

**Recommendations for introducing rubella vaccine into the routine vaccination schedule and determining the target age range for measles and combined measles-rubella SIAs.**

Measles Rubella Working Group

SAGE November 2013

# Outline

## **Three sections:**

1. Introducing rubella vaccine into the routine vaccination schedule
2. Determining the target age range for measles SIAs
3. Determining the target age range for combined measles-rubella SIAs

## **Section 1**

- Optimizing the Use of Rubella Vaccine in the Routine Childhood Schedule

# Current policy guidance

## **The Rubella position paper (2011):**

1. Does not provide unequivocal guidance as to the optimal timing for administration of RCV and
2. Does not clearly explain the value of using the same formulation of RCV for both routine doses
3. Does not indicate that if MMR vaccine is used 2 doses are needed to protect against mumps

## Current Practice

| Vaccine used for first dose | Vaccine used for second dose | Number of countries   |
|-----------------------------|------------------------------|-----------------------|
| <b>M</b>                    | <b>none</b>                  | <b>42</b>             |
| <b>M</b>                    | <b>M</b>                     | <b>20</b>             |
| <b>M</b>                    | <b>MR or MMR</b>             | <b>8 <sup>γ</sup></b> |
| <b>MR or MMR</b>            | <b>none</b>                  | <b>6</b>              |
| <b>MR or MMR</b>            | <b>M</b>                     | <b>1 <sup>γ</sup></b> |
| <b>MR or MMR</b>            | <b>MR or MMR</b>             | <b>117*</b>           |
| <b>Total</b>                |                              | <b>194</b>            |

<sup>γ</sup> 9 countries use different M, MR, MMR formulations at 1<sup>st</sup> and 2<sup>nd</sup> dose

\* 104 of these have MMR as both doses; 8 have MR as both doses; 3 use MMR as 1<sup>st</sup> and MR as 2<sup>nd</sup> dose; and 2 use MR as 1<sup>st</sup> and MMR as 2<sup>nd</sup> dose.

# Issue 1: Timing of 1st dose of rubella vaccine

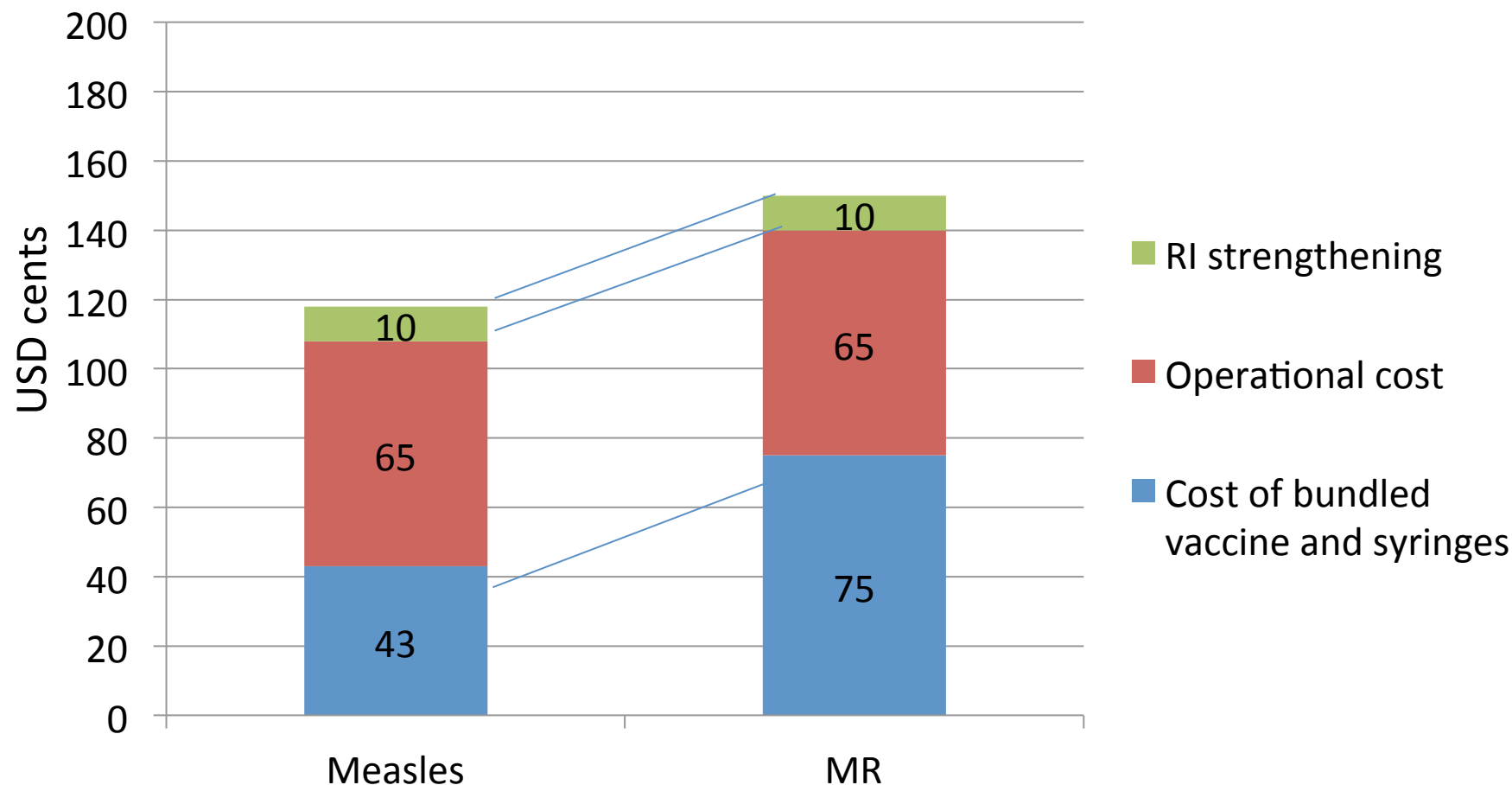
## Give R1 with M1 as MR or MMR

- Global MCV1 coverage is considerably higher than MCV2 coverage (84% versus 36% for 2 year old cohorts in 2012)
- Giving RCV1 at the MCV2 dose delays protection of children against rubella and achieves lower coverage
- 8 countries give RCV with MCV2
- Philippines and Lebanon can gain 47% and 10% points coverage by including RCV with MCV1.

## **Issue 2: Advantages of using one vaccine (MR or MMR) for both doses**

- Simplifies vaccine procurement, logistics, recording, and reporting
- Lowers vaccine wastage especially with smaller session sizes
- Higher coverage – providing RCV at two different opportunities rather than only once increases coverage
- These advantages outweigh the marginal increase in cost of the combination vaccine

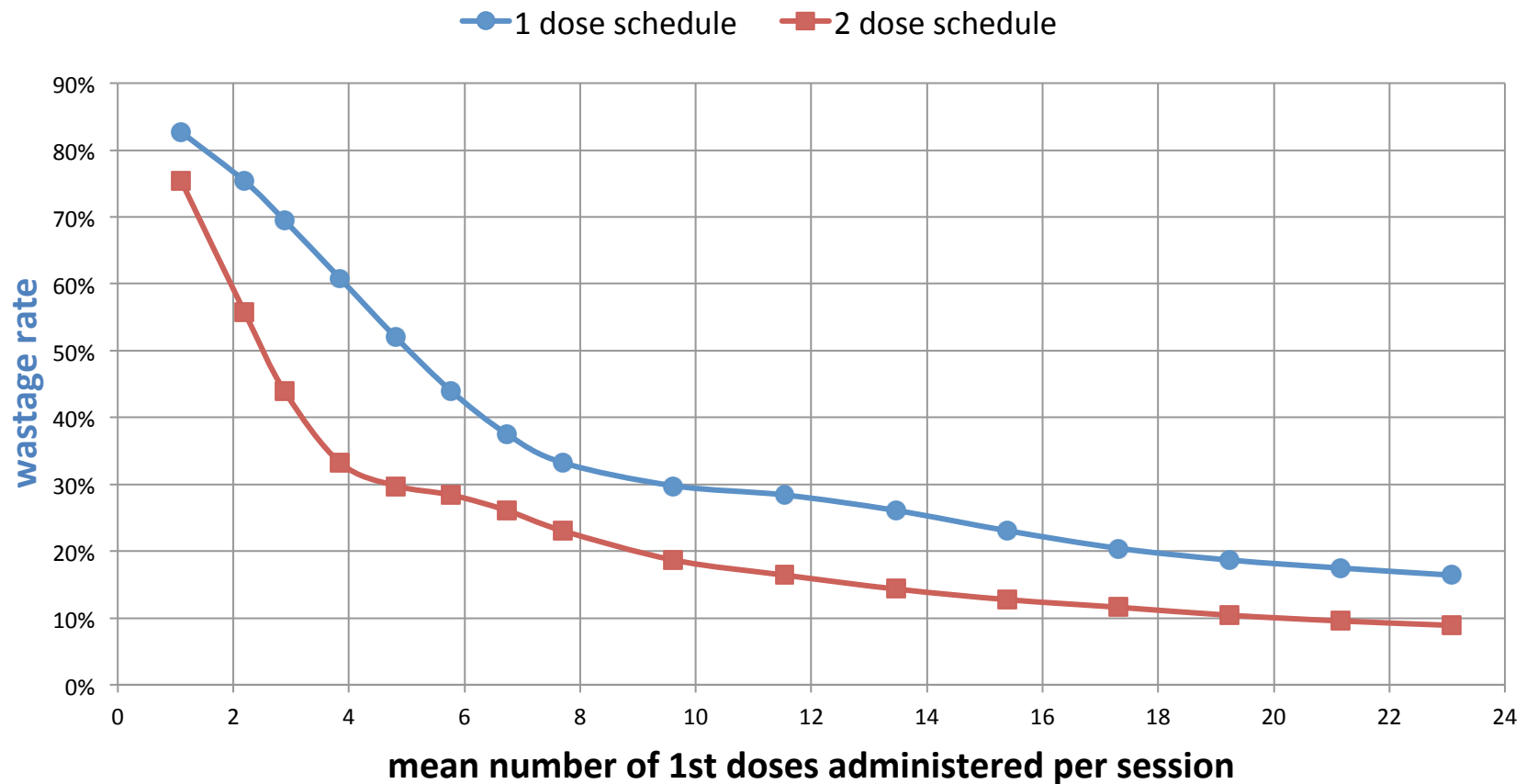
# 30 cents (US) cost differential\* between M vs. MR for the 2<sup>nd</sup> dose



