# Vaccinology - introduction

Gregory Hussey

Vaccines for Africa Initiative

Institute of Infectious Diseases

University of Cape Town




www.vacfa.com gregory.hussey@uct.ac.za

# Outline

- Information sources
- History of vaccines
- Recent developments
- Where are the vaccines being made
- Impact of vaccines
- Trends in vaccinology
- Expanded Programme on Immunization
- The future


KIA

# THE NEW ENGLAND JOURNAL OF MEDICINE PUBLISHES RESULTS OF FINAL LANDMARK PHASE III EFFICACY CLINICAL STUDY OF SANOFI PASTEUR'S DENGUE VACCINE CANDIDATE

**November 03, 2014**

## The New England Journal of Medicine Publishes Results of Final Landmark Phase III Efficacy Clinical Study of Sanofi Pasteur's Dengue Vaccine Candidate

***- Study successfully met primary objective and confirms high efficacy against severe dengue and hospitalization -***

***- Sanofi Pasteur intends to file for registration in several endemic countries in 2015 -***

***- Dengue vaccine candidate would address an urgent unmet medical need in tropical and sub-tropical regions of the world -***

# Pfizer Receives FDA Accelerated Approval for TRUMENBA® (Meningococcal Group B Vaccine) for the Prevention of Invasive Meningococcal B Disease in Adolescents and Young Adults

TRUMENBA is the First and Only Approved Vaccine in the U.S. for the Prevention of Meningococcal Meningitis B

Wednesday, October 29, 2014 - 2:44pm EDT

Pfizer Inc. (NYSE:PFE) announced today that the U.S. Food and Drug Administration (FDA) has granted accelerated approval of TRUMENBA® (meningococcal group B vaccine) for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B in individuals 10 through 25 years of age. Approval of TRUMENBA is based on demonstration of immune response, as measured by serum bactericidal activity against four serogroup B strains representative of prevalent strains in the United States. The effectiveness of TRUMENBA against diverse serogroup B strains has not been confirmed. As part of the accelerated approval process, Pfizer will complete its ongoing studies to confirm the effectiveness of TRUMENBA against diverse serogroup B strains.

TRUMENBA was reviewed and approved under the FDA's Breakthrough Therapy designation and Priority Review programs.

# GSK hepatitis C shot shows promise, bodes well for Ebola vaccines

BY **KATE KELLAND**

LONDON | Wed Nov 5, 2014 2:01pm EST



**RELATED NEWS**

German doctors use experimental heart drug in treating Ebola patient

Exclusive: U.S. Ebola researchers plead for access to virus samples

(Reuters) - A new hepatitis C vaccine from GlaxoSmithKline based on the same technology as an experimental Ebola shot being fast-tracked through human trials has shown promise in early clinical tests, prompting strong and broad immune responses.

# ACIP considers data on 9-valent HPV vaccine

February 28, 2014



The Advisory Committee on Immunization Practices heard data on an investigational 9-valent HPV vaccine being developed by Merck.

**See Also**

Data indicate qHPV vaccine provides long-term protection ...

HPV vaccine coverage rates equal call to action for providers ...

New HPV seroprevalence data may help guide vaccine ...

**Featured**

The vaccine demonstrated noninferior immunogenicity for HPV types 6, 7, 16 and 18 compared with the quadrivalent HPV vaccine (Gardasil, Merck) and offered 97% protection against the five additional HPV serotypes: 31, 33, 45, 52 and 58. In addition, the vaccine demonstrated noninferior immunogenicity in adolescents compared with adults.

Additional data presented indicate that 50% of high-grade cervical lesions are attributable to HPV types 16 and 18 and another 25% are attributable to the five additional serotypes in the 9-valent vaccine. Other data indicate that 62% of HPV-associated cancers are attributable to HPV types 16 and 18 and another 11% are attributable to the five additional serotypes.

# AN HIV VACCINE:

## THE WORLD'S BEST LONG-TERM HOPE FOR ENDING AIDS

### WHO WE ARE

We are the world's largest publicly-funded international collaboration focused on the development of vaccines to prevent HIV/AIDS. Learn more >

### WHAT WE DO

Our sites conduct all phases of clinical trials - from evaluating experimental vaccines for safety and immunogenicity to testing vaccine efficacy. Learn more >

### GET INVOLVED

Worldwide, thousands of people have participated in HIV vaccine trials. Volunteers are the heroes of vaccine development. Learn more >

## NEWS FEATURE

**HIV vaccine trial passes first hurdle in South Africa**

The first in a series of clinical trials designed to build on the promise of an HIV vaccine that showed modest protection when tested in Thailand has passed a key hurdle, according to a new study. It paves the way for larger HIV vaccine trials to move forward in South Africa.

# www.vacfa.com

VACFA
vaccines
for africa


home | about vacfa | links | resources | news | glossary | feedback | contact | ssa pvpd

An Africa free of vaccine preventable diseases.

Our mission is to increase awareness of the benefits of vaccines and to promote uptake of traditional and new vaccines in Africa.

**Search**

Search this site...

**Interactive Map**

Vaccination statistics in Africa

**Vaccines**

The importance of vaccines

Expanded Programme on Immunisation

## latest news

**Tenth Annual African Vaccinology Course**

VACFA
vaccines
for africa

***Tenth Annual African Vaccinology Course***

***10-14 November 2014, Cape Town, South Africa***

***About the course:***

- Convened by Prof. Gregory D. Hussey of the VACFA, University of Cape Town, the annual

***Special course session on meet the specialist:***

- Participants ask any vaccines-related

World Health Organization

Health topics | Data | Media centre | Publications | Countries | Programmes | About WHO | Search

Health topics

## Immunization

WHO/Sergei Deshevoi

Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine. Vaccines stimulate the body's own immune system to protect the person against subsequent infection or disease.

Immunization is a proven tool for controlling and eliminating life-threatening infectious diseases and is estimated to avert between 2 and 3 million deaths each year. It is one of the most cost-effective health investments, with proven strategies that make it accessible to even the most hard-to-reach and vulnerable populations. It has clearly defined target groups; it can be delivered effectively through outreach activities; and vaccination does not require any major lifestyle change.

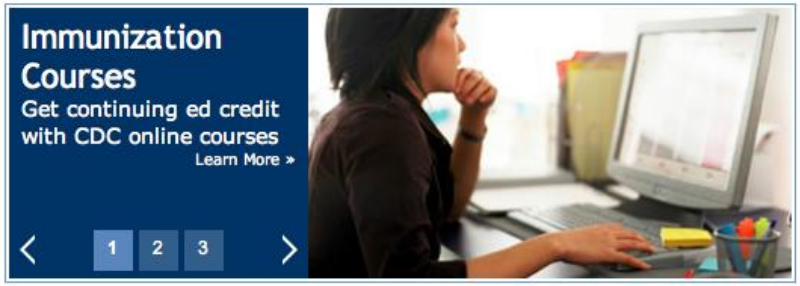
CDC Home

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

Vaccines and Immunizations | All CDC Topics | Choose a topic above | SEARCH

A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

## Vaccines & Immunizations




Past Vaccine Features

### In the Spotlight

- VFC: 20 years of preventing disease and saving lives (Apr 24)
- NEW Standards for Adult Immunization Practice (Apr 9)
- Noninfluenza Vaccination Coverage Among Adults – United States, 2012, MMWR (Feb 7)
- View all...

Email page link
Print page

Get email updates
To receive email updates about this page, enter your email address:
What's this? Submit

### Vaccines & Immunizations Topics


Vaccine Information for Parents

Immunization, Vaccines and Biologicals
Vaccines and diseases
Global Vaccine Action Plan
WHO policy recommendations
National programmes and systems
Monitoring and surveillance
Quality, safety and standards
Research and development
Research by disease
Implementation research
Advisory committees
Resource materials
Newsroom

# WHO Product development for vaccines advisory committee meeting

Share Print

1. Background, objectives and background documents
2. Presentations

## Presentations

### Day one

Why do we need PD VAC?
pdf, 1.05Mb
Vasee Moorthy, WHO Secretariat, Geneva, Switzerland

WHO written standards for regulatory evaluation of vaccines and biotherapeutic products
pdf, 603kb
Ivana Knezevic, WHO Secretariat, Geneva, Switzerland

The decade of vaccines global vaccine action plan
pdf, 1.62Mb
Joachim Hombach, WHO Secretariat, Geneva, Switzerland

GAVI's vaccine investment strategy
pdf, 1.07Mb
Judith Kallenberg, GAVI Alliance, Geneva, Switzerland

Tuberculosis vaccines
pdf, 1.99Mb
Georges Thiry, Tuberculosis Vaccine Initiative

RSV: The disease, the pathogen and the unmet medical need
pdf, 1.21Mb
Eric A.F. Simões, University of Colorado, Denver, USA

RSV vaccine development
pdf, 1.22Mb
Ruth Karron,

http://who.int/immunization/research/meetings_workshops/pdvac/en/index1.html

# A Photo Collection of Vaccine-Preventable Diseases

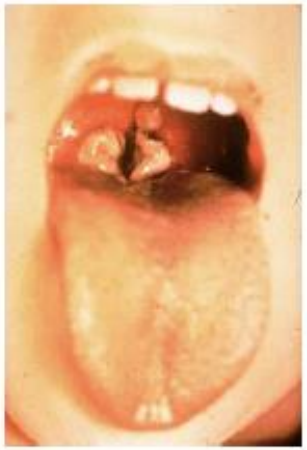
Created by the
Immunization Action Coalition

Updated May 2013

## Diseases for which vaccination is routinely recommended

- Diphtheria
- *Haemophilus influenzae* type b (Hib)
- Hepatitis A
- Hepatitis B
- Herpes zoster (shingles)
- Human papillomavirus (HPV)
- Influenza
- Measles
- Meningococcal disease
- Mumps
- Pertussis
- Pneumococcal disease
- Polio
- Rotavirus
- Rubella
- Tetanus
- Varicella (chickenpox)

Immunization Action Coalition • www.vaccineinformation.org • www.immunize.org



**Diphtheria:** This is a picture of the throat of a child who has diphtheria. Notice the thick gray coating over the back of the throat. If not treated, this child could die from suffocation.

Photo courtesy of the Centers for Disease Control and Prevention (CDC)

**Diphtheria:** This child has bullneck diphtheria.

Photo courtesy of the Centers for Disease Control and Prevention (CDC)

## Description

Quick access from CDC to ACIP-recommended immunization schedules, complete with footnotes. Intended for healthcare professionals recommending and administering vaccines to infants, children, adolescents, and adults. This app is one of an expanding collection of applications from CDC on a variety of specific topics, each optimized

CDC Vaccine Schedules Support ›

...More

## What's New in Version 1.1

Added 'Share This App' feature.

View in iTunes

This app is designed for both iPhone and iPad

**Free**

Category: Medical
Updated: May 29, 2014
Version: 1.1
Size: 3.9 MB
Languages: English, German
Seller: Centers for Disease Control and Prevention
© Centers for Disease Control and Prevention
Rated 12+ for the following:
Infrequent/Mild Medical/Treatment Information

**Compatibility:** Requires iOS 5.0 or later. Compatible with iPhone, iPad, and iPod touch. This app is optimized for iPhone 5.

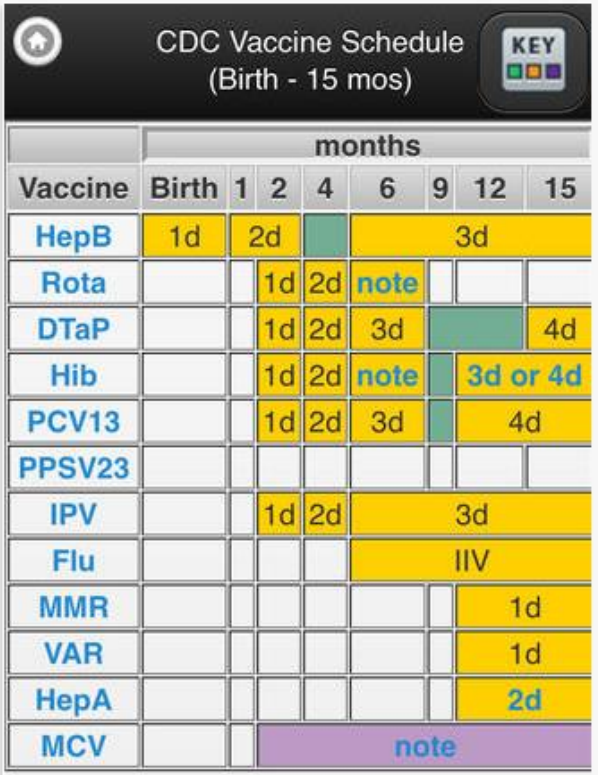
## Customer Ratings

We have not received enough ratings to display an average for the current version of this application.

## More by Centers For Disease Control and

## Screenshots

iPhone | iPad

Open iTunes to buy and download apps.


View in iTunes

**Free**

Category: Medical
Released: Aug 30, 2013
Version: 1.0
Size: 5.3 MB
Language: English
Seller: The Children's Hospital of Philadelphia

Rated 4+

**Compatibility:** Requires iOS 6.0 or later. Compatible with iPhone, iPad, and iPod touch. This app is optimized for iPhone 5.

## Customer Ratings

Current Version:
★★★★½ 6 Ratings

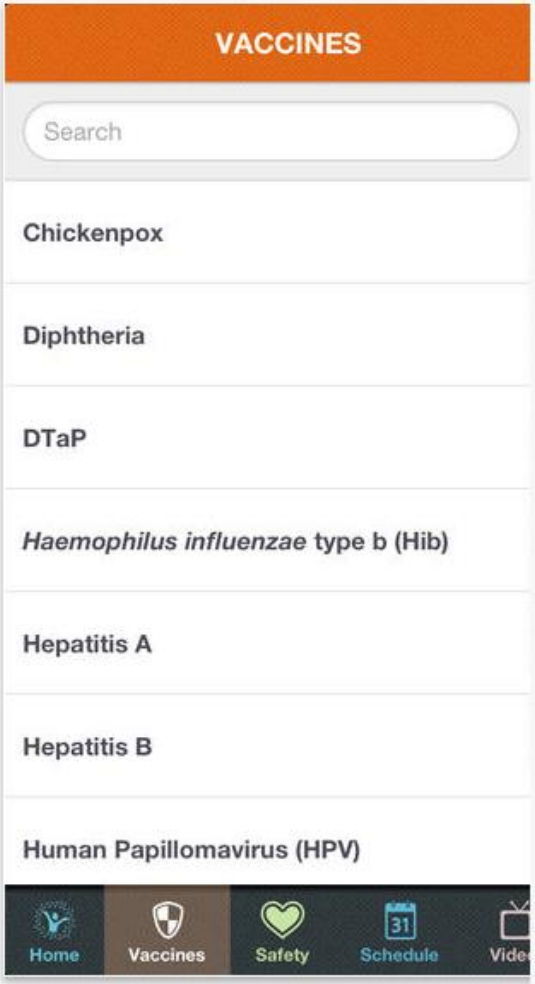
## More iPhone Apps by The Children's Hospital of Philadelphia


## Description

It is easier than ever to get health information; sometimes, however, it's difficult to weed out the "good" information (which is scientifically accurate) from the "bad" information (which is not based on science). This is especially true for vaccines.

The Children's Hospital of Philadelphia Web Site ▸ Vaccines on the Go: What You Should Know ...More
Support ▸ Application License Agreement ▸

## iPhone Screenshot

# Importance of Vaccines

- **Vaccines promote health:** unlike many other health interventions, they help healthy people stay healthy, removing a major obstacle to human development.

- **Vaccines have an expansive reach:** they protect individuals, communities, and entire populations (the eradication of smallpox is a case in point).

- **Vaccines have rapid impact:** the impact of most vaccines on communities and populations is almost immediate. For example, between 2000 and 2008, vaccination against measles reduced global deaths by 78% (from 750 000 deaths to 164 000 deaths per year).

- **Vaccines save lives and costs:** recently, a panel of distinguished economists put expanded immunization coverage for children in fourth place on a list of 30 cost-effective ways of advancing global welfare (Copenhagen Consensus, 2008).

Ack. WHO

# Child mortality in Africa

- Current estimates – 7.6m child deaths <5yrs of age
- Africa, which is home for about 20% of the world's children accounts for approximately 50% of global child deaths.
- 30-40% of deaths in children 1-59 months of age are vaccine preventable.
- Unlikely that Africa will meet the MDG4 target of reducing child mortality by 2/3 by 2015.

# 1.5 m Deaths due to vaccine preventable diseases

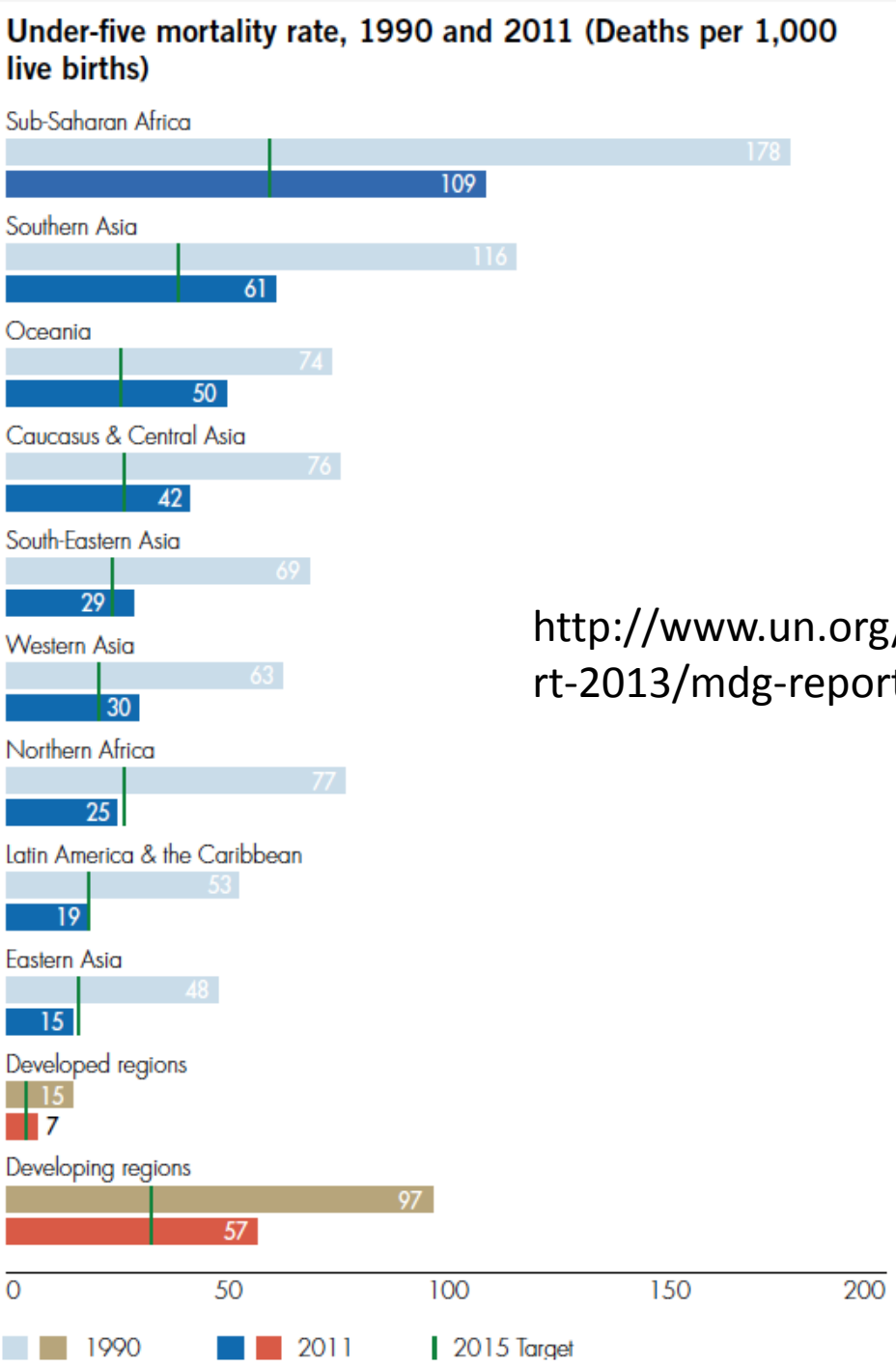
| Disease | Children < 5years |
|---|---|
| Pneumococcal disease | 476000 |
| Measles | 118000 |
| Rotavirus | 453000 |
| Heamophilus inf type b | 199000 |
| Pertussis | 195000 |
| Neonatal Tetanus | 59000 |
| Meningococcal disease | 10000 |
| Others | 19000 |

WHO Global Immunization data, Jul 2013

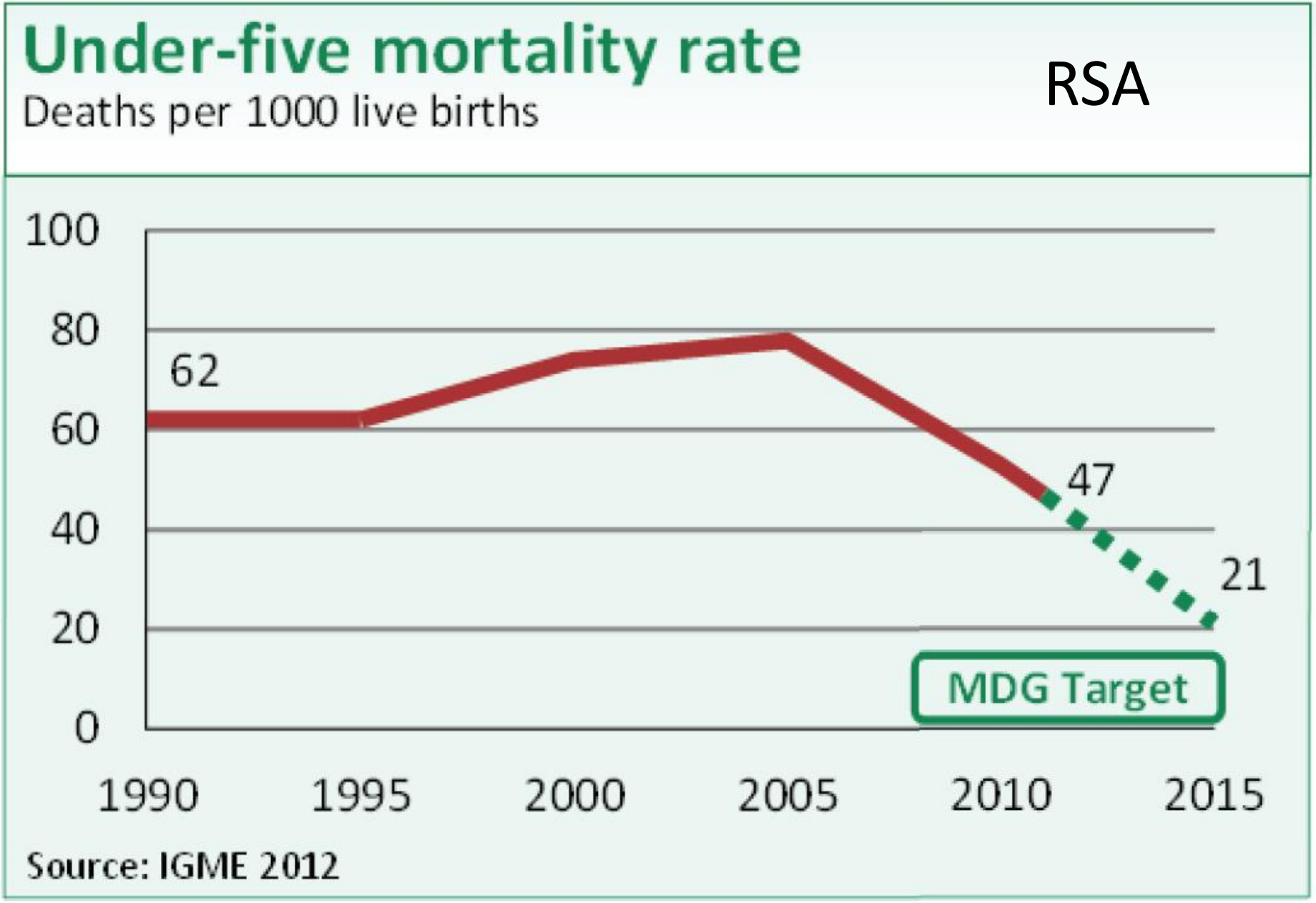
# MDGs

The Millennium Development Goals are eight goals to be achieved by 2015 that respond to the world's main development challenges. The MDGs are drawn from the actions and targets contained in the **Millennium Declaration** that was adopted by 189 nations-and signed by 147 heads of state and governments during the **UN Millennium Summit** in September 2000.

- Goal 1: Eradicate extreme poverty and hunger
- Goal 2: Achieve universal primary education
- Goal 3: Promote gender equality and empower women
- Goal 4: Reduce child mortality
- Goal 5: Improve maternal health
- Goal 6: Combat HIV/AIDS, malaria and other diseases
- Goal 7: Ensure environmental sustainability
- Goal 8: Develop a Global Partnership for Development




http://www.un.org/millenniumgoals/pdf/report-2013/mdg-report-2013-english.pdf




http://www.countdown2015mnch.org/documents/2013Report/South_Africa_Accountability_profile_2013.pdf

# Definitions

A vaccine is a product that produces immunity from a disease and can be administered through needle injections, by mouth, or by aerosol.

Vaccination is the injection of a killed or weakened organism that produces immunity in the body against that organism.

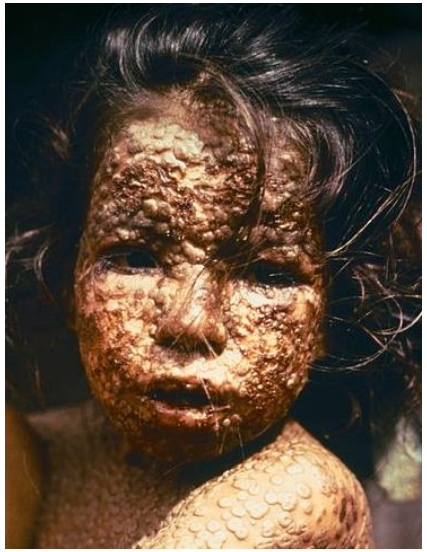
Immunization is the process by which a person or animal becomes protected from a disease. Vaccines cause immunization, and there are also some diseases that cause immunization after an individual recovers from the disease.

