



VACCINOLOGY 2016

X International Symposium for Latin American Experts
September 20 - 22 | Brasília

Vaccination: lost opportunities

José Esparza MD, PhD

- **Adjunct Professor, Institute of Human Virology, University of Maryland School of Medicine, Baltimore, MD, USA.**
- **Formerly at the World Health Organization (Geneva, Switzerland) and the Bill & Melinda Gates Foundation (Seattle, WA, USA).**

Outline

- The public health value of vaccination
- Different types of vaccine hesitancy
- Some historical examples of vaccine introduction and impact
- The case of dengue vaccines
- Conclusions

Ten Great Public Health Achievements of the 20th Century (in the US)

1. **Vaccines**
2. Motor vehicle safety
3. Workplace safety
4. Control of infectious diseases
5. Decline in deaths from heart disease and stroke
6. Safer and healthier foods
7. Healthier mothers and babies
8. Family planning
9. Fluoridation of drinking water
10. Tobacco as a health hazard

The value of vaccination

“The impact of vaccination on the health of the world’s people is hard to exaggerate. With the exception of safe water, no other modality has had such a major effect on mortality reduction and population growth”



Stanley Plotkin (2013)

Vaccine-preventable diseases, by year of vaccine development or licensure. United States, 1798-1998.

Vaccine	Introduction
Smallpox	1798
Rabies	1885
Typhoid	1896
Cholera	1896
Plague	1897
Diphtheria	1923
Pertussis	1926
Tetanus	1927
Tuberculosis	1927
Influenza	1945
Yellow fever	1953
Polio (Salk)	1955
Measles	1963

1963: OPV

Vaccine	Introduction
Rubella	1969
Anthrax	1970
Meningitis	1975
Pneumonia	1977
Adenovirus	1980
Hepatitis B	1981
H. Influenza B	1985
Japanese encephalitis	1992
Hepatitis A	1995
Varicella	1995
Lyme disease	1998
Rotavirus	1998

2009: HPV

More vaccines are available to protect against more diseases (US)

VACCINES IN 1990	
Diphtheria Tetanus Pertussis	DTP
Polio- OPV	
Measles Mumps Rubella	
Hib conjugate	

VACCINES IN 2011		
Diphtheria Tetanus Pertussis	DTaP	Hepatitis B
Polio- IPV		Varicella
Measles Mumps Rubella		HPV
Hib conjugate	MMR	Pneumococcal disease
		Influenza
		Rotavirus
		Hepatitis A
		Meningococcal disease

Timelines of currently available vaccines

B



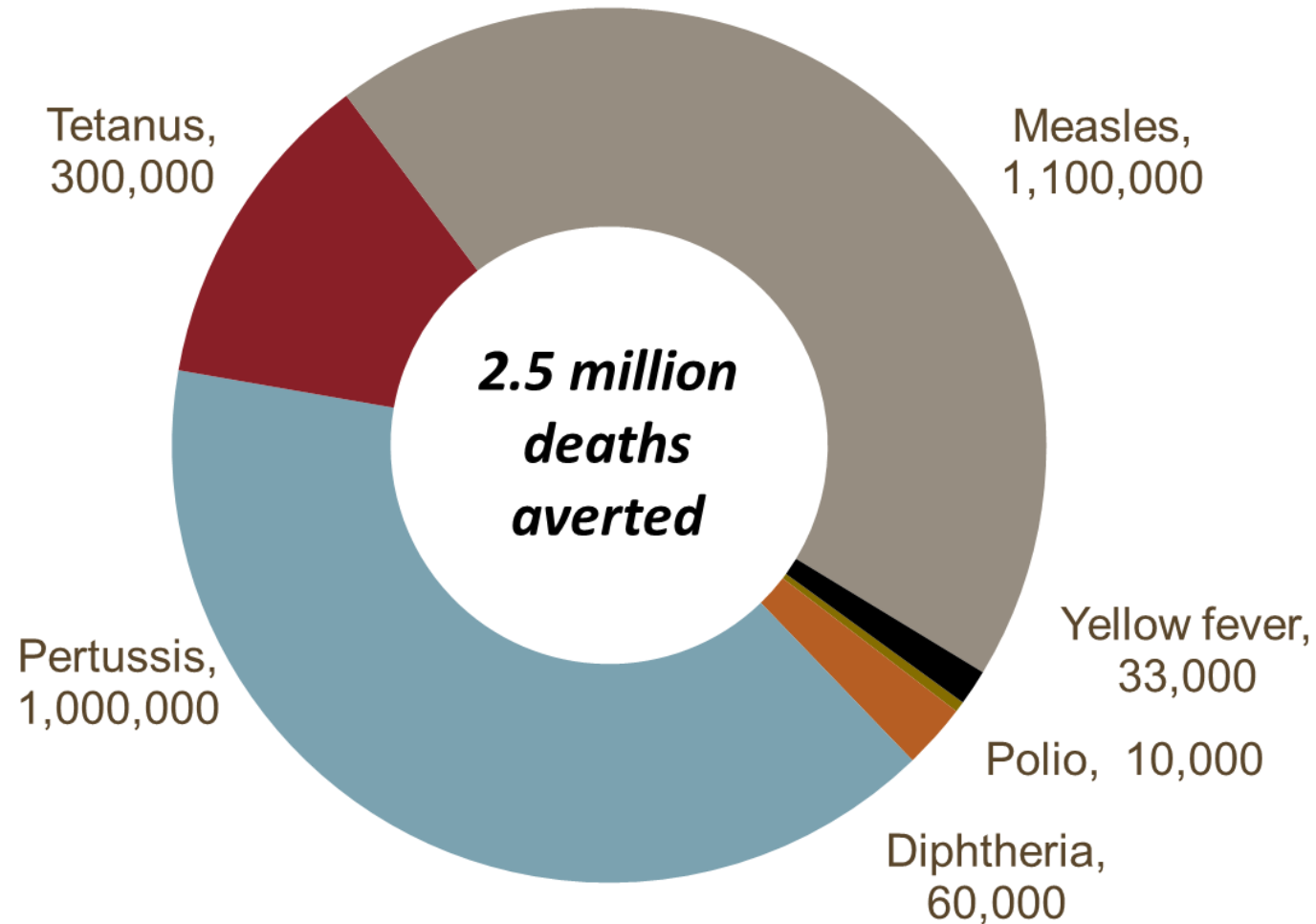
Vaccine preventable diseases: then and now (2010). United States.

