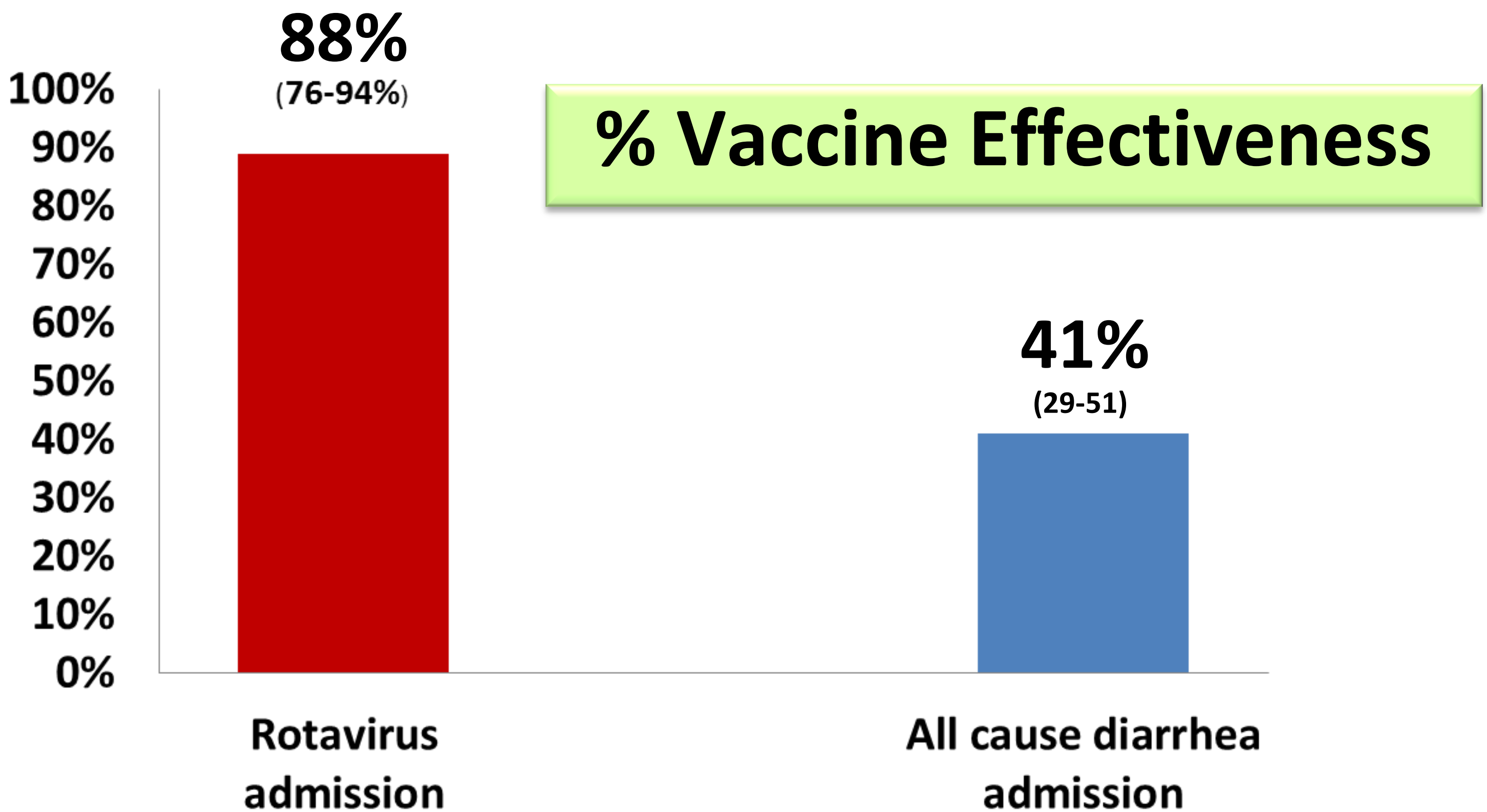
- No intussusception

The first child to receiving rotavirus vaccine under EPI. Picture courtesy of MOPH

RV1 effectiveness study comparing Sukhothai (vaccinated) with Petchaboon (non vaccinated) Sep 2012-14

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

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



- 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.

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

Age at onset (months)	RV vaccine coverage in Sukhothai (%)	% decline in Rotavirus hospitalization
6-11	97	90
12-23	97	85
24-35	68	60
36-47	<1	69
48-59	<1	40

HERD PROTECTION: Older children not vaccinated experienced a 40-69% reduction in RV hospitalization

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

Vaccine. 2017 Feb 1;35(5):796-801. doi: 10.1016/j.vaccine.2016.12.043. Epub 2017 Jan 3.