Edward Jenner vaccinating
James Phipps
14 May 1796

Blossum infected
Sarah Nelmes,

*Veemeer,*
*The milkmaid*
*1658*

# Parchment signed at Geneva on 9 December 1979, by the members of the Global Commission for Certification of Smallpox Eradication

# Pasteur principles

1822 - 1895

**Isolate**

**Inactivate**

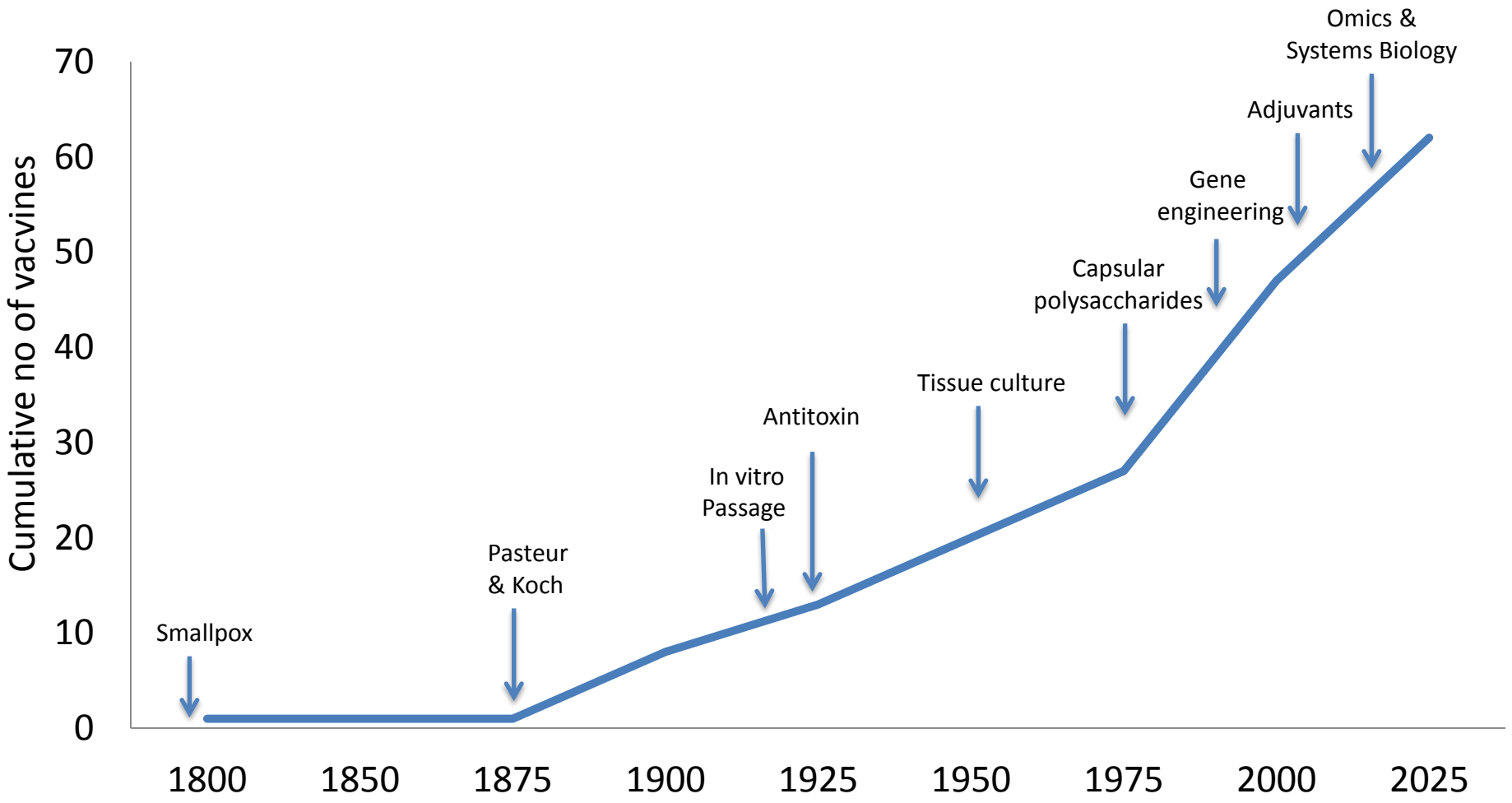
**Inject**

The causative organisms

Killed vaccines

Live attenuated vaccines

# Major milestones in vaccine development




Adapted from NEJM 2013:368:6

# Strategies used in the development of live vaccines

| Development strategy | Date | Vaccine |
|---|---|---|
| Use of related animal virus | 1789 | Smallpox |
| Chemical attenuation | 1881 | Anthrax |
| | 1885 | Rabies |
| Passage in vitro | 1927 | BCG |
| | 1935 | Yellow fever |
| Passage in cell culture | 1962 | OPV |
| | 1963 | Measles |
| | 1971 | Adenovirus |
| | 1995 | Varicella |
| | 2005 | Rotavirus 89-12 |
| Cell culture passage with cold adaptation | 1969 | Rubella |
| | 2003 | Live influenza |
| Auxotrophy | 1989 | Ty21a typoid |
| Reassortments | 2003 | Live influenza |
| | 2005 | Rotavirus bovine-human |

Plotkin. Nat Med, Apr 2005

# Strategies used in the development of inactivated vaccines

| Vaccine strategy | Date | Vaccine |
|---|---|---|
| Inactivated whole organisms | 1896 | Typhoid and cholera |
| | 1897 | Plague |
| | 1926 | Whole cell pertussis |
| | 1938 | Influenza |
| | 1955 | IPV (polio) and Hepatitis A |
| Subunits | 1944 | Japanese encephalitis |
| | 1970 | Influenza |
| | 1960 | Anthrax |
| | 1976 | Cell culture rabies |
| Toxoids | 1923 | Diphtheria |
| | 1927 | Tetanus |
| Capsular polysaccharides | 1974 | Meningococcal |
| | 1977 | Pneumococcal |
| | 1995 | Typhoid |
| Protein –Capsular polysaccharide | 1987 | H influenzae type b |
| | 2002 | Pneumococcal and meningococcal |
| Purified or recombinant proteins | 1986 | Hepatitis B |
| | 1996 | Acellular pertussis |

# Newer strategies for vaccine development starting from microbial DNA or RNA

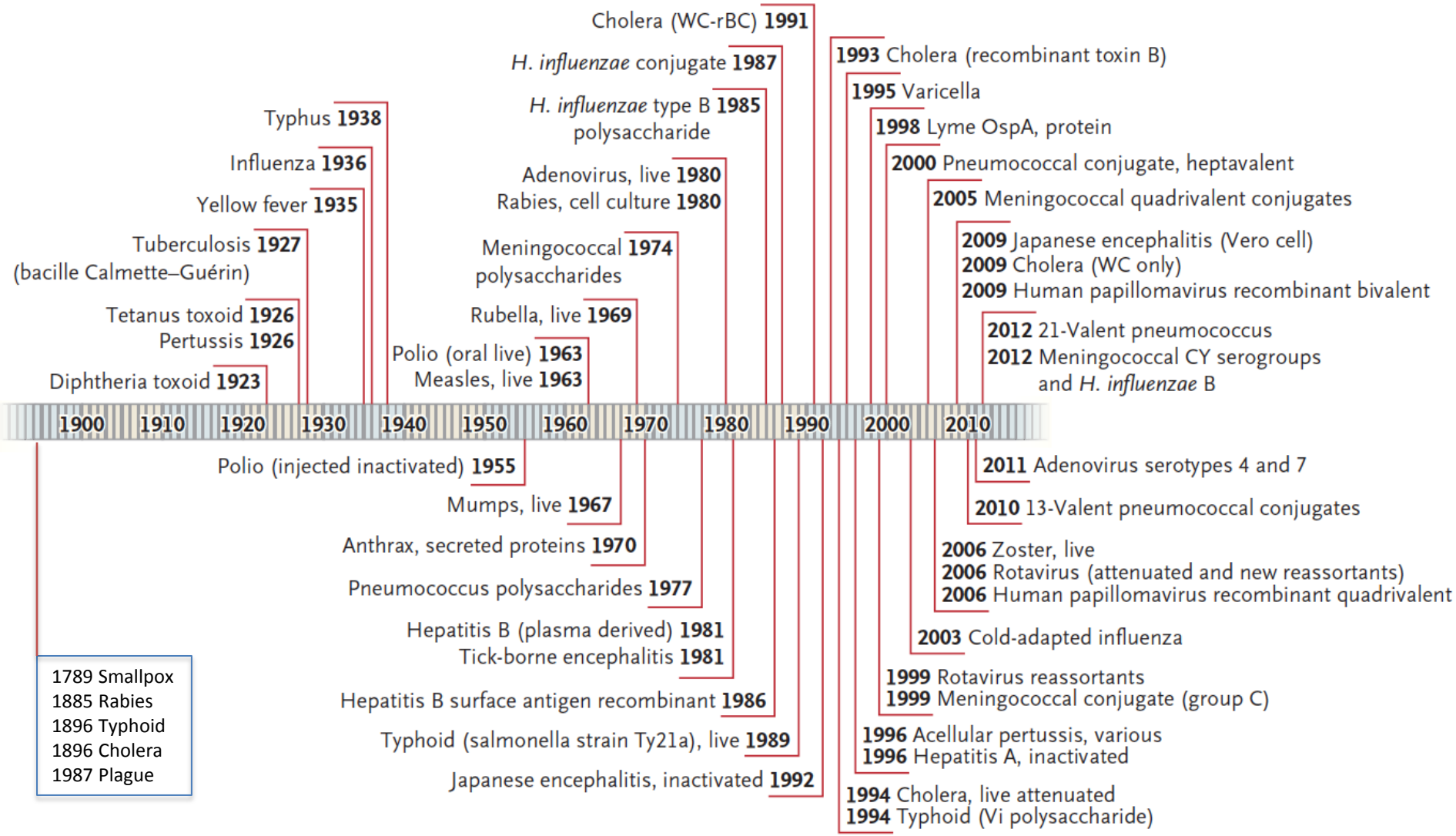
| Strategy | Examples of pathogens targeted |
|---|---|
| Recombinant protein production | Hepatitis B Sag, pertussis toxin, CMV |
| Live recombinants carrying genes from related agents | Dengue genes in yellow fever, MTB genes in BCG |
| Recombinant vectors recombining genes from pathogens | HIV, CMV |
| Replication defective particles | HPV, SARS |
| Naked DNA plasmids | HIV |
| Prime boost using DNA and / or vectors | HIV, malatia, TB |
| Reverse vaccinology | Meningococcus B |
| Synthetic peptides | Cancer, ctl vaccines |
| Reverse genetics | RSV, influenza |
| Synthetic capsular polysaccharides | Hib |

Plotkin. Nat Med, Apr 2005

# Traditional approaches to vaccine development

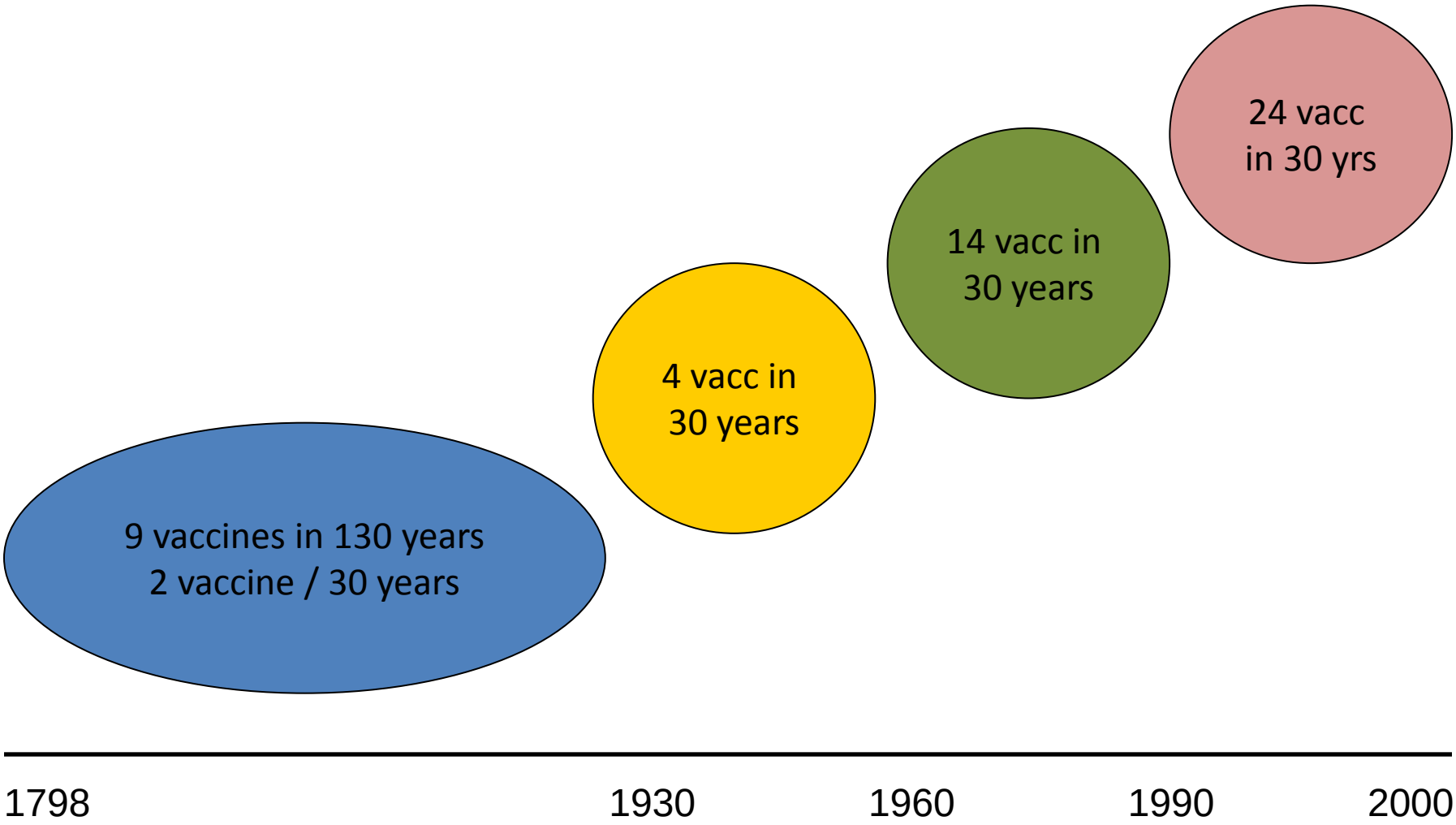
- Live, attenuated vaccines – Live organisms which through culture under certain conditions have lost their virulent properties.
- Whole cell inactivated vaccines – Organisms innately capable of causing disease that have undergone treatment with chemicals or heat, which has rendered them unable to cause the disease.
- Toxoids - Illness-causing components produced by pathogens that have been inactivated.
- Subunit - A part of the organism, rather than the whole organism, is used to create an immune response.
- Conjugate vaccines - Linking the outer polysaccharide coats of certain organisms to proteins can lead to a better immune response

# Timeline for licensure of human vaccines

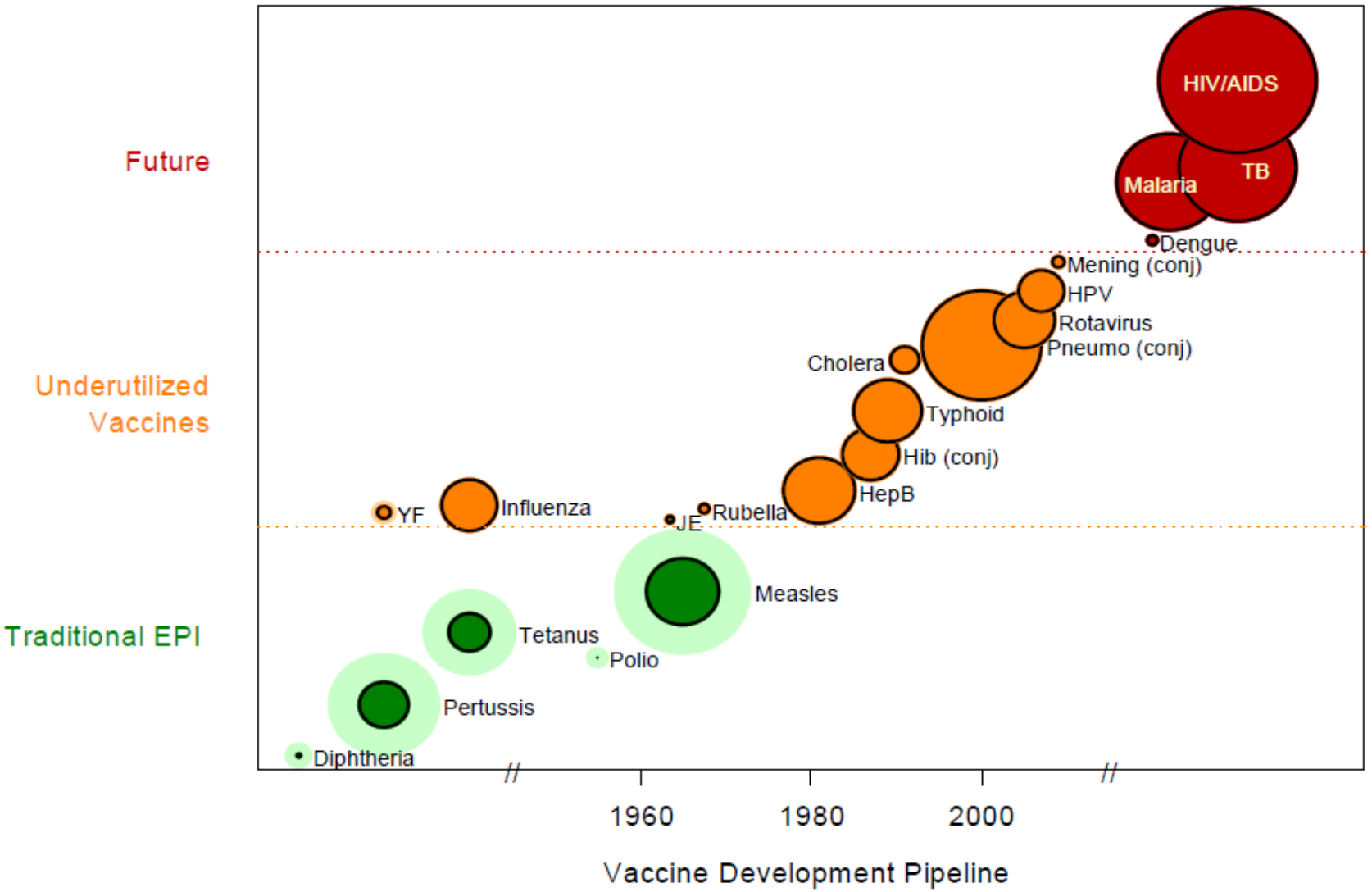



N ENGL J MED 368;6 NEJM.ORG FEBRUARY 7, 2013

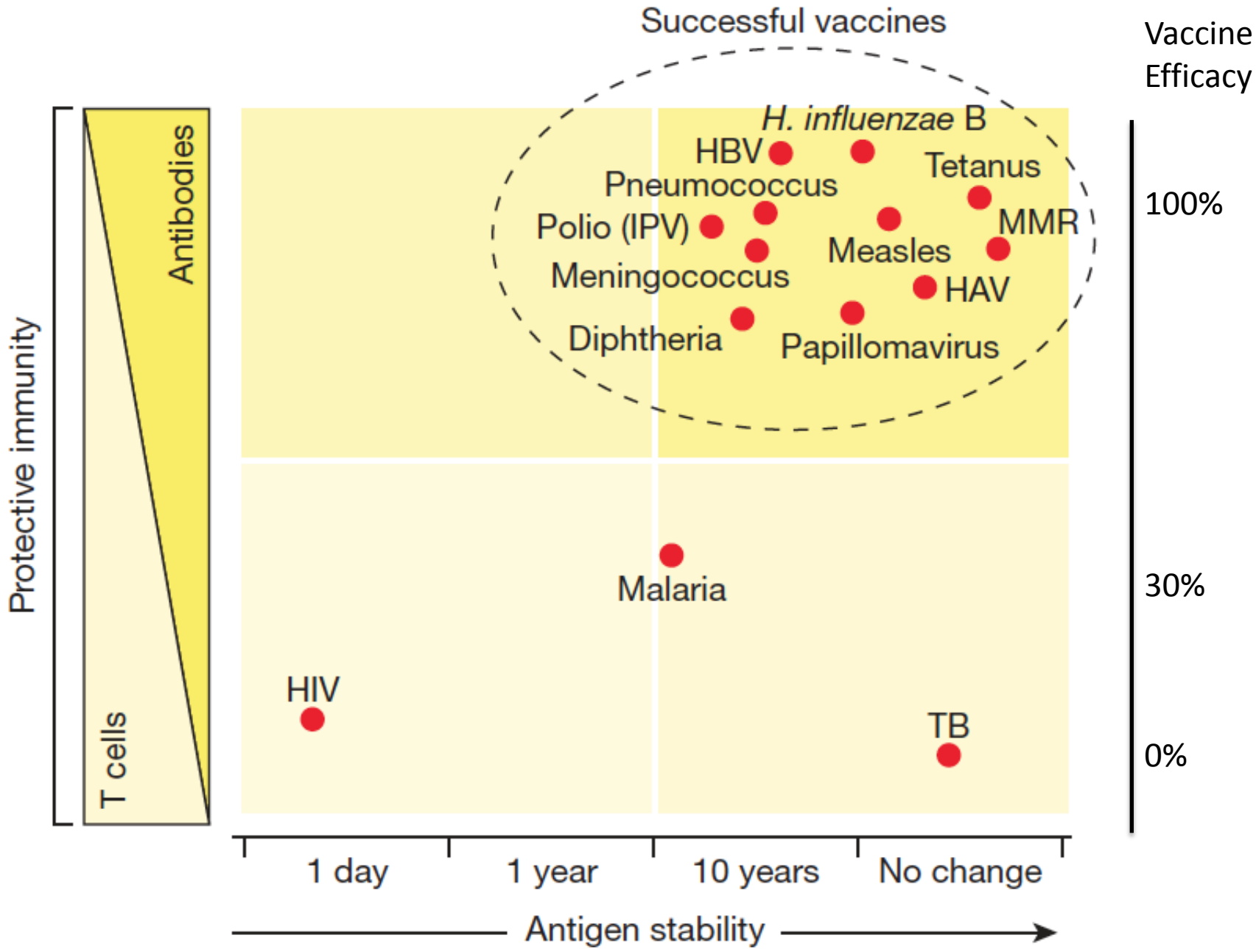
# Vaccines developed over the years



# Vaccine pipeline



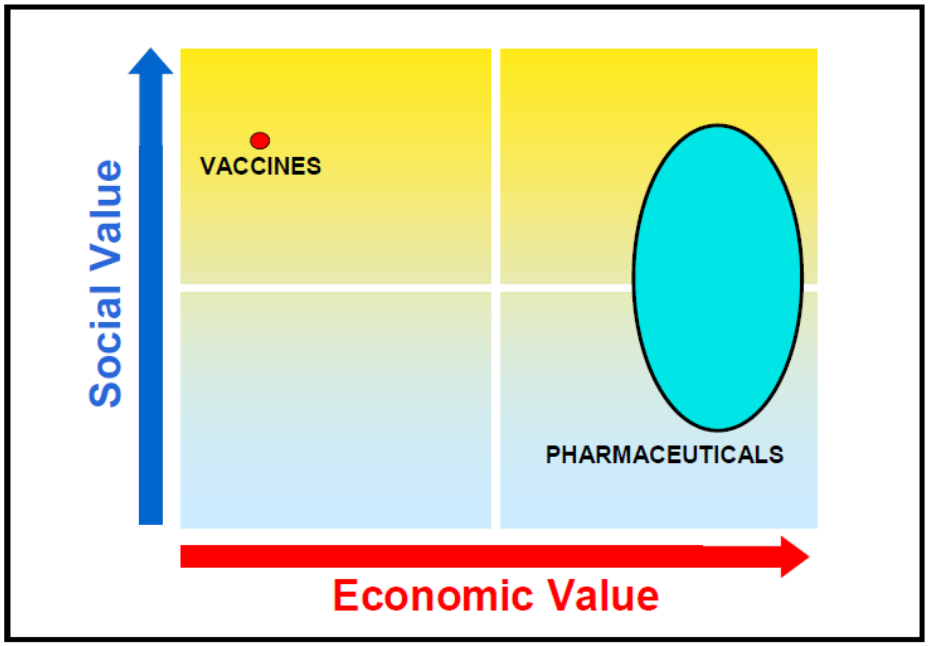

*Area of circle is proportional to number of deaths (2002 data)*
*Shaded area is proportional to number of deaths prevented by vaccination.*



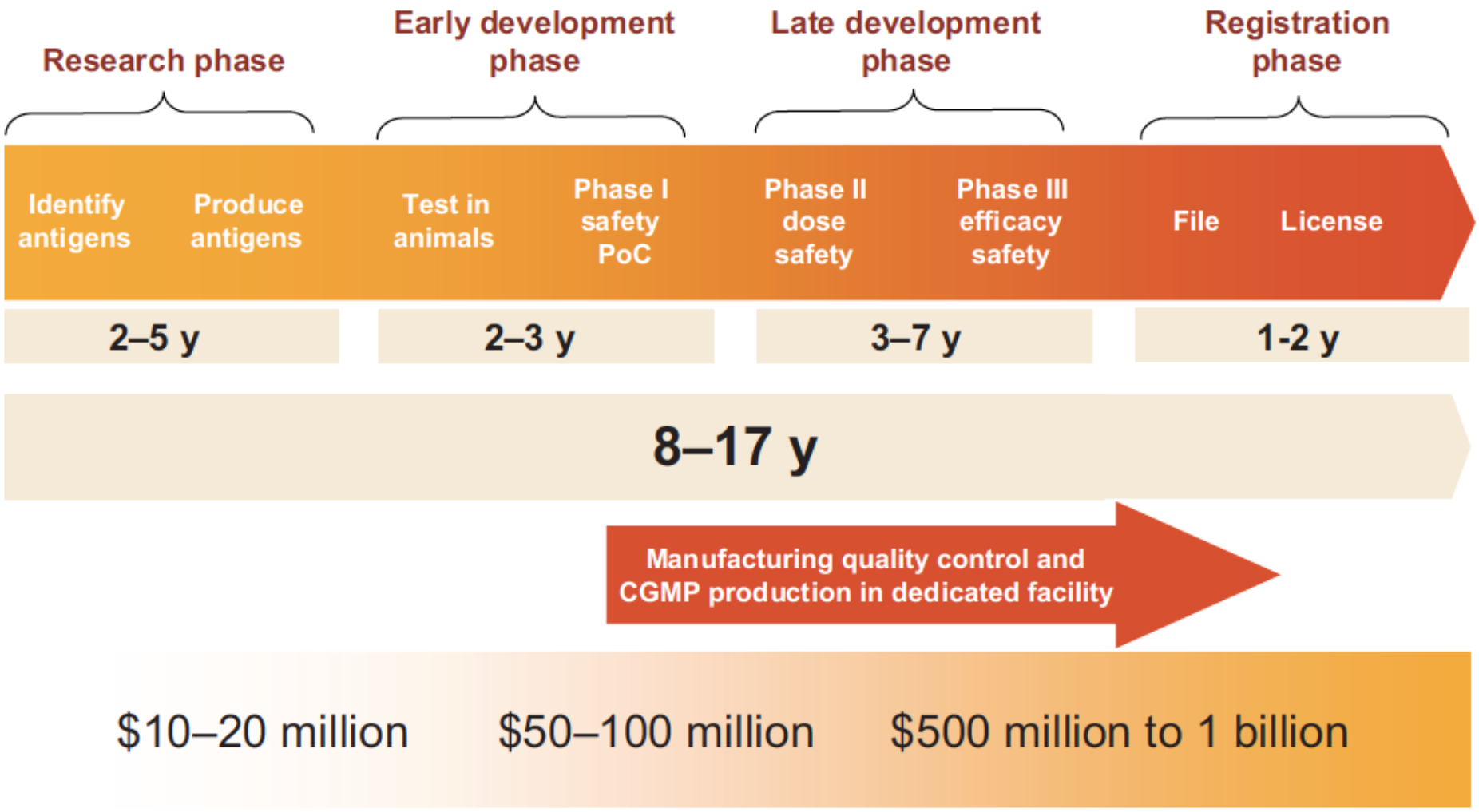

NATURE | VOL 473 | 26 MAY 2011

# Vaccines are different from drugs

- They are given to healthy people – infants in particular.
- They need to hav
  profile.
- A low efficacy is
- It is given once o
- It technically sho

