

Global Health  
Is Good Ever Good Enough?

Jon S. Abramson MD\*  
Chair, Department of Pediatrics  
Wake Forest University Medical School  
&  
Member of the World Health Organization Strategic  
Advisory Group of Experts on Immunizations  
(SAGE)

\*I have no financial relationships with the manufacturers of any commercial products and/or provider of commercial services discussed in this CME activity.

1

---

---

---

---

---

---

---

---

Objectives

- Understand the negative impact that poverty has on global health
- Understand how the eight WHO Millennium Development Goals (MDGs) have lead to substantial improvement in global health
- Discuss new WHO recommendations for meningococcal and influenza vaccines
- Discuss the complexity of considerations when deciding whether good is ever good enough in the following cases:
  - Consideration of removing the age restriction for rotavirus vaccine
  - Ongoing attempt to eradicate polio globally
  - Consideration of whether to attempt to eradicate measles

2

---

---

---

---

---

---

---

---

Global Health

“The first decade of the 21<sup>st</sup> century witnessed a series of commitments, opportunities, innovations, successes, setbacks, surprises, and new realities unprecedented in the history of public health. Equally unprecedented has been the vulnerability of health to new threats arising from the **radically increased interdependence of nations and policy spheres**. The forces driving these changes are powerful, virtually universal, and almost certain to continue to shape health for years to come.” The future of financing for WHO. Report to the Director-General. May 5, 2011

Since the 1970s newly emerging diseases have been identified at the unprecedented rate of  $\geq 1/\text{yr}$ .

3

---

---

---

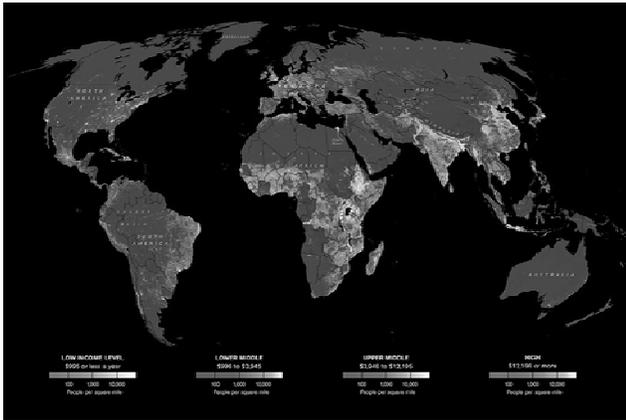
---

---

---

---

---




---

---

---

---

---

---

---

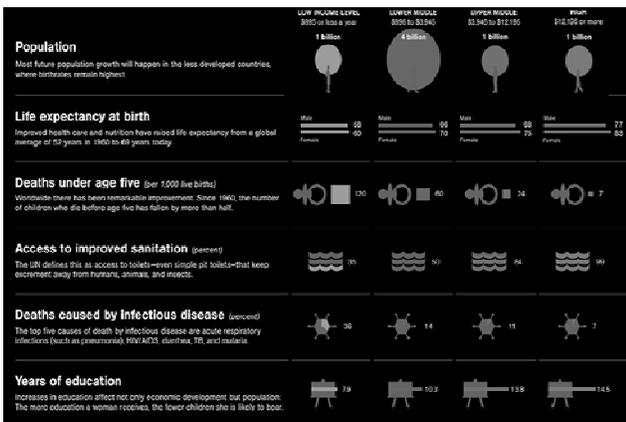
---

---

---

---

---




---

---

---

---

---

---

---

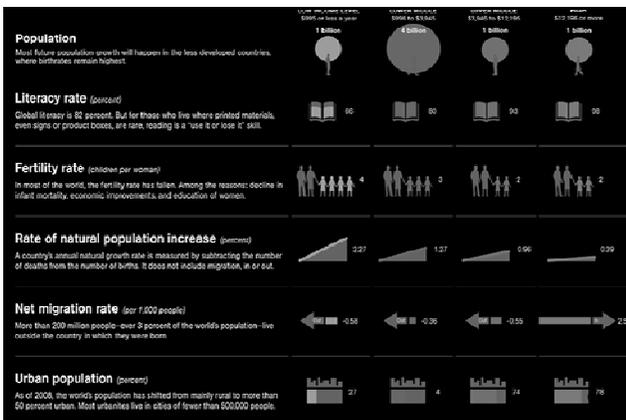
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

---

---



**Purpose of Millennium Development Goals (MDGs)**  
**A Bold Vision**

- Adopted by >190 countries in 2000.
- The goals are set to be achieved by 2015 and use 1990 data as the starting point.
- The MDGs provide a framework for the entire international community to work towards a common end – making sure that human development reaches everyone, everywhere.
- If all MDGs are achieved, world poverty will be cut by half, and tens of millions of lives will be saved.

