Vaccines
Global impact of a preventive technology

Edwin J. Asturias, MD
Associate Professor of Pediatrics and Epidemiology
Director for Latin America
Center for Global Health, Colorado School of Public Health

Global Health and Disasters Course
University of Colorado, November, 2015
Objectives

• How vaccines work and impact global health for children and women
• Apply lessons learned from global experience in vaccine policy
• Summarize current priorities and strategies for universal vaccine coverage
• Understand the new vaccine pipeline and challenges ahead
Childhood deaths reducing worldwide!
Impact of vaccines, malaria prevention and neonatal health
Projected under-5 mortality rate in 2030, on the basis of the observed rate of change for each country, 2000–13
Establishing population immunity to eliminate disease transmission

Number of Countries Reporting Smallpox Cases
1960-1976

Beginning of WHO Intensified Worldwide Smallpox Eradication Program
Situation as of 2015

- 51 cases compared to 256 (22%)
- 38 from Pakistan, 13 Afghanistan
- 15 VDPV cases (40 in 2014)
- None in Africa since 07/14
- No wild PV2 or PV3

Data in WHO HQ as of 27 October 2015

Excludes viruses detected from environmental surveillance.
Lessons learned from the global use of vaccines

• Eradication is possible but seldom feasible
• Value of vaccines as a preventive technology is best when it reaches all
How to deliver vaccines to the whole world?

• Data on disease burden
• Immunization systems ready
  • Health workforce
  • Adequate cold chain
  • Vaccine schedule platform
• Financing for sustainability
• Overcome political and social barriers
Vaccination: WHO main functions

Immunization Policies
- Develop recommendations and strategies on vaccine use
- Support strengthening of national decision making

Research on vaccines and implementation of vaccination
- Development of vaccines and related technologies
- Implementation research
- Evidence for decision making

Vaccine Quality and Safety
- Norms and Standards
- Prequalification
- Strengthening National Regulatory Authorities
- Global safety issues

Programme performance and new vaccines introduction
- Immunization system strengthening
- Accelerating disease control
- Support New Vaccine Introduction
- Strategic information and surveillance
Mission and strategic goals 2011–2015

To save children’s lives and protect people’s health by increasing access to immunisation in poor countries

1. The vaccine goal
   Accelerate the uptake and use of underused and new vaccines

2. The health systems goal
   Contribute to strengthening the capacity of integrated health systems to deliver immunisation

3. The financing goal
   Increase the predictability of global financing and improve the sustainability of national financing for immunisation

4. The market shaping goal
   Shape vaccine markets to ensure adequate supply of appropriate, quality vaccines at low and sustainable prices
Immunization financing per infant through time and by WHO region

Notes: * = Baseline years.

GAVI programmatic policies

Co-financing Policy

• Objective: to enhance ownership and put countries on a trajectory towards financial sustainability to prepare for phasing out of GAVI support.
  • All countries applying for NVS are required to co-finance a portion of the cost of requested vaccines*
  • 3 country groupings according to GNI per capita:

<table>
<thead>
<tr>
<th>Country group</th>
<th>GNI per capita threshold</th>
<th>Co-financing requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low income</td>
<td>currently &lt;$1,005</td>
<td>$0.20 per dose</td>
</tr>
<tr>
<td>Intermediary</td>
<td>currently &gt;$1,005 to &lt;$1,520</td>
<td>$0.20 per dose + 15% annual increase</td>
</tr>
<tr>
<td>Graduating</td>
<td>Currently &gt; $1,520</td>
<td>Gradual ramp up over five years to reach projected price after GAVI</td>
</tr>
</tbody>
</table>

*The only exceptions from co-financing are vaccines for measles second dose, MenA and YF preventive campaigns and MR. Countries are however expected to pay a share of operational costs of campaigns.
84% of children in the world now reached with DTP3 vaccine