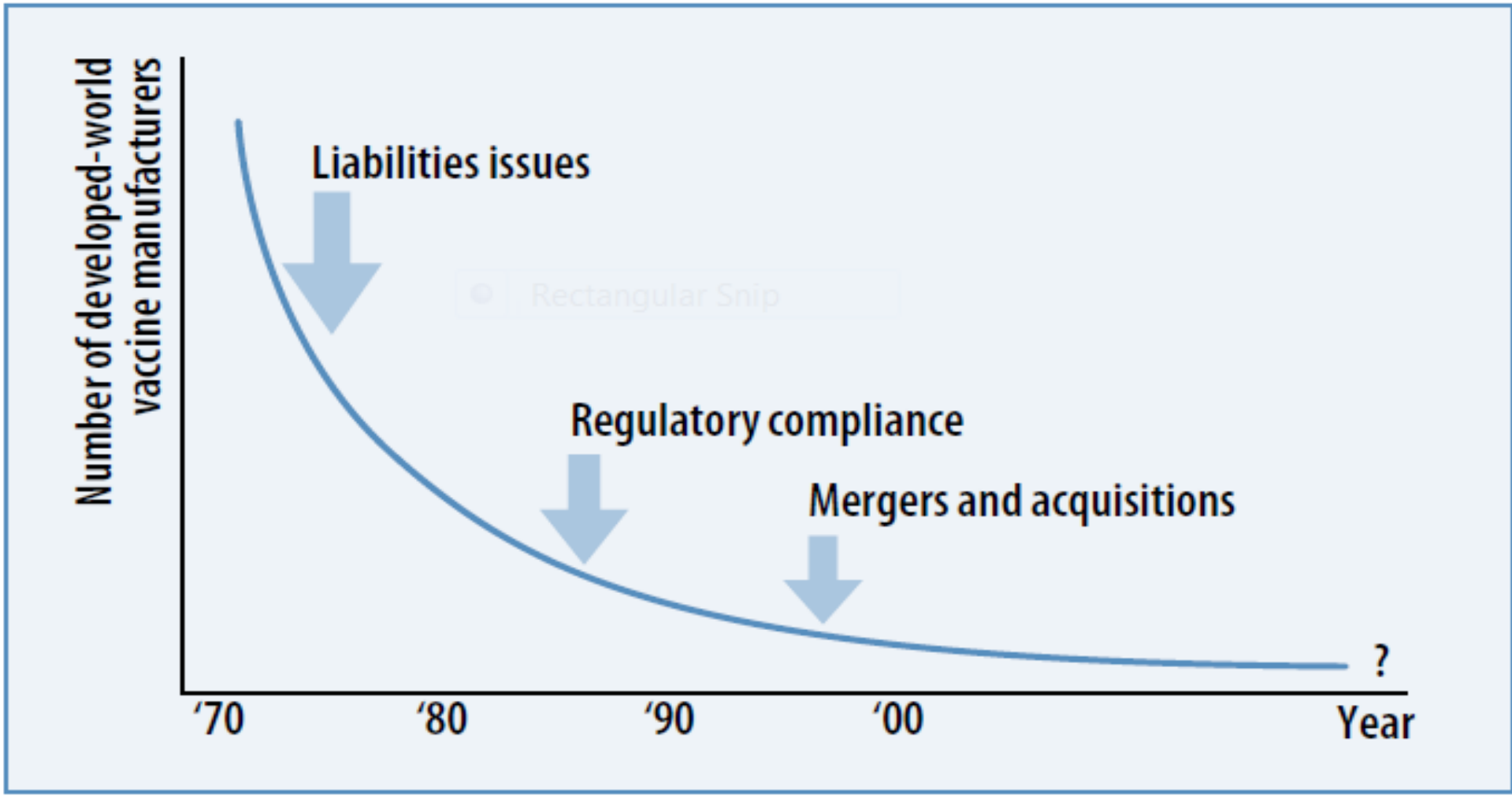


# Timeline for vaccines to get into the community



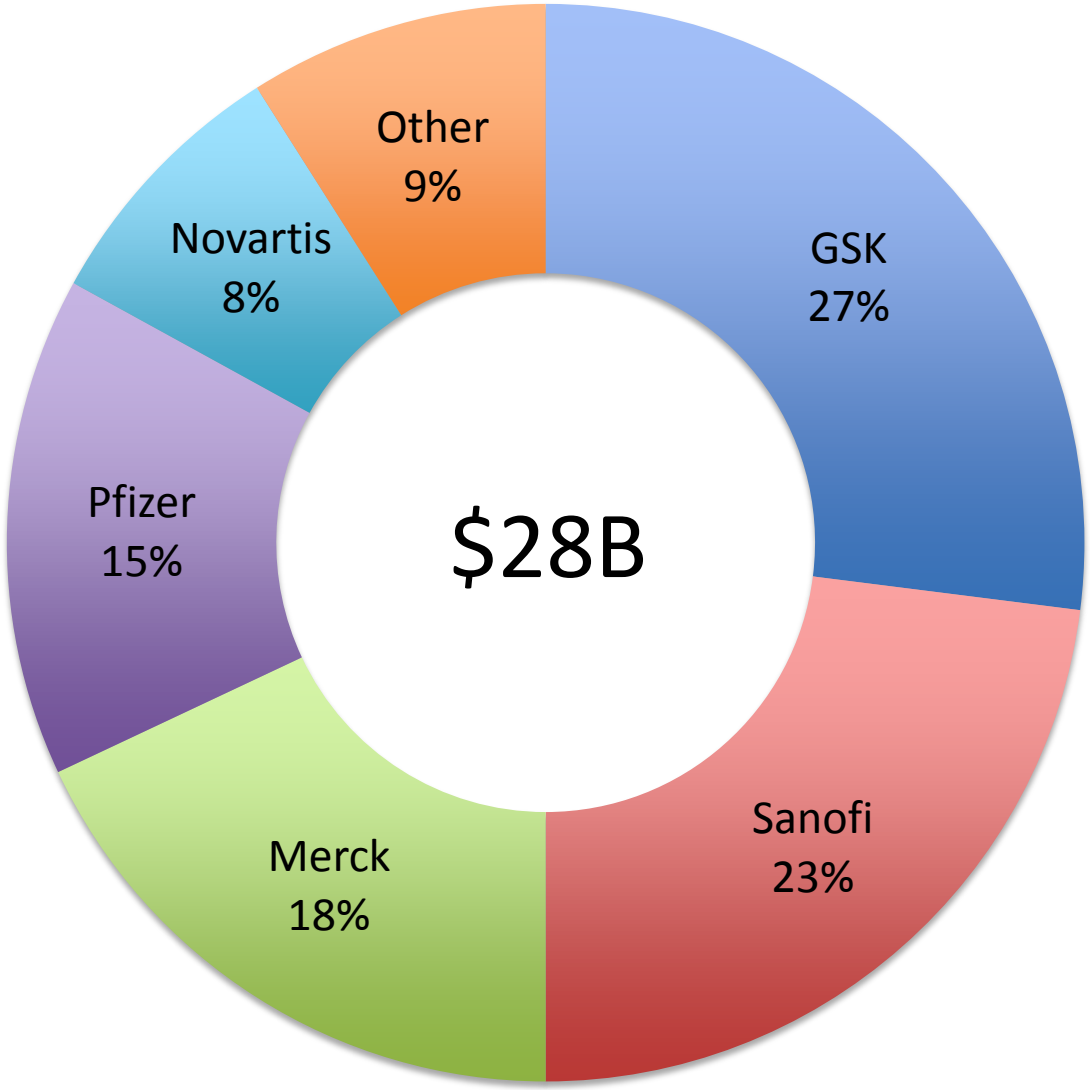

KANESA-THASAN et al Ped 2011

# Number of Vaccine Manufacturers in Industrialised Countries

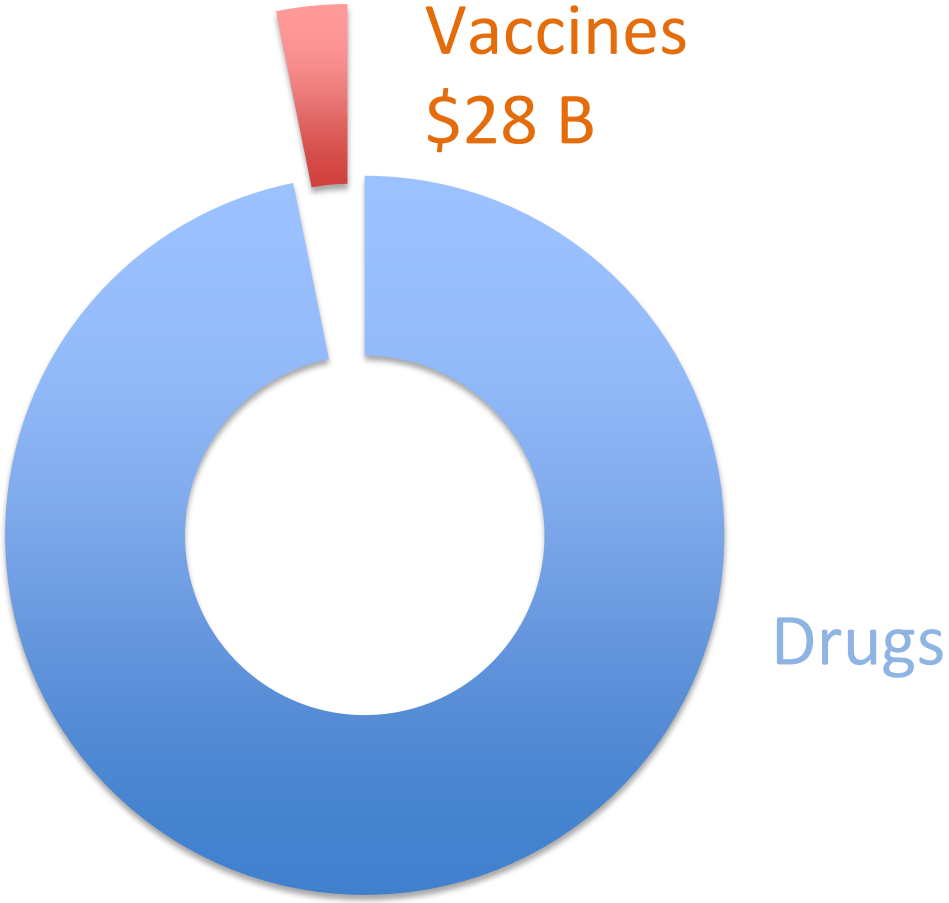



Ackn. WHO

# Vaccine companies market share 2010



# Global Pharma Company Sales 2010



# UN MARKET (in value)

| | 2002 | 2011 | % |
|---|---|---|---|
| UNICEF SD | $ 220 million | $ 1,03 Billion | + 468% |
| PAHO RF | $ 120 million | $ 400 million | + 333% |
| Total | $ 340 million | $1,430 billion | + 420% |

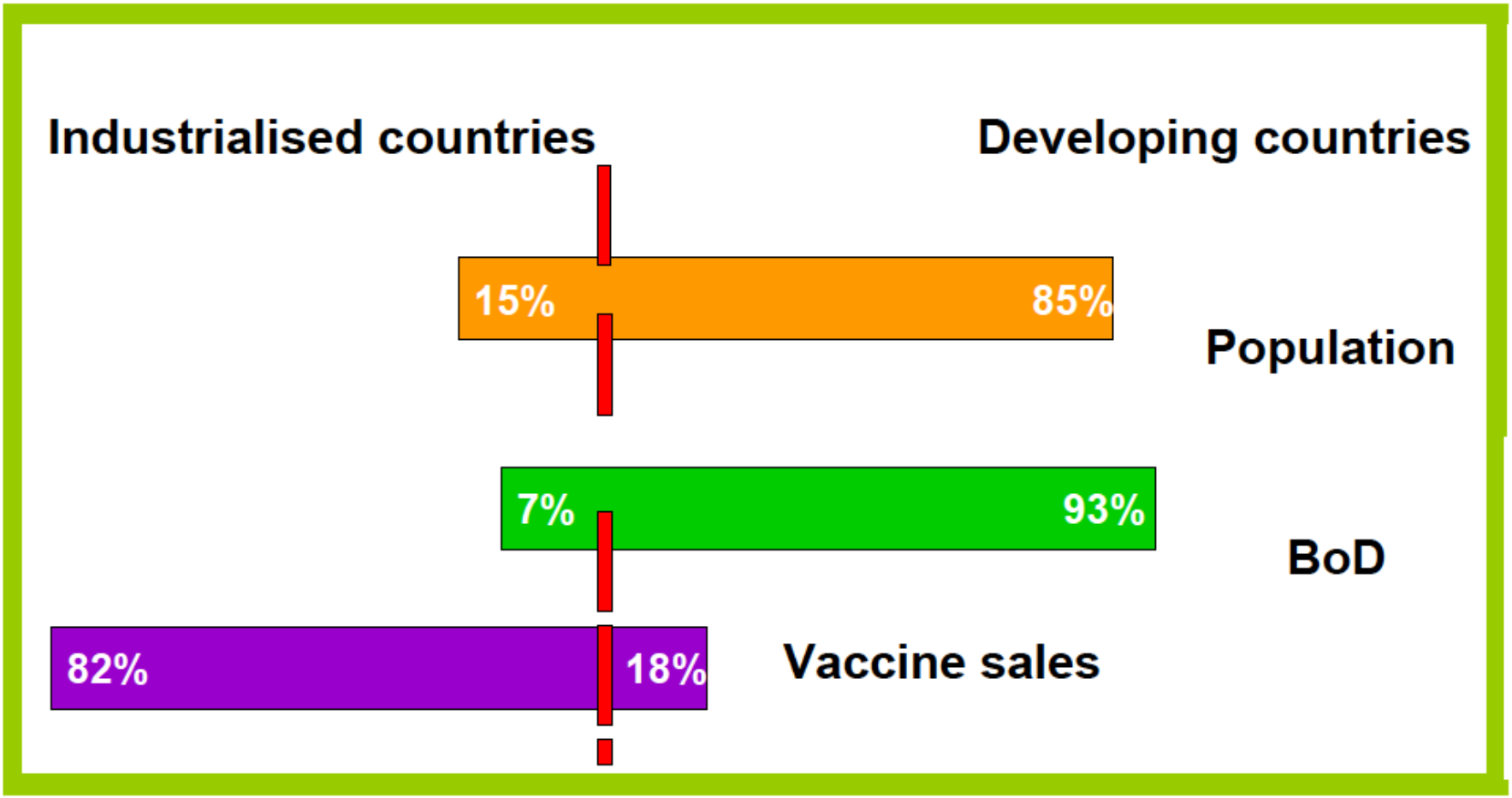
**Around 7, 5 % of total vaccine sales**

Sources: our WHO estimates based on UNICEF SD and PAHO RF data



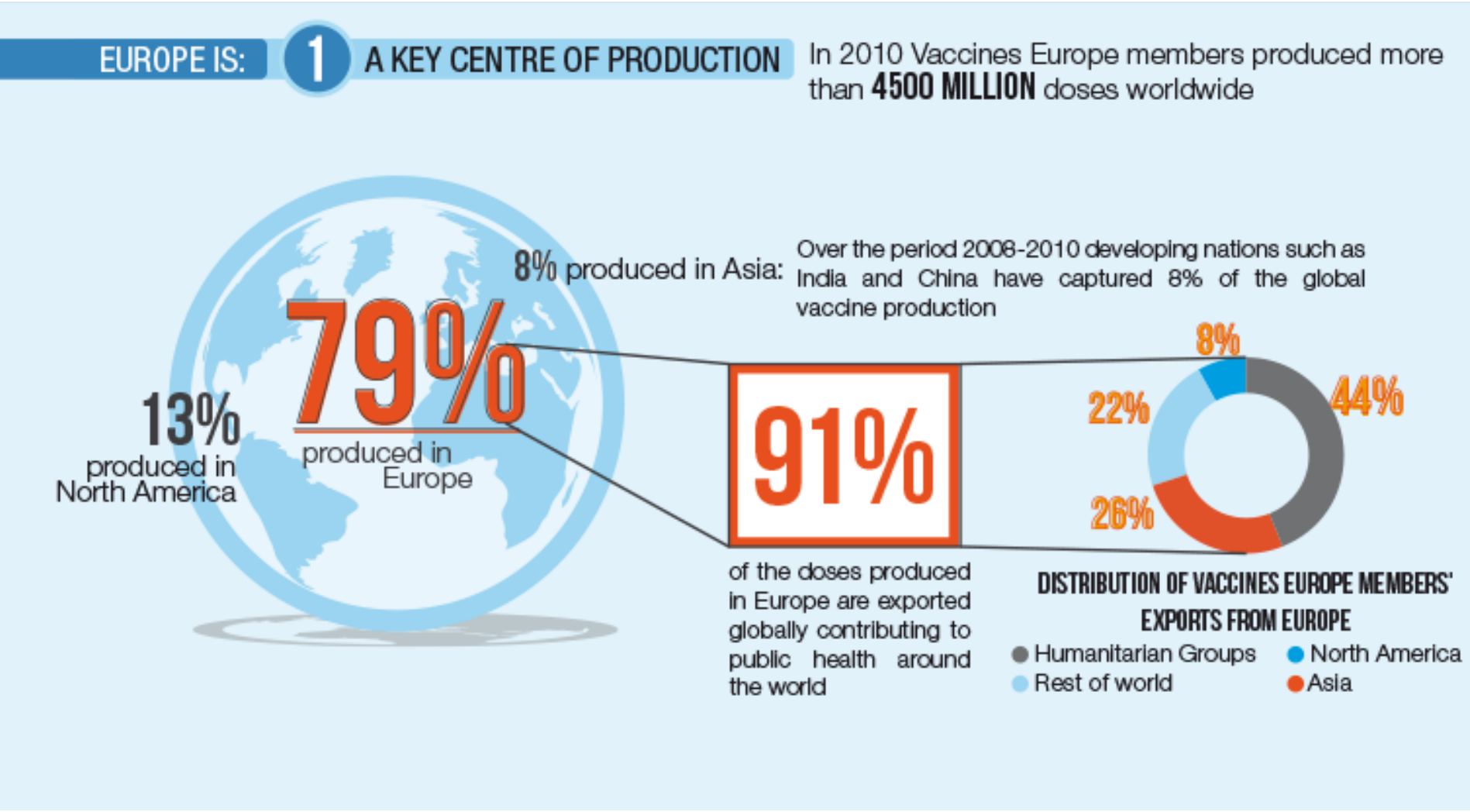
World Health Organization

# Vaccine Market
# North – South GAP






World Health Organization

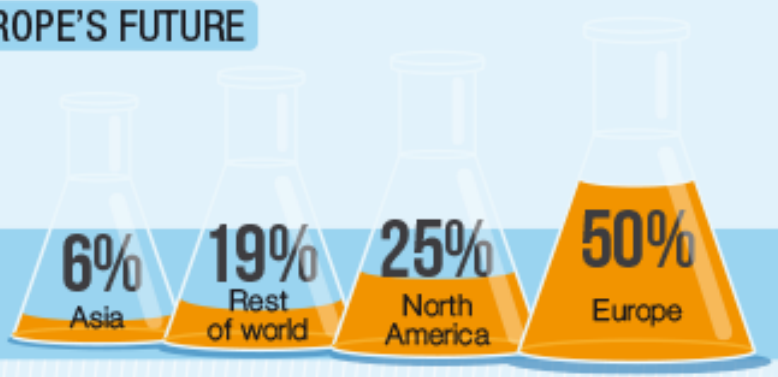



http://www.vaccineseurope.eu/about-vaccines-europe/vaccines-europe-in-figures/

EUROPE IS: **2** A LEADER IN R&D INVESTING IN EUROPE'S FUTURE

Vaccines Industry

Half of all R&D projects undertaken by Vaccines Europe members are based in Europe



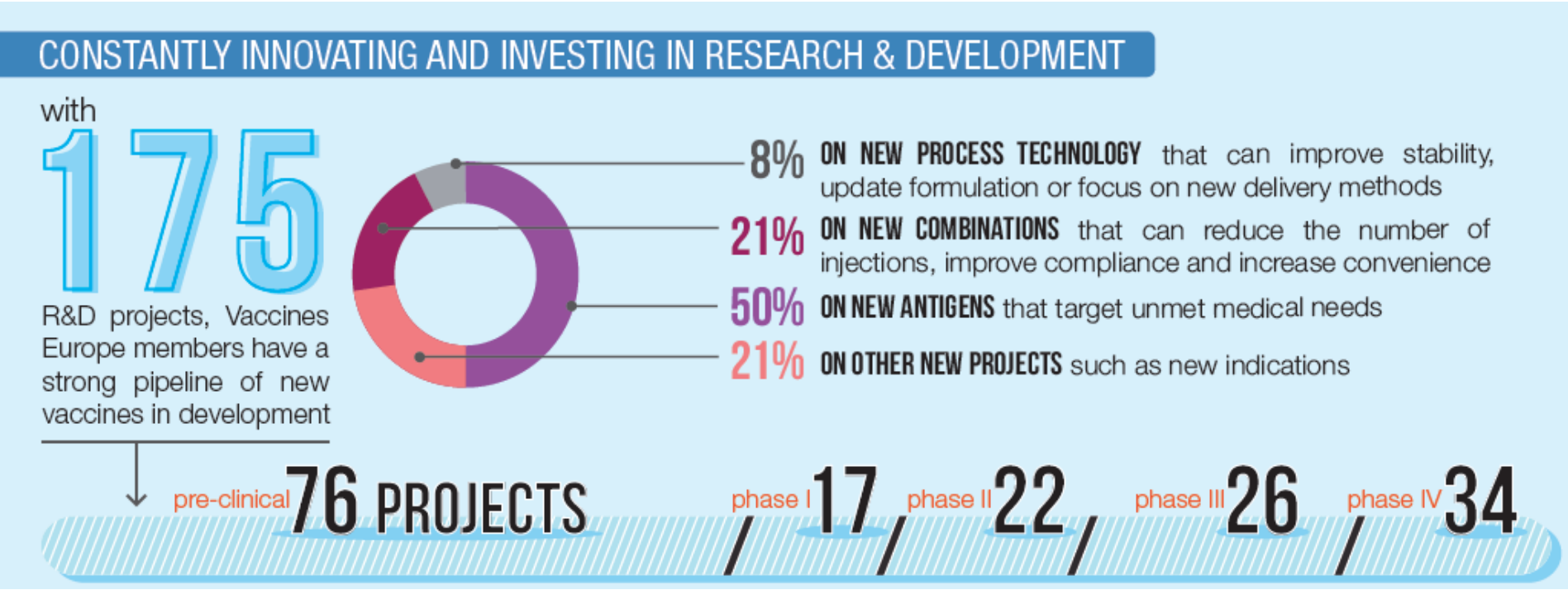


Vaccines Europe members commit

**58%**

of their total R&D investment to Europe

# The future - Investing in Vaccine R&D




* Vaccines Europe, formerly European Vaccine Manufacturers (EVM), is a specialised group within the European Federation of Pharmaceutical Industries and Associations (EFPIA) representing all the major vaccine companies operating in Europe.
Vaccines Europe conducts a biennial survey that provides an insight into the innovation, research and development (R&D), employment and manufacturing undertaken by its members: Abbott Biologicals, AstraZeneca, Baxter, Crucell, GSK Vaccines, MSD, Novartis Vaccines, Pfizer, Sanofi Pasteur and Sanofi Pasteur MSD.

OCTOBER 2012

# DCVMN: 37 manufacturers from 14 countries

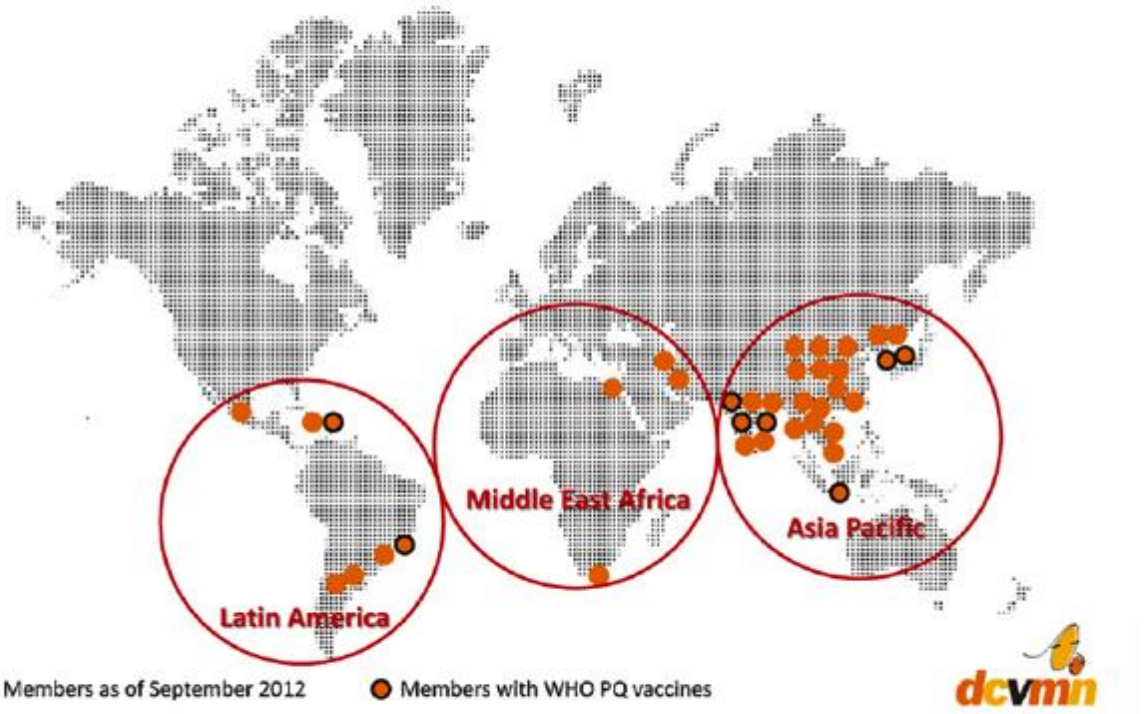



**Fig. 1.** Distribution of 37 DCVMN members in 14 countries: Argentina, Bangladesh, Brazil, China, Cuba, Egypt, India, Indonesia, Mexico, Republic of Iran, Republic of Korea, ) have products that have been prequalified by the World Health Organization.