Evaluating the first introduction of rotavirus vaccine in Thailand: Moving from evidence to policy.

Tharmaphornpilas P[1], Jiamsiri S[2], Boonchaiya S[2], Rochanathimoke O[3], Thinyounyong W[4], Tuntiwitayapun S[5], Guntapong R[6], Riewpaiboon A[3], Rasdjarmrearnsook AO[2], Glass RI[7].

Author information

Abstract

BACKGROUND: We assessed the effectiveness and possible impact of introducing rotavirus vaccine into the routine immunization program.

METHODS: Two provinces were selected for an observational study, one where vaccine was introduced and another where vaccine was not available. In these areas, two sub-studies were linked. The prospective cohort study enrolled children 2month old and followed them to the age of 18months to detect all diarrhea episodes. The hospital surveillance study enrolled all children up to age 5 hospitalized with diarrhea whose fecal samples were tested for rotavirus. Rates of rotavirus hospitalizations in older children who had not been vaccinated in both settings provided data to determine whether immunization had an indirect herd effect. The key endpoints for the study were both vaccine effectiveness (VE) based upon hospitalized rotavirus diarrhea and herd protection.

FINDINGS: From the cohort study, the overall VE for hospitalized rotavirus diarrhea was 88% (95%CI 76-94). Data from hospital surveillance indicated that for 2 consecutive years, the seasonal peak of rotavirus admissions was no longer present in the vaccinated area. Herd protection was observed among older children born before the rotavirus vaccine program was introduced, who experienced a 40-69% reduction in admission for rotavirus.

CONCLUSIONS: Rotavirus vaccine was highly effective in preventing diarrheal hospitalizations and in conferring herd protection among older children who had not been vaccinated.

KEYWORDS: Rotavirus vaccine; Vaccine effectiveness; Vaccine impact

PMID: 28057385 DOI: 10.1016/j.vaccine.2016.12.043

Economic & Financial Issues (Public Health & Individual Perspective)

