Introduction to Measles – a Priority Vaccine Preventable Disease (VPD) in Africa

Nigeria Center for Disease Control

Federal Ministry of Health

Abuja

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Outline

1. Measles disease
2. Progress towards measles mortality reduction
3. Mortality reduction strategies
4. Measles outbreak

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2. Progress towards measles mortality reduction
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4. Measles outbreak

Measles disease

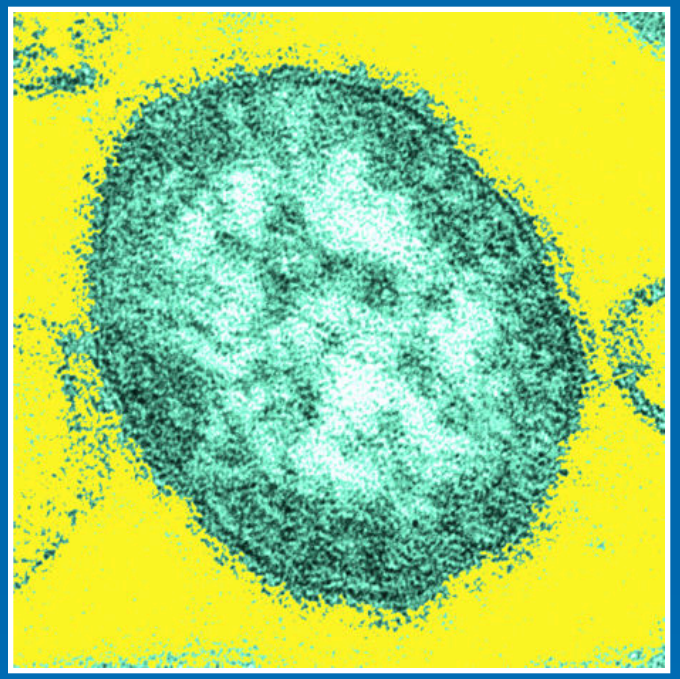
- **An acute and highly infectious disease**
  - Caused by measles virus
  - Everyone exposed gets the disease if not immune (R_0 = 12.5 – 18.0)
  - Without vaccination program, virtually all are eventually infected
  - Fever, Rash and 3Cs (Cough, Conjunctivitis, Coryza)
- **Transmission**
  - Contact with respiratory secretions or aerosols

Measles disease: Classic manifestations

- Fever
- Maculopapular rash
- The 3C:
  - ✓ Cough
  - ✓ Coryza (runny nose)
  - ✓ Conjunctivitis (red eyes)