\* Prices are in USD cents, assumptions based on budgets for campaign activities

# Lower wastage when using MR for both doses

from 1 dose of MR/MMR to 2 doses



## Recommendations

1. All countries need to introduce Rubella vaccine
2. Rubella vaccine should be given in combination with the first dose of MCV (as MR or MMR)
3. In countries using RCV and a two-dose schedule of MCV, both doses should be the same formulation of MR or MMR
4. When the formulation contains mumps vaccine (MMR) then at least two doses must be given to protect against mumps (and measles)

## Section 2: Policy Question

- What criteria should be used to guide countries on when to expand the **target age range** for:

Follow-up measles SIAs beyond 5 years?

# Measles Position Paper (2009)

## Supplementary Immunization Activities (SIAs)

- All countries should provide 2 doses of measles vaccine and reach population immunity  $\geq 95\%$ 
  - 2<sup>nd</sup> dose through routine services and/or periodic SIAs, whichever has higher coverage
- Recommended SIA strategy:
  - Initial catch-up SIA targeting 9m-14y
  - Periodic follow-up SIA targeting 9-59m
  - Continue follow-ups until MCV1 and MCV2 coverage  $>90-95\%$

# Measles Position Paper and AFRO TAG (2005)

## Interval between SIAs

- Interval based on “birth cohort rule”
  - Use MCV1 coverage to calculate cumulative number of susceptible children
  - Conduct follow-up SIA before the number of susceptible children of pre-school age reaches the size of 1 birth cohort
- Rule was basis for AFRO TAG recommendations:

### Routine MCV1

| Coverage | SIA interval | SIA target age |
|----------|--------------|----------------|
| <60%     | 2 years      | 9-35 m         |
| 60-79%   | 3 years      | 9-47 m         |
| >80%     | 4 years      | 9-59 m         |

# Problems in the field

- Outbreaks have occurred after preventive measles SIAs because of:
  - Low SIA coverage (most common)
  - Age range targeted is too narrow (this is difficult to separate from low coverage)
- Uncertainty about which age groups to target
  - Coverage data are often unreliable
  - Age distribution of cases are often used
  - Wider age range is not budgeted for
- Programme capacity to reach the 95% coverage target is variable
- Concern about the impact of repeat SIAs on routine services and programme fatigue

# Methods

- Systematic analysis of measles epidemiology and vaccination programmes in countries
  - Main limitation is the quality of the data
- Work with 3 groups of modelers is ongoing
  - Different dynamic models are used by 3 groups
  - They have applied their models to a number of countries including India, Kenya, DRC, Ethiopia, Burkina Faso

# Preliminary Results of the Modelers

## **Impact of the SIA depends on:**

- Target age range
- Frequency of the SIA campaigns
- Coverage of the SIA is critical

**However, clear criteria for determining the target age range for SIAs have not yet been identified**

- “90% rule” of basing the target age range for SIA on the age distribution of measles cases can be misleading (Matt Ferrari)
- If proportion of population susceptible is known, age distribution of cases can be used to set SIA age target

\* Use the 90<sup>th</sup> percentile of the cumulative age distribution of recent cases to define the upper age of the SIA

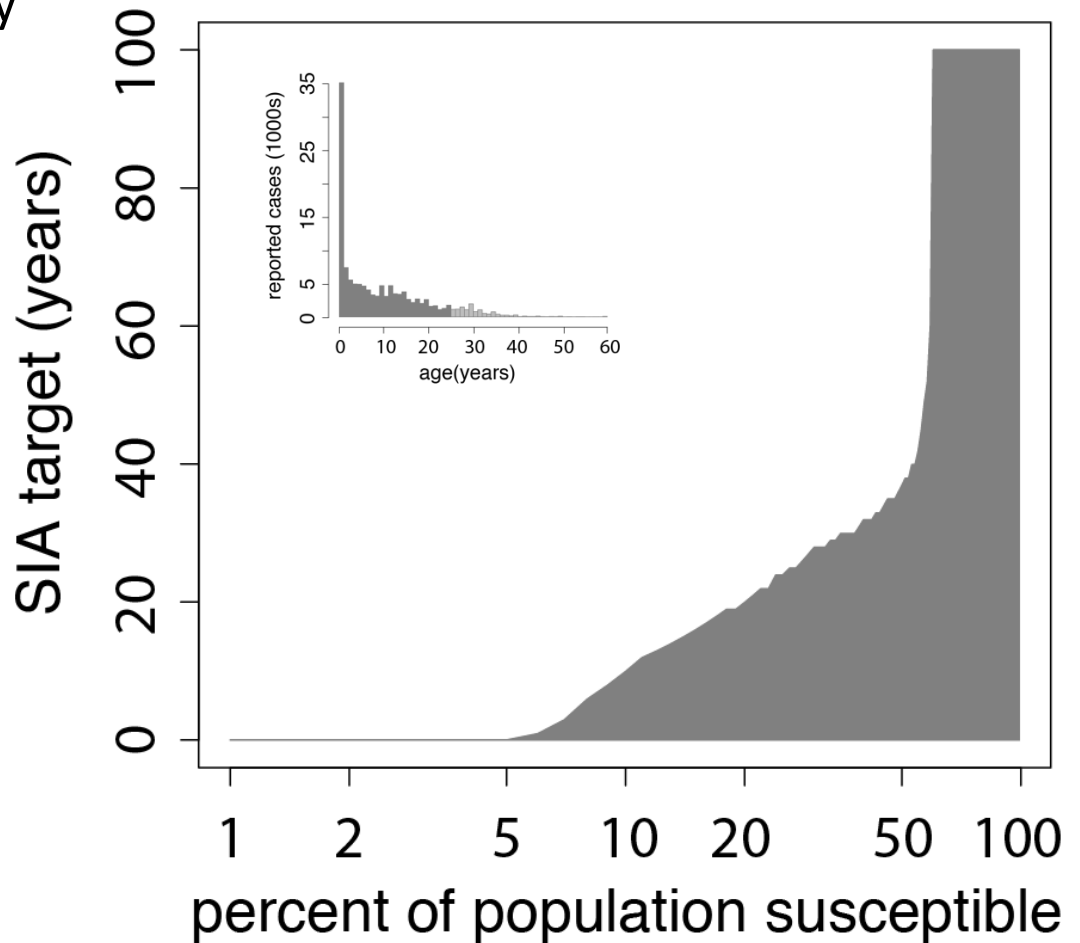
# Target Age Range to Achieve Herd Immunity

Age target to achieve herd immunity for a population with the 2010 Malawi susceptible age structure.

| Percent of Population Susceptible | Upper Age Target for SIA |
|-----------------------------------|--------------------------|
| 6%                                | 1yr                      |
| 7.5%                              | 6yr                      |
| 10%                               | 12yr                     |
| 20%                               | 28yr                     |