Vaccine 31S (2013) B176–B183

Contents lists available at SciVerse ScienceDirect

Vaccine

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

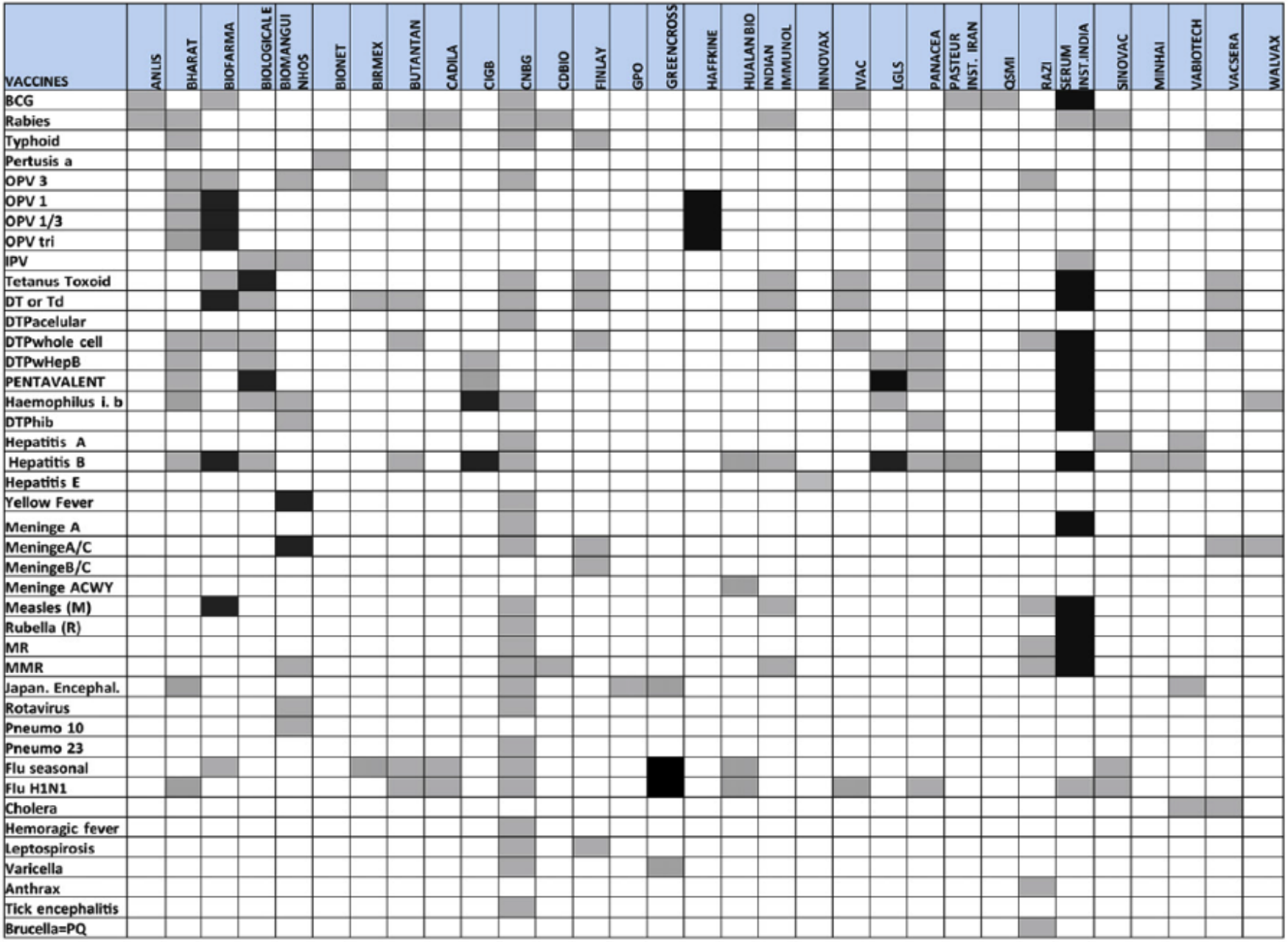
Review

## Developing Countries Vaccine Manufacturers Network: Doing good by making high-quality vaccines affordable for all☆

Sonia Pagliusi[a,*], Luciana C.C. Leite[b,1], Mahima Datla[c,2], Morena Makhoana[d,3], Yongzhong Gao[e,4], Mahendra Suhardono[f,5], Suresh Jadhav[g,6], Gutla V.J.A. Harshavardhan[h,7], Akira Homma[i,8]

[a] DCVMN International, Chemin du Canal 5, 1260 Nyon, Switzerland
[b] Instituto Butantan, Av. Vital Brazil 1500, Sao Paulo 05503-900, Brazil
[c] Biological E Ltd, 18/19/3, Azamabad, Hyderabad 500 020, A.P., India
[d] The Biovac Institute, 15, Alexandra Road, Pinelands, Cape Town, South Africa
[e] Xiamen Innovax Biotech Co., Ltd. No. 130 XinYuan Road, Haicang District, Xiamen, Fujian 361022, China
[f] PT. Biofarma, Jl. Pasteur no. 28, Bandung 40181, Indonesia
[g] Serum Institute of India, 212/2, Off. Poonawalla Road, Hadapsar, Pune 411 028, India
[h] Bharat Biotech International Ltd, Genome Valley, Turkapally, Shameerpet (M), Hyderabad 500 078, India
[i] Bio-Manguinhos | Fiocruz, Av. Brasil, 4365 – Manguinhos, Rio de Janeiro 21040-360, Brazil

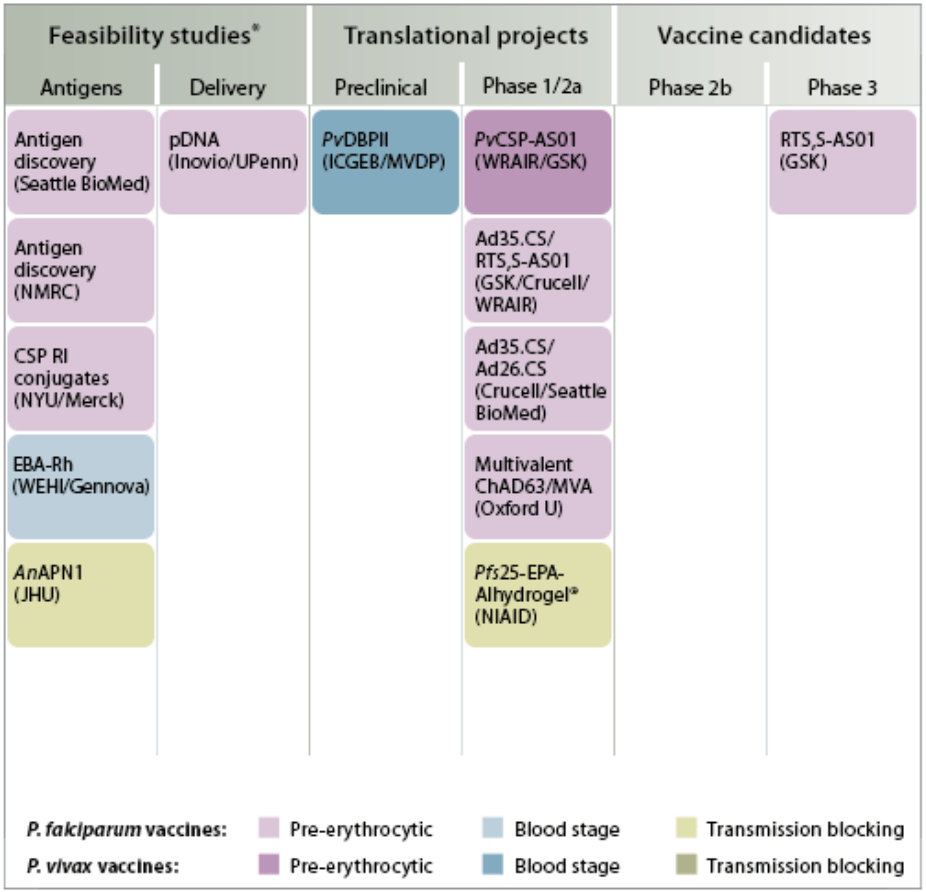
# Developing Countries Vaccine Manufacturers



# Our portfolio

MVI is accelerating the development of malaria vaccines by testing multiple candidates simultaneously. We are strategically using our resources to support and advance a range of vaccine approaches that target both humoral and cellular immunity.

## MVI portfolio




RESEARCH AND DEVELOPMENT

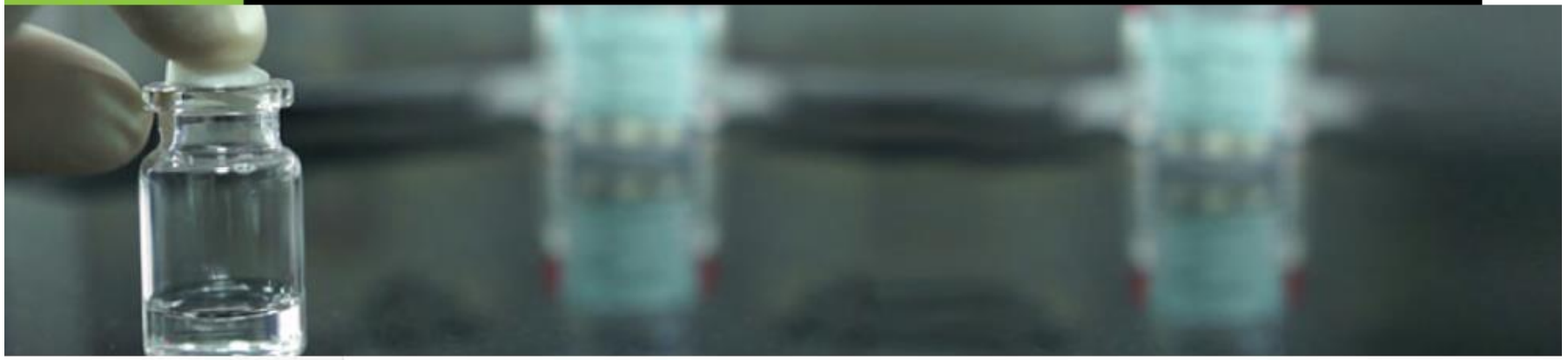
Overview
Our R&D strategy
Our portfolio
Vaccine candidates
Translational projects
Feasibility studies
Evaluation technologies
Immunoassays
Challenge models
Clinical trials
RTS,S malaria vaccine candidate
Trial sites
Partnering with us
Our partners
RFPs

MSD · Wellcome Trust
Hilleman Laboratories
*Developing vaccines for global health*

http://www.hillemanlabs.org/

HOME SITEMAP

PROGRAMS HIGHLIGHTS | ABOUT US | SCIENCE | PROGRAMS | MEDIA | CAREERS | CONTACT US



**Programs**

- Overview
- **Current Projects**
- Project Partners

Home » Programs » Current Projects

# Current Projects

It is estimated that globally 0.6 million children under the age of 5 die annually due to rotavirus diarrhea and another 2 million are hospitalized. 90% of these deaths occur in developing countries.


## Thermostable Rotavirus Vaccine

International research data suggests that current rotavirus vaccines have 85-95% efficacy against severe rotavirus gastroenteritis (RVGE). There are concerns while using the same in developing countries.

# What We Do

Why Vaccines?
Our Research
Meet Our Scientists
Vaccine Portfolio
Translational Research
Laboratory Sciences
Capacity-building

# Vaccine Portfolio

IVI is involved in the development of a number of vaccines against diseases such as cholera, typhoid, paratyphoid, and pneumonia (due to *Streptococcus pneumoniae* infection). The Institute's Microbiology Program is also working on the development of the first universal vaccine against shigellosis (bacillary dysentery).


| Vaccine | IVI's Role | Status |
|---|---|---|
| Killed whole-cell oral cholera vaccine | IVI, in collaboration with partners in Sweden, Vietnam and India, enhanced an existing oral cholera vaccine to meet international standards set by WHO, thereby allowing global access of the vaccine. | Licensed in India as Shanchol™. Received WHO prequalification in 2011. Currently deployed in endemic and epidemic areas in countries around the world. |
| Vi polysaccharide typhoid vaccine | IVI improved the production technology of Vi polysaccharide, resulting in higher yield Vi. | Technology transferred to Shantha Biotechnics in 2009 as part of transfer of Vi-DT conjugate vaccine technology (see below). |
| Vi-diptheria toxoid (Vi-DT) conjugate typhoid vaccine | IVI developed this new vaccine using conjugation technology from the U.S. National Institutes of Health. | Technology transferred to Shantha in 2009 and pilot lots were produced. Clinical trials to follow. |
| Bivalent enteric fever conjugate vaccine (protects against typhoid and paratyphoid) | IVI developed the typhoid and paratyphoid conjugates for the vaccine; formulation work is ongoing. | Under preclinical development. |

MOST POPULAR STORIES

Most Read | Most Emailed | Latest News

10 Promising Therapeutic Vaccines
FDA warns against needleless flu shots
New job opportunities emerging in Big Pharma
Swiss activists plan 'occupy' protest at Novartis chair's house
U.S. considers anthrax vaccine trials--for kids
Diabetics under 60 should get hep B vaccine

Related Topics >> cancer vaccine | therapeutic vaccines

# 10 Promising Therapeutic Vaccines

October 27, 2011 — 8:08am ET



*by Deborah Erickson*

Scientists have long figured it should be possible to rev up the immune system on command, to give the body's own natural defenses an extra surge of power to attack tumors and fight diseases. But decades of working on the challenge have seen many promising clinical trials of potential "immune modulators," "immune stimulators" and "therapeutic vaccines" end in disappointment.



- **ICT-107** - Glioblastoma
- **VGX-3100** - Cervical cancer
- **MAGE-A3** - Skin, lung cancer
- **NeuVax** - Breast cancer
- **AE37** - Breast cancer
- **NexVax2** - Celiac disease
- **ADXS-HPV** - Cervical, head and neck cancer
- **CRS-207** - Pancreatic cancer
- **PEV7** - Recurrent vulvovaginal candidiasis
- **GI-4000** - Pancreatic cancer

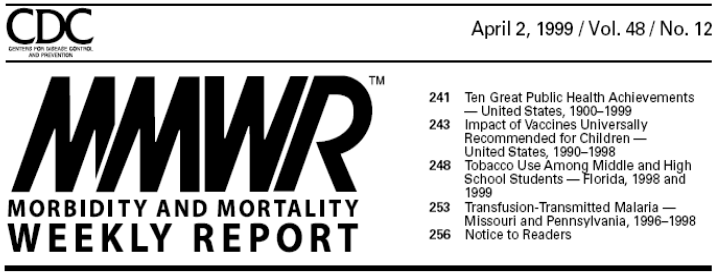
# Impact of immunization

- Immunization is the most cost effective public health discovery.

# Public health achievements of the 20th century

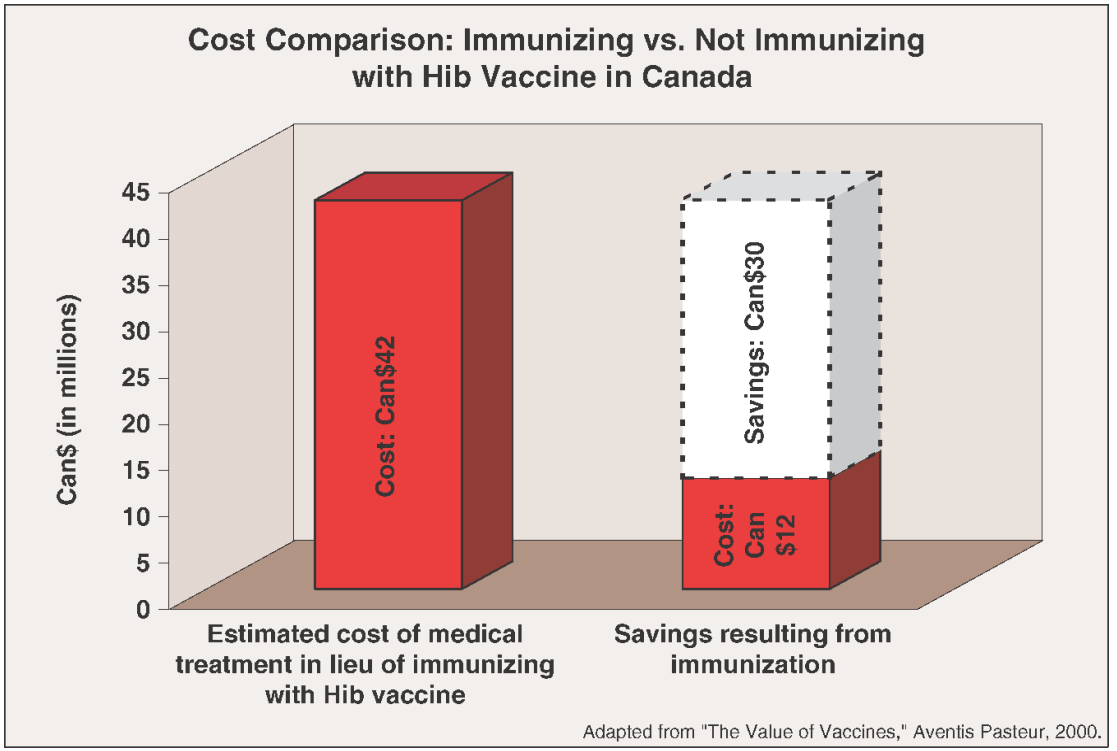
**Ten Great Public Health Achievements — United States, 1900–1999**

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary heart disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard



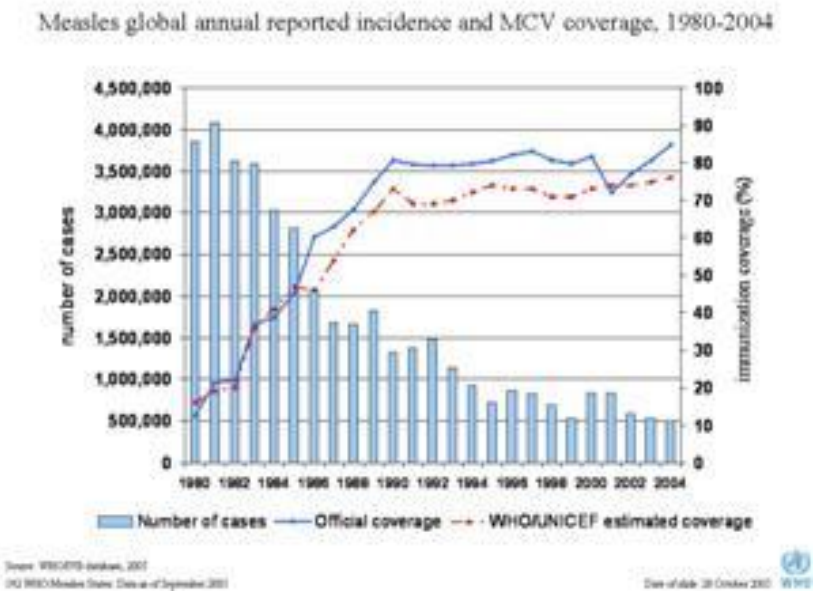
# Immunization can save money

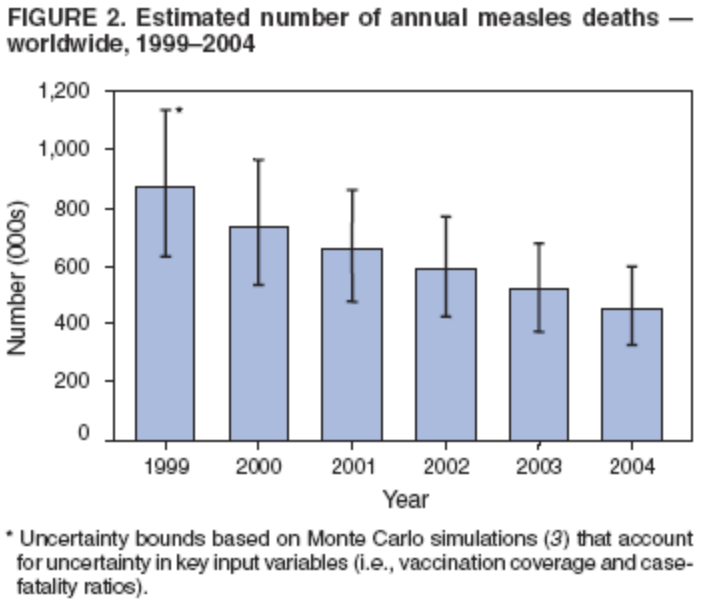
- Immunization is one of the most cost-effective health interventions.
- Investing in vaccines SAVES more money than it costs.



# Impact of immunization

- Immunization is the most cost effective public health discovery.
- Immunization has reduced childhood morbidity and mortality dramatically…..



# Impact of Vaccines in the 20th C.

| Disease | 20th Century Annual Morbidity | 2005 Total | % Decrease |
|---|---|---|---|
| Smallpox | 48,164 | 0 | 100 |
| Diphtheria | 175,885 | 0 | 100 |
| Pertussis | 147,271 | 25,616 | 83 |
| Tetanus | 1,314 | 27 | 98 |
| Polio (paralytic) | 16,316 | 1* | >99.9 |
| Measles | 503,282 | 66 | >99.9 |
| Mumps | 152,209 | 314 | >99 |
| Rubella | 47,745 | 11 | >99.9 |
| Congenital rubella | 823 | 1 | 99.8 |
| *Haemophilus influenzae* (<5 years) | 20,000 (est) | 226 (serotype B or unknown serotype) | 99 |

Atkinson, W., Wolfe, S., Hamborsky, J., & McIntyre, L. (Eds.). (2009). Impact of vaccines in the 20th & 21st Centuries. In *Centers for disease control and prevention: Epidemiology and prevention of vaccine-preventable diseases* (Appendix G: Data and statistics) (11th ed.). Washington, D.C.: Public Health Foundation.
Retrieved from http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/impact-of-vaccines.pdf

# 1.5 m Deaths due to vaccine preventable diseases

| Disease | Children < 5years |
|---|---|
| Pneumococcal disease | 476000 |
| Measles | 118000 |
| Rotavirus | 453000 |
| Heamophilus inf type b | 199000 |
| Pertussis | 195000 |
| Neonatal Tetanus | 59000 |
| Meningococcal disease | 10000 |
| Others | 19000 |

WHO Global Immunization data, Jul 2013

# Deaths due to VPDs in context of global child deaths

- 1.5 million of the 5.2 (29%) of deaths in children 1-59 months of age are vaccine preventable.
- Africa, which is home for about 20% of the world's children accounts for approximately 50% of all child deaths.

# Impact of immunization

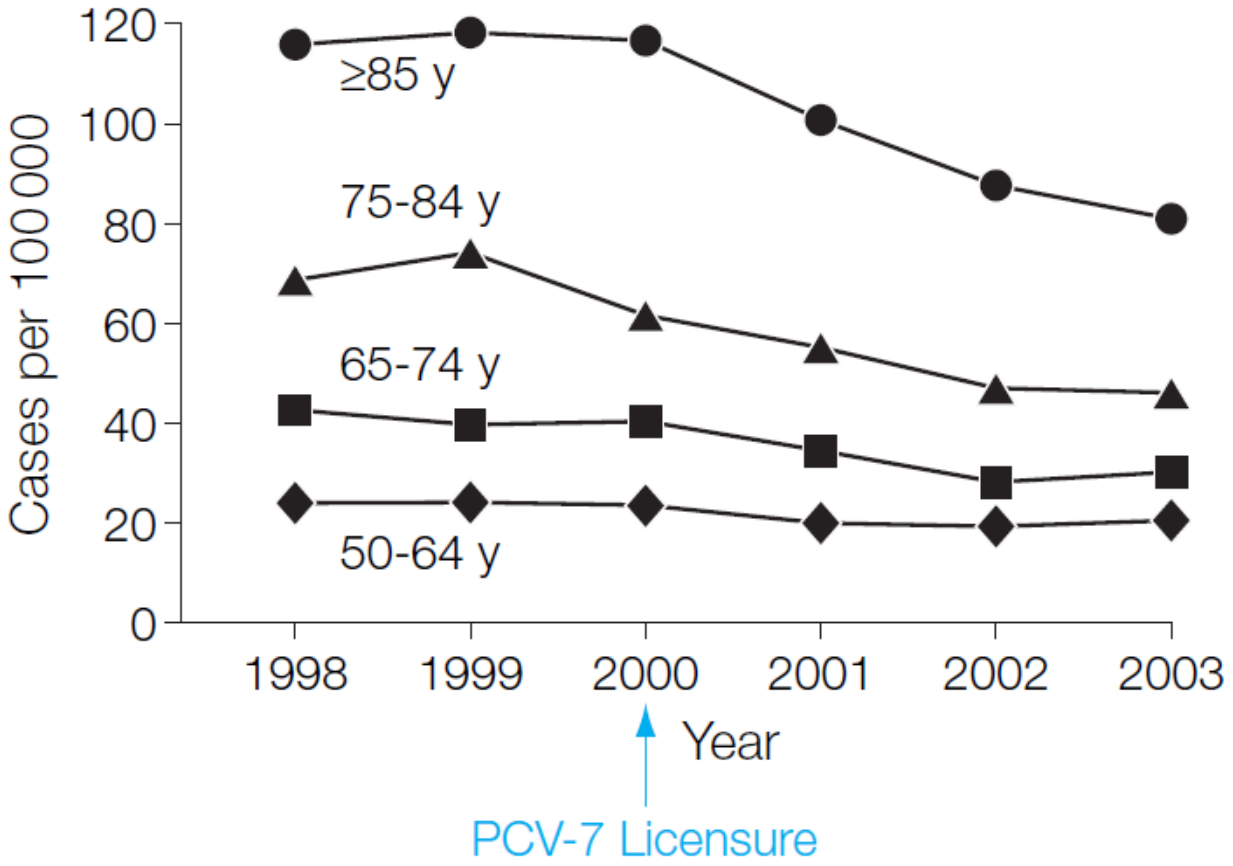
- Immunization is the most cost effective public health discovery.
- Immunization has reduced childhood morbidity and mortality.
- Immunization can protect the unprotected.