Measles virus

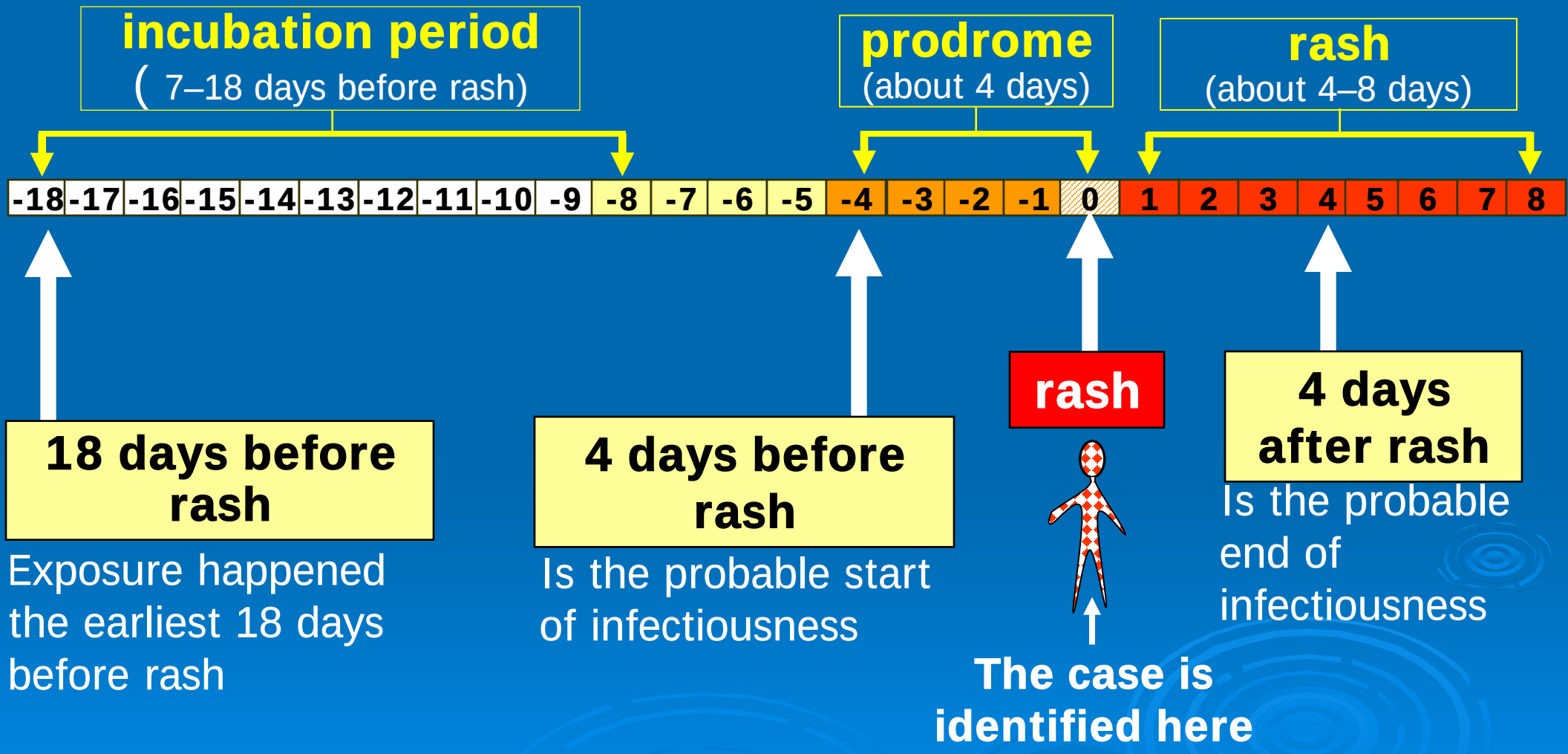
- RNA virus
- Family: Paramyxoviridae.
- Genus: Morbillivirus
- Humans are the only reservoir
- Multiplies in the respiratory tract
- Transmitted via respiratory secretions or aerosols



Clinical course of measles

- **Incubation period: 14 days (range, 7 – 18 days)**
- **Prodrome: begins 10 – 14 days after exposure**
  - High fever, cough, coryza, conjunctivitis
  - Period of greatest infectiousness (virus shedding)
- **Rash begins: 2 – 4 days after prodrome starts**
- **Complications: occur mostly in 2nd and 3rd weeks**
  - Any disease or death not clearly due to another cause (e.g., trauma) during the 30 days following rash onset
- **Case Fatality Ratio (CFR)** 0.1 – 10 %
  - Up to 30% in humanitarian emergencies