Disease	20 th Century Annual Mortality	2010 Reported Cases	% reduction
Smallpox	29,005	0	100 %
Diphtheria	21,053	0	100 %
Measles	530,217	61	> 99 %
Mumps	162,344	2,528	98 %
Pertussis	200,752	1,291	89 %
Polio (paralytic)	16,316	0	100 %
Rubella	47,745	6	> 99 %
Congenital rubella syndrome	152	0	100 %
Tetanus	580	8	99 %
Haemophilus influenza B	20,000	270	99 %



†Source: JAMA. 2007;298(18):2155-2163
 †† Source: CDC. MMWR January 7, 2011;59(52);1704-1716. (provisional MMWR week 52 data)
 * 16 type b and 254 unknown serotype (< 5 years of age)

Vaccines save millions of lives annually

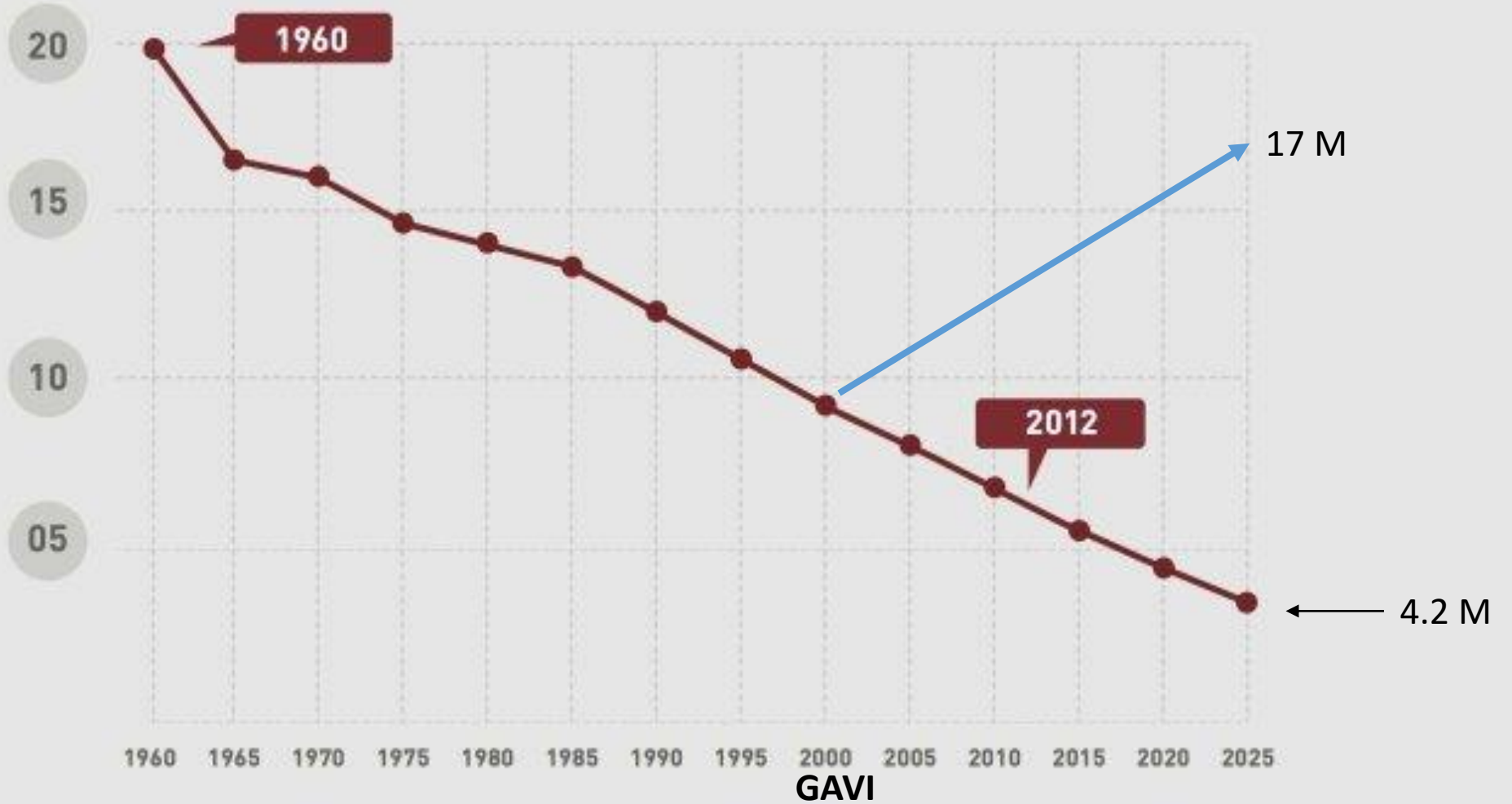




“Bill Gates Chart”