# Immunization can protect the unprotected

- When immunization coverage is high, it can prevent viruses and bacteria from circulating.
- The more children in a community that are fully immunized, the more everyone is safe.
- Even the elderly are protected

Ack:PATH

**Figure.** Annual Incidence of Invasive Pneumococcal Disease by Age Group for Adults ≥50 Years—Active Bacterial Core Surveillance, 1998-2003



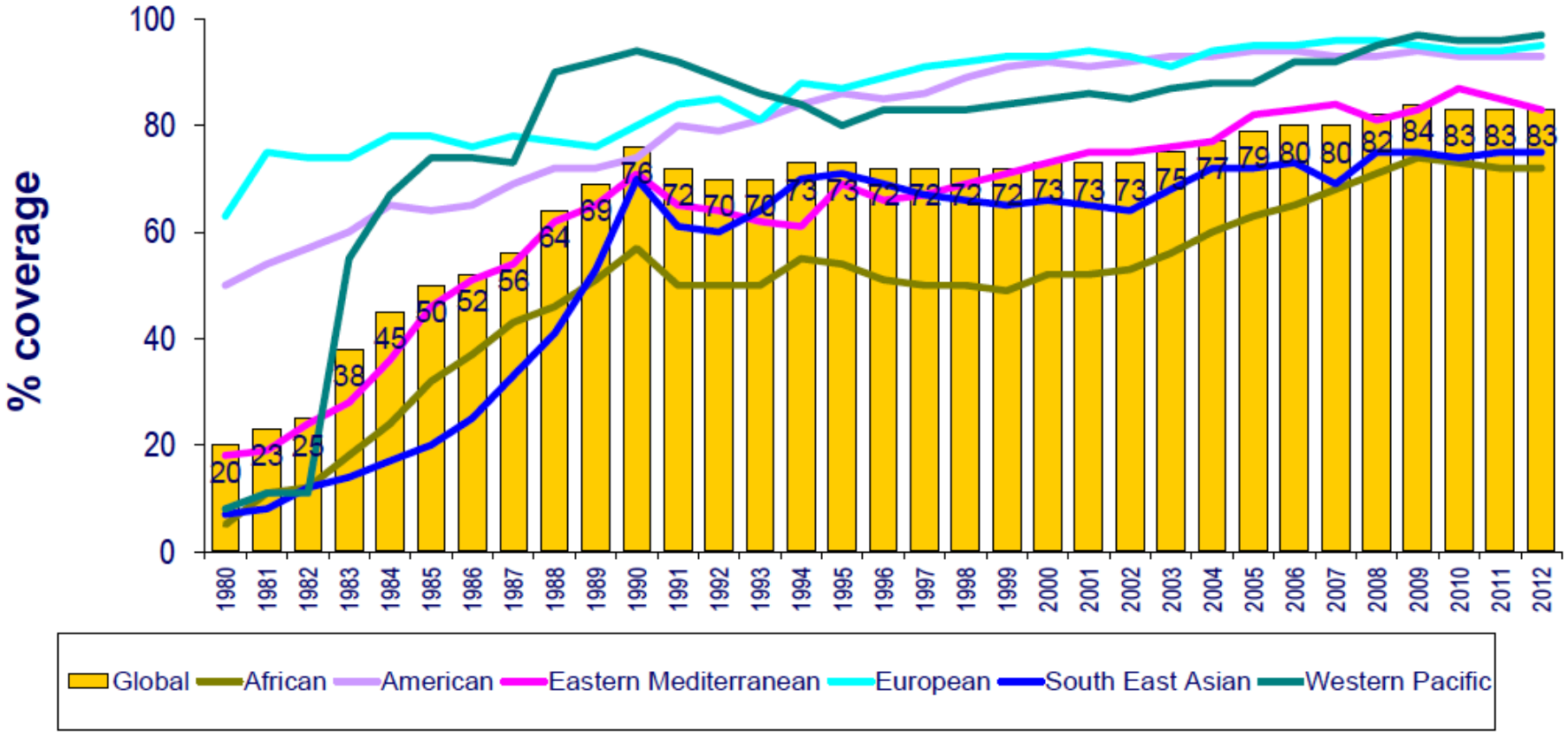

JAMA 2005

# Impact of immunization

- Immunization is the most cost effective public health discovery.
- Immunization has reduced childhood morbidity and mortality.
- Immunization can protect the unprotected..
- However, many children are denied these benefits….

# Global Immunization 1980-2012, DTP3 coverage

## global coverage at 83% in 2012

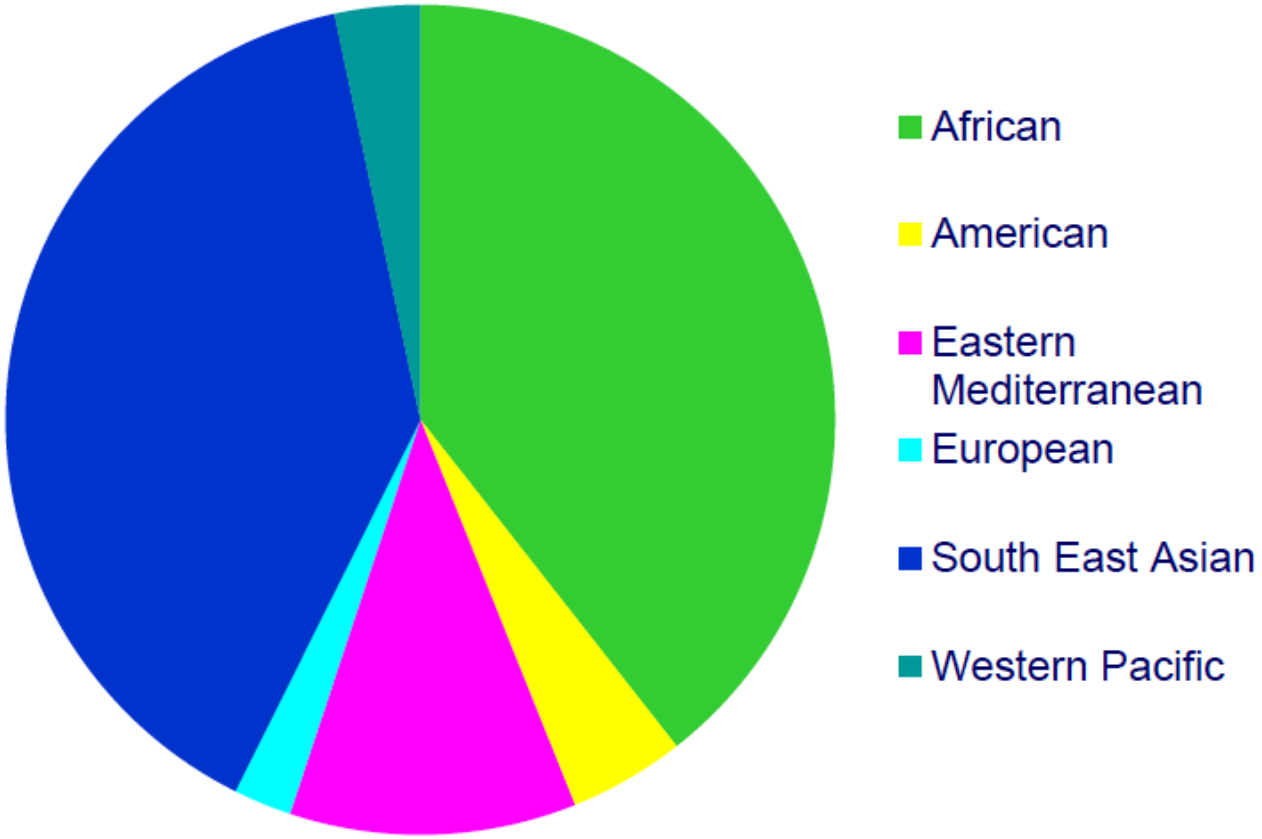



Source: WHO/UNICEF coverage estimates 2012 revision. July 2013
Immunization Vaccines and Biologicals, (IVB), World Health Organization.
194 WHO Member States. Date of slide: 27 August 2013.

unicef

World Health Organization

# 22.6 million infants not immunized (DTP3), 2012




Source: WHO/UNICEF coverage estimates 2012 revision. July 2013 / United Nations, Population Division. The World Population Prospects - the 2012 revision". New York, 2013.
Immunization Vaccines and Biologicals, (IVB), World Health Organization.
194 WHO Member States. Date of slide: 22 July 2013.

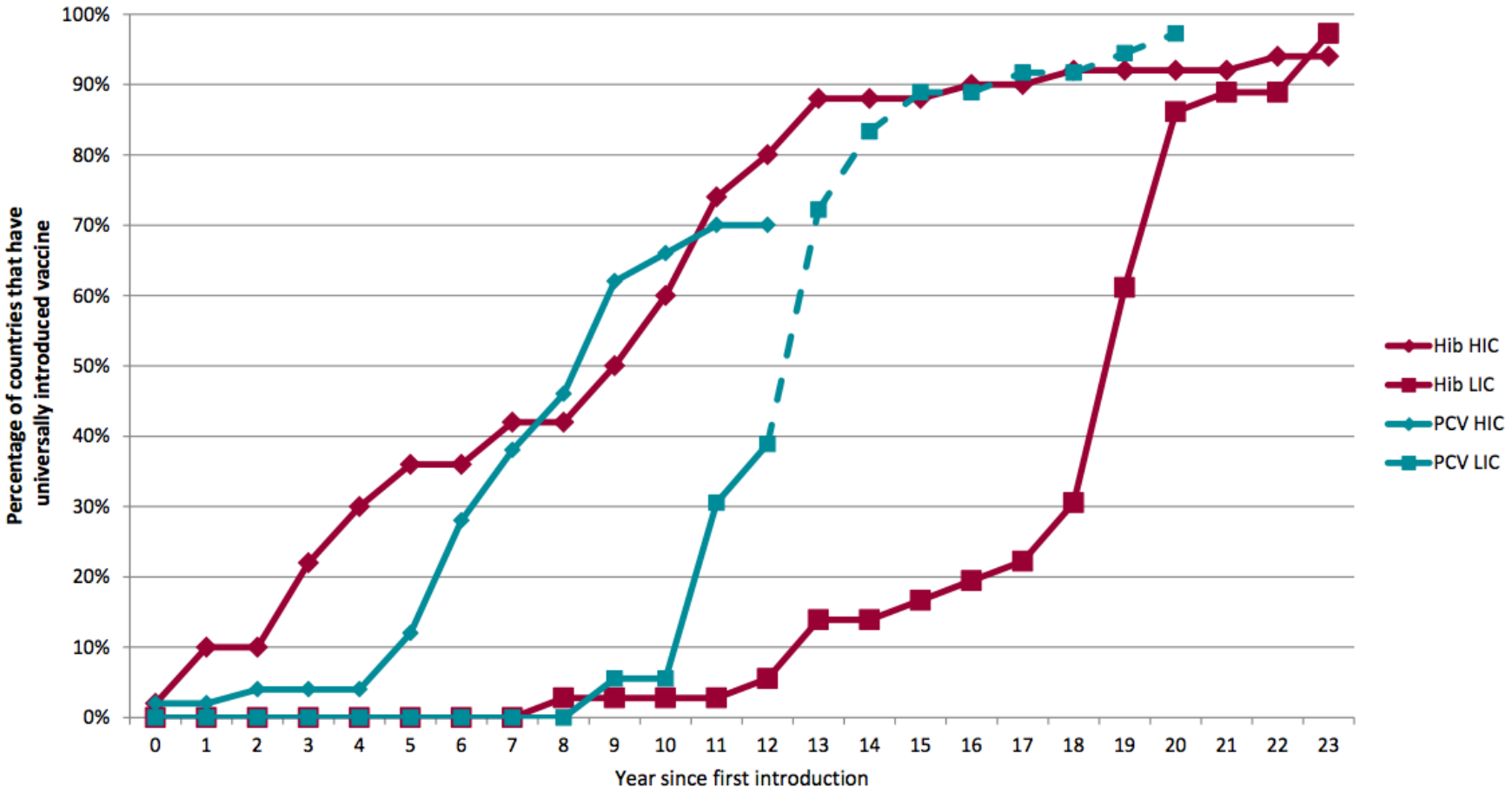
# Review of non and under-vaccination

- Swiss Tropical Institute
- Centres for Disease Control and Prevention
- IMMUNIZATIONbasics
- Vaccines for Africa
- Recent publications from South Africa

# Conclusion

- Non-vaccination and under-vaccination is a significant problem.
- Multiplicity of causes (from individual to societal) highlights the complexity of the issue.
- A number of themes have emerged from the reviews
  - Weaknesses in the immunisation system
  - Problems with communication and information
  - Knowledge, attitudes and beliefs of parents and health care workers
  - Problems in family structures and community characteristics
- Calls for a multi-faceted approach.

# Vaccine Introduction by Income Group




Note: Limited projections are available for PCV introduction in High Income Countries

A line graph showing the proportion of high and low income countries that have introduced or are projected to introduce PCV and Hib vaccine over time. Year of first introduction is 1989 for Hib vaccine and 2000 for PCV. It took 20 years for Hib vaccine to reach 70% of low income countries. PCV is projected to reach 70% of low income countries seven years faster, protecting millions of children sooner from deadly pneumococcal disease.



IVAC
Evidence ➤ Policy ➤ Access

## VACCINE INTRODUCTION DASHBOARD

### Year of First Vaccine Introduction

| Income Level | Hib Vaccine | PCV | Rotavirus Vaccine |
|---|---|---|---|
| High-Income | 1989 (Iceland) | 2000 (US) | 2006 (3 countries) |
| Middle-Income | 1994 (2 countries) | 2008 (5 countries) | 2006 (5 countries) |
| Low-Income | 1997 (Gambia) | 2009 (Rwanda) | 2012 (Rwanda) |
| GAVI Supported | 2001 (2 countries) | 2009 (2 countries) | 2008 (Bolivia) |

### Total number of countries that have introduced each vaccine

| Vaccine | Global Introductions (194 Countries) | | | GAVI Introductions (73 Countries) | Total |
|---|---|---|---|---|---|
| | Universal | At-Risk | Regional/Phased | | |
| Hib | 182 | 0 | 5 | 72 | 187 |
| PCV | 92 | 9 | 1 | 31 | 102 |
| Rotavirus | 46 | 0 | 5 | 16 | 51 |

http://www.jhsph.edu/research/centers-and-institutes/ivac/vims/IVAC_VIMS_Report2013Oct.pdf

# Access to vaccines

> "We can distribute Coca-Cola all around the world, but we can't seem to get medication to save a child from something as simple as diarrhea …."
>
> **Annie Lennox, 2008**[1]

# Expanded Programme on Immunization (EPI)

- Established 1974
- Building on advances in smallpox eradication
- Objective – raise childhood immunization coverage with *expanded* number of antigens
- Vaccines – BCG, DTP, OPV, measles
- Strategy – routine immunization services

# Routine vs Supplemental immunization

## Routine:

Day to day immunisation according to country immunisation schedule

## Supplemental:

In addition to/adding to routine/ strengthening routine immunisation coverage

# Standard EPI schedule

| | |
|---|---|
| BCG/OPV | Birth |
| DTP/Hib/HBV/OPV | 6 wks |
| DTP/Hib/HBV/OPV | 10 wks |
| DTP/Hib/HBV/OPV | 14 wks |
| Measles | 9 mths |
| Measles | 18mths |

# 2013 Recommended Immunizations for Children from Birth Through 6 Years Old

| Birth | 1 month | 2 months | 4 months | 6 months | 12 months | 15 months | 18 months | 19–23 months | 2–3 years | 4–6 years |
|---|---|---|---|---|---|---|---|---|---|---|
| HepB | HepB | | | HepB | | | | | | |
| | | RV | RV | RV | | | | | | |
| | | DTaP | DTaP | DTaP | | DTaP | | | | DTaP |
| | | Hib | Hib | Hib | Hib | | | | | |
| | | PCV | PCV | PCV | PCV | | | | | |
| | | IPV | IPV | | IPV | | | | | IPV |
| | | | | | Influenza (Yearly)* | | | | | |
| | | | | | | MMR | | | | MMR |
| | | | | | | Varicella | | | | Varicella |
| | | | | | | | HepA§ | | | |

**Is your family growing?** To protect your new baby and yourself against whooping cough, get a Tdap vaccine towards the end of each pregnancy. Talk to your doctor for more details.

Shaded boxes indicate the vaccine can be given during shown age range.

**NOTE:** If your child misses a shot, you don't need to start over, just go back to your child's doctor for the next shot. Talk with your child's doctor if you have questions about vaccines.

**FOOTNOTES:**

* Two doses given at least four weeks apart are recommended for children aged 6 months through 8 years of age who are getting a flu vaccine for the first time and for some other children in this age group.

§ Two doses of HepA vaccine are needed for lasting protection. The first dose of HepA vaccine should be given between 12 months and 23 months of age. The second dose should be given 6 to 18 months later. HepA vaccination may be given to any child 12 months and older to protect against HepA. Children and adolescents who did not receive the HepA vaccine and are at high-risk, should be vaccinated against HepA.

*If your child has any medical conditions that put him at risk for infection or is traveling outside the United States, talk to your child's doctor about additional vaccines that he may need.*

SEE BACK PAGE FOR MORE INFORMATION ON VACCINE-PREVENTABLE DISEASES AND THE VACCINES THAT PREVENT THEM.

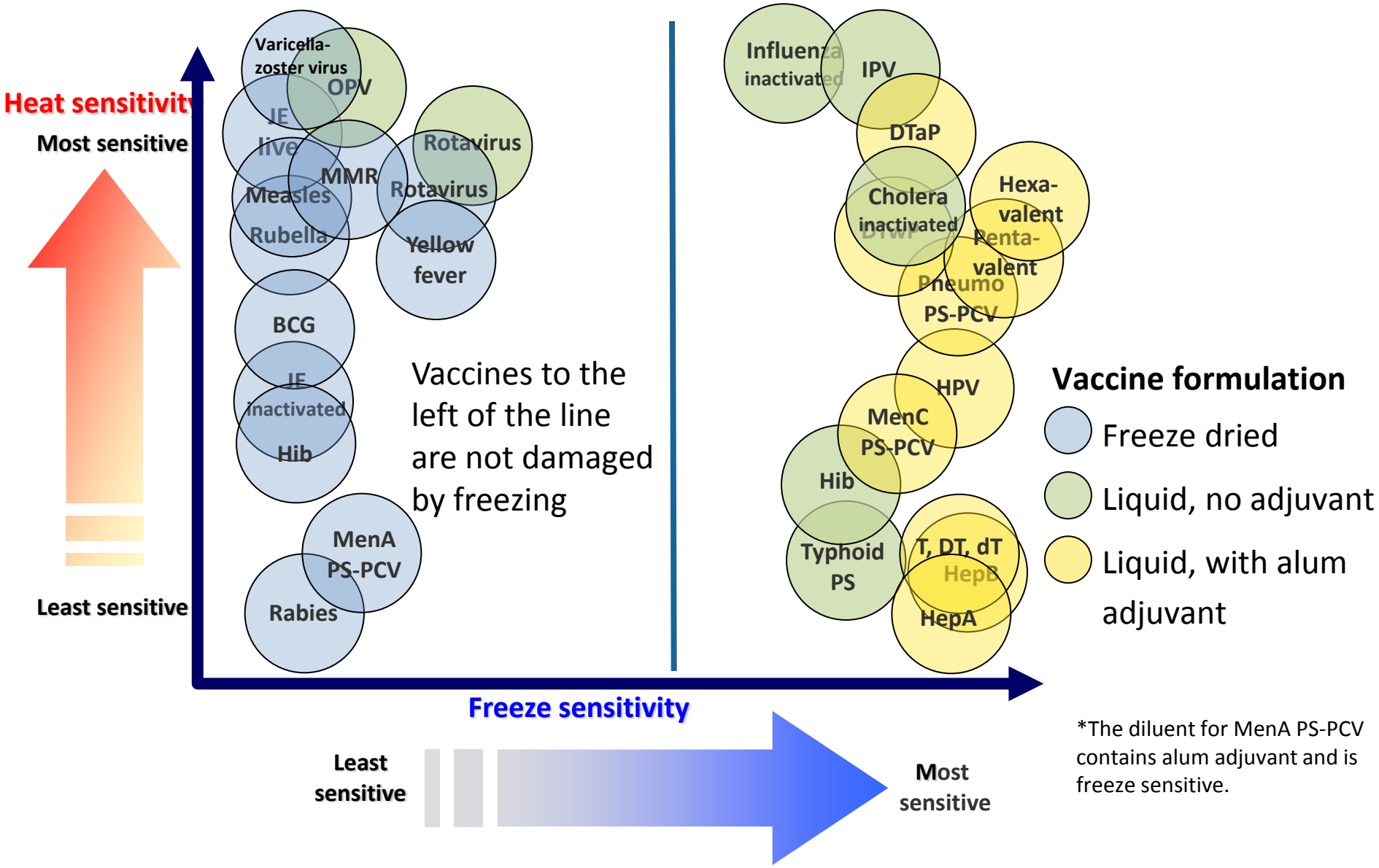
For more information, call toll free
**1-800-CDC-INFO** (1-800-232-4636)
or visit
**http://www.cdc.gov/vaccines**

**U.S. Department of Health and Human Services**
Centers for Disease Control and Prevention

AMERICAN ACADEMY OF FAMILY PHYSICIANS
STRONG MEDICINE FOR AMERICA

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

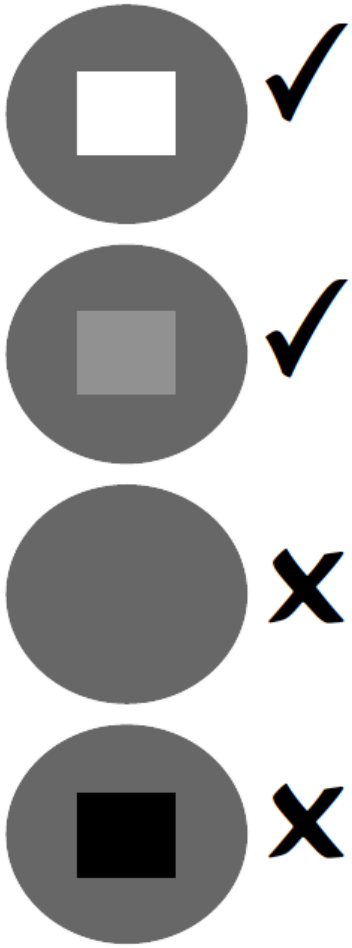
# Temperature sensitivity of vaccines




*The diluent for MenA PS-PCV contains alum adjuvant and is freeze sensitive.

Ack, WHO

Figure 1: Vaccine vial monitor showing four stages of exposure



Inner square is lighter than outer ring.
**If the expiry date is not passed,**
**USE the vaccine.**

As time passes: Inner square is still lighter than outer ring.
**If the expiry date is not passed,**
**USE the vaccine.**

**Discard point:** Inner square matches the colour of outer ring.
**DO NOT use the vaccine.**

**Beyond the discard point:** Inner square is darker than outer ring.
**DO NOT use the vaccine.**

# Vaccine delivery

- Almost all vaccines are currently delivered by injections; exceptions are oral polio, rotavirus, cholera, and salmonella vaccines.
- Unsafe injections have been linked to around 23 million new hepatitis B, hepatitis C, and HIV infections each year (WHO, 2004).
- Autodisabled syringes has reduced reuse of needles and syringes
- Needlestick injuries and unsafe disposal of sharps waste still leave health care workers, patients, and the community at risk

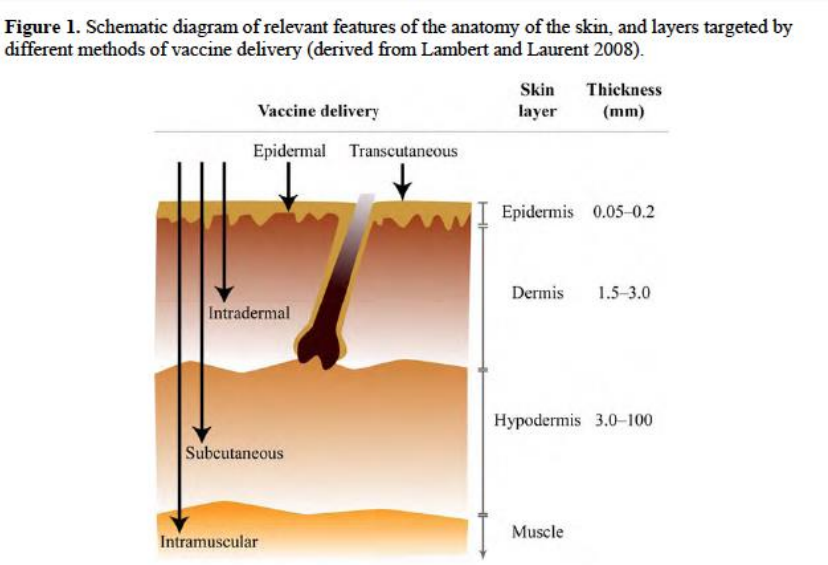



**Figure 1.** Schematic diagram of relevant features of the anatomy of the skin, and layers targeted by different methods of vaccine delivery (derived from Lambert and Laurent 2008).

# Transcutaneous vaccine delivery systems

| Technique | Principle |
|---|---|
| Electroporation | Method to transiently increase permeability of a membrane by applying a single or multiple short-duration pulses |
| Iontophoresis | Method to enhance transport of ionic or charged molecules through a biological membrane by the passage of direct or periodic electric current through an electrolyte solution with an appropriate electrode polarity |
| Sonophoresis | Method to enhance substance penetration through the SC by disrupting the structure of the membrane with low-frequency ultrasound |
| Jet injectors | Devices that use pressure to deliver substances into the skin |
| Patch formulations | Devices to enhance penetration of antigens into the skin |
| Microneedles | Devices that can create a transport pathway large enough for proteins and nanoparticles but small enough to avoid pain |
| Nanoparticles | Nano-bio interaction, Consequent induction of transient and reversible opening of SC, through hair follicles |
| Lipid-based vesicles | Nano-bio interaction, flexible bilayer mixes with SC and disrupts it |

Vaccine 31 (2013) 2403– 2415

# Global Immunisation Vision and Strategy (GIVS)

A joint WHO/UNICEF framework for immunization was developed to guide countries and international partners over a 10 year period

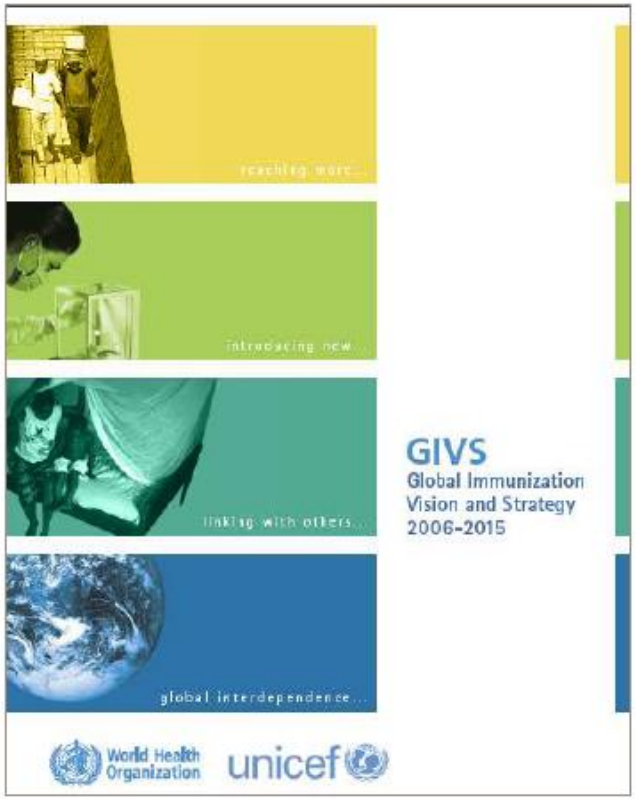
## Four strategic areas

1. Protecting more people:
   → Expand immunisation beyond infancy to older age groups

2. Introducing new vaccines and technologies

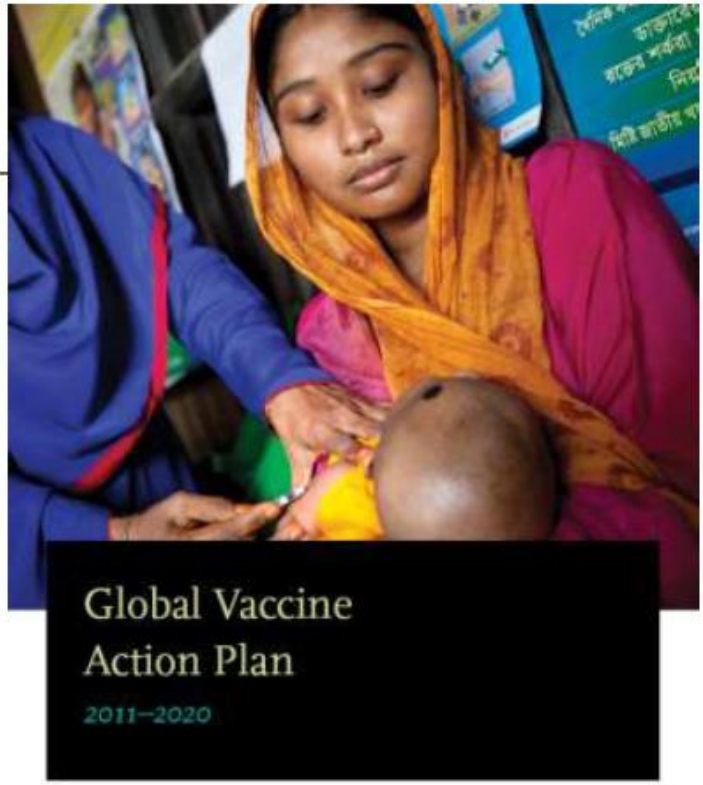
3. Integration with other interventions and surveillance in the health system context

4. Immunization in a context of global interdependence




http://www.who.int/immunization/givs/GIVS_strategies.pdf

# The Global Vaccine Action Plan




- The Global Vaccine Action Plan (GVAP) builds on the success of **GIVS**.
- **GVAP** was endorsed by the 194 Members of the World Health Assembly in May 2012.
- It is a framework to prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all communities.