10

---

---

---

---

---

---

---

---

**World Health Organization MDGs**

- Goals that stretch the vision
  - The eight MDGs have 21 quantifiable targets that are measured by 60 indicators.
- Tools that can enable the vision
  - Enhanced public health and education infrastructure
  - Immunizations
  - Technologies- e.g., mobile phones, internet access
- Donors that believe in the vision
  - Global Alliance for Vaccines and Immunizations (GAVI)
  - Gates Foundation
  - Various high income country governments
  - Others

11

---

---

---

---

---

---

---

---

**MDGs 1 & 2**

**Goal 1- Eradicate extreme poverty and hunger**

- Reduce by half the proportion of people whose income is less than \$1.25 a day.
- Reduce by half the proportion of people who suffer from hunger.

**\*Status- poverty target already achieved. Hunger target is not on tract**

**Goal 2- Achieve universal primary education**

- Ensure that all boys and girls complete a full course of primary schooling.

**\*Status- increased from 58% to 76%**

\*United Nations MDG Report 2012

12

---

---

---

---

---

---

---

---

**MDGs 3 & 4**

**Goal 3- Promote gender equality and empower women**

-Eliminate gender disparity in primary and secondary education preferably by 2005, and in all levels of education no later than 2015.

**\*Status- gender equity already achieved for primary education**

**Goal 4- Reduce child mortality**

-Reduce by two thirds the mortality of children under-five years of age.

**\*Status- deaths decreased from 12M in 1990 to 7.6M in 2010 (37%)**

\*United Nations MDG Report 2012

13

---

---

---

---

---

---

---

---

**MDGs 5 & 6**

**Goal 5- Improve maternal health**

-Reduce maternal mortality by three quarters.

**\*Status- not on target**

**Goal 6- Combat HIV/AIDS, malaria and other diseases**

-Halt and reverse the spread of HIV/AIDS.

-Halt and reverse the incidence of malaria, TB & other major diseases.

**\*Status- 6.5M people receiving HIV treatment in 2010, but did not achieve 2010 target of universal access. Malaria deaths have decreased by 25% and TB by 50%**

\*United Nations MDG Report 2012

14

---

---

---

---

---

---

---

---

**MDG 7**

**Goal 7- Ensure environmental sustainability**

- Halve the proportion of people without access to safe drinking water and basic sanitation

- Improve the lives of at least 100 million slum dwellers by 2020

- Integrate principles of sustainable development into country policies and programs; reverse the loss of environmental resources.

**\*\*Status- Water and slum dwelling targets achieved. Sustainable development targets not on track.**

\*United Nations MDG Report 2012

15

\*\*Sachs JD, From MDGs to Sustainable Development Goals. Lancet 2012;379:2206-11

---

---

---

---

---

---

---

---

## MDG 8

### Goal 8- Develop a global partnership for development

- Further develop an open, rule-based, predictable, non-discriminatory trading and financial system.
- Address special needs of the least developed countries, landlocked countries and small island developing States.
- Deal with developing countries' debt.
- In cooperation with developing countries, develop and implement strategies for decent work for youth.
- In cooperation with the private sector, make available the benefits of new technologies, especially information and communications.

**\*Status- Technology targets are progressing well. The other targets are mixed with several of them impacted by the global recession.**

\*United Nations MDG Report 2012

16

---

---

---

---

---

---

---

---

---

---

## A Further Look at MDG 4

### MDG 4- reduce by two thirds the mortality of children < 5 years of age

- As of 2012, the mortality rate has been reduced by ~50%
- Vaccines have played the biggest role in achieving this success

17

---

---

---

---

---

---

---

---

---

---

### The Global Alliance Vaccine and Immunization (GAVI) Enhanced Funding of the Global Vaccination Program

- The GAVI was formed in 2005 and is a combined public (various developed countries) and private (e.g., Gates Foundation) initiative that provides immunization funding support to countries with a per capita income less than \$1000.
- GAVI's support has resulted in an additional 288 million children in the world's poorest countries being immunized.