CHILDREN WHO DIE BEFORE AGE 5

MILLIONS



The current world immunization efforts are achieving:

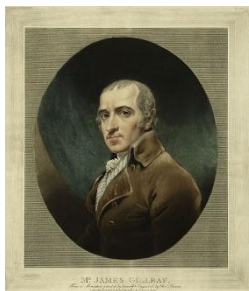
- **Equity between high and low-income countries**
- **Bringing the power of vaccines to even the world's poorest countries**
- **Reducing morbidity and mortality in developing countries**
- **Eliminating and eradicating disease**



Vaccine hesitancy: WHO definition

“Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services.”

Vaccine hesitancy started with the introduction of the smallpox vaccine more than two hundred years ago.



James Gillray, 1802

Six reasons to oppose vaccination (England, 19th Century)

- Business competition with variolation.
- Principles are not well understood (especially after the Age of Enlightenment).
- Vaccination is ineffective.
- Vaccination is not safe.
- Religious and philosophical concerns.
- Resistance to compulsory vaccination.

J. Esparza. "A historical perspective on public trust in vaccines." *Symposium on Public Confidence on Vaccines*
London School of Hygiene and Tropical Medicine, 25 April 2014

Five reasons to oppose vaccination (in the 21st Century)

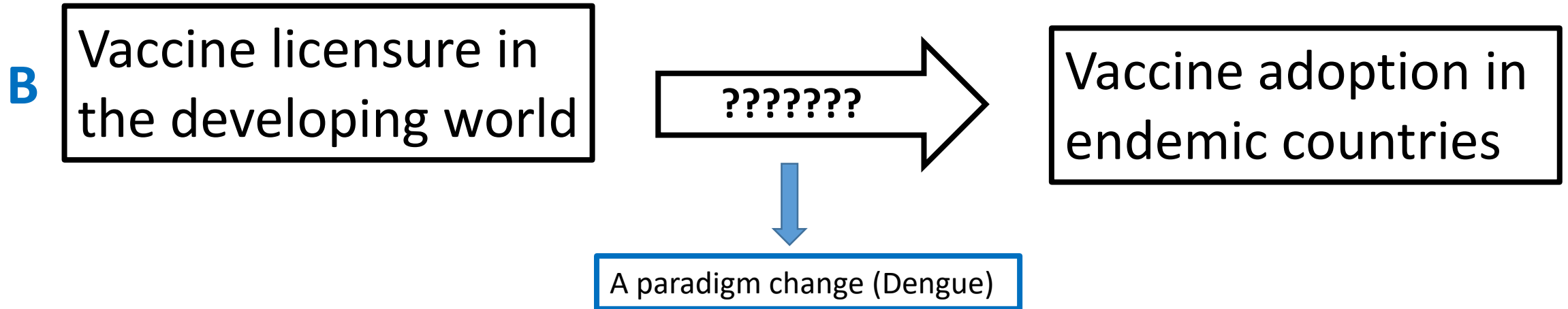
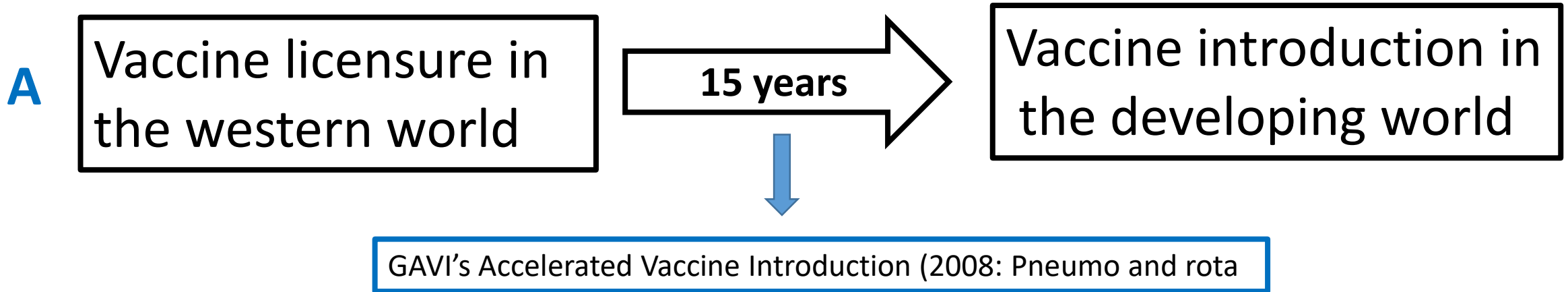
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**Same reasons for
vaccine hesitancy in
the 21st century!**

C McKee, K. Bohannon. Exploring the reasons behind parenteral refusal to vaccines.