**Developing the plan brought together more than 1100 individuals in 140 countries, representing 290 distinct organizations**

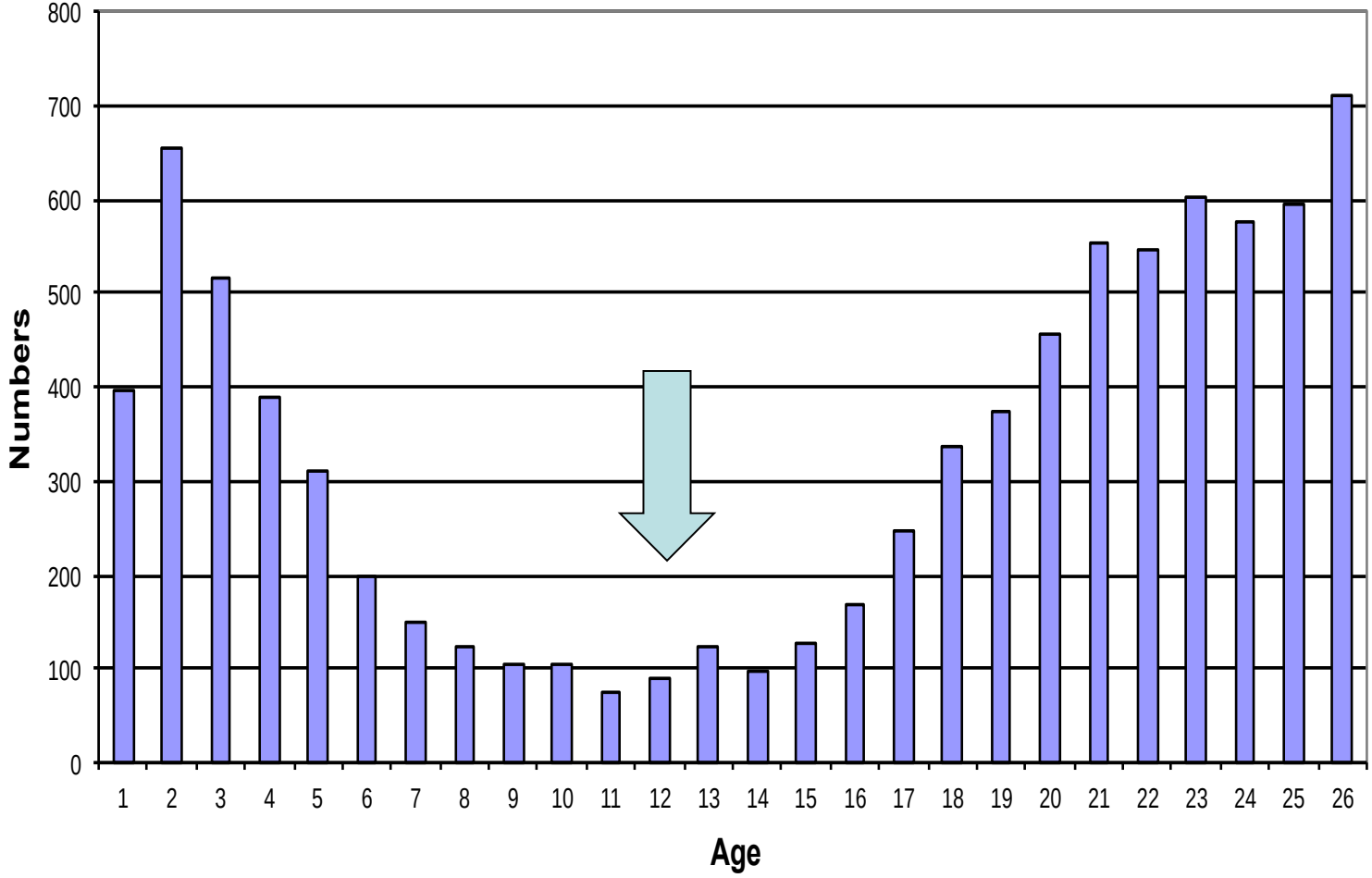
GVAP was the product of the **Decade of Vaccines** (DoV) Collaboration.

*http://www.dovcollaboration.org/action-plan/*

# Why vaccinate in adolescents.

- Optimal time – before development of disease in adulthood eg TB and HIV.

# Numbers of TB cases by age in Cape Town in 2002/2003



# Why vaccinate in adolescents.

- Optimal time – before development of disease in adulthood eg TB and HIV.
- Adolescents are a reservoir for infection for infants, the elderly and at risk populations.

# Pertussis in Australia today

## A disease of adolescents and adults that can kill infants


**BACKGROUND**

Adolescents and adults are the main reservoir of pertussis infection in Australia today. Diagnosis in these age groups can be difficult because of atypical clinical presentations and limitations of laboratory investigations.

**OBJECTIVE**

This article discusses the common presentation of pertussis in adults and adolescents, the use and limitations of laboratory testing, and appropriate treatment and prophylaxis.

**DISCUSSION**

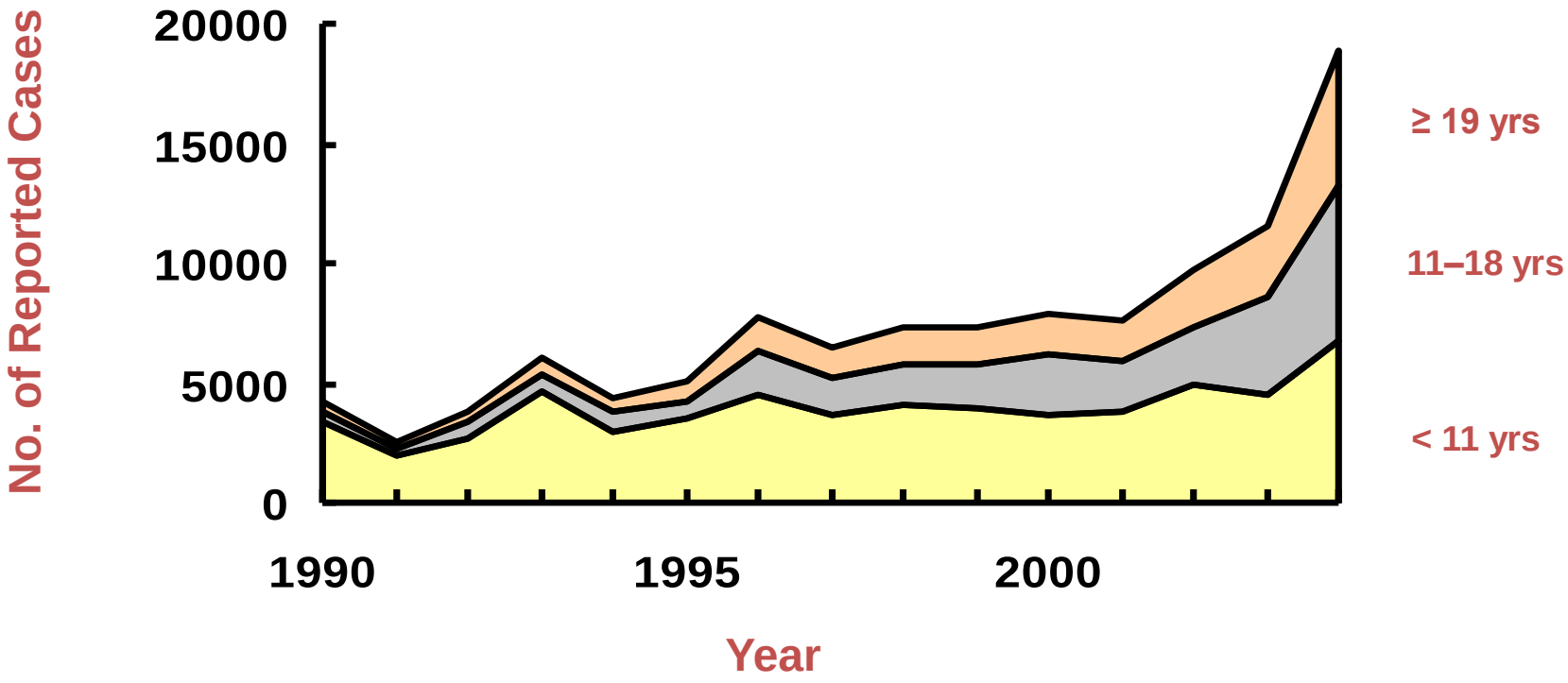
The reason for treating cases and providing chemoprophylaxis for contacts is to prevent infection in infants, who account for 90% of deaths from pertussis. Treatment with the newer macrolides appears to be as effective as erythromycin and with less side effects; however, roxithromycin should not be used as its in vivo efficacy is unproven. The majority of pertussis cases will be seen in general practice – most likely during the infectious period – therefore general practitioners need to consider being vaccinated with dTpa against pertussis.


Aust Fam Physician Jan 2007

# Why vaccinate in adolescents.

- Optimal time – before development of disease in adulthood eg TB and HIV.
- Adolescents are a reservoir for infection for infants, the elderly and at risk populations.
- Waning infant vaccine induced immunity results in cases occurring in adolescents

# Reported Pertussis by Age Group, 1980-2004*




*2004 data provisional
National Immunization Program unpublished data

# Loss in vaccine induced immunity to varicella over time

- Sentinel population of 350000 - children 8-12
- Universal vaccination in 1995
- Those vaccinated > 5 years previously had more severe disease than those vaccinated < 5 years previously (RR2.6)
- Annual rate of breakthrough varicella increased from 1.6/1000 py since vaccination within 1 year to 9/1000 at 5 years

NEJM 15 Mar 2007

# Why vaccinate in adolescents.

- Optimal time – before development of disease in adulthood eg TB and HIV.
- Adolescents are a reservoir for infection for infants, the elderly and at risk populations.
- Waning infant vaccine induced immunity results in cases occurring in adolescents
- Catch – up vaccinations

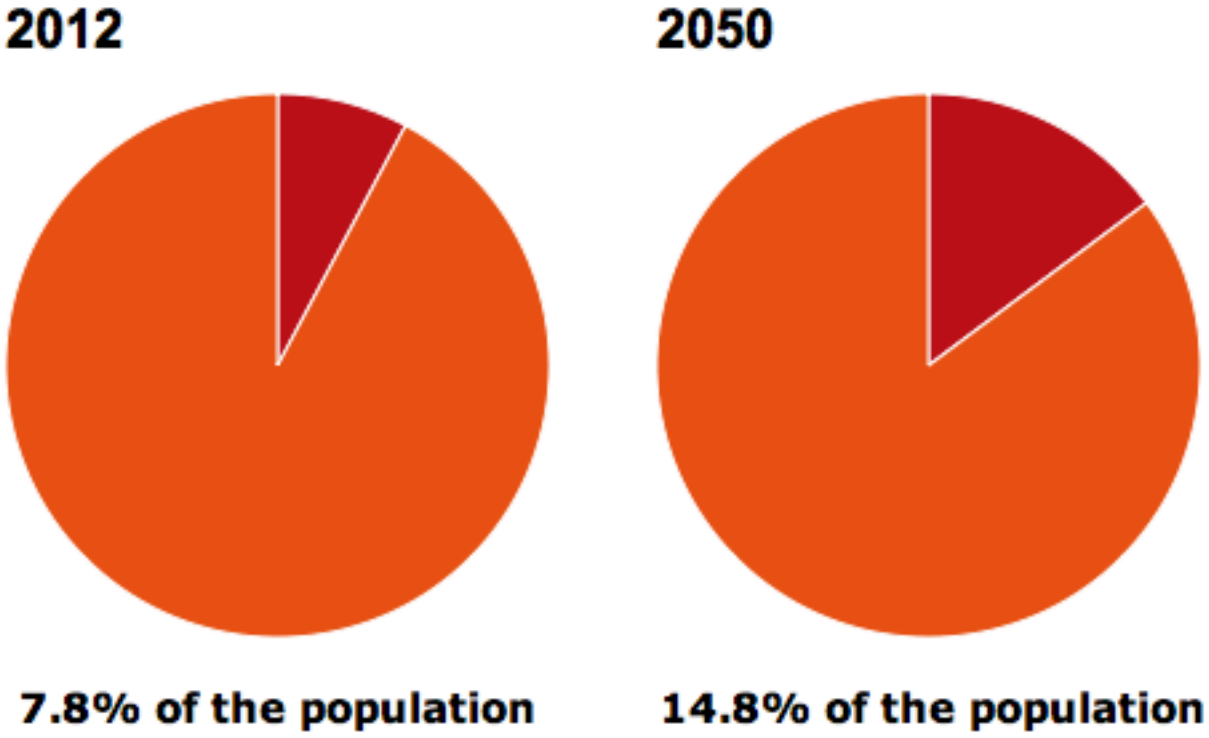
# Why vaccinate adults?

- Vaccine preventable diseases cause significant morbidity and mortality.
- Waning vaccine induced immunity.
- Immune senecence.
- Concomitant health problems.
- Herd immunity.
- High risk situations including:
  - Pregnancy.
  - Health care workers.
  - People in institutions.

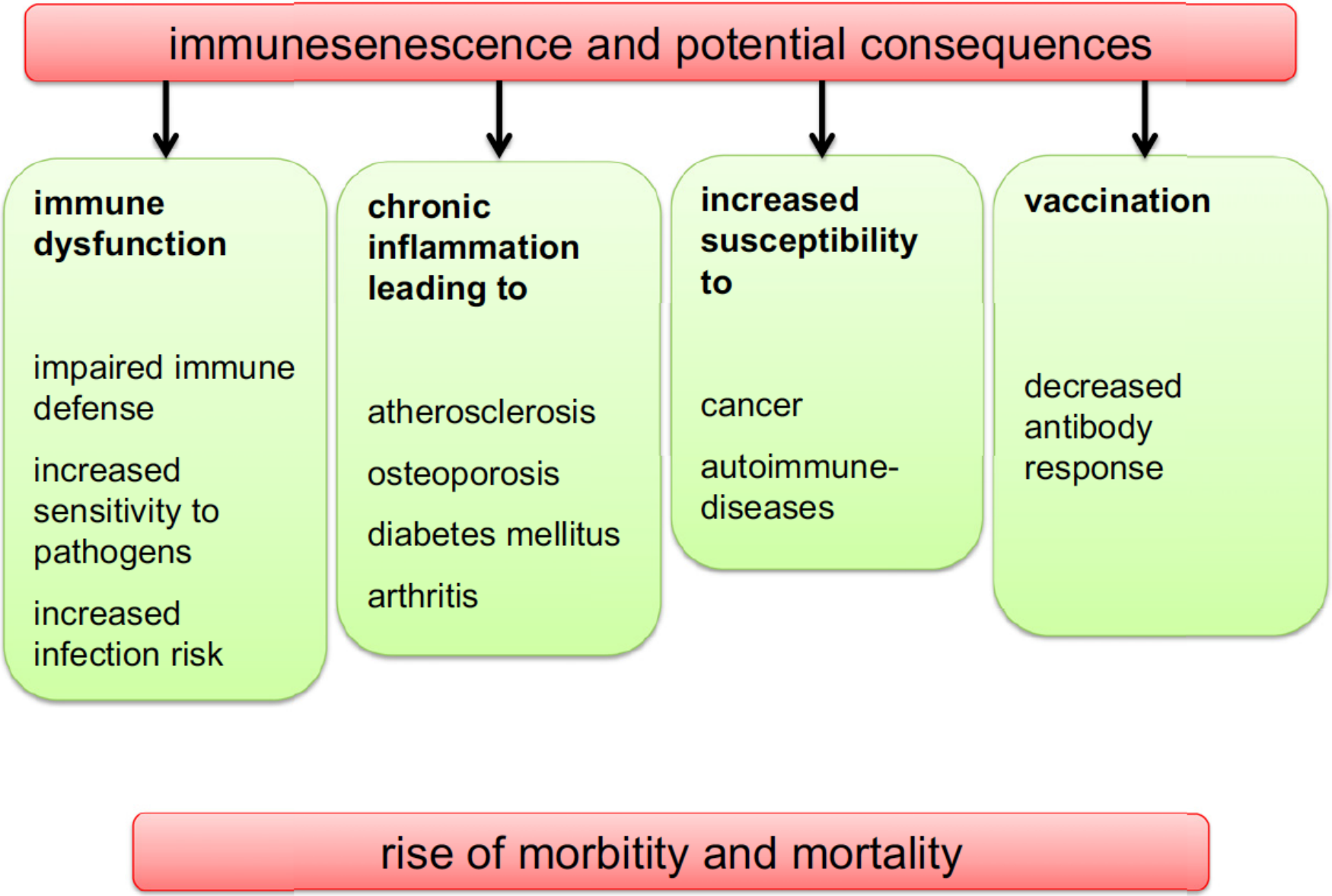
# South Africa

Percentage of population aged

60+




| Population over 60 | 2012 | % of population over 60 |
|---|---|---|
| 14.4 million | UK | 23.0% |
| 21.6 million | Brazil | 10.9% |
| 8.8 million | Nigeria | 5.3% |


immunesenescence and potential consequences
immune dysfunction
impaired immune defense
increased sensitivity to pathogens
increased infection risk
chronic inflammation leading to
atherosclerosis
osteoporosis
diabetes mellitus
arthritis
increased susceptibility to
cancer
autoimmune-diseases
vaccination
decreased antibody response
rise of morbitity and mortality

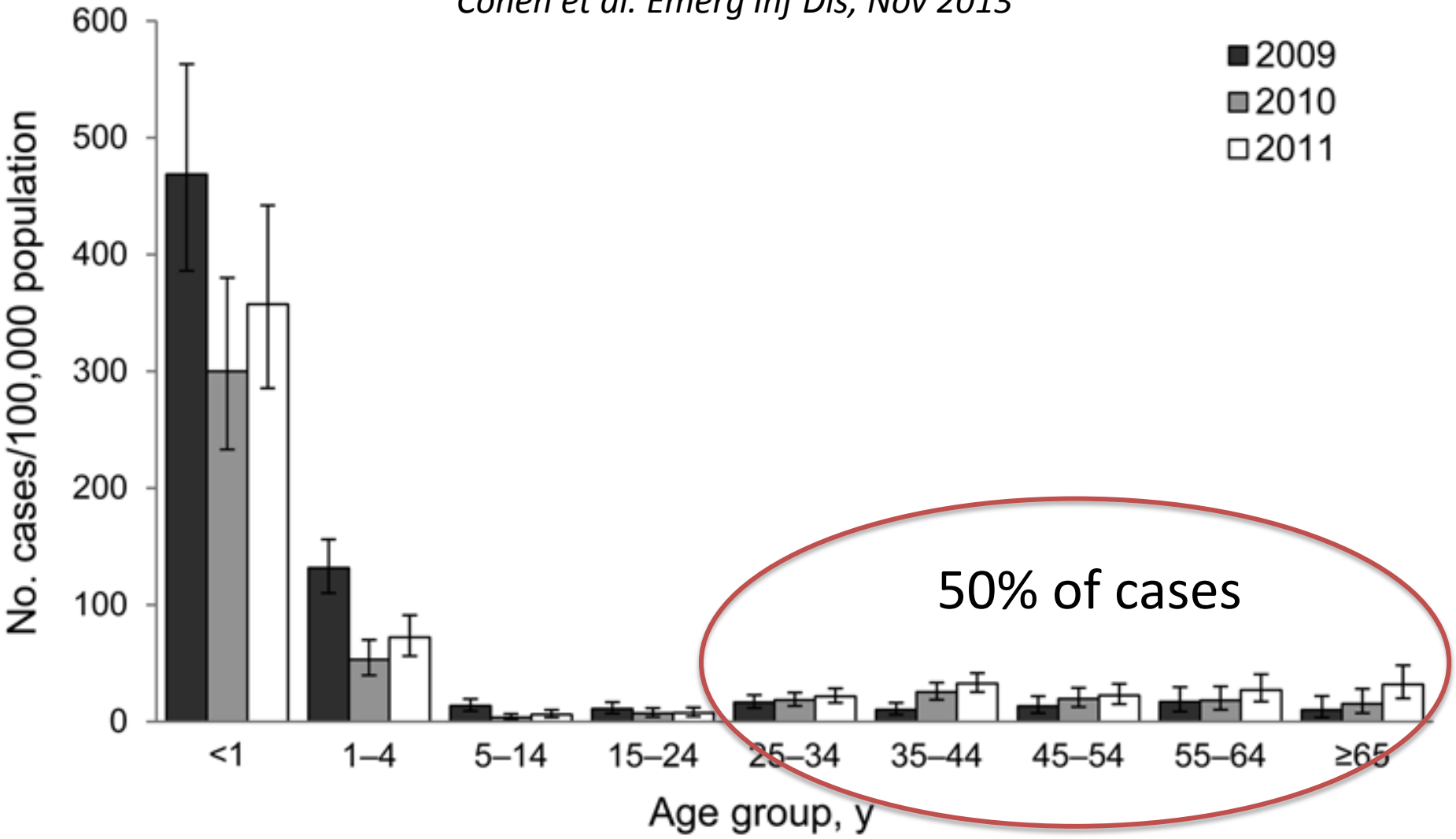
# VPDs in the USA

- Causes significant morbidity and is a common cause for hospitalisation in adults.
- 60000 adults and 300 children die each year.
- 200 fold greater mortality due to VPDs in adults
- “What would our response be if 60000 children were dying from VPDs?”