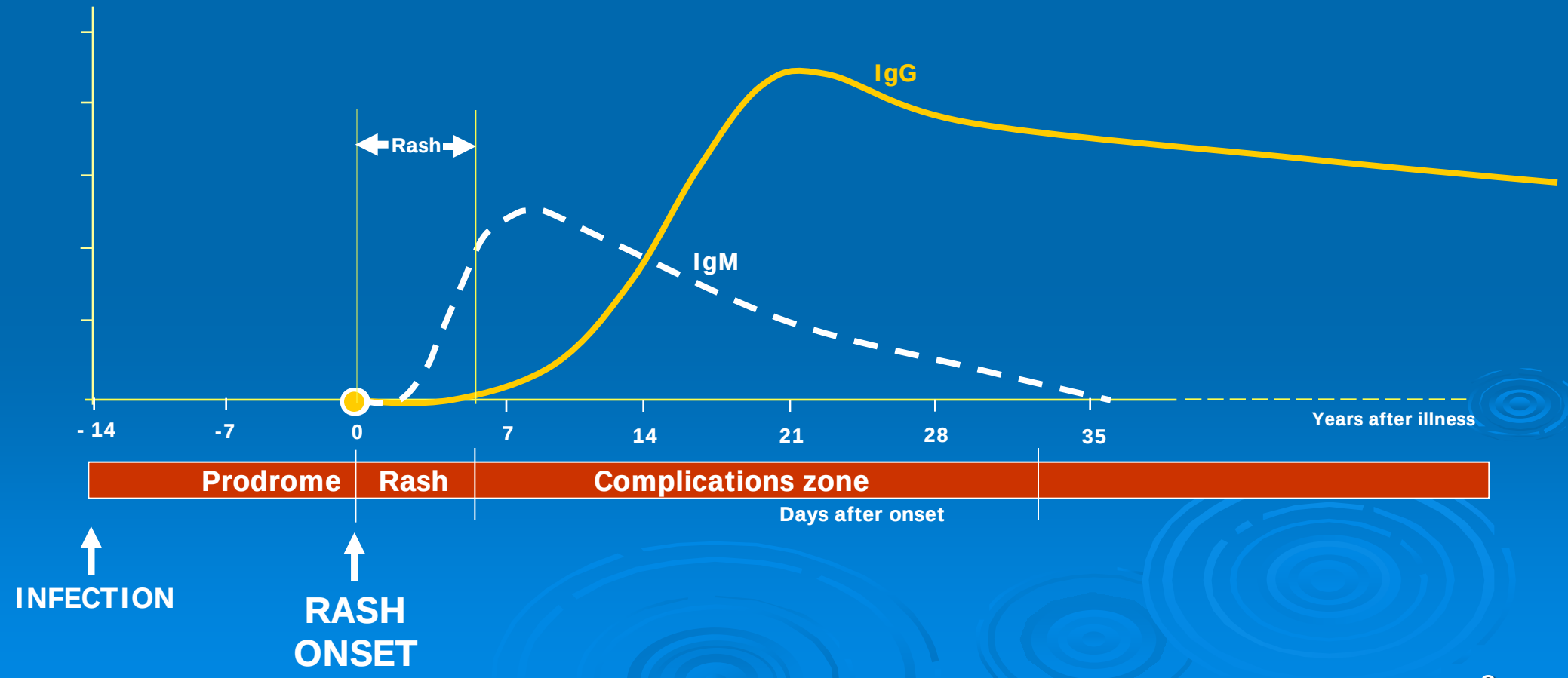
Clinical course of measles



Clinical course of measles and antibody dynamics

IgM appear first and disappear within 30 days. Marks the acute infection

IgG appear later and remain high for years. Mark immunity



Complications….1

- **Complications:** any disease or death not clearly due to another cause during the 30 days following rash onset
  - Corneal scaring (aggravated by Vit A deficiency)
  - Encephalitis (higher children and adults, 0.1%)
  - Diarrhea
  - Pneumonia (major cause of death)
- **Mortality rate**
  - 0.1 – 10%
  - Up to 30% in humanitarian emergencies

Complications….2

Corneal scarring causing blindness

Vitamin A deficiency

Encephalitis

Older children, adults

≈ 0.1% of cases

Chronic disability

desquamation

Pneumonia & diarrhea

Diarrhea common in developing countries

Pneumonia ~ 5-10% of cases, usually bacterial

Complications…3

Sub-acute Sclerosing Panencephalitis (SSPE)

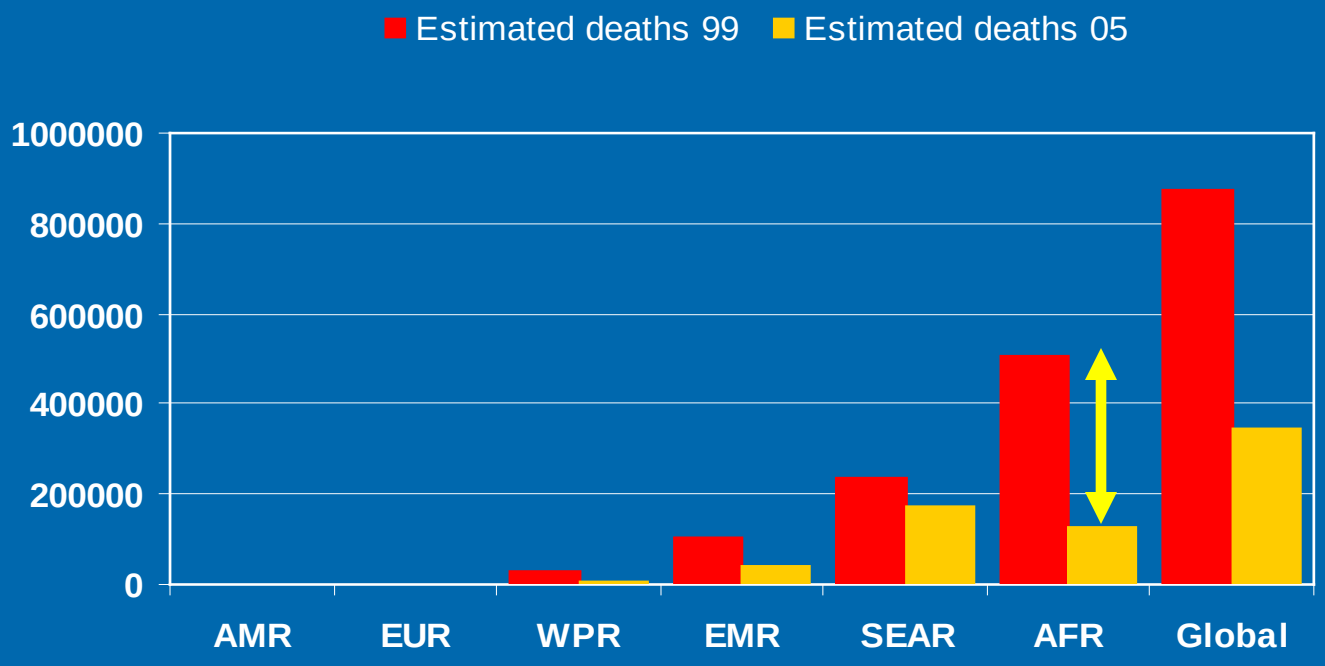
- Delayed complication: avg. 7 years after measles infection
- Rare (1 in 100,000 cases)
- Degenerative CNS disorder with personality changes, seizures, motor disability, progressing to coma and death