J Pediatr Pharmacol Ther 2016 21(2):104-109

Other types of vaccine hesitancy: delays in adopting new vaccines



GAVI's approach to accelerate new vaccine introduction

- Ensure sufficient supply
- Secure adequate funding
- Support informed country decisions
- Facilitate country introduction
- Establish a platform for future vaccines

A historical example of vaccine introduction: Smallpox vaccination and eradication

- 1796-1798: Smallpox vaccine developed by Edward Jenner
- From early 1800s: Vaccine rapidly introduced, worldwide
 - 1800: Introduced in the US (Boston) by Benjamin Waterhouse
 - 1803-1806: Balmis Expedition to vaccinate Spanish colonies
- Smallpox eradication
 - 1967: Initiation of the WHO Smallpox Eradication Programme
 - 1977: Last case of naturally occurred smallpox (Somalia)
 - Total cost of the eradication campaign: Around USD 300 M
 - 1980: WHO declares smallpox to be eradicated

The Vaccination Monster (London, 1880)



The National Anti-Vaccination League argued that in 1880 smallpox vaccination was causing the deaths of 25,000 children.

The power of (smallpox) vaccines

- **In 1967 WHO initiated the Intensified Smallpox Eradication Campaign**
 - **Estimated number of cases in 1967: ?**
 - **Estimated number of deaths in 1967: ?**
 - **Number of countries affected: ?**

The power of (smallpox) vaccines

- In 1967 WHO initiated the Intensified Smallpox Eradication Campaign
 - Estimated number of cases in 1967: **10-15 million**
 - Estimated number of deaths in 1967: **2.6 million**
 - Number of countries affected: **31**

The power of vaccines is such that they do not only eradicate the disease, *but also the memory of the disease.*

A historical example of vaccine introduction: Polio vaccination and potential eradication

- 1908: First isolation of the poliovirus in Austria (Karl Landsteiner and Erwin Popper)
- 1935: Failed vaccine trials in the US (Maurice Brodie; William Park and John Kolmer)
- 1954-1955: Salk (IPV) vaccine trial involved 1.8 million volunteers mostly in the US
 - **Results announced at the University of Michigan on April 12, 1955 at 10:20 am**
 - **Vaccine licensed by the NIH the same day at 5:15 pm**
 - **Within the next five days five pharmaceutical companies were mass producing the vaccine**
 - **The “March of Dimes” had invested USD 9 million (USD 109 in today’s money) to manufacture the vaccine.**
 - **The goal was to prevent the next epidemic wave in the US during the Summer of 1955.**
- 1959: Sabin (OPV) vaccine trial involved 15 million volunteers in the former Soviet Union
 - Vaccine licensed in the US in 1963.
- Both vaccines, IPV and OPV, have contributed to the control and hopefully to the future eradication of poliomyelitis.

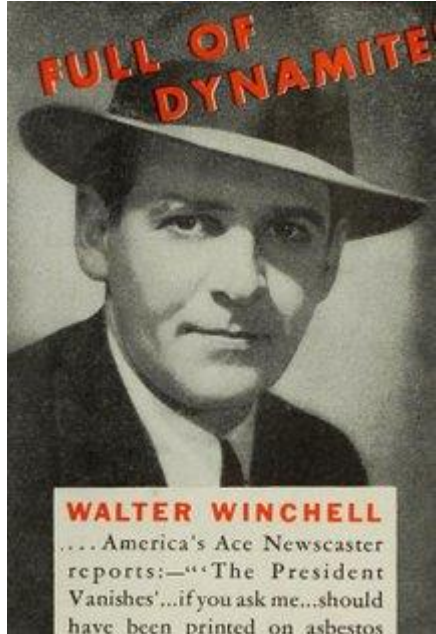
“Little white coffins”

April 4, 1954

"Good evening, Mr. and Mrs. America ... and all the ships at sea. Attention everyone. In a few moments I will report on a new polio vaccine claimed to be a polio cure. It may be a killer."

Commercial pause.

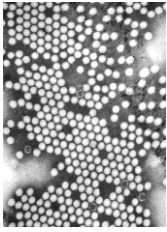
"Good evening, Mr. and Mrs. America, and all the ships at the sea... Attention all doctors and families: the National Foundation for Infantile Paralysis Plans to inoculate one million children with a new vaccine this months... The U.S. Public Health Service tested ten batches... They have found (I am told) that seven of the ten contained live (not dead) poliovirus... That it killed several monkeys... The name of the vaccine is the Salk Vaccine; named for Dr. Jonas Salk of the University of Pittsburg."