18

---

---

---

---

---

---

---

---

---

---

### Impact of GAVIs Enhanced Vaccination Program

- To date this program has prevented >5,000,000 deaths in children <5 yrs of age.
- However, ~24 million children <1 yr of age (20%) of the worldwide annual birth cohort are still not being vaccinated.
- If the vaccines currently recommended against childhood diseases were widely adopted with >90% coverage worldwide an additional 2 million deaths/yr would be averted.

19

---

---

---

---

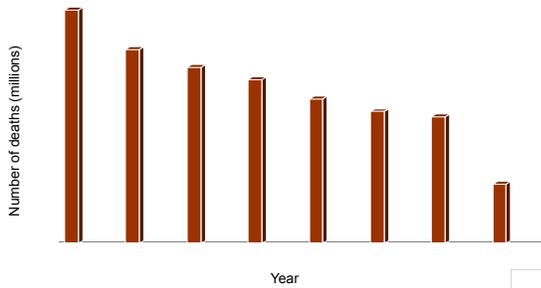
---

---

---

---

### Trends in Global Mortality in Children Under Five Years of Age



WHO Department of Immunization, Vaccines and Biologicals estimates

---

---

---

---

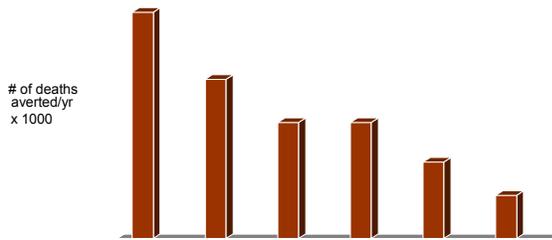
---

---

---

---

### Impact of Enhanced Funding on Various Diseases



WHO Department of Immunization, Vaccines and Biologicals estimates based on Global Burden of Disease, 2004 estimates. Pneumococcal Diseases and Hib estimates are for the year 2000.

---

---

---

---

---

---

---

---

### GAVI's Vaccine Price Shaping Program

- GAVI's 2011–2015 strategic plan includes price shaping activities to minimize the cost of vaccines to GAVI while providing a sufficient supply of high-quality vaccines and fostering an environment for innovation. For example
  - GSK will supply up to 125M doses of its Rotarix® vaccine over 5 yrs to GAVI at \$2.50/dose (\$5.00/course), which is ~95% reduction to the Western market price and a 67% reduction from the lowest price available on the public market today.
  - Merck will supply its RotaTeq® vaccine to GAVI at \$5.00/dose (\$15.00/course), with the purchase price decreasing to \$3.50/dose (\$10.50/course) once the volume increases to 30M doses.
  - Bharat Biotech has offered a future price to GAVI of \$1.00/dose (\$3.00/course) for ROTAVAC® (currently in Phase 3 clinical trials), which is anticipated to be ready for purchase by 2015.

22

---

---

---

---

---

---

---

---

### United States Healthy People Global Health Initiative

- In February 2010, the US announced a new Global Health Initiative which invests \$63 billion over 6 years to help partner countries improve health outcomes through strengthened health systems, with a particular focus on improving health in women, newborns and children.
- Motives are both altruistic and self serving. Decreasing the incidence of disease in other countries will also decrease disease in the US (e.g., measles).

23

---

---

---

---

---

---

---

---

### The Future of the WHO Vaccination Program

- Based on the success to date with MDG 4, the Gates Foundation has declared 2010 – 2020 the Decade of Vaccines and pledged \$10 billion towards fulfilling this goal.
- Plans for the Decade of Vaccines will include:
  - Completion of plans with currently recommended vaccines
  - Expansion of the use of influenza vaccines
  - Initiation of programs involving new vaccines including
    - Malaria- in phase 3 trials
    - TB- in phase 3 trials
    - Development of an effective HIV vaccine
    - Expansion of maternal infant immunization program beyond just tetanus vaccine (e.g., influenza)