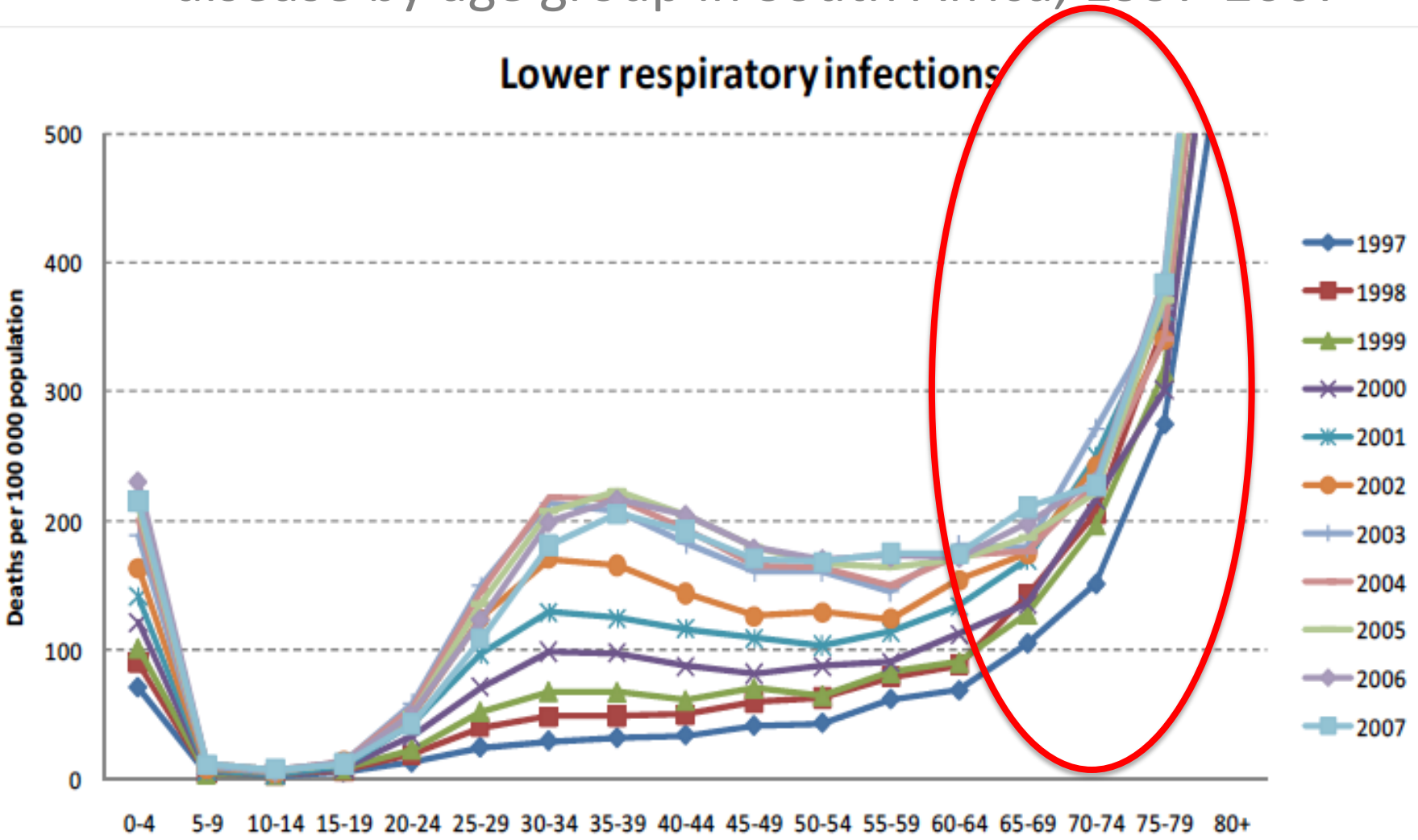
*Institute of Medicine, 2000*

# Severe Influenza-associated Respiratory Infection in South Africa, 2009–2011

*Cohen et al. Emerg Inf Dis, Nov 2013*



# Age specific mortality rates for common infectious disease by age group in South Africa, 1997-2007

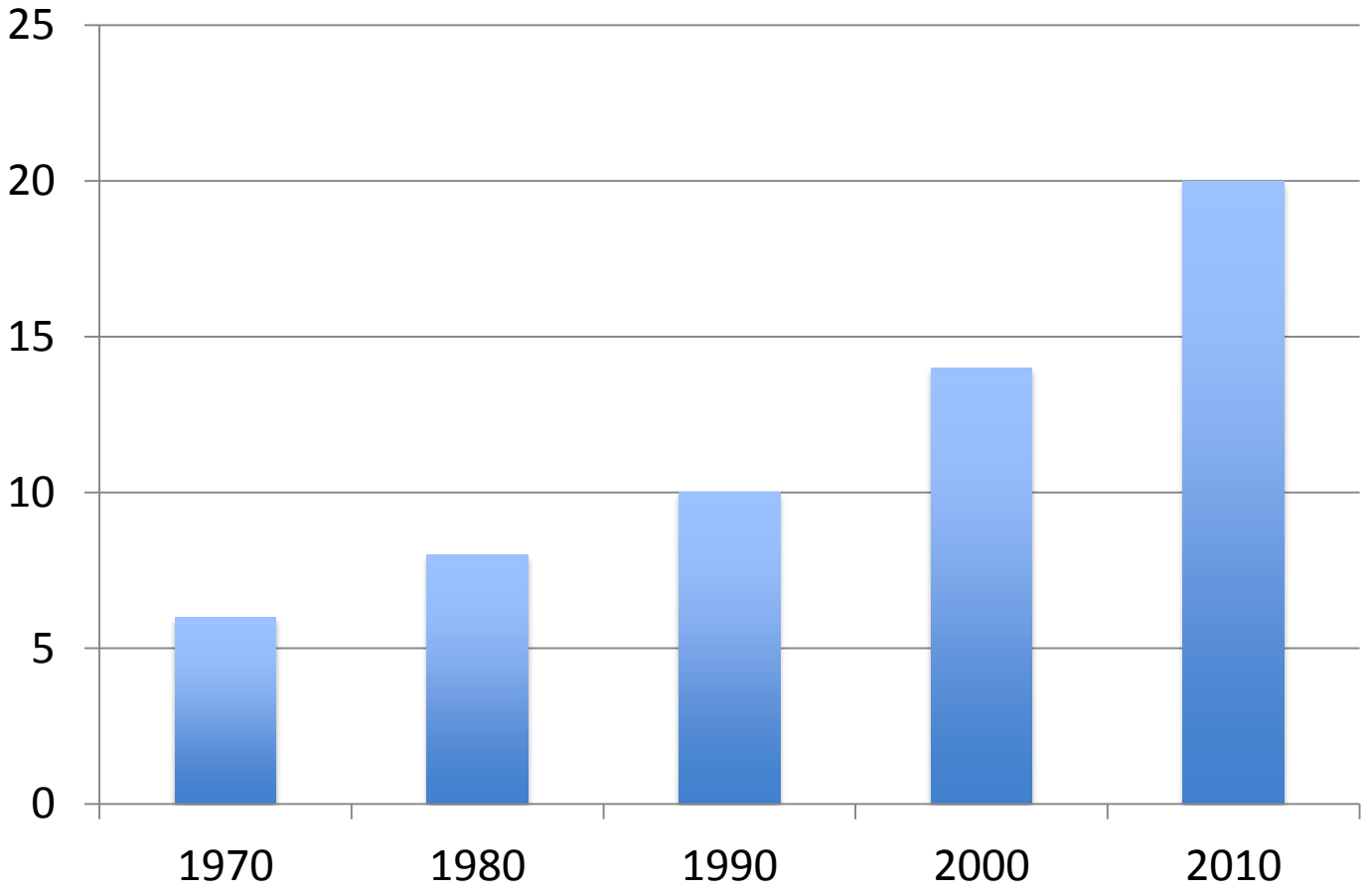



*http://www.mrc.ac.za/bod/cause_death_statsSA.pdf*

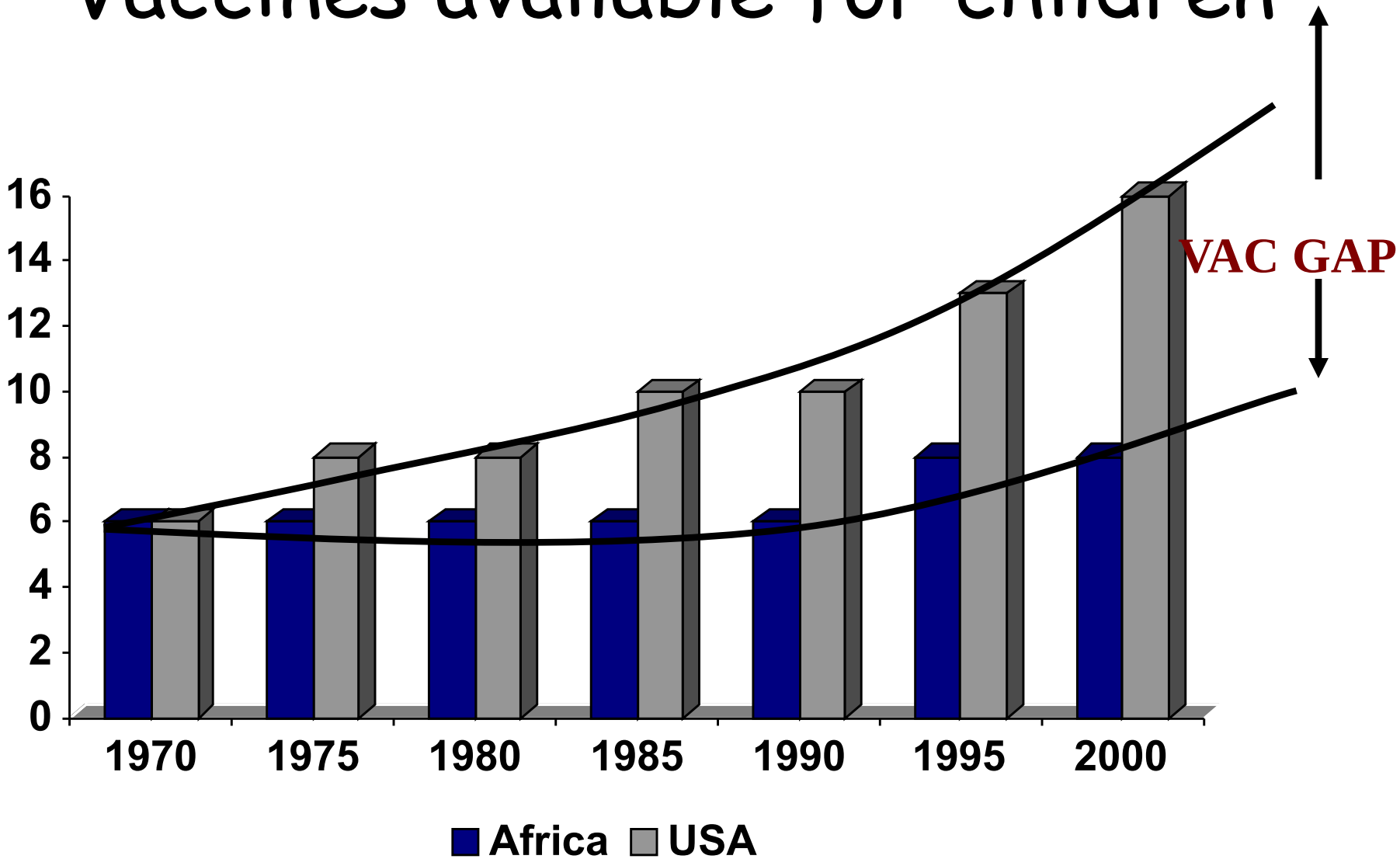
# Major trends in vaccinology

1. Steady increase in the number of vaccines included in the routine immunization program.

# Vaccines available for children in developed countries



# Vaccines available for children



# The vaccination gap

- Exists between regions and countries
- Exists within countries

In developing countries

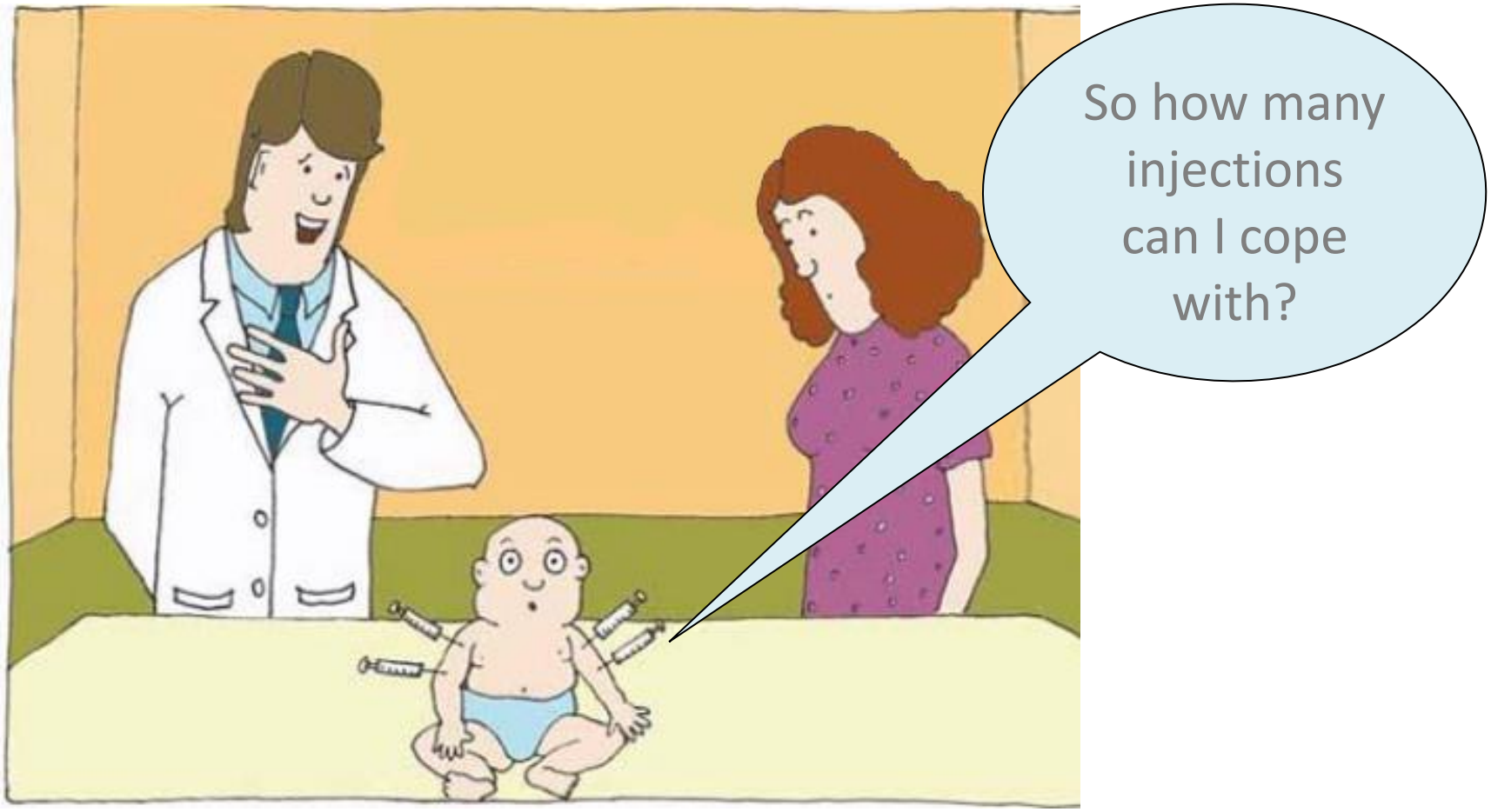
- Children have access to fewer vaccines
- Do not have access to basic vaccines

# Major trends in vaccinology

1. Steady increase in the number of vaccines included in the routine immunization program.
2. Move towards more purified, safer and more effective vaccines.

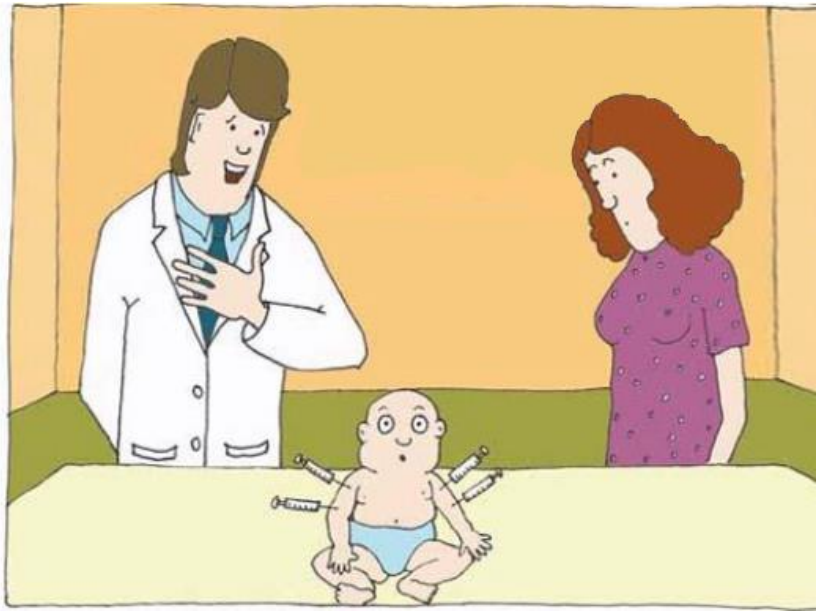
# Major trends in vaccinology

1. Steady increase in the number of vaccines included in the routine immunization program.
2. Move towards more purified, safer and more effective vaccines.
3. Use of increasingly sophisticated combinations, to deliver more vaccines with fewer injections.


So how many injections can I cope with?

# Combination vaccines

- Combination vaccines increase acceptability of multiple vaccines at one visit.
- Vaccinated children get fewer injections.
- Combination vaccines simplify logistics.



# Challenges to universal vaccination

- Social, political and economic factors
- Vaccine costs and funding
- Health service problems
- Community problems
- HIV epidemic
- Anti-vaccination lobby
- Vaccine shortages


Gillray, 1802

# HIV epidemic

- Impact on health and social services
- Diverting scarce resources
- Strain on health workers
- Direct effect on health workers
- Impact on vaccine efficacy

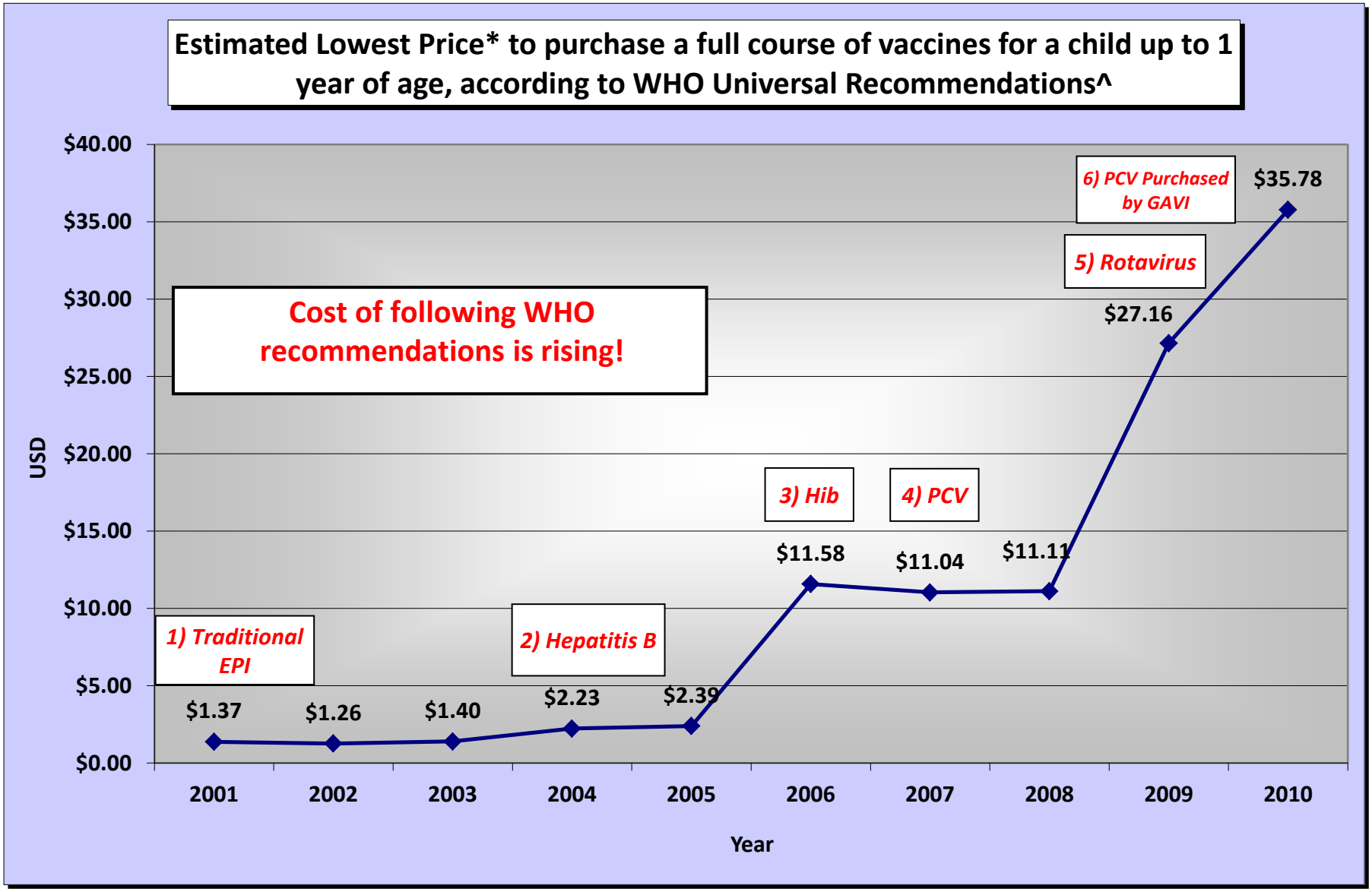
# Vaccine costs

WHO estimates

- $20 per child for basic EPI vaccines
- incl. vaccines and delivery costs.

Viewed in context of current health expenditure

- many African countries: <$50 per person pa
- SA : $819 per person pa (2007)


Estimated Lowest Price* to purchase a full course of vaccines for a child up to 1 year of age, according to WHO Universal Recommendations^
$40.00
$35.00
$30.00
$25.00
$20.00
$15.00
$10.00
$5.00
$0.00
USD
Cost of following WHO recommendations is rising!
1) Traditional EPI
2) Hepatitis B
3) Hib
4) PCV
5) Rotavirus
6) PCV Purchased by GAVI
$1.37
$1.26
$1.40
$2.23
$2.39
$11.58
$11.04
$11.11
$27.16
$35.78
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
Year

# Vaccine costs for SA

| | |
|---|---|
| • BCG | R4 |
| • OPV | R2 |
| • Measles | R8 |
| • Hep B | R16 |
| • Hib/DTP/IPV | R408 |
| • SUB TOTAL | R438 |
| • Rota | R160 |
| • Pneumo | R510 |
| • TOTAL | R1008 |
| • HPV | R1800 |

# United Nations Convention on the Rights of the Child

Article 24 – right to good health

includes the right to immunization against the major infectious diseases

How do we ensure this right?

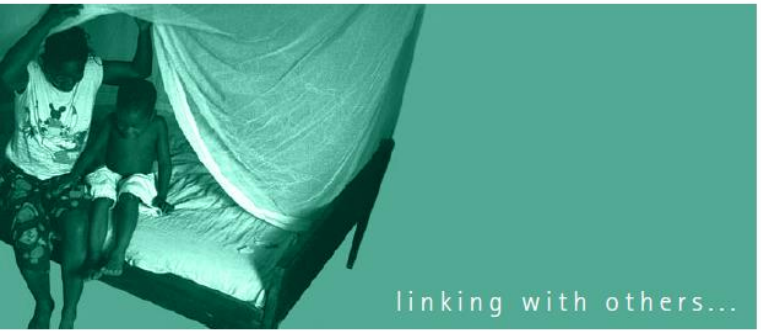
# Action - 1.

- Political commitment.
- Increasing resources for vaccination.
- Promoting the concept of vaccination.
- Increasing community awareness.

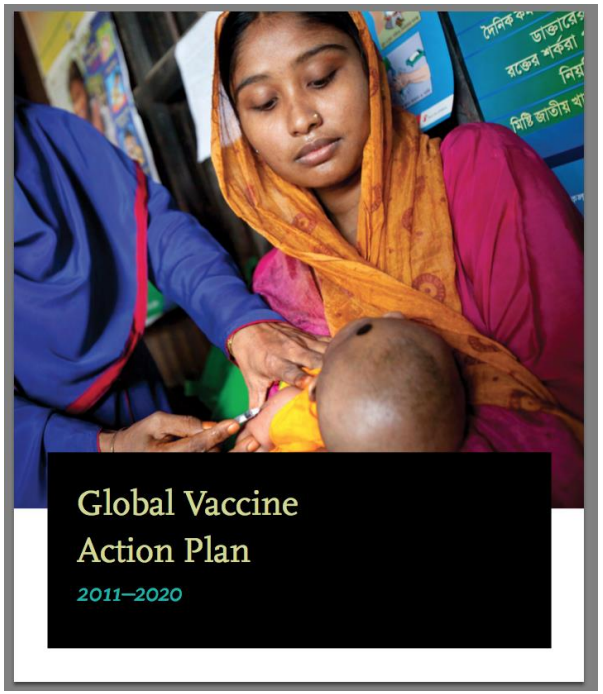
# Action - 2

- Improve access to sustainable immunisation services
- Expand use of existing vaccines
- Introduce new vaccines
- Accelerate R&D for vaccines needed in developing countries

# Global response to existing, new and anticipated challenges to immunization




**GIVS**
Global Immunization Vision and Strategy 2006–2015




DECADE of VACCINES COLLABORATION

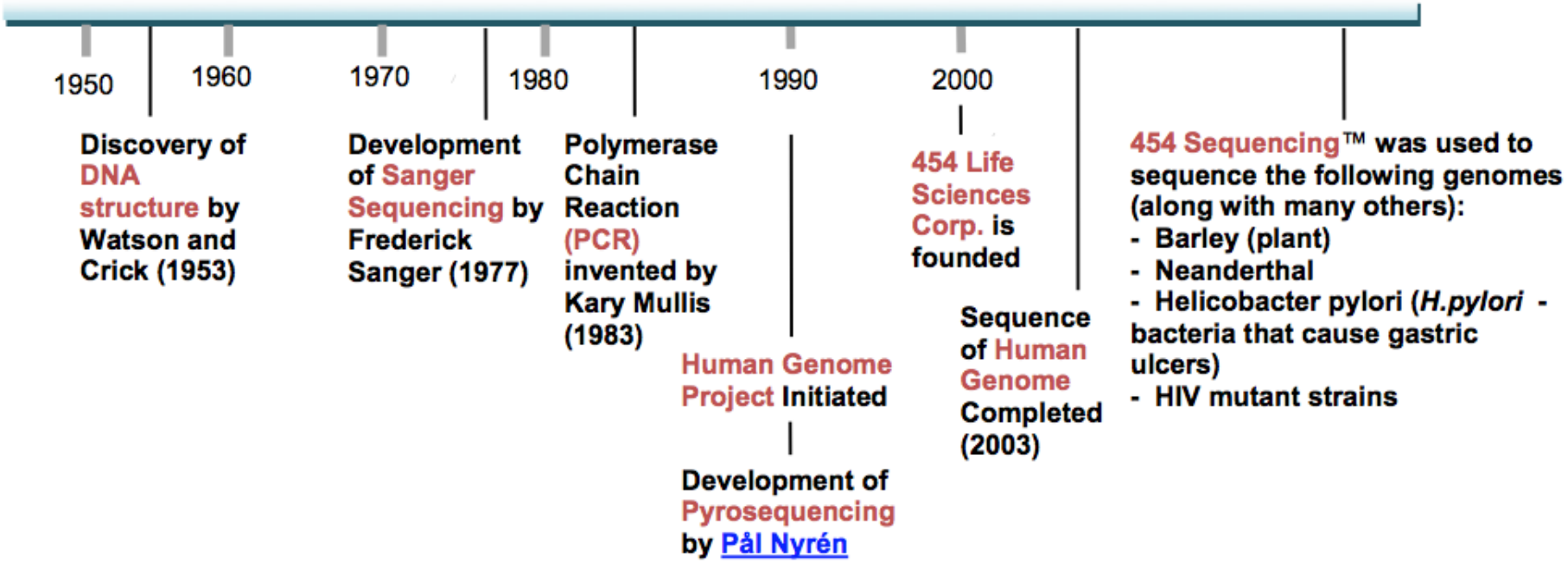
# Cape Town Declaration on Vaccines

## Adopted at the 1st International African Vaccinology Conference
## 11 November 2012

The First International African Vaccine Conference (IAVC) held in Cape Town, South Africa, brought together 500 health workers, program managers, researchers, representatives of civil society, government, and international agencies to discuss successes and challenges of immunization program in Africa and to explore regionally appropriate solution

- Ownership
- Accountability
- Advocate for sustainable funding
- Enhance programme performance
- Encourage indigenous vaccine development

# History of Genome Sequencing

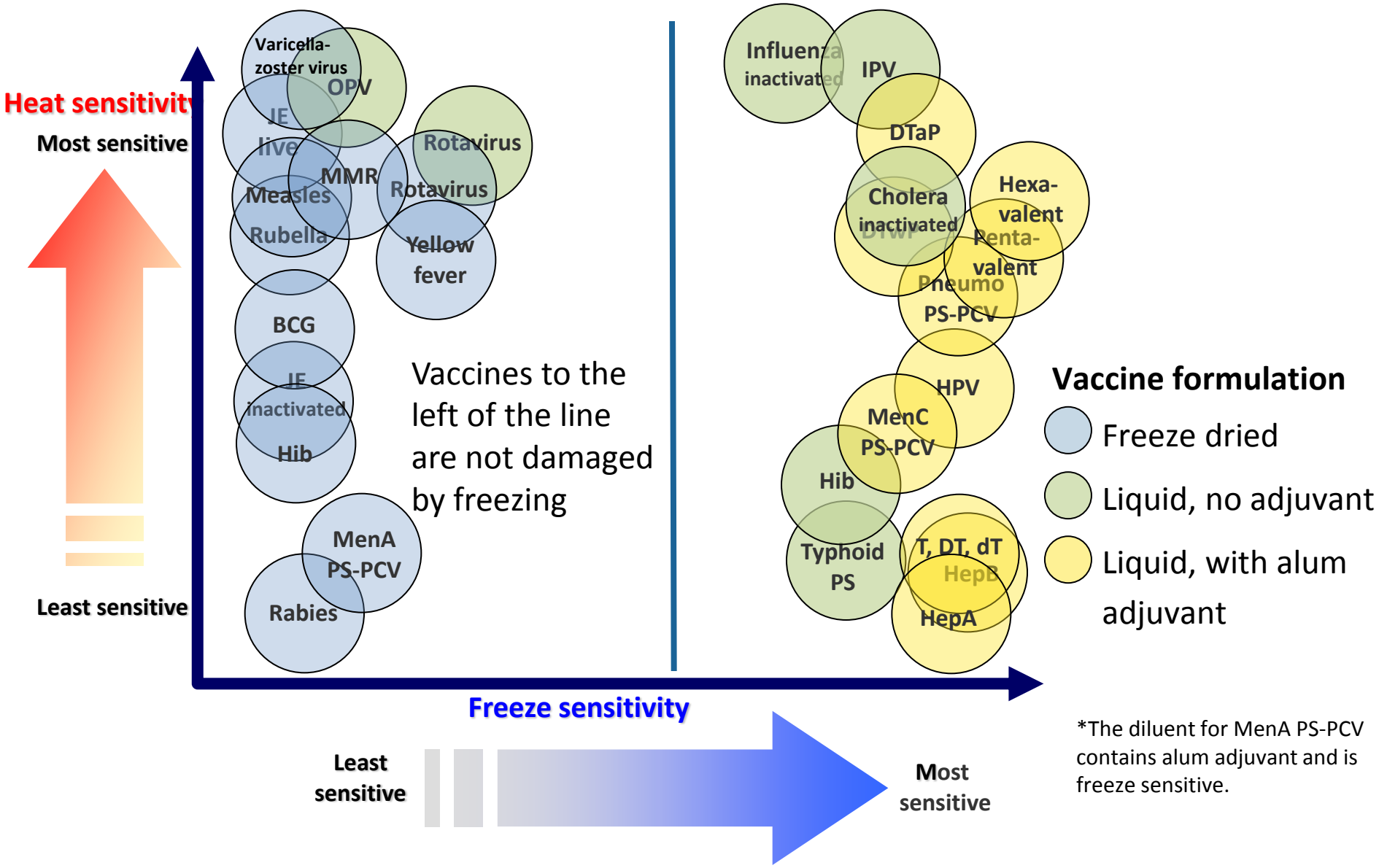



Source: U.S. Department of Energy Office of Science, Systems Biology for Energy and the Environment, Human Genome Project Information
Base URL: http://genomics.energy.gov/

# Whole-Genome Random Sequencing and Assembly of *Haemophilus influenzae* Rd

Robert D. Fleischmann, Mark D. Adams, Owen White, Rebecca A. Clayton, Ewen F. Kirkness, Anthony R. Kerlavage, Carol J. Bult, Jean-Francois Tomb, Brian A. Dougherty, Joseph M. Merrick, Keith McKenney, Granger Sutton, Will FitzHugh, Chris Fields,* Jeannine D. Gocayne, John Scott, Robert Shirley, Li-Ing Liu, Anna Glodek, Jenny M. Kelley, Janice F. Weidman, Cheryl A. Phillips, Tracy Spriggs, Eva Hedblom, Matthew D. Cotton, Teresa R. Utterback,

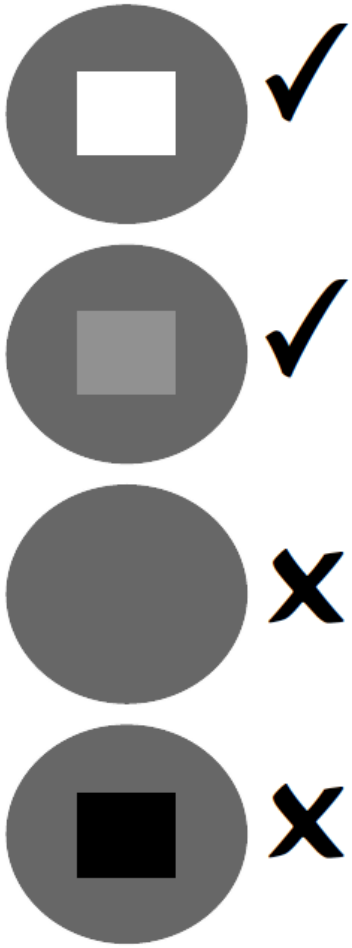
# Temperature sensitivity of vaccines




*The diluent for MenA PS-PCV contains alum adjuvant and is freeze sensitive.