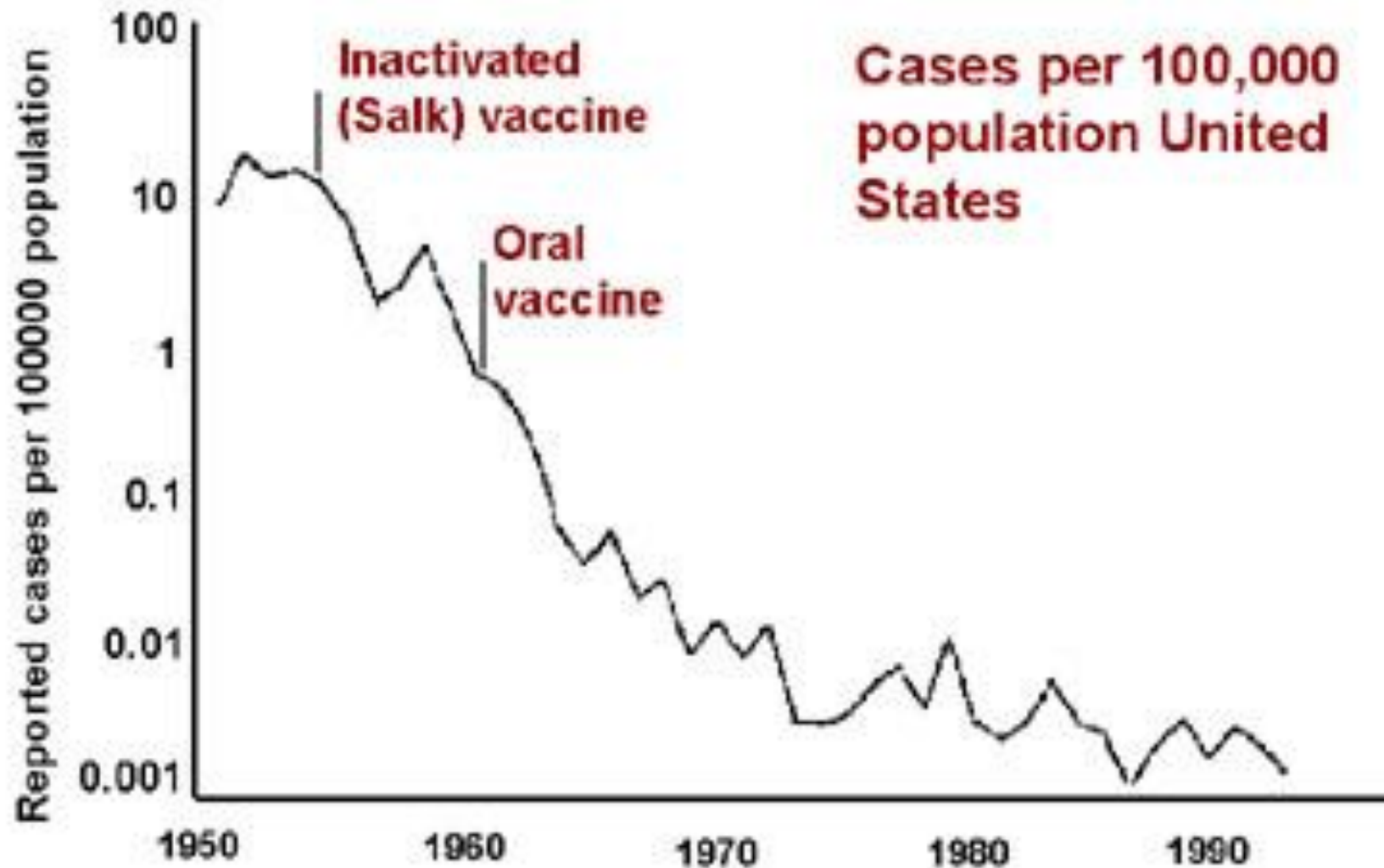
Walter Winchell

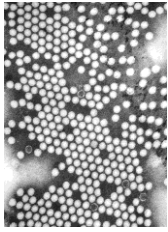
THE SALK VACCINE MUST NOT BE LICENSED!

EVERY U. S. SENATOR & U. S. CONGRESSMAN OWE IT TO YOU (THE PUBLIC) TO DEMAND AN IMMEDIATE OPEN HEARING ON "THE TRUTH ABOUT POLIO" INVITING DOCTORS OF EVERY HEALING PROFESSION TO TESTIFY. WHEN "POLIOPHOBIA" IS EXPOSED AND REPLACED WITH "TRUTH" NO POLIO VACCINE WILL EVER BE LICENSED.