24

---

---

---

---

---

---

---

---

### Examples of Current WHO Vaccine Initiatives

- Conjugated Meningococcal vaccine
- Influenza vaccine

25

---

---

---

---

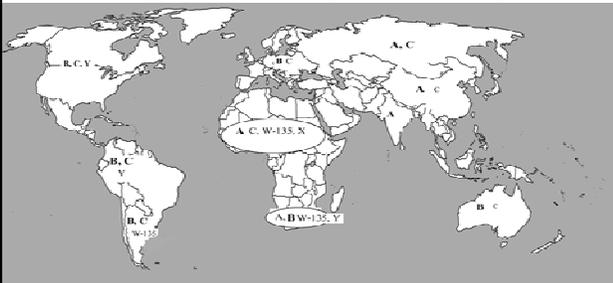
---

---

---

---

### Distribution of common and predominant meningococcal serogroups by region\*



\* Predominant strains highlighted in bold

Meningococcal Vaccines: WHO Position Paper, 2011. Weekly Epidemiologic Record 2011;86:521-40 <sup>26</sup>

---

---

---

---

---

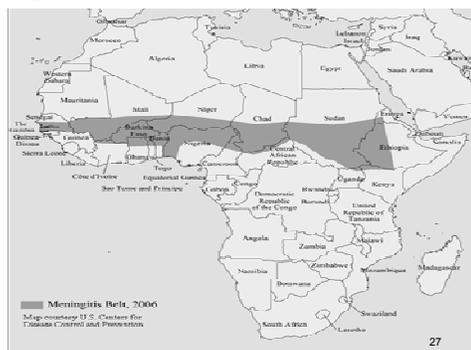
---

---

---

### The "Meningitis Belt" of sub-Saharan Africa

430 million people live in the meningitis belt



■ Meningitis Belt, 2006  
Map courtesy U.S. Centers for Disease Control and Prevention

27

---

---

---

---

---

---

---

---

### Meningococcal Disease

- Worldwide- five serotypes cause most disease (A, B, C, Y and W-135)
  - ~500,000 cases/yr and ~50,000 deaths/yr
  - Majority of disease presents as meningitis
  - ~20% of survivors have major sequelae
- Sub-Saharan Africa contains the meningococcal meningitis belt spans (from Senegal in the west to Ethiopia in the east)
  - epidemics due to serotype A occur every 7 – 12 yrs
  - In 2009 ~88,000 cases and ~10,000 deaths
  - In conjunction with Gates Foundation a massive immunization program is underway using a conjugate meningococcal A vaccine (\$0.40/ dose) has been initiated in this region for everyone 1 – 29 yrs of age.
    - In those countries where the vaccine has been used the disease incidence has decreased >95%

28

---

---

---

---

---

---

---

---

### Impact of Influenza on Maternal and Newborn Outcomes

- Increase risk of severe infection is 4–10 fold greater in pregnant women compared to non-pregnant women
- Disease severity increases during the 2<sup>nd</sup> and 3<sup>rd</sup> trimester. For example in the 2009 pandemic
  - for pregnant women who were hospitalized, 30% of cases occurred in the 2<sup>nd</sup> trimester and 65% in the 3<sup>rd</sup> trimester
  - the risk of being admitted to ICU was increased 7-fold in the 2<sup>nd</sup> trimester and 13-fold in the 3<sup>rd</sup> trimester
  - Overall risk of death for pregnant women who were hospitalized was 11%

---

---

---

---

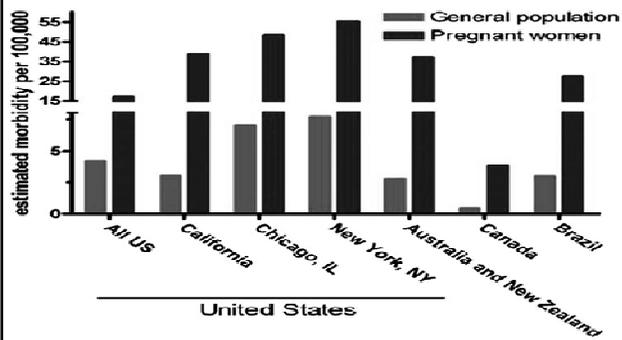
---

---

---

---

### Rates of Severe Influenza Disease Among Pregnant Women and the General Population




---

---

---

---

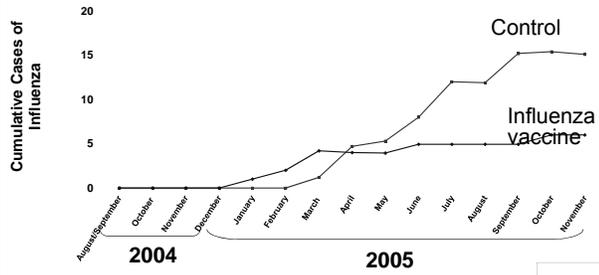
---

---

---

---

Cumulative Cases of Lab-Proven Influenza in Infants of Mothers Receiving Influenza Vaccine vs Controls