Source: Matt Ferrari

Target based on Malawi case distribution

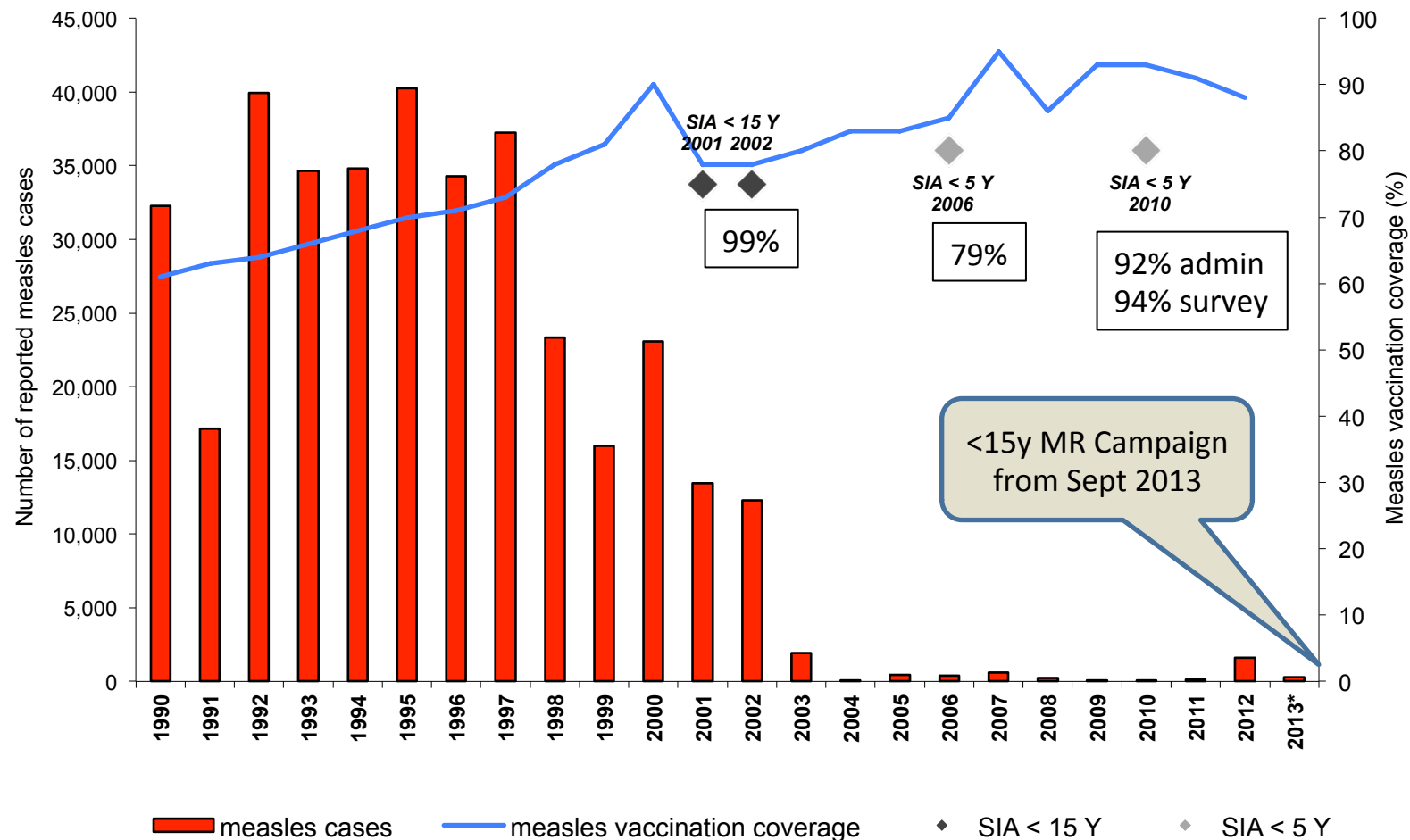


# Country Analysis

Grouped by Vaccine Delivery Strategy

| Delivery Strategy       | No. of Countries | Example         |
|-------------------------|------------------|-----------------|
| MCV1/MCV2, no SIAs      | 41               |                 |
| MCV1/MCV2, 1 SIAs       | 26               | S. Korea        |
| MCV1/MCV2, regular SIAs | 77               | Vietnam, Brazil |
| MCV1, regular SIAs      | 50               | Ghana, Malawi   |

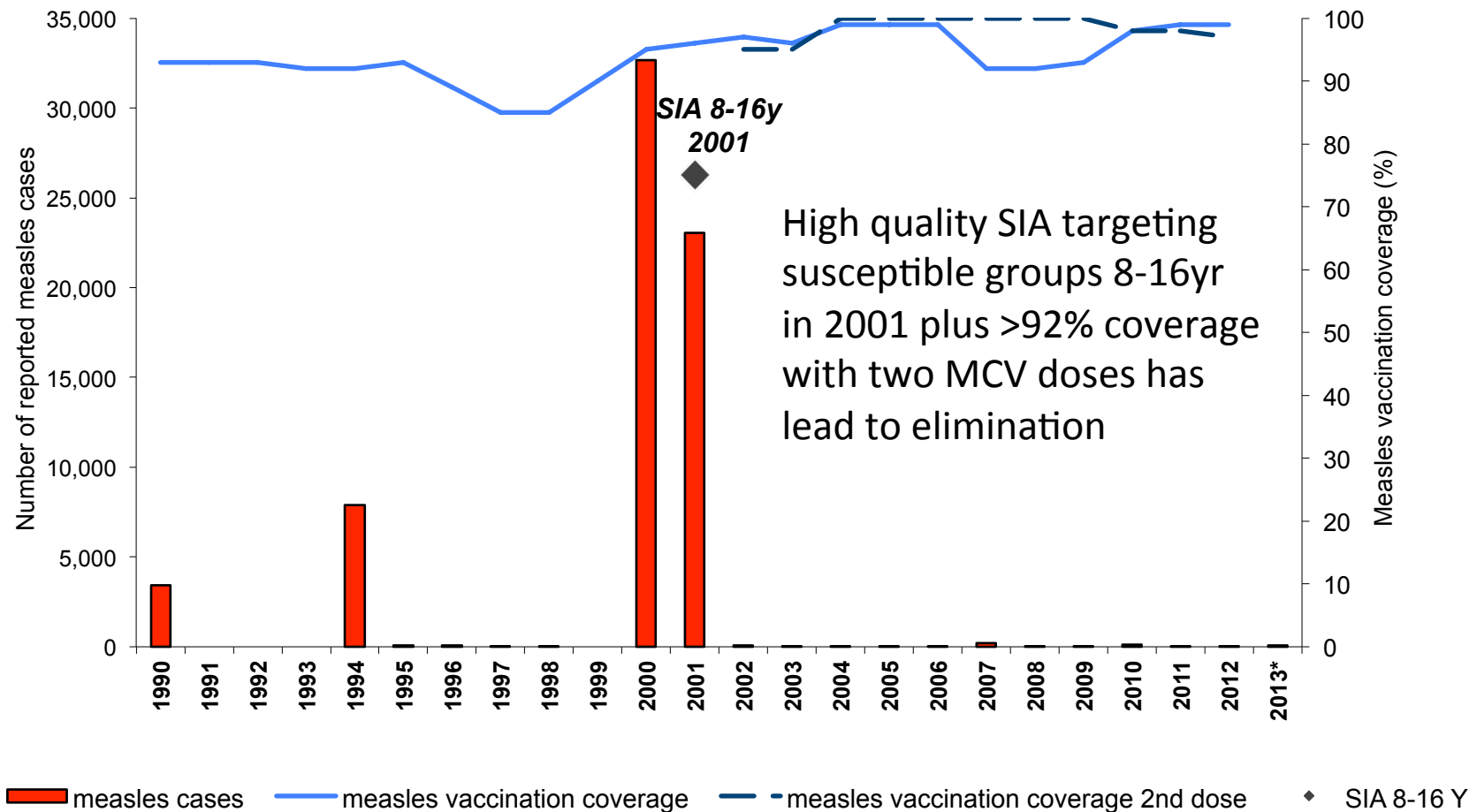
# Reported measles cases and measles vaccination coverage, 1990-2013\*, Ghana



Data source:  
 measles cases - reported by national authorities to WHO annually; monthly reports used for 2013  
 measles vaccination coverage - WHO/UNICEF immunization coverage estimates 1990-2012, as of July 2013;  
 SIA activities: WHO/EPI supplementary immunization activities database