Prevention: Measles vaccine

- Live attenuated virus vaccine
- Excellent safety records
- Among most effective public health interventions
- Lifelong immunity
- Efficacy:

Age (Months)	Seroconversion* (%)
6	50
9	85 (Routine EPI dose)
12	90
15	95 (SIA dose)

Progress in measles elimination in Africa



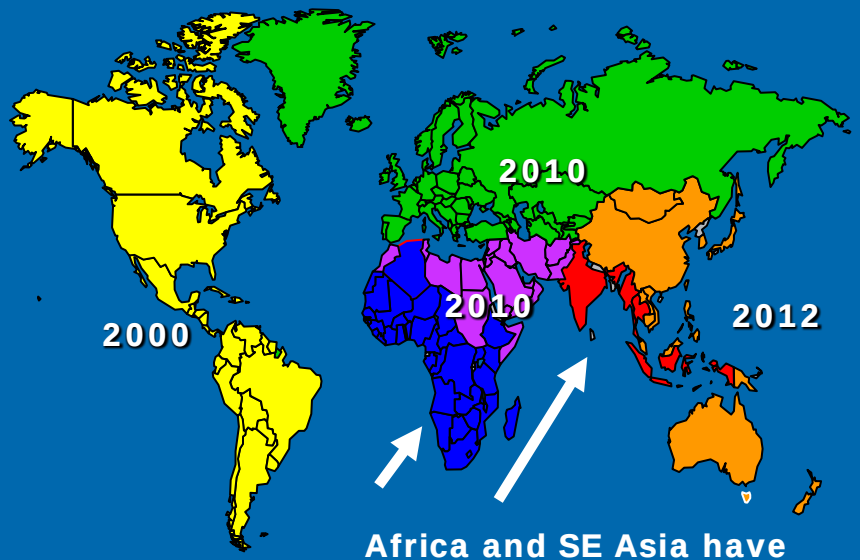
Estimated number of measles deaths by region, 1999 vs. 2005

- **60% reduction worldwide**
- **75% in Africa**
- **2.3 mil additional deaths prevented**

Engine behind this progress

Global commitment

Americas, Europe, E. Mediterranean, W. Pacific have elimination goals



Africa and SE Asia have mortality reduction goals

Partnership for Reduction of Measles Mortality in Africa 2001–2005

- Partners: ARC, UNF, IFRC, CIDA, UNICEF, WHO & CDC
- Measles SIAs in 40 countries
- 217 million children immunized
- Est. 1.2 million deaths averted