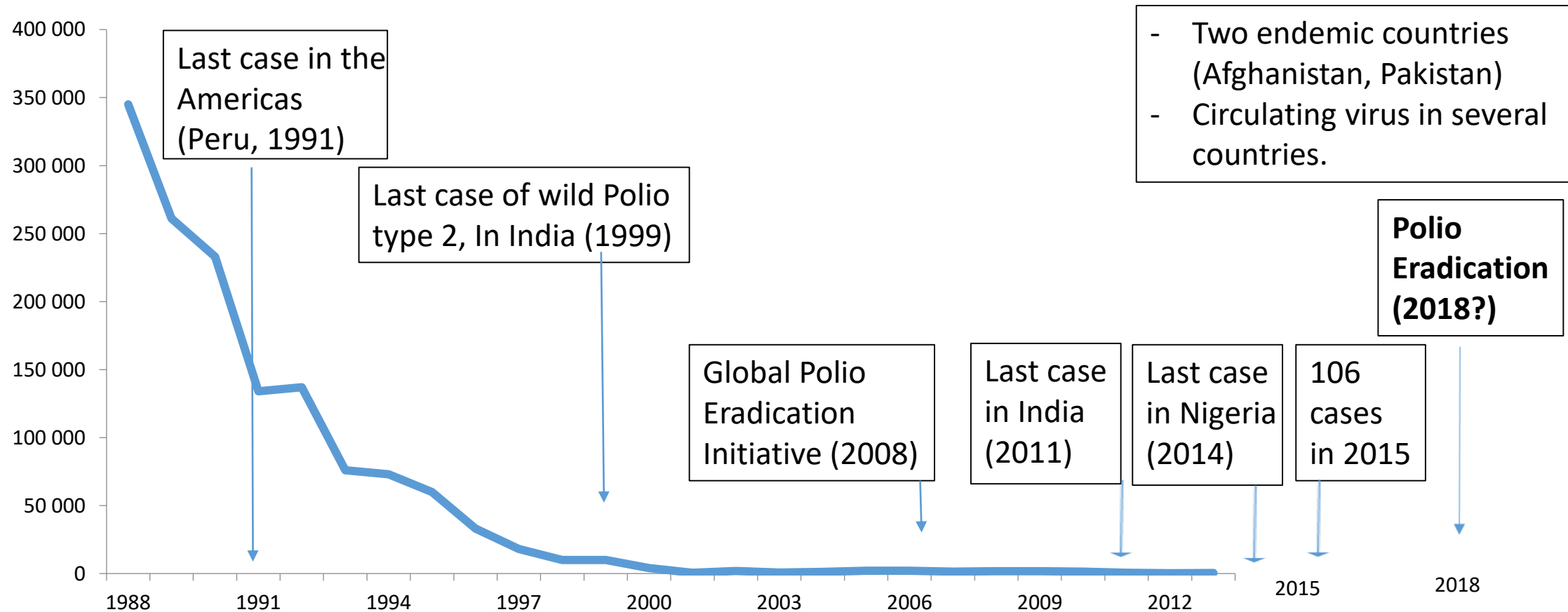
Impact of polio vaccination in the US





The job is not completed: final push on polio eradication

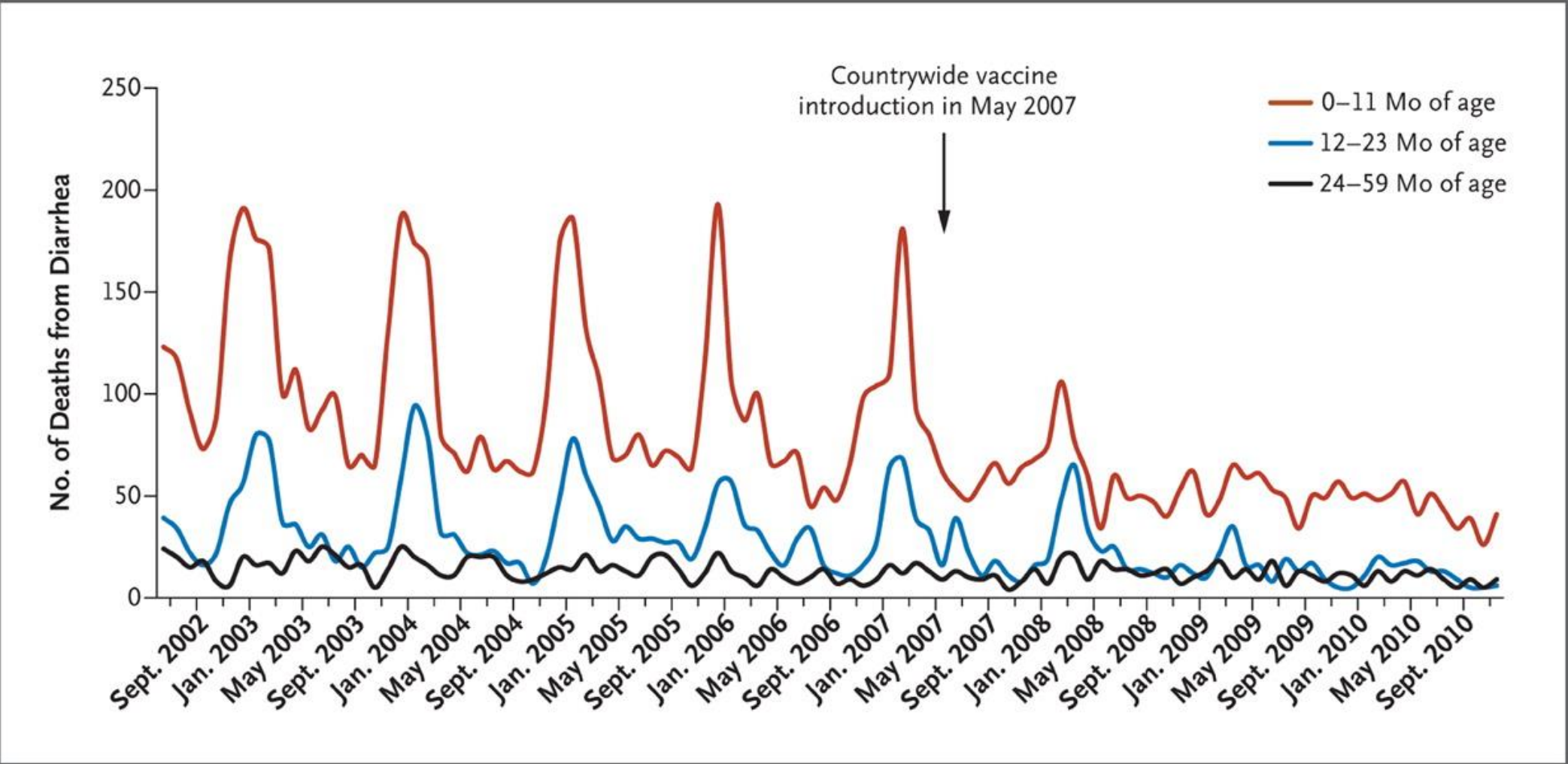
Global Polio Cases



A historical example of vaccine introduction: Rotavirus vaccines

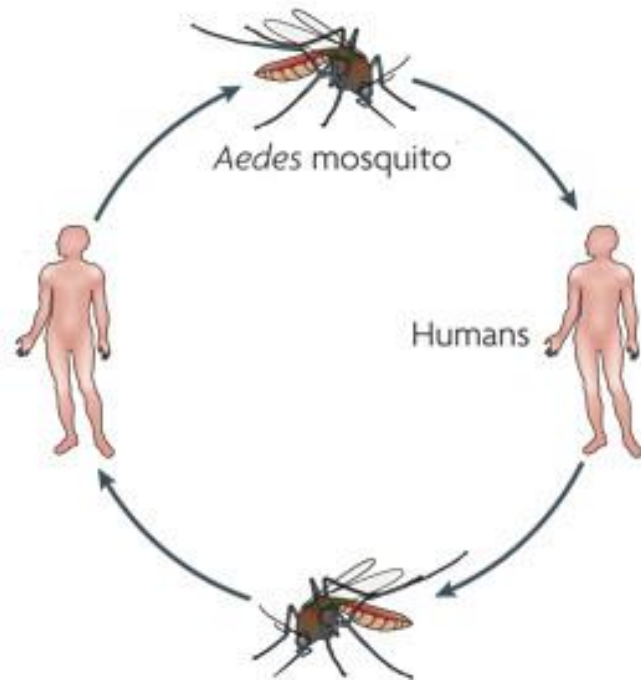
- 1973: Rotavirus discovered in Australia (Ruth Bishop et al)
- 1998: Licensing of RotaShield® from Wyeth
- 1999: Fatal cases of intussusception associated with vaccination
- Paradigm change: vaccine prevention of severe disease
- Subsequent rotavirus vaccines:
 - 2006: RotaTeq® from Merck (bovine-human rotavirus gene reassortant)
 - 2008: Rotarix® from GSK (attenuated human rotavirus)

Rotavirus vaccine effectiveness in Mexico



V Richardson, U Parashar, M Patel. *N Engl J Med* 2011; 365:772-773