**Immunisation coverage rate (%)**

- **High-income countries**: 96%
- **Global**: 84%
- **Gavi-supported countries**: 76%

*Based on data officially reported to WHO and UNICEF by current member states. Note: Includes DTP-containing vaccines, such as pentavalent vaccine. Source: WHO/UNICEF vaccine coverage estimates (July 2014).*
Uptake of Hib and pneumococcal vaccines in high-income versus low-income countries

Hib = Haemophilus influenzae type b. PCV=pneumococcal vaccine.
Dashed line=projected uptake. Solid line=actual uptake

Countries having introduced Hib vaccine in 1997 and 2014

1997
- 29 countries introduced
- 2 countries partially introduced

2014
- 190 countries introduced
- 2 countries partially introduced

Map production: Immunization Vaccines and Biologicals (IVB), World Health Organization.
194 WHO Member States. Date of slide: 28 July 2014
EPI program success around the world as of 2014 – WHO databases

<table>
<thead>
<tr>
<th>Vaccine Preventable Disease</th>
<th>Global cases (2014)</th>
<th>Estimated Global Deaths (2013)</th>
<th>%Global Vaccine Coverage (2014)</th>
<th>% Reduction from reported peak</th>
<th>Target GVAP &gt;90% coverage (No. of gap countries)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>7,321</td>
<td>5,000</td>
<td>86</td>
<td>92</td>
<td>65</td>
</tr>
<tr>
<td>Tetanus neo</td>
<td>2,161</td>
<td>49,000</td>
<td>64</td>
<td>94</td>
<td>24</td>
</tr>
<tr>
<td>Pertussis</td>
<td>139,786</td>
<td>254,000</td>
<td>86</td>
<td>93</td>
<td>65</td>
</tr>
<tr>
<td>Polio</td>
<td>376</td>
<td>&lt;50</td>
<td>86</td>
<td>99</td>
<td>3</td>
</tr>
<tr>
<td>Measles</td>
<td>266,701</td>
<td>145,700</td>
<td>85</td>
<td>94</td>
<td>§16%</td>
</tr>
<tr>
<td>Hib</td>
<td>8,371</td>
<td>10,000</td>
<td>56</td>
<td>98</td>
<td>65</td>
</tr>
</tbody>
</table>

http://www.who.int/immunization_monitoring/diseases/en/  § children not receiving

Prepared by E. Asturias
Vaccine-Preventable Mortality
Among Children Under 5

- Rotavirus*: 30%
- Pneumococcal diseases*: 32%
- Hib*: 13%
- Pertussis: 13%
- Measles: 8%
- Tetanus: 4%

*WHO estimates
Progress in Introduction of Pneumococcal Conjugate Vaccine Worldwide, 2000–2012

- 36 (73%) of 50 high-income countries introduced PCV
- 13 (37%) of 36 low-income
- 18 (35%) of 52 lower-middle income
Rates of Pneumococcal invasive diseases death around the world 2012
Countries that have introduced pneumococcal conjugate vaccines in their national Immunization programs, by income status* — worldwide, 2012
Cervical cancer burden of disease
world map
Availability of data per country to estimate cervical cancer incidence

By the end of 2014, 75 countries had introduced HPV vaccination in their national programs...
73% of the 24 million unimmunized children live in 10 countries

- India, 9.7 million
- Nigeria, 2.4 million
- Indonesia, 1.1 million
- China, 1.2 million
- Ethiopia, 0.8 million
- Pakistan, 0.7 million
- Uganda, 0.5 million
- Niger, 0.4 million
- Bangladesh, 0.4 million
- Congo, Democratic Republic, 0.4 million
- Rest of the world, 6.6 million
Why are vaccines key for global health?