Adapted from Zaman K et al., *N Engl J Med.* 2008 Oct 9;359(15):1555-64

---

---

---

---

---

---

---

---

---

---

---

---

Reduction in Hospitalizations Due to Influenza in Infants of Pregnant Mothers Receiving Influenza Vaccine vs Those Not Vaccinated



Adapted from Poehling KA et al. *AJOG* 2011;204:S141-8.

32

---

---

---

---

---

---

---

---

---

---

---

---

Neonatal Outcomes During 2009 Influenza Pandemic

- One study showed severe neonatal outcomes (NICU or death) in 83% of pregnant women with severe illness
- In another study 57% of neonates born to pregnant women admitted for influenza were admitted to NICU
- Incidence of prematurity in infants born to mothers with influenza was increased 4-7 fold

---

---

---

---

---

---

---

---

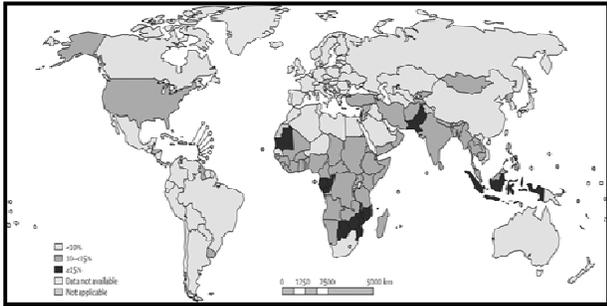
---

---

---

---

### Estimated Global Preterm Birth Rates by Country 2010



Adapted from The Lancet 2012; 379:2162-2172

34

---

---

---

---

---

---

---

---

---

---

### Assessment of Influenza Risk and Influenza Vaccine Characteristics in Various Risk Groups (SAGE meeting- April 2012)

| Risk Group                   | Feasibility of Delivery | Disease Severity | Vaccine Effectiveness | Indirect Benefits |
|------------------------------|-------------------------|------------------|-----------------------|-------------------|
| Pregnant women               | ++                      | +++              | +++                   | ++                |
| Healthcare workers           | ++                      | +                | +++                   | +                 |
| Children, 2-5 years          | +                       | ++               | ++                    | -                 |
| Children, < 2 years          | ++                      | +++              | +                     | -                 |
| Elderly                      | +                       | +++              | +                     | -                 |
| Underlying Health Conditions | +                       | +++              | +                     | -                 |

35

---

---

---

---

---

---

---

---

---

---

### Use of Influenza Vaccine SAGE Recommendations

- In countries using or considering introducing seasonal influenza vaccination SAGE recommends that:
  - Influenza vaccination of all pregnant women as the highest priority group
  - Based on local circumstances (e.g. burden of disease, vaccine availability, cost-effectiveness considerations, competing priorities, and programmatic constraints), countries consider annual influenza vaccination of healthcare workers, children (< 2 years and 2-5 years of age), the elderly, and individuals with underlying health conditions, with. Countries should decide the relative priority to assign to targeting these groups for influenza vaccination.

36

---

---

---

---

---

---

---

---

---

---

### Is Good Ever Good Enough?

My own view- the answer depends on the specific question.  
For example:

- 1) Should the age restrictions for rotavirus vaccine be discontinued?
- 2) Should the global polio eradication be continued?
- 3) Should a global measles eradication deadline be declared?