\*2013 data through 10.09.2013

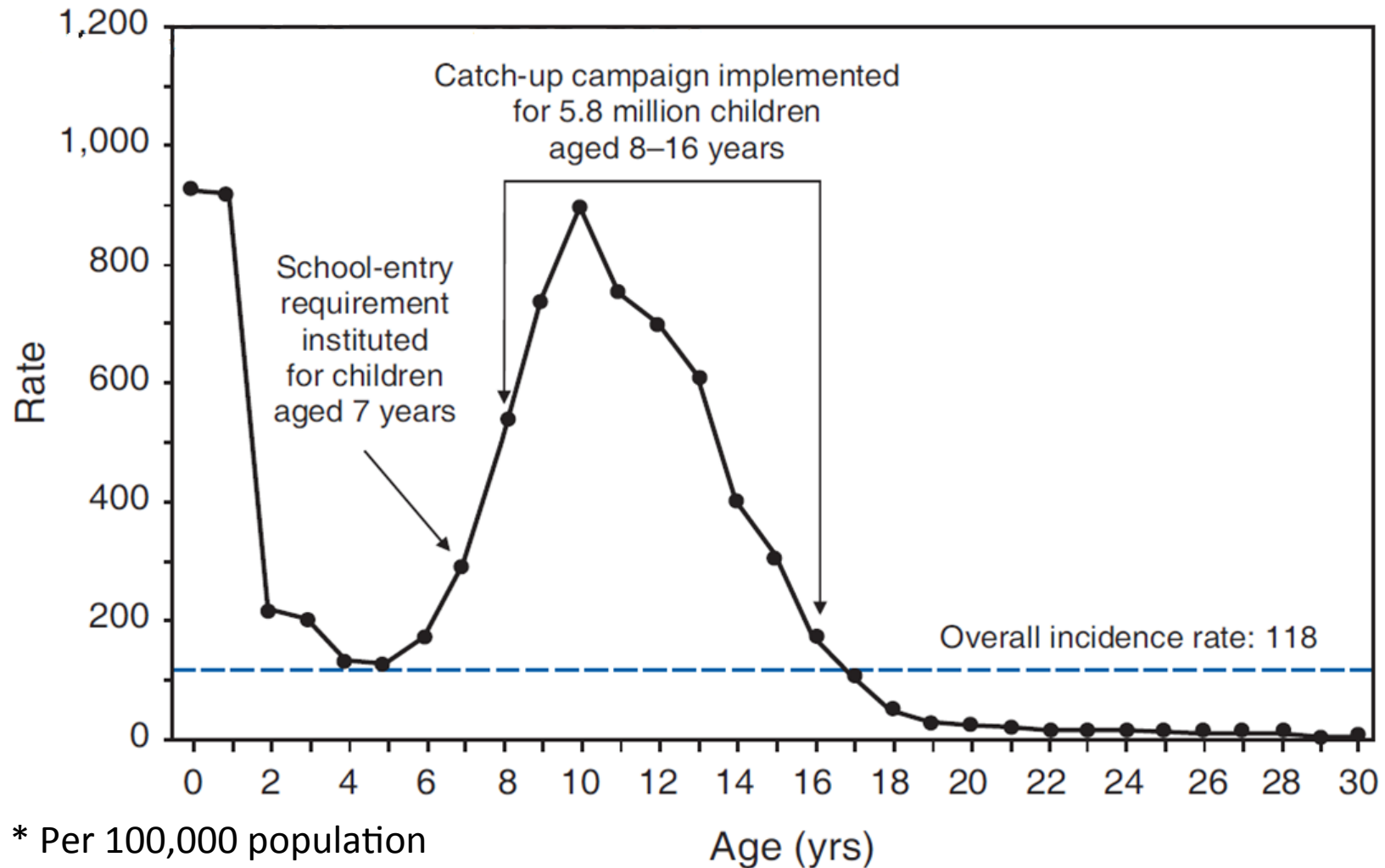
# Reported measles cases and measles vaccination coverage, 1990-2013\*, Republic of Korea



\*2013 data through 20.08.2013

Data source:  
 measles cases - reported by national authorities to WHO annually; monthly reports used for 2013  
 measles vaccination coverage - WHO/UNICEF immunization coverage estimates 1990-2012, as of July 2013;  
 SIA activities: WHO/EPI supplementary immunization activities database

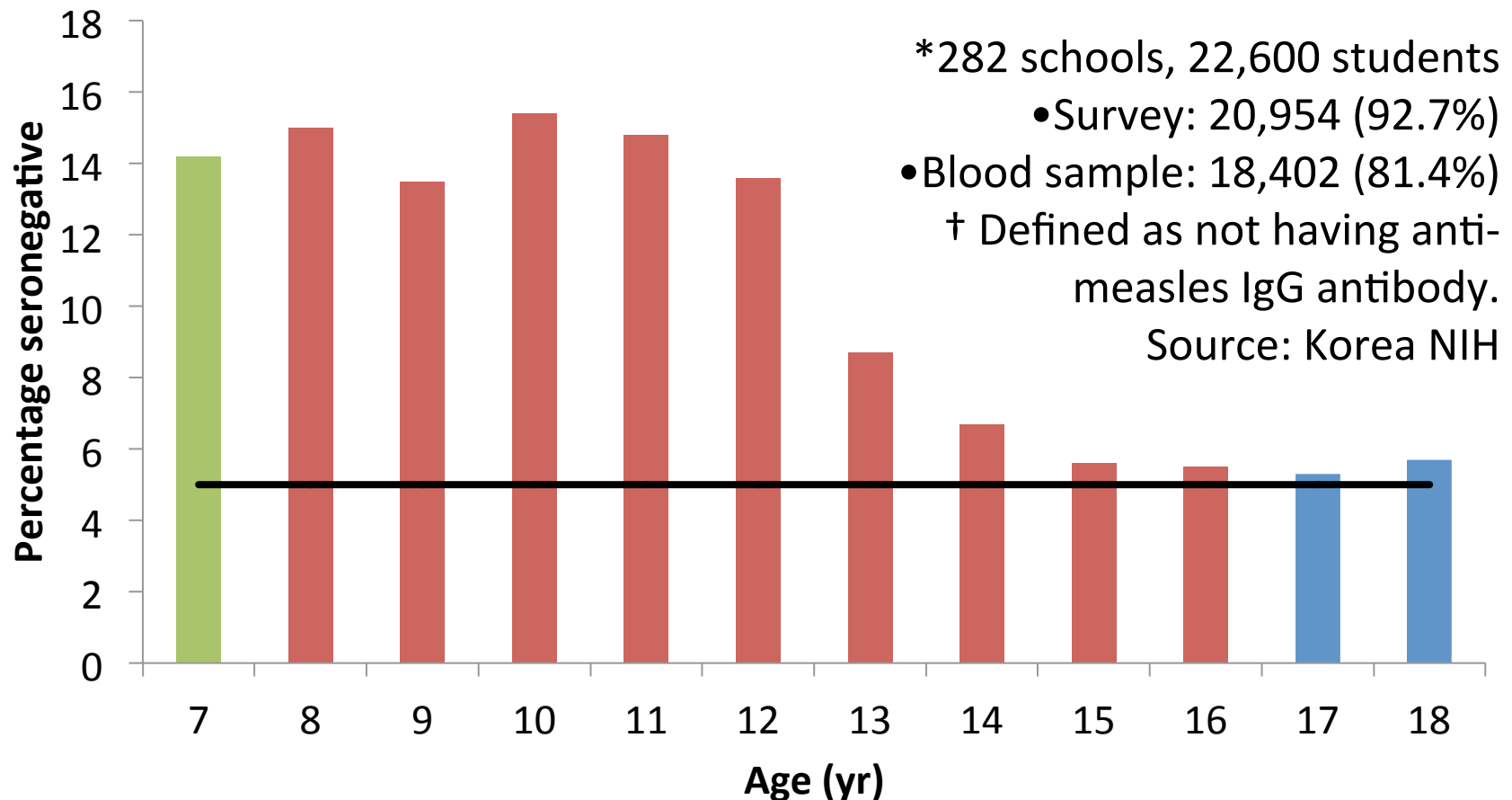
# Incidence rate\* of reported measles cases by age — Republic of Korea, 2000–2001