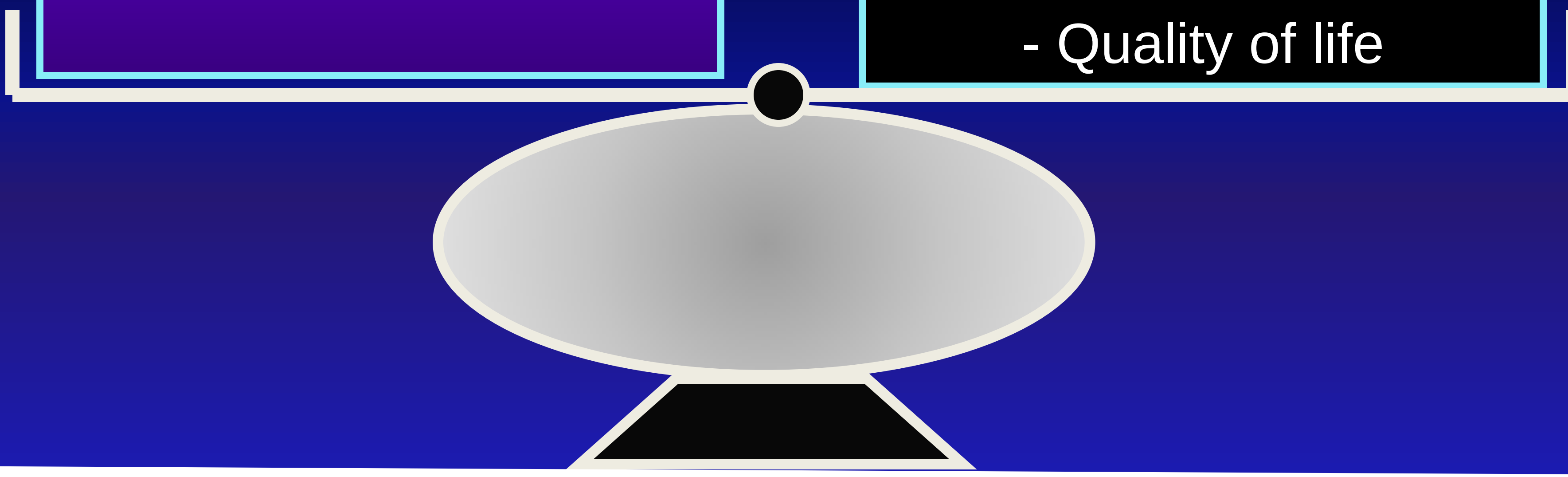
Cost of Programs/Services

Cost-averted

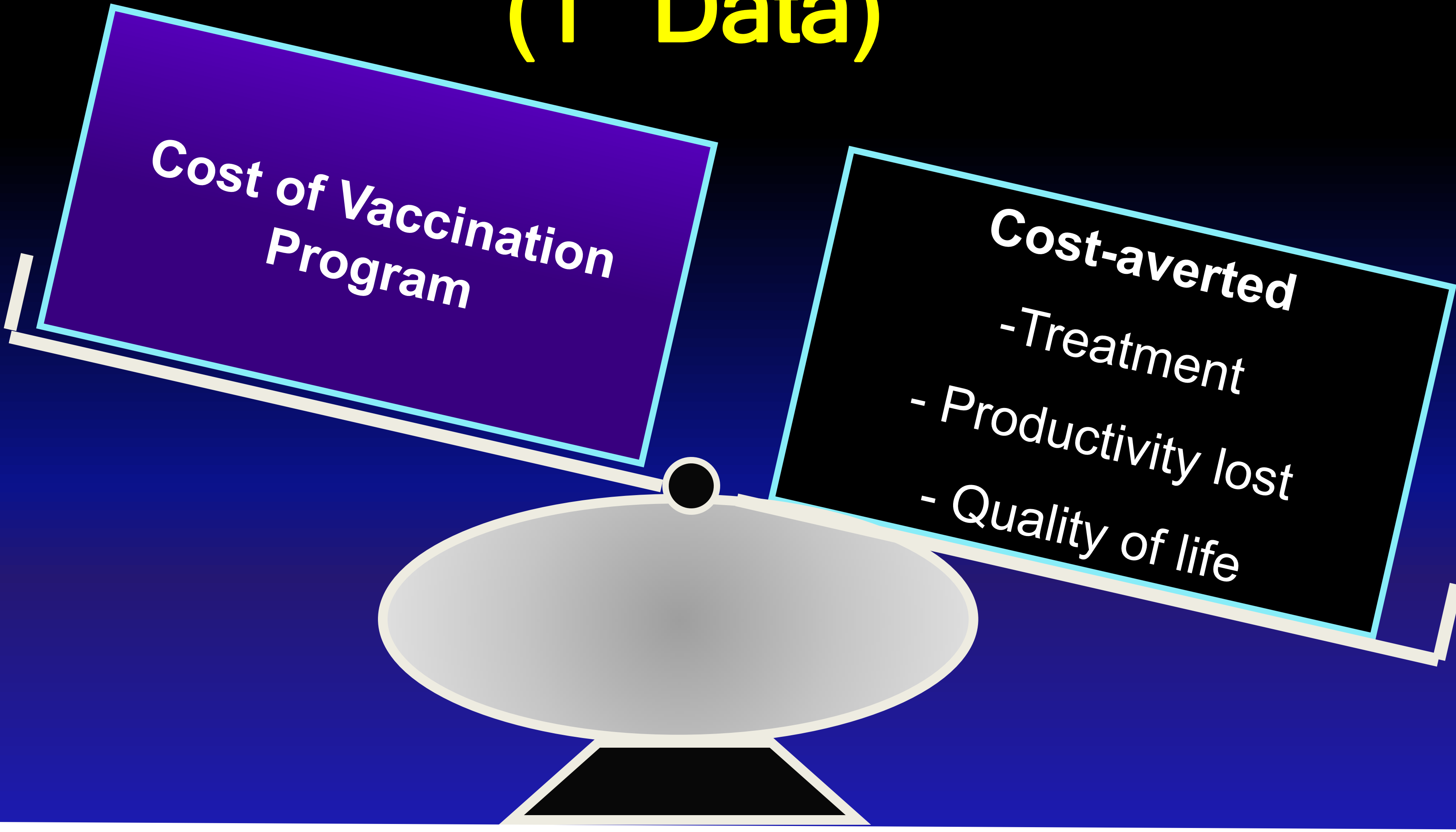