37

---

---

---

---

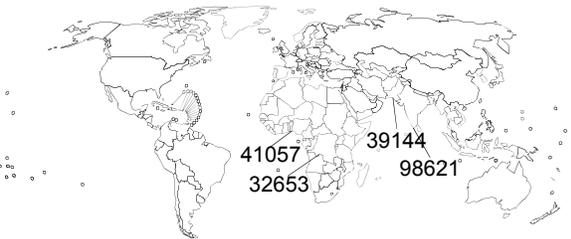
---

---

---

---

### Global Impact of Rotavirus Disease



~453,000 child deaths/yr with 82% of these deaths occurring in 20 countries

Presentation at April 2012 WHO SAGE meeting, Geneva, Switzerland

---

---

---

---

---

---

---

---

### Rotavirus (RV) Disease

- RV is the most common cause of severe diarrhea disease in young children worldwide
  - >2,000,000 children are hospitalized/yr with ~453,000 deaths/yr.
  - Vaccine effectiveness in preventing hospitalization due to RV is 44 – 100% in countries where studied
  - A small increase in intussusception rate with first dose including in US (~4/100,000 infants)
- In 2009 the WHO recommended that RV vaccine for infants should be included in all national immunization programs.
  - In countries where deaths due to diarrhea account for  $\geq 10\%$  of mortality among children <5 years, the introduction of the vaccine is strongly recommended.
  - Due to concerns about intussusception 1<sup>st</sup> dose should be given before 15 weeks and last dose by 32 weeks

39

---

---

---

---

---

---

---

---

| <b>What are the Trade-offs when Considering Whether to Remove the Age Restrictions for Rotavirus Vaccine?</b> |  |   |
|---|--|---|
|   | Median (5 <sup>th</sup> and 95 <sup>th</sup> percentiles)            |   |
|   | Rotavirus Deaths Averted   | Associated Intussusception Deaths                       |
| Restricted  | 156,100<br>(110,100 to 201,800)                                      | 288<br>(99 to 688)*                                     |
| No age restriction  | 199,200<br>(140,700 to 255,400)                                      | 605<br>(310 to 1,133)*                                  |
| <b>No age restriction (vs. age restriction)</b>   | <b>43,100 additional rotavirus deaths averted (30,600 to 53,500)</b> | <b>317 additional IS deaths associated (211 to 445)</b> |
| <b>Conclusion- remove the age restriction</b>   |  | 40  |

---

---

---

---

---

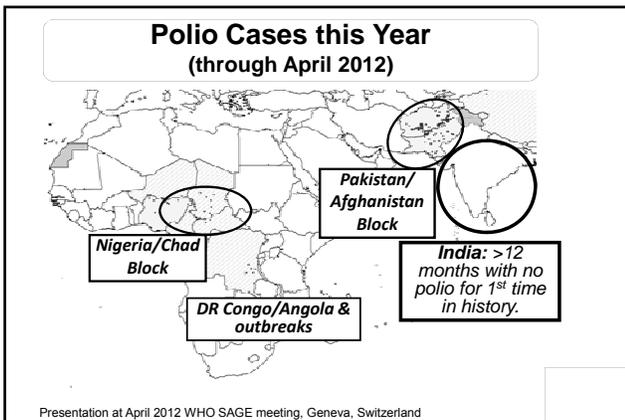
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

**Polio Eradication**

- The global effort to eradicate polio is now costing ~ 2 billion dollars/yr
- In 2011 the eradication of polio was designated by the WHO to be a **global emergency**.
- "Loss of this opportunity to eradicate polio would be extremely tragic and unacceptable and a waste of the considerable investment already made in polio eradication with consequences for all of immunization activities, especially in the poorest countries. Any diminution of polio eradication activities due to a lack of funds is completely unacceptable. We urge all governments and partners to act immediately to meet the polio eradication funding needs if we are to wipe out this crippling disease (SAGE meeting, Geneva, April 2012).

42

---

---

---

---

---

---

---

---

---

---

**What are the Trade-offs when Considering Whether to Continue the Polio Eradication Program?**

Reasons to continue

- Polio was eliminated from India in 2011 using an improved vaccine (i.e., bivalent OPV)
- Polio is now endemic in only 3 remaining countries
- Not finishing the job would be a huge public health failure and would impact donor funding for other programs

Reasons to not continue

- Two deadlines for polio eradication have already been missed (i.e., 2000 and 2010)
- Many billions of dollars have been spent and donors are fatiguing
- Funding is being diverted from other programs