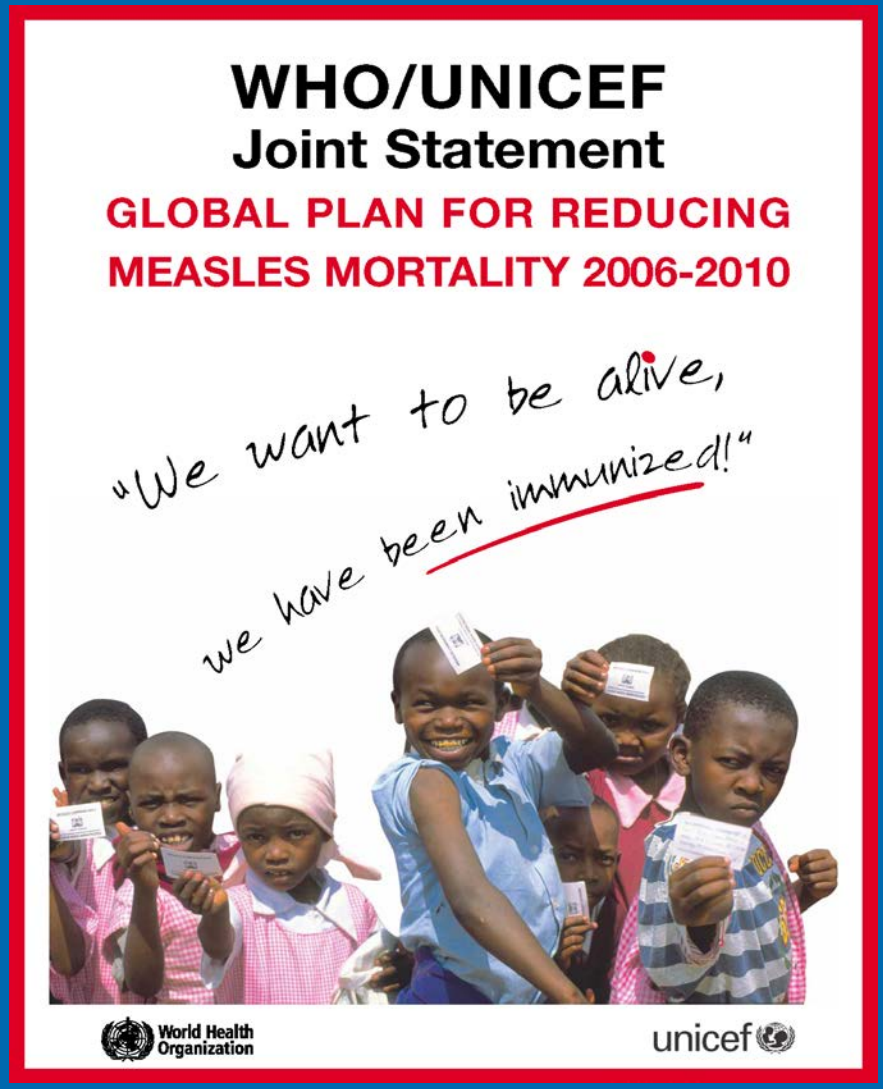
Effective strategic plans

WHO/UNICEF strategic plan for reducing measles mortality 2006 – 2010

- 90% reduction in measles-associated child mortality compared to 2000
- 47 priority countries
- 4 strategies

WHO/UNICEF Strategic Plan 2006-2010

- 47 Priority Countries
- Goal: reduce measles mortality by 90% by 2010 vs. 2000
- Based on 4 strategies



Measles Mortality Reduction Strategies

1. Improve case management (Vitamin A supplementation++)
2. Achieve high 1st dose routine vaccination coverage
3. Provide 2nd opportunity for vaccination through routine or supplemental activities
4. Establish an effective measles surveillance

1 – Improve case management: strategies to improve case management

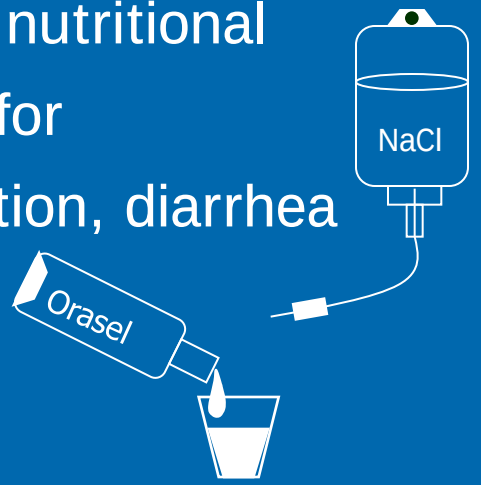
Measles case

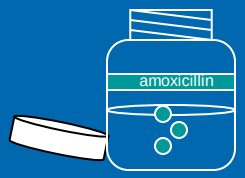
Vitamin A supplementation

Measures to reduce fever (antipyretics, tepid sponge)

Advise mother to bring the child back if the illness worsens

Fluids + nutritional support for malnutrition, diarrhea





Antibiotics for secondary infections (Pneumonia, ear infection..)