\* Per 100,000 population

Source: MMWR 2007; 56:304-307

## Proportion of persons aged 7–18 yr\* with measles susceptibility† by age — Republic of Korea, 2000

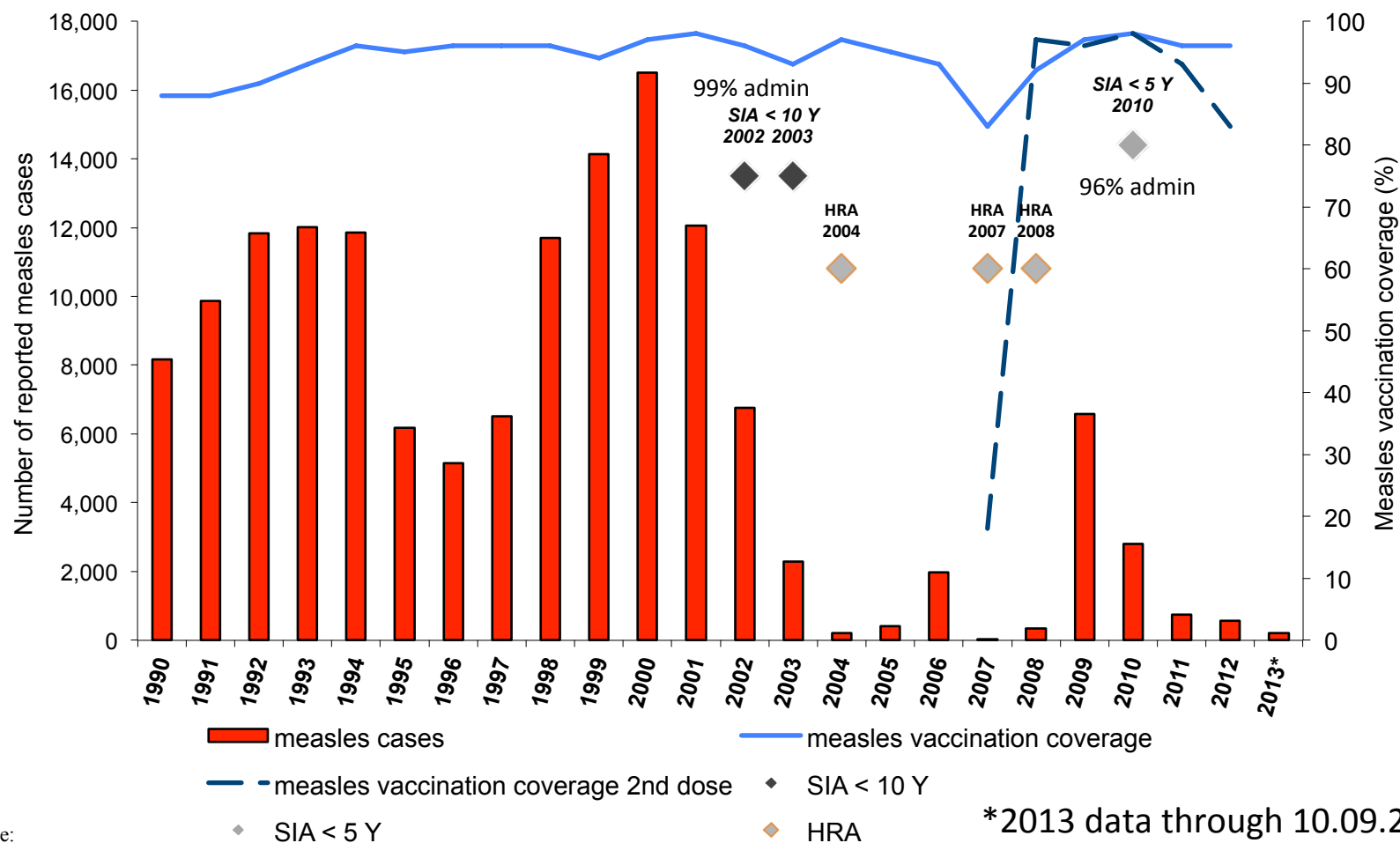


# Reported measles cases and measles vaccination coverage 1990-2013\* Viet Nam

Large outbreak in 2009-2010 revealed immunity gaps:

Cohorts 10-14 years were not covered by 2002-03 catch-up SIA

Children born since 2002 catch-up were missed due to low MCV1, no MCV2 in routine until 2007, choice of older age (6y) for MCV2 and no follow-up SIA in 2006



Data source:

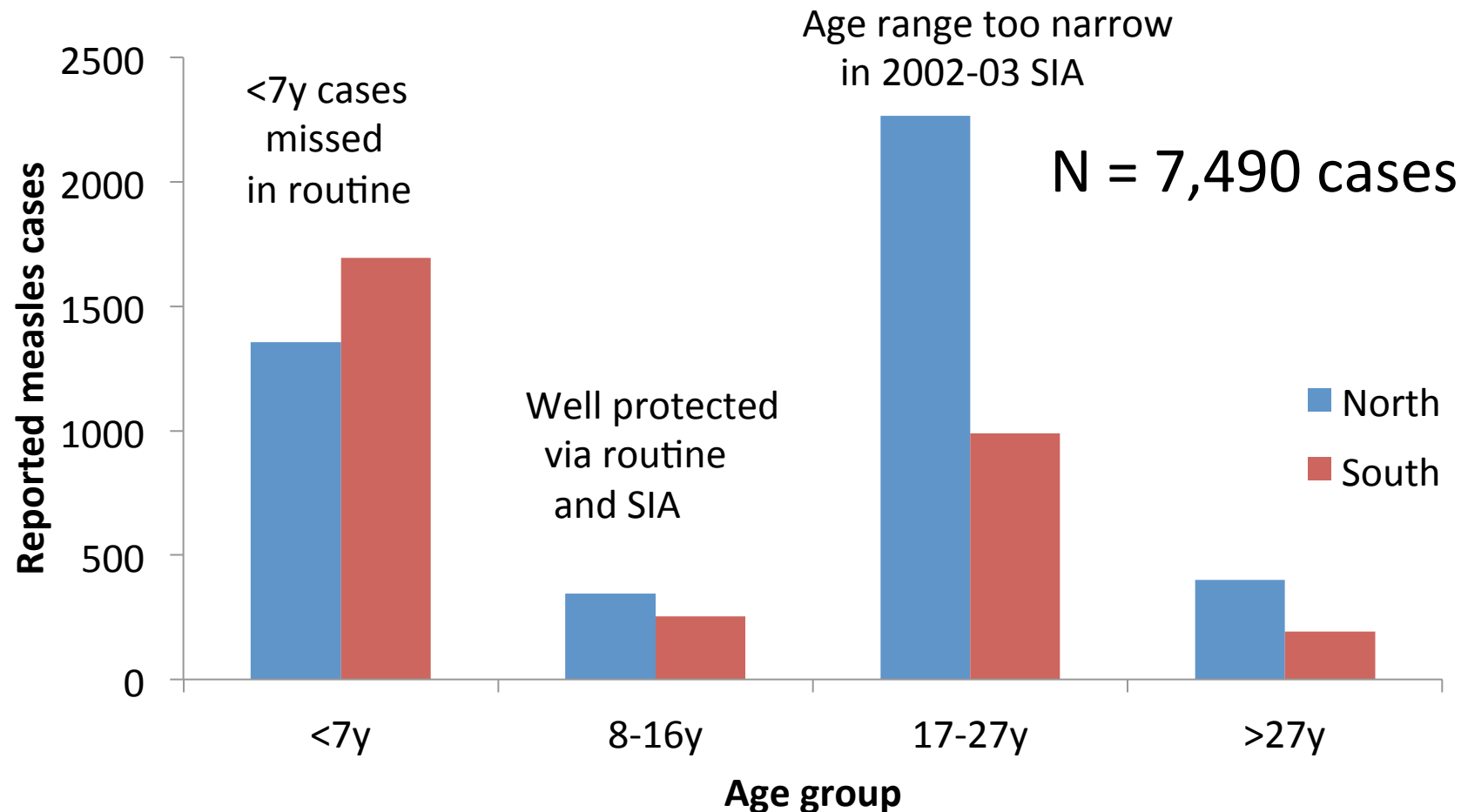
measles cases - reported by national authorities to WHO annually; monthly reports used for 2013

measles vaccination coverage - WHO/UNICEF immunization coverage estimates 1990-2012, as of July 23232013;