**Conclusion**

One more intense effort accompanied by a deadline

43

---

---

---

---

---

---

---

---

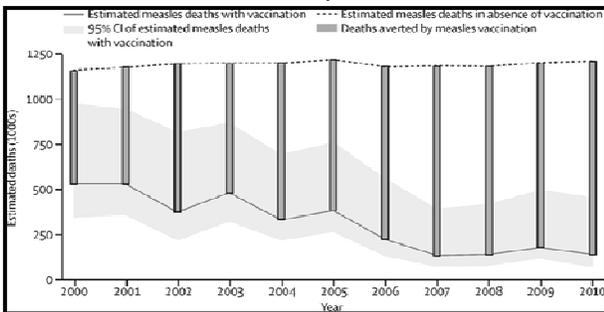
---

---

---

---

**Global Estimated Measles Mortality & Measles Deaths Averted**



Adapted from the Lancet 2012; 379:2173-2178

44

---

---

---

---

---

---

---

---

---

---

---

---

**What are the Trade-offs when Considering Whether to Introduce a Global Measles Eradication Program?**

Reasons to try

- Measles vaccine was introduced in 1963
- Measles caused ~2.6 million deaths/yr as recently as 1980 and decreased to ~140,000 deaths in 2010.
- From a logistics standpoint measles is easier to eliminate than polio
- Endemic measles has been eliminated from the Americas
- Congenital rubella could also be eliminated at the same time as measles
- Measles incidence quadrupled to 222 cases in the United States in 2011 compared to the previous year.
  - A third of these cases required hospitalization.
  - Most of the 17 outbreaks began in foreign visitors or in Americans returning from abroad — usually from Europe.

45

---

---

---

---

---

---

---

---

---

---

---

---

**What are the Trade-offs when Considering Whether to Introduce a Global Measles Eradication Program?**

**Reasons to not continue**

- Donor fatigue from effort to eradicate polio
- Vaccine hesitancy/refusal – vaccine attitudes can be seen on a continuum ranging from total acceptance to complete refusal. Vaccine hesitant individuals are a heterogeneous group in the middle of this continuum.
  - This problem has different underlying causes that often vary between regions and within countries
  - To date, efforts to overcome this problem have been relatively ineffective
  - Europe had >37,000 measles cases during the past year
    - a small percentage of people refusing measles vaccine causes large outbreaks
  - WHO recently formed a Vaccine Hesitancy work group

46

---

---

---

---

---

---

---

---

---

---

---

---

**Vaccine Hesitancy Issues**

| <u>Influences</u>  | <u>Vaccine-specific issues</u>  | <u>Individual/social group influences</u>   |
|--|---|---|
| Socio-economic   | History of AEFI (e.g. rotavirus and intussusceptions)   | Experience with past vaccination  |
| Religious/cultural/historic  | Risk/benefit (scientifically based and relevant to the specific context)                              | Risk/benefit (perceived, heuristic) perception of disease risk as well as vaccine risk/benefit<br>Perception of immune system<br>Immunization is a social norm vs not needed or harmful |
| Politics/policies (e.g., mandates)                                     | Vaccination schedule (evidence based, relevant to context)  | Perception of immune system (preference to separate, delay vaccines due to perceptions of overload) and vaccination schedule (starts too early, too many doses)                         |
| Communication and media  | Mode of delivery: Routine/health centre-based vs campaign   | Individual knowledge of why/what/when vaccines are needed   |
| Role of HCW (vaccine recommendations, delivery, ? hesitant themselves) | -New vaccines or formulations may not be trusted by HCW<br>-Erratic vaccine supply affects confidence | Individual knowledge, beliefs and attitudes about health and prevention   |

47

---

---

---

---

---

---

---

---

---

---

---

---

**Should We Attempt Measles Eradication?**

**Conclusion- Measles eradication can not be achieved without overcoming vaccine hesitancy**

48

---

---

---

---

---

---

---

---

---

---

---

---

## Questions and Comments

49

---

---

---

---

---

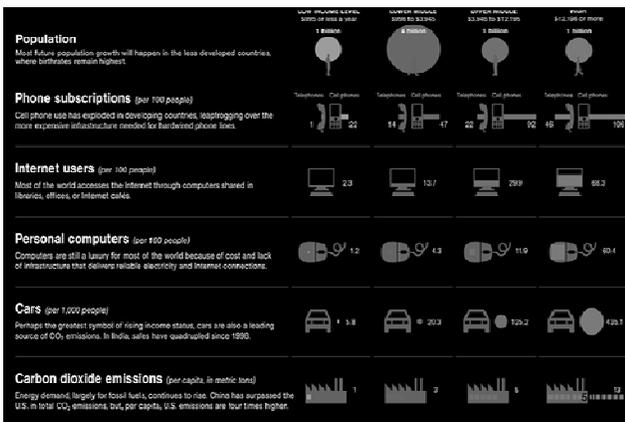
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