• Most impactful and equitable preventive technology
• Effective at reducing the infectious diseases burden in target populations
• Direct and indirect effects
• Societal value and economic value
Global Vaccine Action Plan (GVAP)

• Framework to prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all communities
• Endorsed at 2012 World Health Assembly
• Developed by Decade of Vaccines (DoV) Collaboration
Effect of vaccine prevention on earnings and wealth

- Fewer missed school days (better attendance)
- Less long term disability
- Changes in household behavior after survival
- Better cognitive development
  - Philippines: vaccination effect on scores in math, language and cognition
  - Estimated return on investment of \(21\%\)
Beyond preventing 426 million cases of illness and averting 6.4 million deaths in the next 10 years…

Stack et al. and Ozawa et al. *Health Affairs* – June 2011
Perception of Safety of Vaccines according to the Program Effectiveness

Robert T. Chen, CDC
Vaccine safety going viral and global

Donald J. Trump
@realDonaldTrump

Healthy young child goes to doctor, gets pumped with massive shot of many vaccines, doesn't feel good and changes - AUTISM. Many such cases!
Consequences of exemptions and vaccine safety scares – US (measles)

2015 Measles Cases in the U.S.
January 1 to August 21, 2015

MMR coverage

Exemptions
- <1% (n = 8)
- 1%-2% (n = 18)
- 2%-<4% (n = 10)
- >4% (n = 11)
- Data not available

Cases:
- 0
- 1-4
- 5-9
- 10-19
- 20+

*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases
Number of cases of measles in Europe and rate of 2 doses of MCV 2011
Parental Vaccine Preferences in Guatemala 2009

- Urban areas more concerned with safety
- Safety overrides decision of number of injections
Knowledge on HPV Vaccine and Cervical Cancer Facilitates Vaccine Acceptability among School Teachers in Kitui County, Kenya.

- HPV infection common Kenya
- HPV vaccine Safe
- School girls should receive sex ed
- School Based Vaccination Should Continue

What is next on vaccines?

• Reduce infectious mortality in children
• Reduce morbidity in young children
• Reduce disability and perinatal infections
• Emerging infections
# Five leading childhood infection killers (aged 1-59 months)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of deaths in 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>570,000</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>63,800</td>
</tr>
<tr>
<td>Syphilis</td>
<td>56,900</td>
</tr>
<tr>
<td>Cholera</td>
<td>45,200</td>
</tr>
<tr>
<td>Respiratory Syncytial virus</td>
<td>41,100</td>
</tr>
</tbody>
</table>
Current vaccines and vaccines on the horizon and impact on mortality

- 1960
- 1980
- 2000

Diphtheria
Pertussis
Tetanus
YF
Influenza
Polio
Measles
JE
Rubella
HepB
Hib (conj)
Typhoid
Mening (conj)
Dengue
Malaria
Rotavirus
HIV/AIDS
HepB (conj)
Typhoid
Cholera
Pneumo (conj)
Rotavirus

Traditional EPI
New and underused vaccines
Future vaccines

Source – WHO, 2005
Global Vaccines in the Horizon

• **Malaria**
  
  • 2012: *Plasmodium falciparum* 207 million cases and 627,000 deaths
  
  • Mortality has decreased by 50% due to bed nets and antimalarial treatment
  
  • Increasing insecticide and resistance
  
  • Vaccine candidate RTS has completed phase III studies
## Dengue Vaccine Candidates

<table>
<thead>
<tr>
<th>Producer (Developer)</th>
<th>Vaccine Type</th>
<th>Clinical Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi Pasteur (Acambis)</td>
<td>Live attenuated - chimera 17D yellow fever + DENV</td>
<td>Phase I, Phase II, Phase III</td>
</tr>
<tr>
<td>Takeda (CDC, Invirogen)</td>
<td>Live attenuated - chimera DENV-2 + DENV 1,3, 4</td>
<td>Phase I, Phase II, Phase III</td>
</tr>
<tr>
<td>Butantan (NIAID)</td>
<td>DENV attenuated - mutations + DENV/DENV chimera</td>
<td>Phase I, Phase II, Phase III</td>
</tr>
<tr>
<td>GSK (WRAIR)</td>
<td>Cell culture derived, inactivated</td>
<td>Phase I, Phase II, Phase III</td>
</tr>
<tr>
<td>MERCK (Hawaii Biotech)</td>
<td>Envelop subunits of DENVs</td>
<td>Phase I, Phase II, Phase III</td>
</tr>
</tbody>
</table>
Global RSV Disease Burden