SIA activities: WHO/EPI supplementary immunization activities database

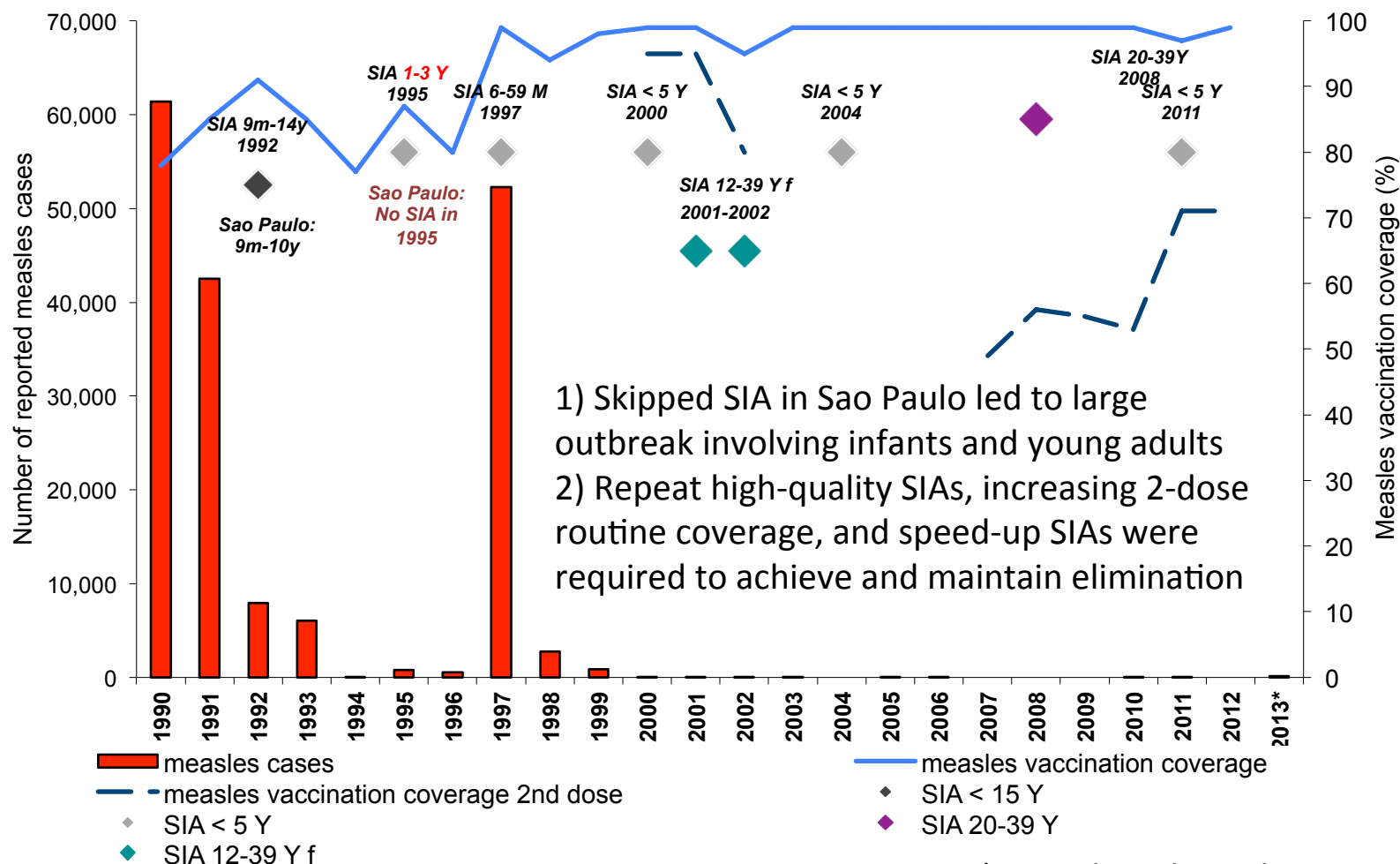
# Measles cases by age and region

## Viet Nam, Oct 2008 – Jan 2010



Source: EPI Viet Nam

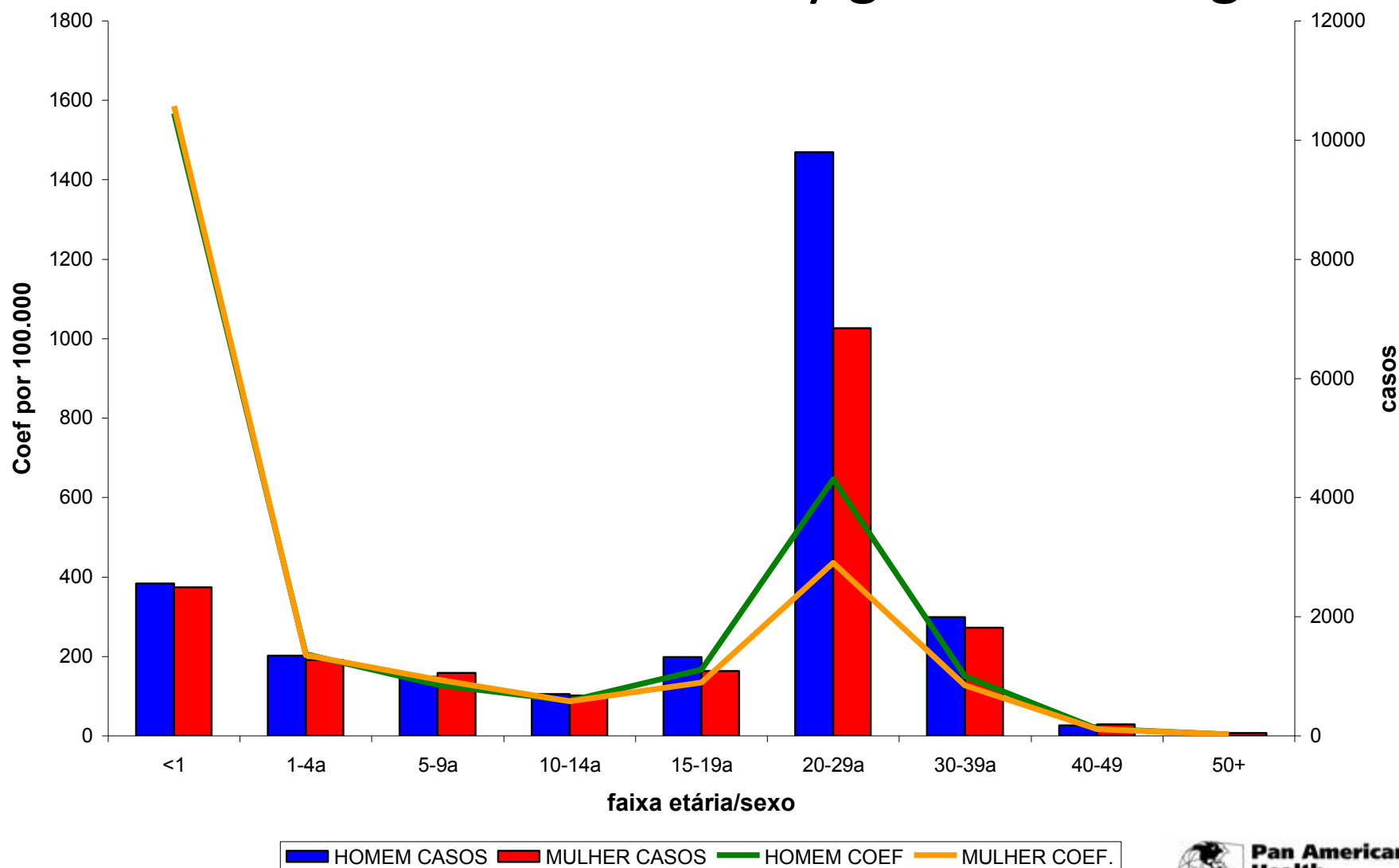
# Reported measles cases and measles vaccination coverage, 1990-2013\*, Brazil



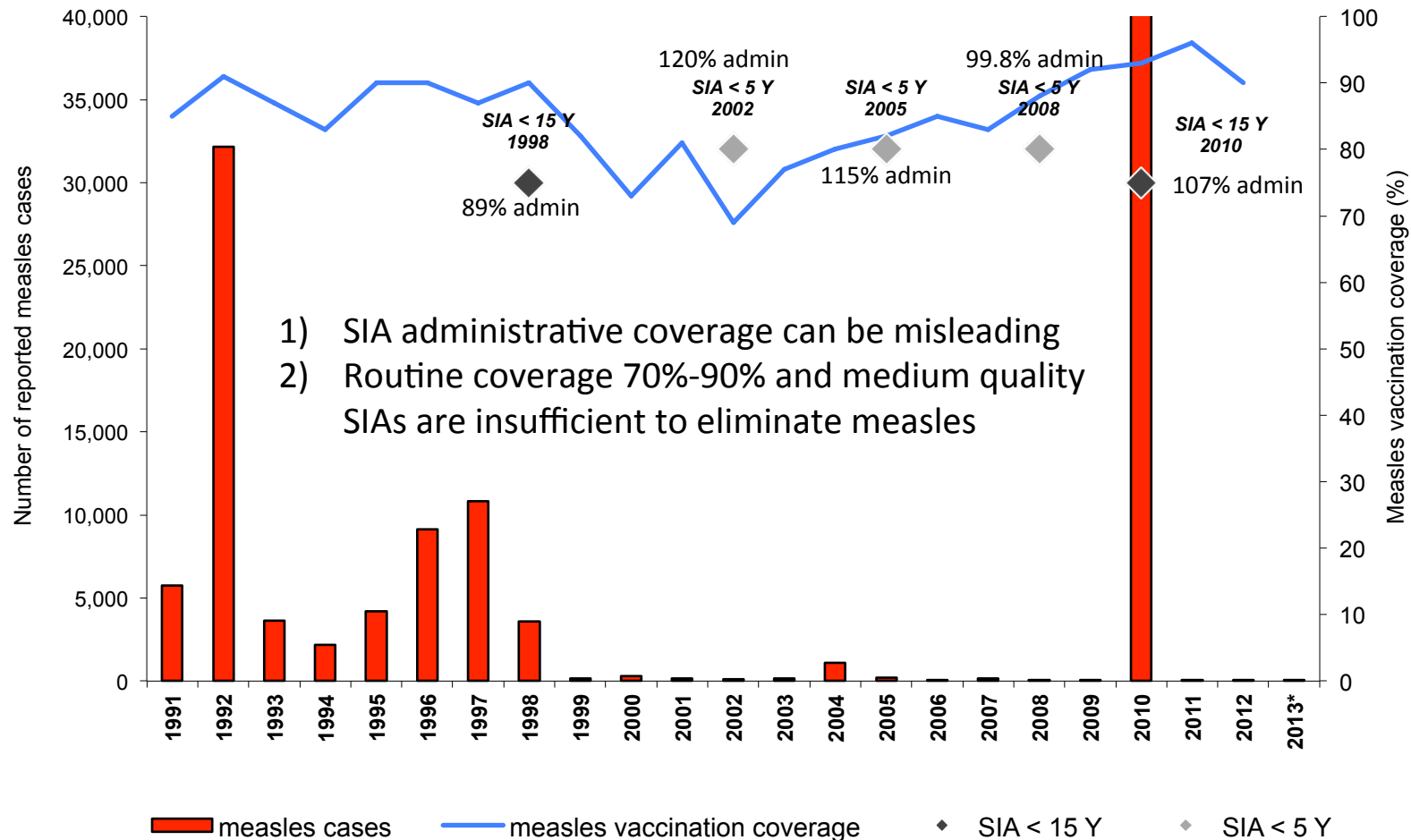
Data source:  
measles cases - reported by national authorities to WHO annually; PAHO monthly reports used for 2013  
measles vaccination coverage - WHO/UNICEF immunization coverage estimates 1990-2012, as of July 2013;  
SIA activities: WHO/EPI supplementary immunization activities database

\*2013 data through 10.09.2013

# Measles in São Paulo metropolitan area, 1997: Cases and incidence by gender and age



# Reported measles cases and measles vaccination coverage, 1996-2013\*, Malawi



Data source:  
measles cases - reported by national authorities to WHO annually; monthly reports used for 2013  
measles vaccination coverage - WHO/UNICEF immunization coverage estimates 1990-2012, as of July 2013;  
SIA activities: WHO/EPI supplementary immunization activities database