## The Leading Causes of Neonatal Deaths Globally

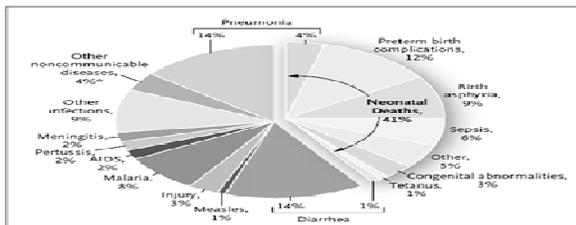


Figure 2. Causes of Childhood Deaths worldwide in 2008. The causes of death during the first 27 days of life are shown in yellow shades. The remainder of the graph shows the causes of death in children 1 to 59 months of age. The asterisk denotes that the data include deaths from congenital anomalies, accidents, and injuries.

Black, RE, Cousens S, Johnson HL, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet 2010;375:1969-87.

---

---

---

---

---

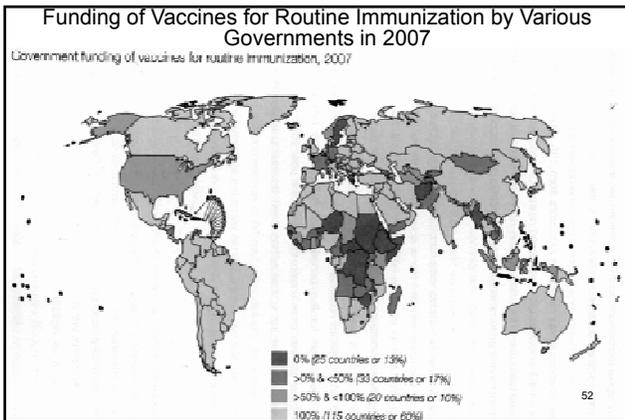
---

---

---

---

---




---

---

---

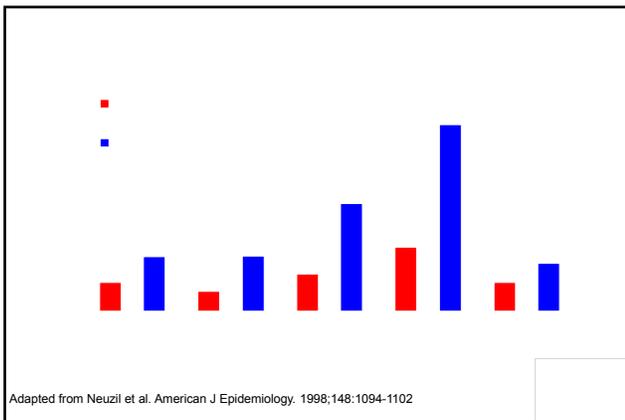
---

---

---

---

---




---

---

---

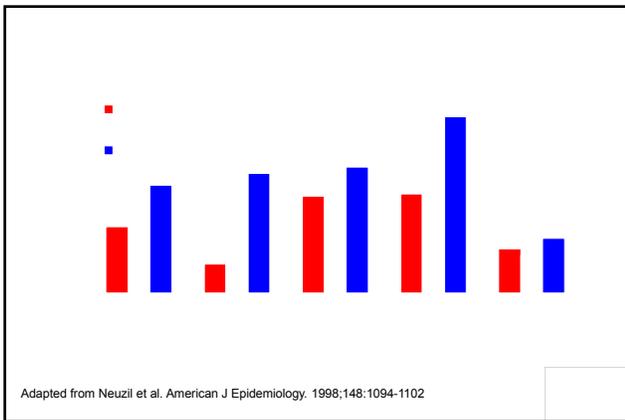
---

---

---

---

---




---

---

---

---

---

---

---

---