- **RSV** kills more children <1 year of age than any other single pathogen except malaria
- **Leading cause of hospitalization in children under 5 years of age in the**
Causes of newborn deaths, global data for the year 2013

- Intrapartum-related complications: 24%
- Complications from preterm birth: 35%
- Severe infections: 23%
- Sepsis, meningitis, tetanus: 17%
- Pneumonia: 5%
- Diarrhoea: 1%
- Other: 8%
- Congenital: 10%

Effect of Maternal Influenza vaccination on confirmed cases of Influenza According to Cohort and Study Group in South Africa

**A** HIV-Uninfected Cohort, Mothers

Proportion of Mothers with Confirmed Influenza

Months since Vaccination

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>10 Months</th>
<th>12 Months</th>
<th>14 Months</th>
<th>16 Months</th>
<th>18 Months</th>
<th>20 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIV3</td>
<td>1062</td>
<td>1047</td>
<td>1007</td>
<td>985</td>
<td>703</td>
<td>159</td>
</tr>
<tr>
<td>Placebo</td>
<td>1054</td>
<td>1023</td>
<td>993</td>
<td>964</td>
<td>685</td>
<td>179</td>
</tr>
</tbody>
</table>

**B** HIV-Uninfected Cohort, Infants

Proportion of Infants with Confirmed Influenza

Age (mo)

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>2 Months</th>
<th>4 Months</th>
<th>6 Months</th>
<th>8 Months</th>
<th>10 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIV3</td>
<td>1026</td>
<td>1004</td>
<td>981</td>
<td>891</td>
<td>873</td>
</tr>
<tr>
<td>Placebo</td>
<td>1023</td>
<td>993</td>
<td>960</td>
<td>873</td>
<td>873</td>
</tr>
</tbody>
</table>

**C** HIV-Infected Cohort, Mothers

Proportion of Mothers with Confirmed Influenza

Months since Vaccination

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>10 Months</th>
<th>12 Months</th>
<th>14 Months</th>
<th>16 Months</th>
<th>18 Months</th>
<th>20 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIV3</td>
<td>100</td>
<td>95</td>
<td>91</td>
<td>86</td>
<td>61</td>
<td>9</td>
</tr>
<tr>
<td>Placebo</td>
<td>94</td>
<td>87</td>
<td>78</td>
<td>74</td>
<td>53</td>
<td>7</td>
</tr>
</tbody>
</table>

**D** HIV-Infected Cohort, Infants

Proportion of Infants with Confirmed Influenza

Age (mo)

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>2 Months</th>
<th>4 Months</th>
<th>6 Months</th>
<th>8 Months</th>
<th>10 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIV3</td>
<td>100</td>
<td>93</td>
<td>86</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>88</td>
<td>81</td>
<td>75</td>
<td>66</td>
<td></td>
</tr>
</tbody>
</table>
Estimate of absolute risk of GBS disease in a neonate as a function of capsular IgG in colonized mother
Final Remarks on Global Vaccines

• One of the most effective and equitable health preventive technologies
• Use of vaccines is key to their preventive success – reach the unimmunized
• Addressing the safety and societal concerns is a priority in the current age
• New vaccines will bring a new paradigm: community protection is the key
Facts to remember

1 in 5 children do not have access to life-saving immunizations

Vaccines prevent 2 to 3 million deaths annually around the world

$20 can fully vaccinate a child against pneumonia, diarrhea, polio and measles

Over 18 million infants remain unimmunized in the world each year