\*2013 data through 10.09.2013



# Draft Recommendations

- Based on current epidemiological and modelling data, it is not possible to have a general rule for when the target age-range of SIAs should be expanded.
- The key issue is achieving  $\geq 95\%$  immunity to measles across all age cohorts. This means ensuring that vaccination coverage, whether by routine and/or SIA, is  $\geq 95\%$
- The quality of SIA is critical to achieving high coverage
- Need to verify coverage for all measles SIAs through statistically valid and generally accepted methodology
- The differential coverage required for elimination vs control must be taken into account

## Draft Recommendations

**Each country has to integrate all of its available data to determine the distribution of immunity deficit.**

- Historical data on measles cases and MCV use
- Demographic data (birth rate and migration patterns)
- Administrative coverage by routine and SIA (for each birth cohort and at lower administrative levels)
- Surveillance (age-specific measles rates, including at lower administrative levels)
- Coverage surveys - routine and post-SIA
- Sero-surveys – planned and opportunistic
- Local knowledge of EPI managers and staff

# Countries with weak health systems

- Need to consider the capacity of the health system to do SIAs and the trade-offs between strengthening routine delivery and the need for high quality SIAs versus attempting wide age range SIAs that result in poor coverage

## Section 3: Policy Question

What criteria should be used to guide countries on when to expand the **target age range** for:

- Catch-up measles-rubella (MR) SIAs beyond 15 years?

## Rubella Position Paper (2011)

- The primary purpose is to prevent the occurrence of congenital rubella infection including CRS
  - In the PP, there are two approaches,
    - 1) CRS prevention
    - 2) rubella elimination
- Rubella elimination:
  - Interruption of rubella virus transmission, thereby eliminating rubella as well as CRS.

# Rubella/CRS Elimination (PP 2011)

- Countries should take the opportunity of the two dose measles vaccine strategy to use MR or MMR vaccine.
- The preferred approach is to begin with MR or MMR vaccine in a wide-age range campaign followed immediately with introduction of MR, or MMR vaccine in the routine programme.
- The first dose of MR vaccine can be delivered at 9 or 12 months of age
- All subsequent follow-up campaigns should use MR vaccine or MMR vaccine.
- Efforts to reach women of child-bearing age

## Current Status of RCV introduction

- 135 countries have introduced RCV
  - Of those 59 countries, 48 countries are GAVI eligible
  - Current GAVI support is for MR campaigns up to 14 years 11 months of age
- However, to achieve the rubella elimination goal by 2020 (only 7 years away) countries may need to expand the age range to older individuals

## SIA target age range

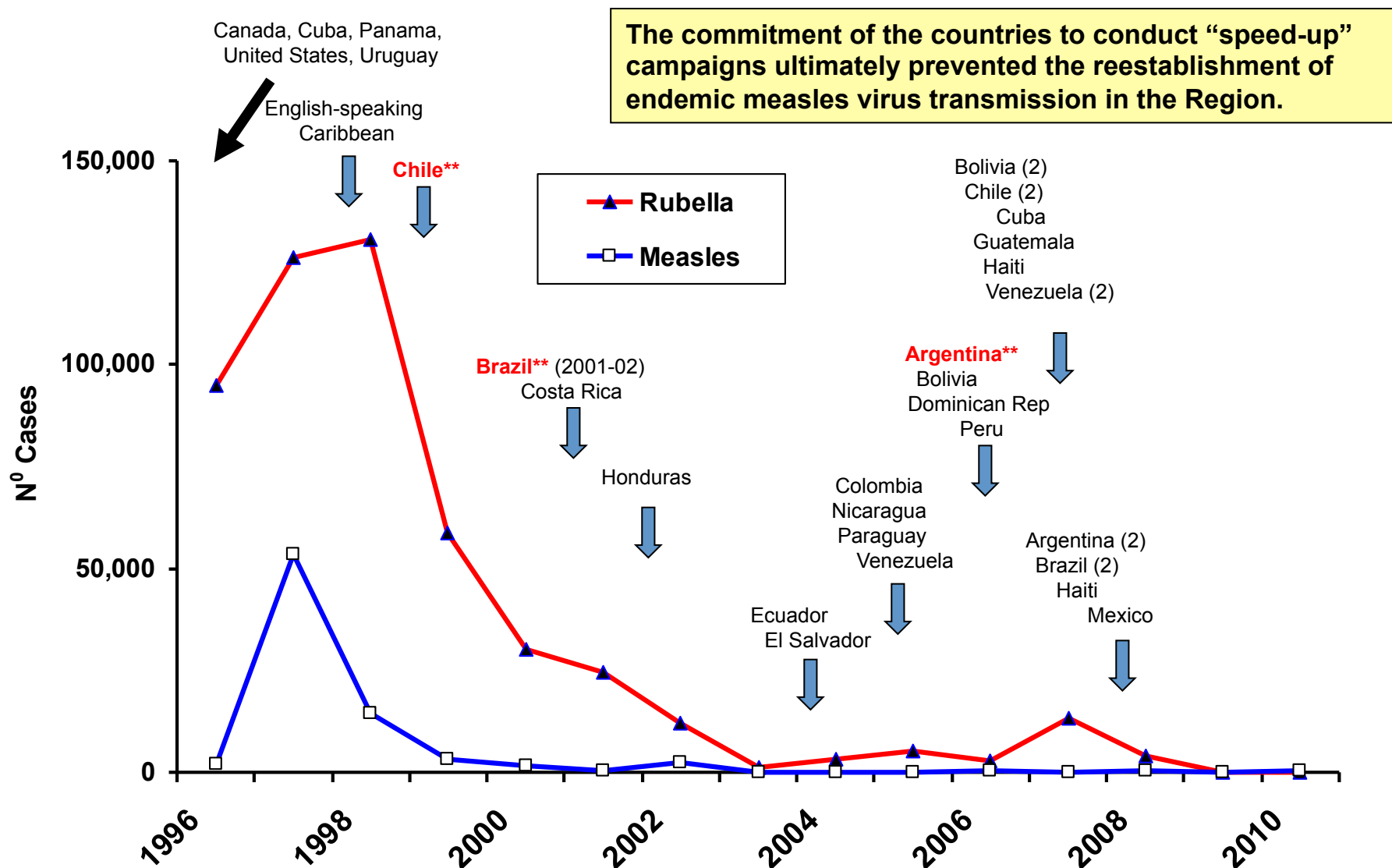
- The Working Group identified 2 situations in which the target age range for MR SIAs should be extended beyond 15 years:
  1. To accelerate achievement of established rubella/CRS elimination goals; and
  2. To fill immunity gaps identified through a thorough analysis of their country data for both measles and rubella.

# 1. Achieving the Elimination Goal

- Two WHO regions with established rubella elimination goals – AMR (2010) and EUR (2015)
- GVAP goals – 5 of the 6 WHO regions are to have achieved by 2020
  - Four more regions need to reach the goal
- PAHO established rubella/CRS elimination goal in 2003.
  - 3 countries (Peru, Haiti, DR) had not introduced RCV
  - 7 countries had introduced RCV within the last 5 years
  - Between 2003 and 2008, 14 countries conducted adult mass campaigns after introduction of RCV in program

**Age range for campaigns was <30 or < 40 years males and females in most PAHO countries**

# Adolescent and Adult Rubella Vaccination (“Speed-up”) Campaigns, The Americas\*



Source: Country reports to FCH/IM.

\* Includes rubella and measles cases reported to PAHO as of epidemiological week 47/2010.

\*\*Countries that implemented “speed-up” campaigns (1<sup>st</sup> phase) in women only.