-Treatment

- Productivity lost

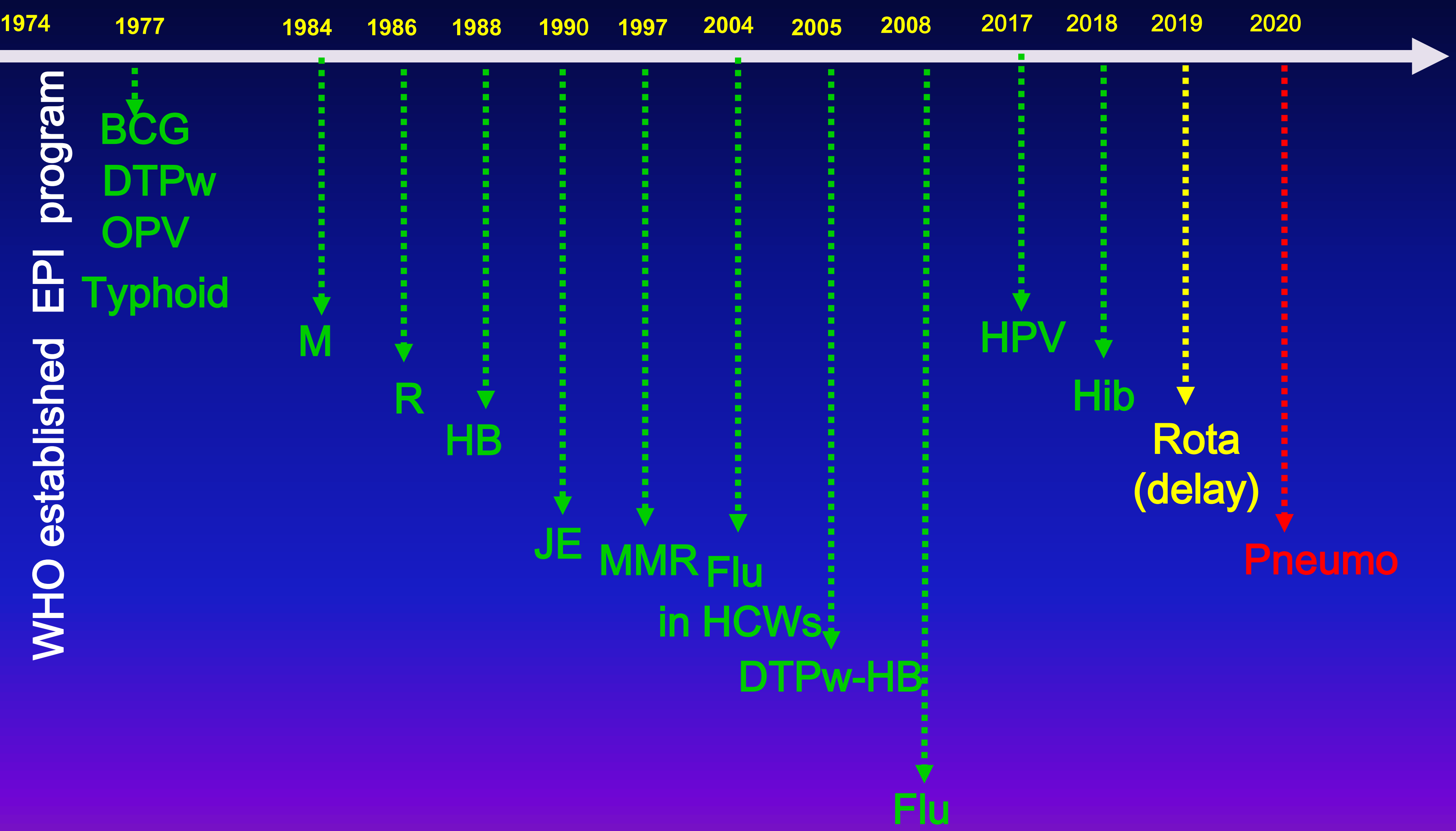
- Quality of life



Economic & Financial Issues (1° Data)