Ack, WHO

Figure 1: Vaccine vial monitor showing four stages of exposure



Inner square is lighter than outer ring.
**If the expiry date is not passed,**
**USE the vaccine.**

As time passes: Inner square is still lighter than outer ring.
**If the expiry date is not passed,**
**USE the vaccine.**

**Discard point:** Inner square matches the colour of outer ring.
**DO NOT use the vaccine.**

**Beyond the discard point:** Inner square is darker than outer ring.
**DO NOT use the vaccine.**

**FIGURE 1:** Distribution improvements for EHPs Can Significantly Reduce Waste and Save Money

| CURRENT SITUATION | IMPROVEMENT BENCHMARKS | POTENTIAL IMPACT |
|---|---|---|
| **151 million vaccine doses were wasted in developing countries in 2007 due to improper refrigeration** | • Develop vaccines that do not require cold chain<br>• 10-50% reduction in heat- or freeze-damaged vaccine doses | • $200 M saved in direct costs for cold chain*<br>• 30.2 M vaccines saved annually<br>• $40.7 M saved annually<br>*(Assumption: 20% reduction)* |
| **100 million doses of DTP-HepB-Hib vaccine were distributed annually with high rates of wastage** | • Eliminate current wastage rates of 25-50% via product innovations and improved management | • $80 M saved annually on DTP-HepB-Hib** vaccine<br>*(Assumption: 25% wastage currently)* |

An estimated 30 million vac- cine doses could be saved annually in developing countries via improvements in the vaccine cold chain.

http://www.jhsph.edu/research/centers-and-institutes/ivac/resources/IVAC-Improving-Access-to-Essential-

# Intradermal delivery of vaccines

## Intradermal Delivery of Vaccines

A review of the literature and the potential for development for use in low- and middle-income countries

August 27, 2009

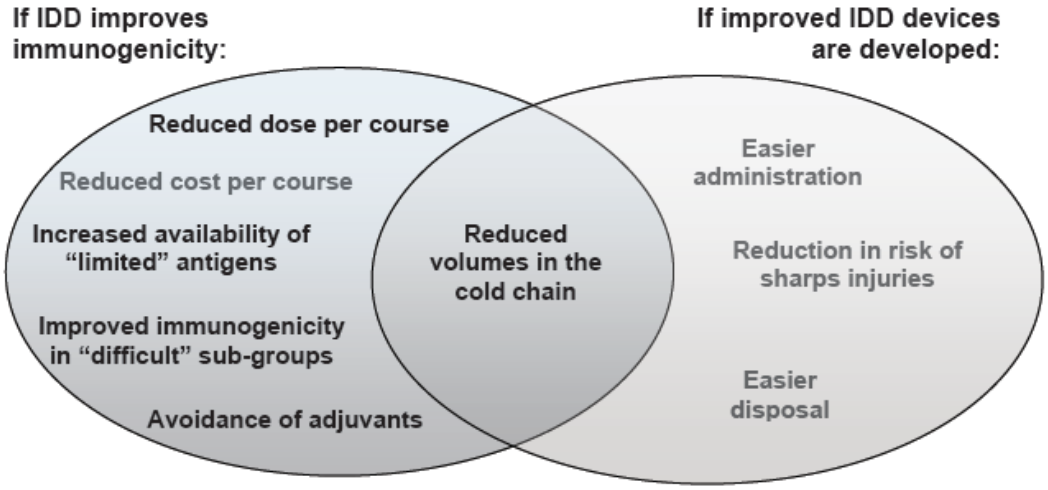
Batiment Avant Centre
13 Chemin du Levant
01210 Ferney Voltaire
France

Phone: 33.450.28.00.49
Fax: 33.450.28.04.07
www.path.org
www.who.int

World Health Organization

PATH

**Figure 2.** Summary of potential benefits of IDD of vaccines.

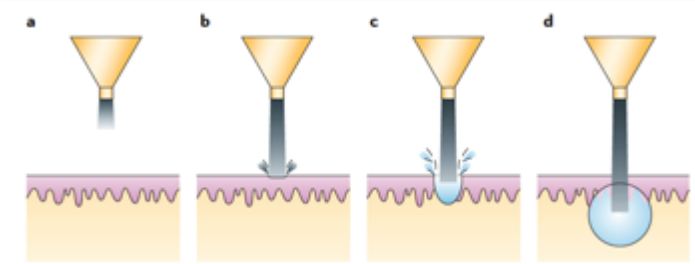



*NATURE REVIEWS | DRUG DISCOVERY VOLUME 5 | JULY 2006 | 543*

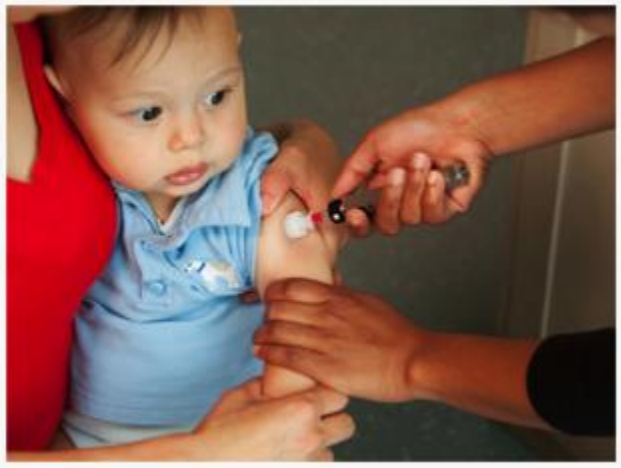
# Jet injectors


Advantages of jet injection

- the elimination of sharps and their associated disposal
- ease of administration
- consistent smaller ID dose equivalent to full SC or IM dose
- smaller individual doses could prevent vaccine shortages
- vaccine costs could be reduced.
- reduce the space required in the cold chain, thereby reducing storage and transportation costs.
- For many needle-phobic patients, they reduce anxiety and offer a preferred mode of delivery.




*Schematic depiction of the jet injection process.*



# Vaccine adaptation

Some characteristics of an ideal vaccine

- Safe in all populations
- Single dose
- Induces lifelong immunity
- Administrable without a needle and syringe
- Thermostable
- Administrable with other vaccines

# Malaria vaccine trials

- The most clinically advanced malaria vaccine candidate in development to prevent clinical disease, RTS,S, is a pre- erythrocytic, subunit vaccine based on a single parasite antigen (the circumsporozoite protein, or CSP), formulated with AS01 adjuvant, and currently undergoing Phase 3 evaluation via a collaboration between GSK, MVI, and 13 clinical sites in eight sub-Saharan African countries.

- One-year follow-up data in 5–17 month-old children revealed a 55% reduction in the incidence of the first or only episode of clinical malaria and a 47% reduction in the incidence of severe malaria, when compared to the control group.

  *N Engl J Med 2011;365:1863-75.*

- In 6–12 week-old infants, for the period 14 months after the first dose of vaccine, the reduction in incidence of first or only episode of clinical malaria was 30%. Vaccine efficacy against severe malaria was 26.0%

  *N Engl J Med 2012;367:2284-95*.

# Phase 3 HIV vaccine trials

- Recombinant protein (HIV gp120) adjuvanted in alum. This candidate failed to prevent or control HIV infection in men who have sex with men and in injection drug users. *Flynn JID 2005.*
- Recombinant adenovirus type 5 vaccine, containing HIV gag, pol and nef genes aimed at stimulating cellular immunity to control infection. Failed to provide any efficacy in preventing or controlling HIV in men who have sex with men (STEP trial). *Buchbinder, Lancet 2008*
- Prime–boost strategy (RV-144) utilizing a canarypox vector prime+ monomeric gp120 boost. Provided the first signal for prevention of HIV infection in humans, albeit with a modest 31.2% efficacy in heterosexuals at moderate risk for HIV infection. *Rerks-Ngarm. N Engl J Med 2009*

# Types of vaccines

- live-attenuated (OPV, MMRV, rota, flu, BCG …)
- killed inactivated (IPV, HepA)
- sub-unit or split (influenza)
- polysaccharide (MenACWY, Vi)
- conjugated (Hib/Men/PCV)
- combined (DTP-HepB/Hib; HAB …)
- recombinant adjuvanted (HepB, HPV, malaria …)
- DNA vaccines, mucosal vaccines
- therapeutic / cancer vaccines

# Cape Town Declaration on Vaccines

## Adopted at the 1st International African Vaccinology Conference
## 11 November 2012

The First International African Vaccine Conference (IAVC) held in Cape Town, South Africa, brought together 500 health workers, program managers, researchers, representatives of civil society, government, and international agencies to discuss successes and challenges of immunization program in Africa and to explore regionally appropriate solution

- Ownership
- Accountability
- Advocate for sustainable funding
- Enhance programme performance
- Encourage indigenous vaccine development

# Reverse vaccinology

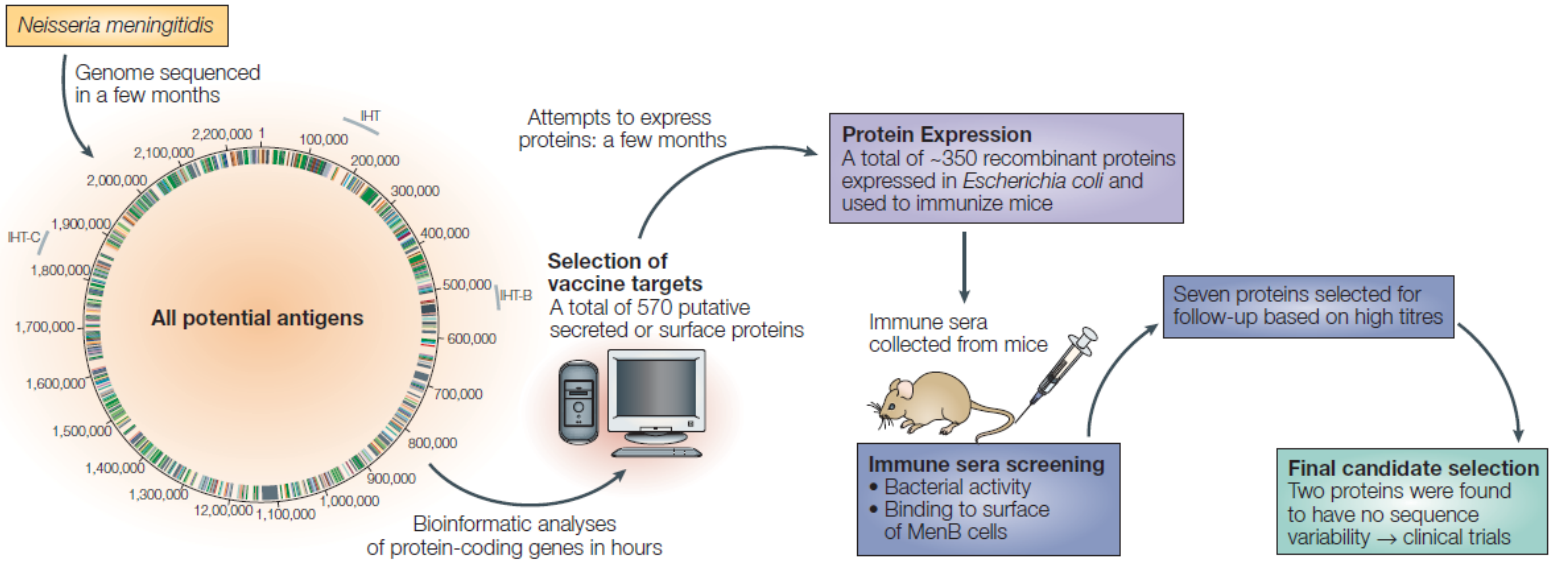
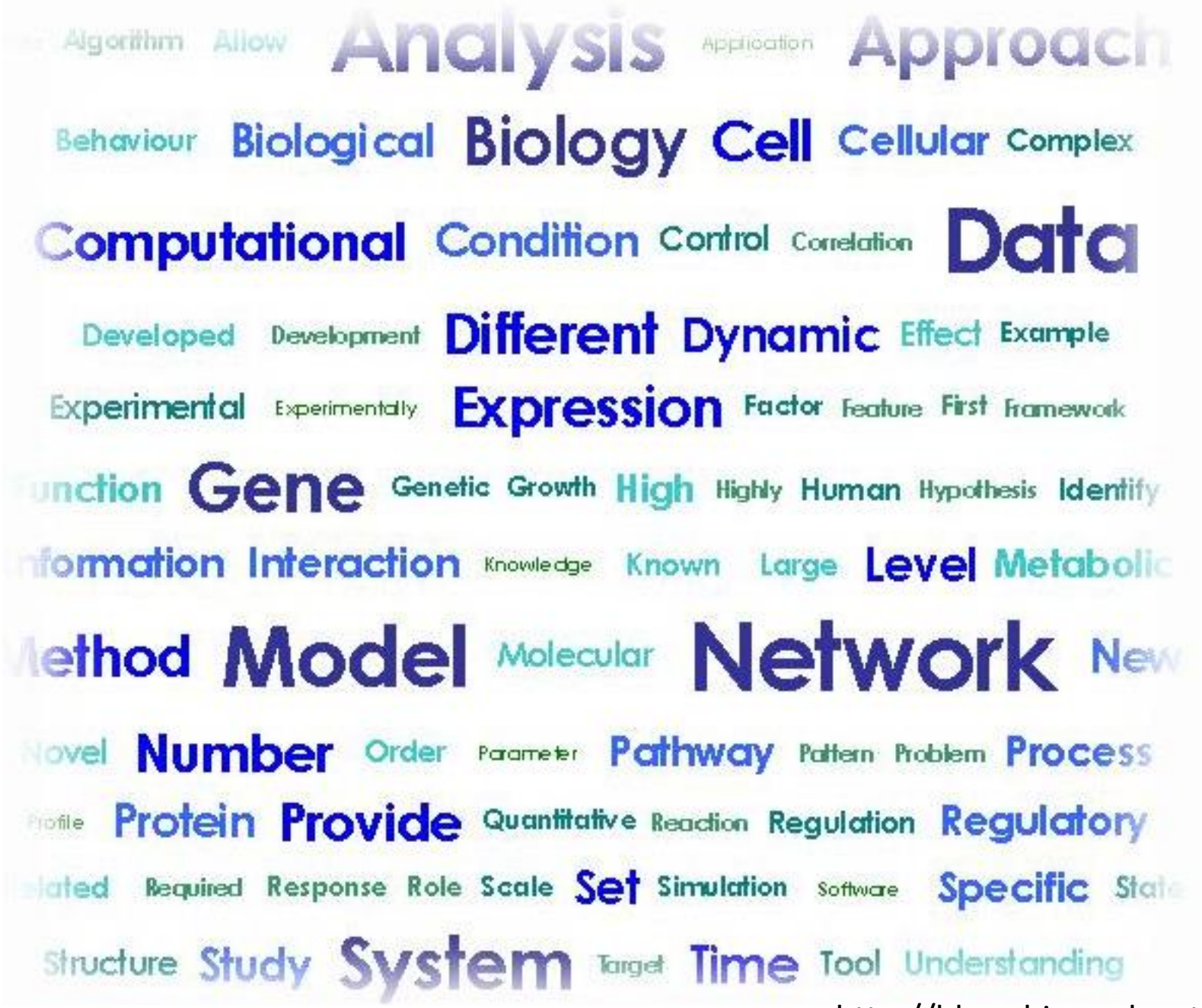



Figure 1 | **Reverse vaccinology: a genomics-enabled approach to vaccine development.** The reverse vaccinology strategy was first successfully used in the search for vaccine candidates against serogroup B *Neisseria meningitidis* (MenB)[53]. The first step in this process is the completion of the genome sequence of the pathogen of interest. In the case of MenB, this took approximately 18 months from the time when it was undertaken in 1998–1999. Today, the complete genome sequence of a pathogen can be obtained in a matter of days to weeks. Several algorithms are used to identify putative cell-surface or secreted proteins that could potentially elicit antibody responses in a human host. For MenB, 570 potential vaccine candidates were identified by bioinformatics approaches. The next step in the process was to produce recombinant proteins in *Escherichia coli*; approximately 350 proteins were expressed at high levels, purified and used as immunogens in mice. Immune sera were collected and assayed for their ability to bind to the surface of MenB cells and for their bactericidal activity *in vitro*. Seven proteins had high titres in all of the assays that were carried out and were taken into the final stage of evaluation, which assessed the extent of protein sequence variability in these proteins across large numbers of MenB isolates. From this large-scale screening process, two new vaccine candidates emerged that met all of the criteria. These vaccine candidates are now in Phase I clinical trials. Modified with permission from REF. 67 © Macmillan Magazines Ltd (2000).

*Nature review: Genetics, Jan 2004*

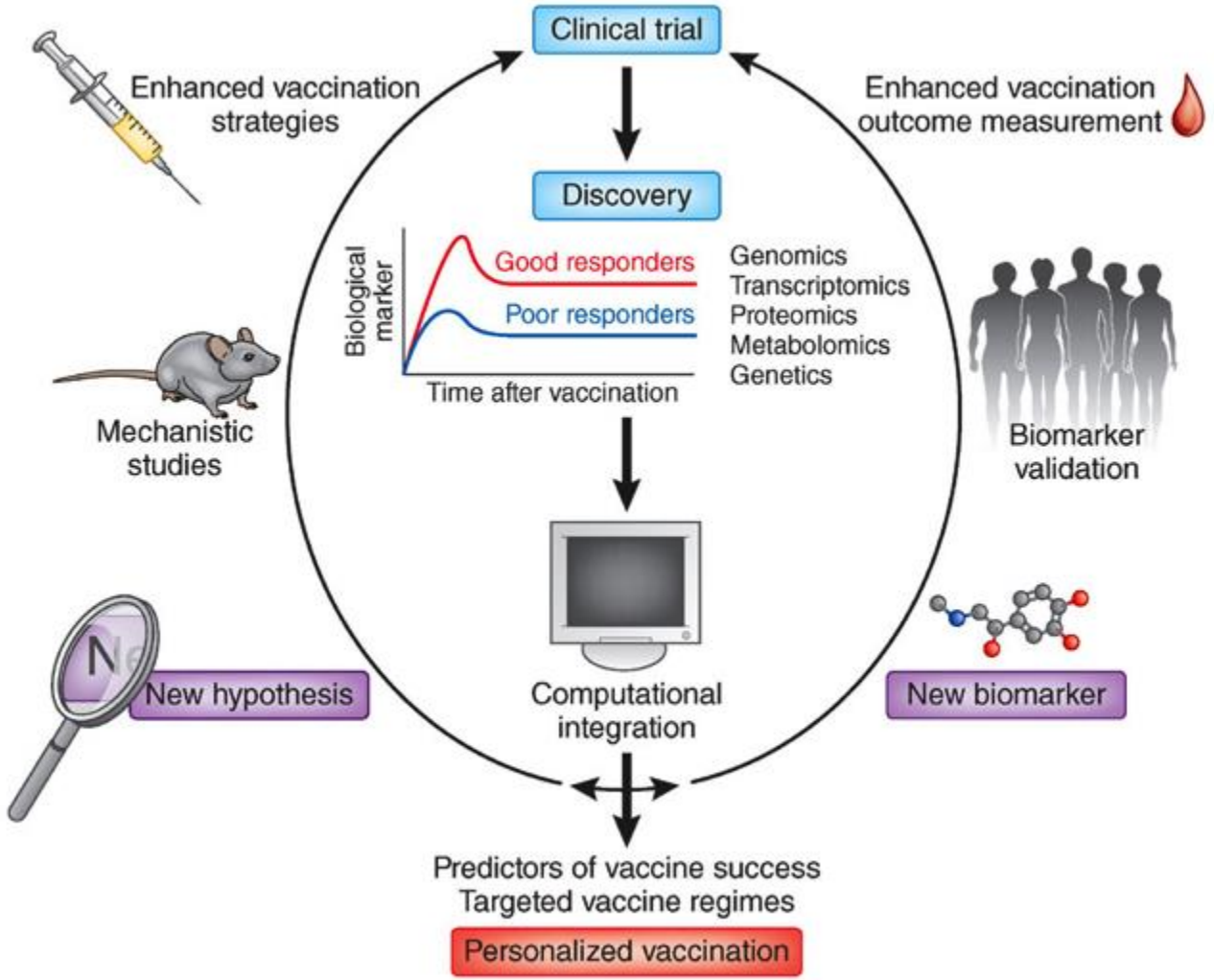



http://blogs.biomedcentral.com

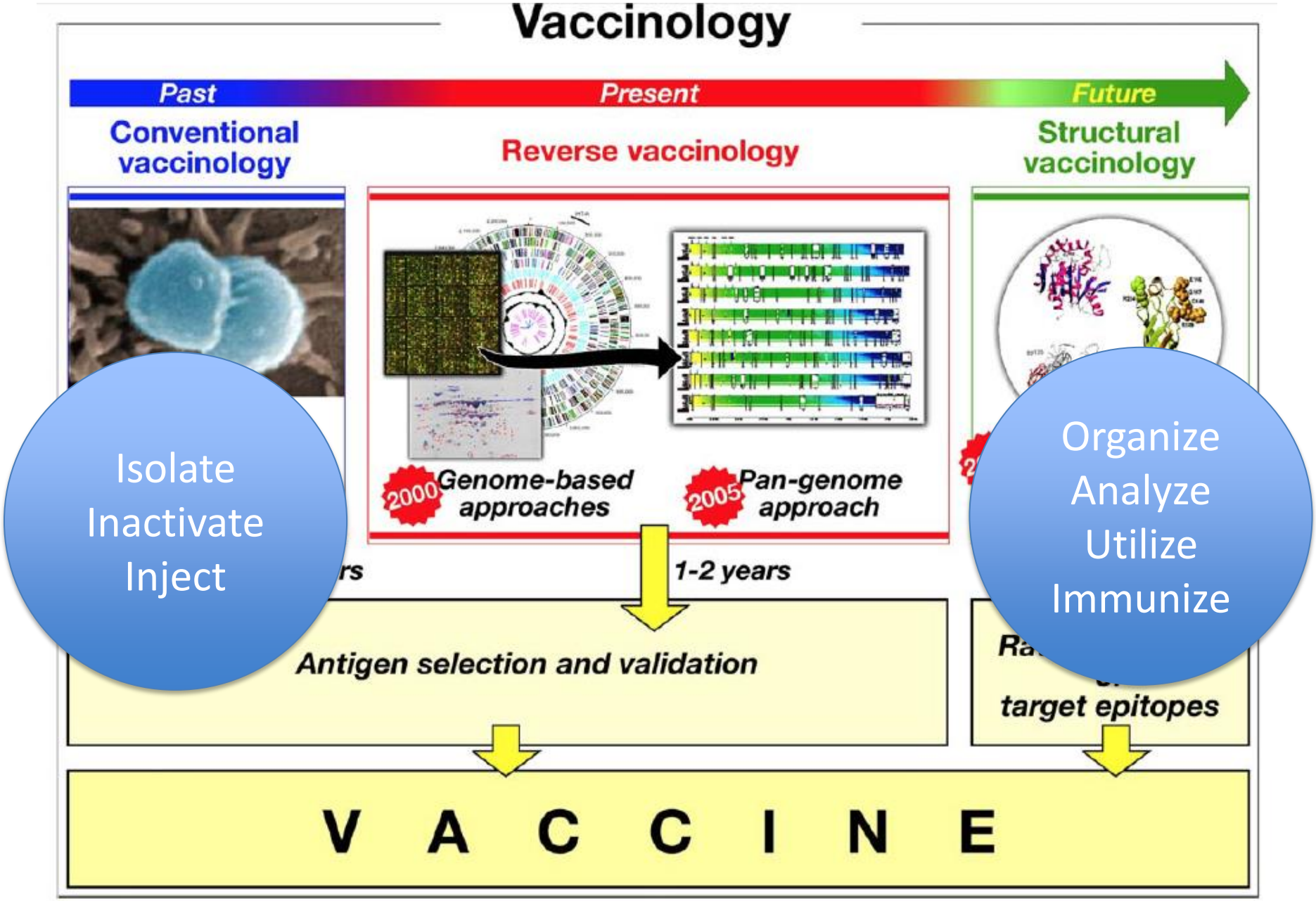
# Systems biology

- A biology based inter-disciplinary field.
- Focuses on complex interactions within biological systems.
- Uses a more holistic perspective compare to the more reductionist approach to biomedical research.
- Has the potential to make development and testing of new vaccines more efficient and faster.

# Systems biology approaches in the vaccine development




Trautmann & Sekaly. Nat Imm Aug 2011




D. Serruto, R. Rappuoli / FEBS Letters 2006, 2985

# Stagnation

- Declining funding for immunization: UNICEF funding fell from $182 million to $51 million between 1990 and 1998
- Hard-to-reach populations
- Declining infrastructure
- Political issues – war and civil unrest
- Increase cost of vaccines

http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RL30793.pdf

# Why are the children in greatest need the last to receive life-saving new vaccines?

- Lack of awareness?
- Uncertainty about disease burden and vaccine impact?
- Concern about cost and sustainability?
- Focus on other priorities?
- Programmatic issues?
- Cost of vaccines