Dengue: Multiple opportunities to intervene



PREVENTING TRANSMISSION TO SUSCEPTIBLE HOSTS:

VECTOR CONTROL

- Environmental Management
- Chemical control
- Biological control
- Wolbachia-based biocontrol
- (Also important for the control of chikungunya and zika)

PREVENTING INFECTION OF SUSCEPTIBLE HOSTS:

VACCINE

- To protect susceptibles and interrupt chain of transmission
- Contribution to both, reduction of morbidity and of mortality

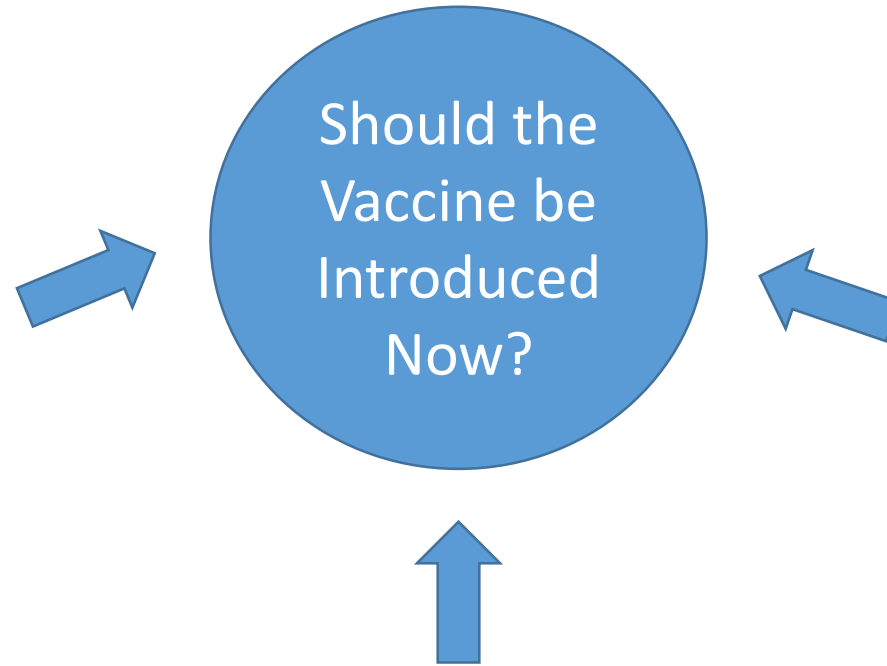
PREVENTING SEVERE DISEASE AND DEATH OF INFECTED PEOPLE:

CASE MANAGEMENT

Overview: Deciding on the introduction of a Vaccine

THE DISEASE

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



THE VACCINE

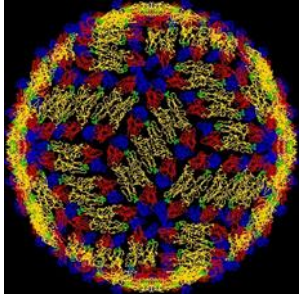
- Performance and characteristics of available vaccines.
- Economic and financial issues.
- Availability of vaccine supply.