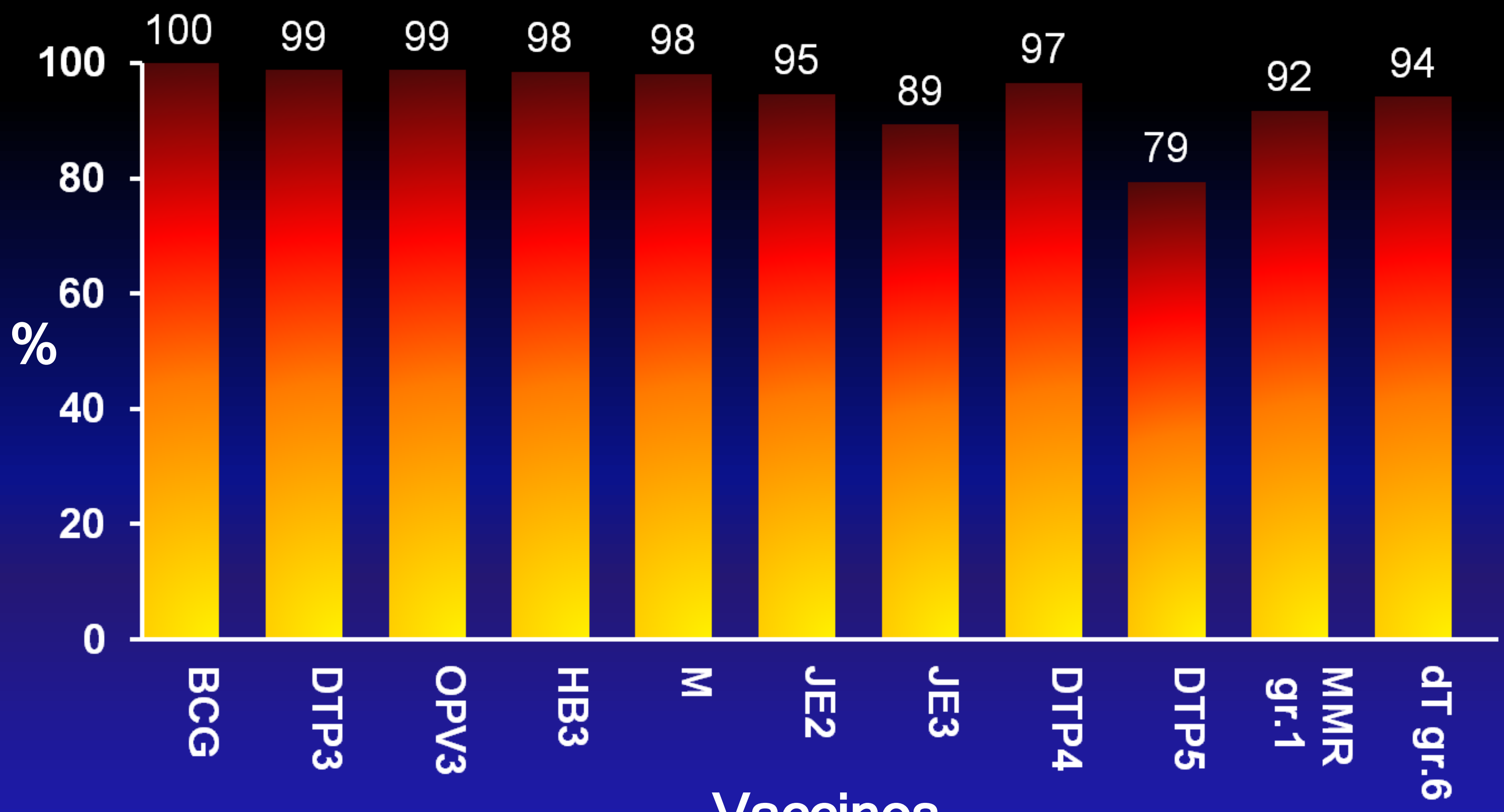


New Vaccine Introduction in Thai EPI



Source: modified from DDC, MOPH 2009

EPI Vaccine Coverage of Thailand



Source: modified from DDC, MOPH 2009

BMA-Bangkok Metropolitan Administration press released on rotavirus vaccine introduction

First campaign of the rotavirus immunization of the BMA-Bangkok Metropolitan Administration, Thailand, in Jan 2019

Conclusion

- Rotavirus is well known for the most common cause of severe diarrhea in infants and young children worldwide, resulting in dehydration with shock, electrolyte imbalance and death
- Vaccination as part of a comprehensive approach to diarrheal disease control offers the best hope for protecting children from rotavirus
- Despite the WHO recommendation that rotavirus vaccines be introduced into every country’s national immunization program, over 90 million children throughout the world still do not have access to this critical intervention

Conclusion 2

- Among middle income countries, **strong & clear system of the introductory consideration at the national level** is the important successful factor (in Thailand), including
  - **Advisory Committee on Immunization Practices (ACIP**), could facilitate the uptake of new vaccines and support evidence-based decision-making in the administration of national immunization programs
  - **Economical analysis and financing mechanisms** for the purchase of new vaccines have shown their potential
  - **Research agenda performed in the country** encouraging for better understanding of the vaccine impact, effectiveness and safety are strongly influential to the decision of introduction

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Thank you