## Lessons learned from AMR

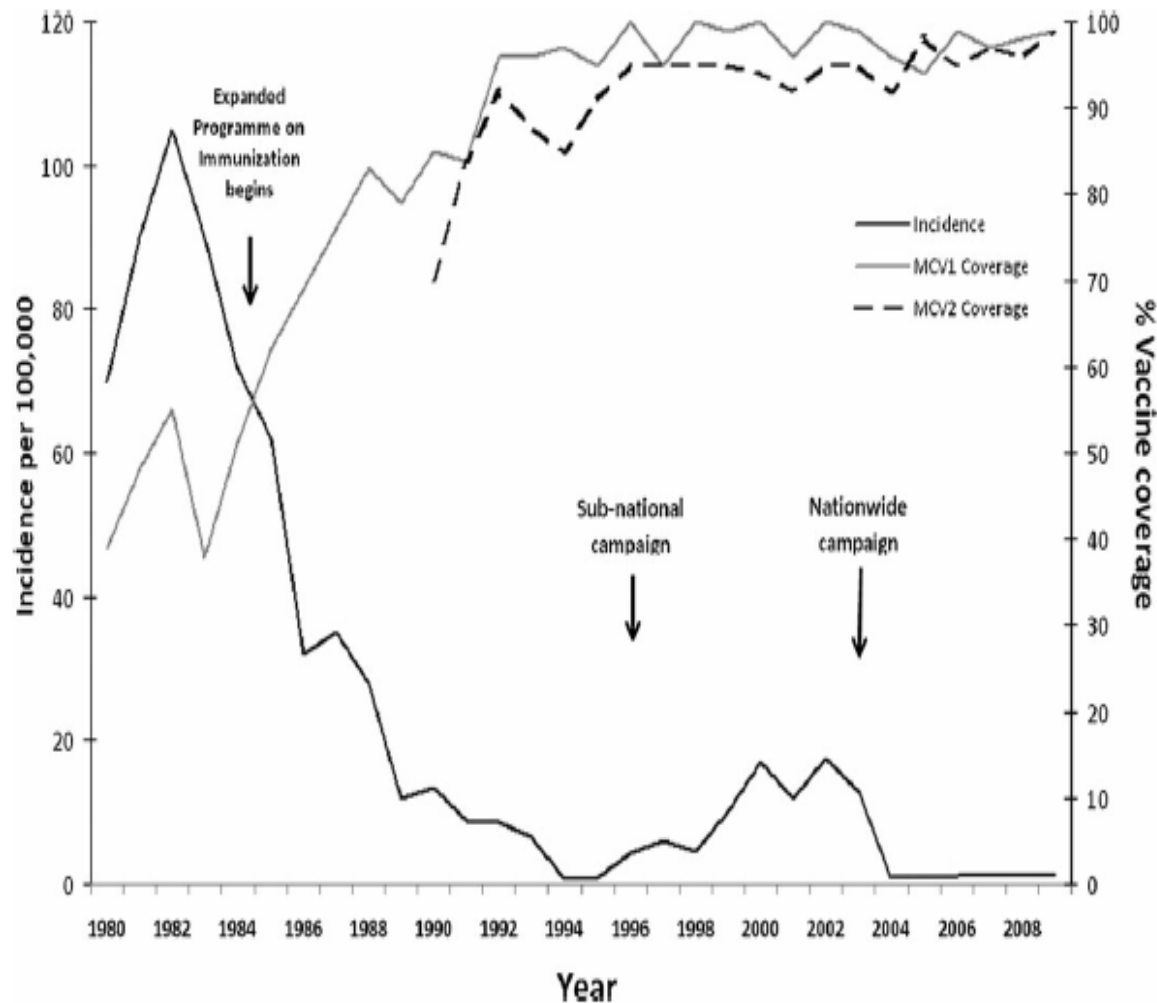
- In the previous 2000 PP, it was recommended to vaccinate WCBA in routine and mass campaigns
- This approach has resulted in large rubella epidemics, particularly in adolescent and adult males (AMR, EUR, WPR)
- In AMR, 3 countries (Brazil, Argentina, Chile) vaccinated adolescent and adult females only which resulted in large epidemics and CRS cases
  - For the countries to achieve their rubella/CRS elimination goal, each country had to conduct a repeat mass campaign.
- **If countries have or anticipate establishing a rubella elimination goal, SIAs in adults must include both females and males.**

## 2. Integration of Measles and Rubella Epidemiology

**Second reason to extend target age range >15y:**

- **To fill gaps in population immunity** based on similar epidemiologic and programmatic considerations described for measles SIAs; however, taking into account both measles and rubella epidemiology

# Iran



In 2002, measles elimination goal established

During 1999-2002, shift in age distribution of measles cases to 10-25y

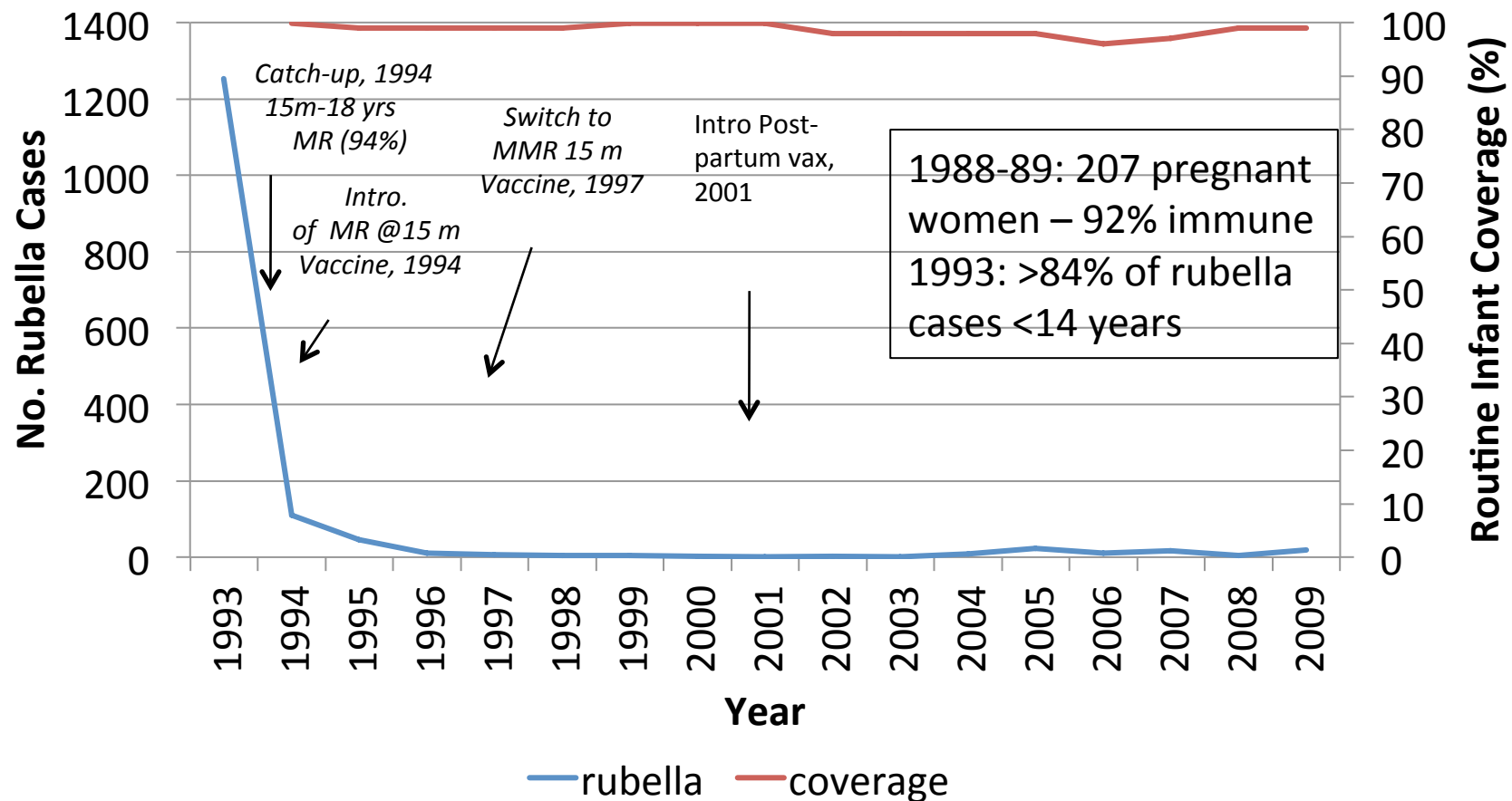
In 2001, rubella seroprevalence study – 14-70y, 96% protected

In 2003, conducted MR SIA targeting 5-25y to address measles susceptibility

# Using data for action

- In reviewing the country information:
  - Epidemiology
    - Age distribution of cases
    - History of vaccination program
  - Seroprevalence data
  - Age specific fertility rates
  - CRS information – age of mother

# Reported rubella and routine infant vaccine coverage, Oman 1993-2009



# Haiti

Haiti was the last country to introduce RCV,

- Used a sero-prevalence study to determine the target age range (9 months - 19 years)
- Based on this survey did a SIA 9m - 19 years to meet the regional 2010 rubella/CRS elimination goal

## Country experience shows that....

- Wide age SIAs can be used to achieve the established goals as demonstrated in AMR
- Integration of measles and rubella epidemiology can be used to target both diseases for elimination
- With the GVAP elimination goals, adolescent and adult women should not be targeted only in SIAs. Must include both males and females.

## Draft Recommendations (1)

- SIAs are done to reach unvaccinated or susceptible children/ persons in order to close immunity gaps
- Each country must analyse its own data in depth to determine the target age range for MR SIAs
- Ensure high coverage ( $\geq 95\%$ ) during MR SIAs
- Verify coverage for all MR SIAs through statistically valid and generally accepted methods
- Record doses given during SIAs (by age group, number of zero-dose children vaccinated)

## Draft Recommendations (2)

- Measles-rubella catch-up SIAs should be extended beyond 15 years in order to:
  - Accelerate the progress toward established rubella/CRS elimination goals
  - Fill gaps in population immunity based on similar epidemiologic and programmatic considerations as for measles SIAs
  - Additional information to consider for MR SIAs
    - Levels of rubella immunity among women of child bearing age
    - Epidemiology of rubella and CRS
    - Population characteristics e.g. age-specific fertility rates
    - Age of mothers of CRS affected infants

Thank you