STRENGTH OF THE IMMUNIZATION PROGRAMME AND HEALTH SYSTEM

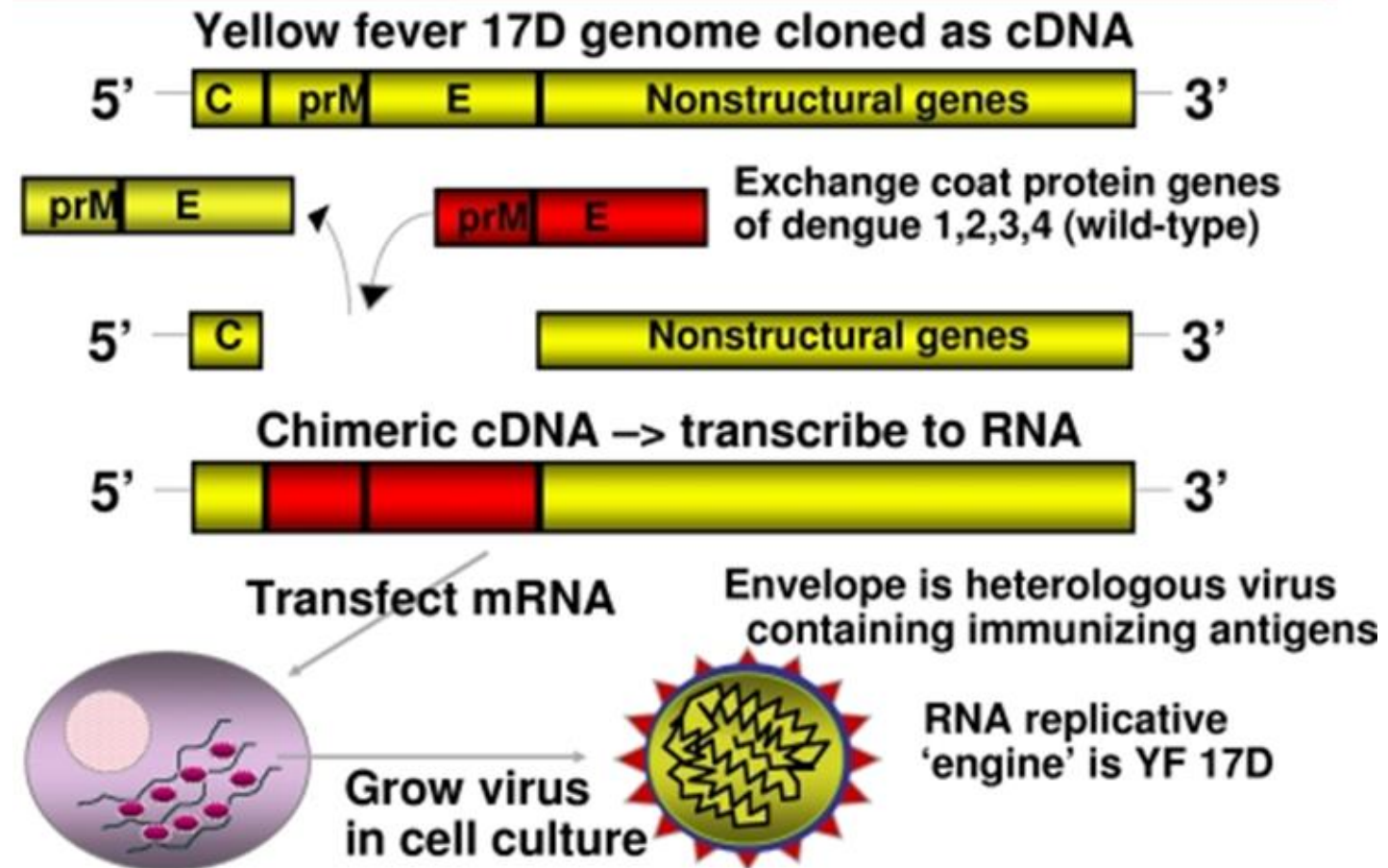
- Consider ways to strengthen these during a new vaccine introduction

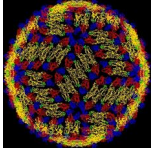


The development of a dengue vaccine



ChimeriVax Technology





Fair questions regarding the CYD-TDV dengue vaccine

- Is the vaccine sufficiently effective?
- Were the number of endpoints in the trials sufficient?
- Is the vaccine sufficiently safe?
- What about if an improved vaccine is developed in the future?
- What would be the consequences of delaying the introduction of the vaccine?
- Would the vaccine be available in sufficient quantity?
- Would the use of the vaccine be cost-efficient?
- Would the vaccine replace other dengue prevention and control interventions?

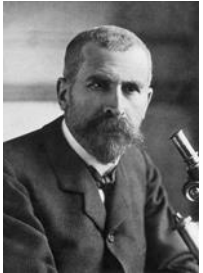
Conclusions 1

- In the past, the rapid introduction of vaccines were critical in the control and eventual eradication of major epidemic diseases.
- A dengue vaccine will complement (not replace) other dengue prevention and control measures.
- A dengue vaccine will be essential to achieve the WHO goals of 25% reduction of morbidity and 50% reduction of mortality by 2020.
- Delaying decision regarding the introduction of dengue vaccines could have important public health and economic implications.

Conclusions 2

- In the case of one CYD-TDV dengue vaccine, the experimental evidence, specially from phase III clinical trials, suggests that its introduction in public health programs is advisable based on its safety and efficacy profiles.
- The recommendations from the **WHO Strategic Advisory Group of Experts on Immunization (SAGE)** (*Weekly epidemiological record, No 30, 91:349-364; 29 July 2016*) provides a rational pathway for future decisions and research.
- If “better” (or improved) vaccines are developed in the future, the adoption of a dengue vaccine strategy now will facilitate future introductions, **and the goal of global control of the dengue pandemic could become a reality.**

**“Science appears calm and triumphant when it is completed;
but science in the process of being done
is only contradiction and torment,
hope and disappointment”**



Emile Roux

Inauguration of monument to Pasteur in Dôle, August 3, 1902

***From Stanley Plotkin’s lecture at the opening session of the
XIII AIDS Vaccine Conference. Barcelona, Spain, October 2013.***



~“Future generations will judge us not by the science we did, but how that science was used to solve inequities in the world.”



Bill Gates

Many thanks for your attention