Enhance infection control in hospitals

2. Achieve high 1st dose routine vaccination coverage

- Administered at 9 months in Nigeria
- Sero-conversion at this age is 85%
- Sub-cutaneaous

3 – Provide second opportunity

Important concept: Herd Immunity

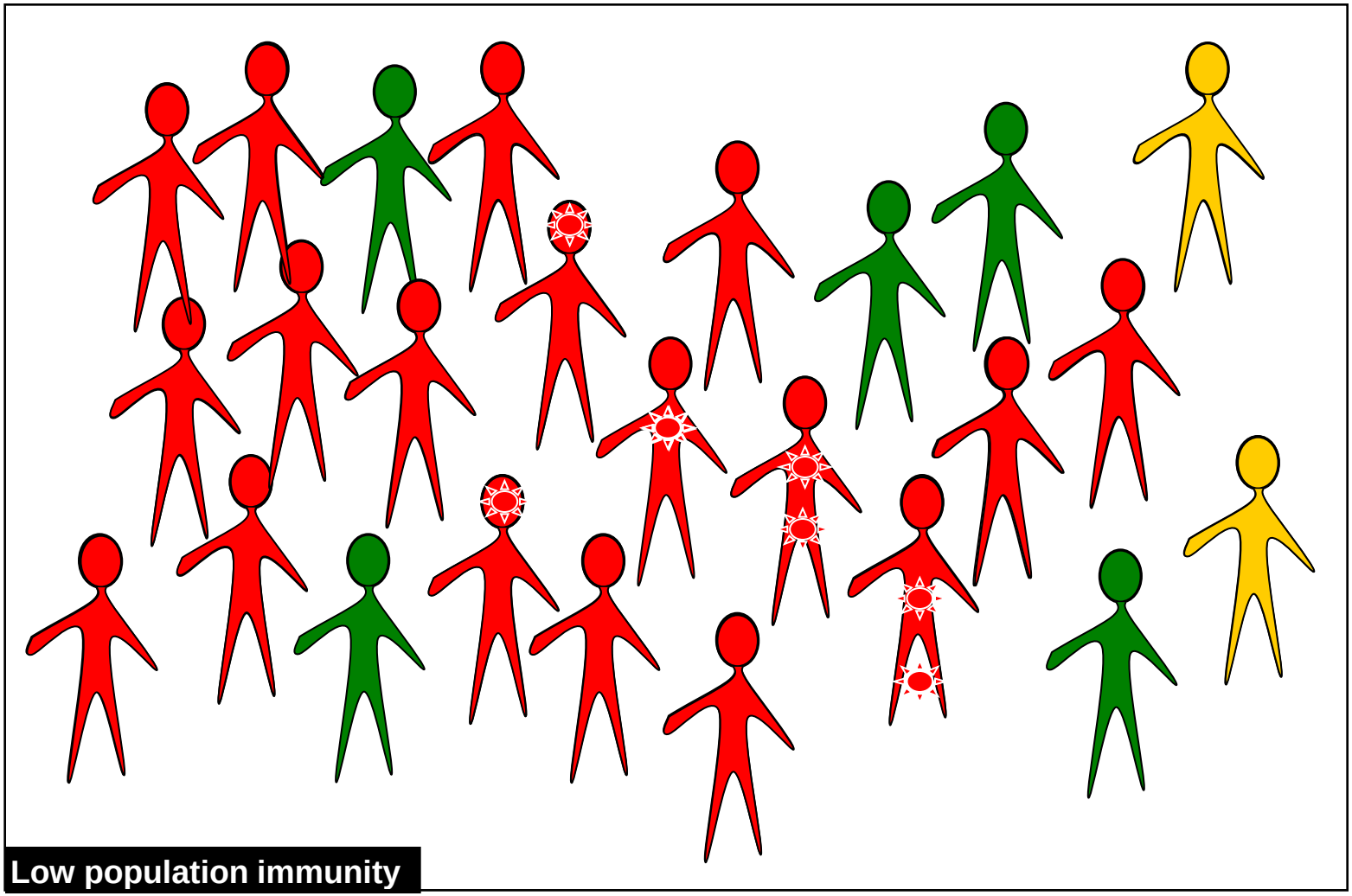
Definition

The resistance of a population to attack by a disease to which a large proportion of the members are immune.

For measles, this proportion is **95%**

What is Herd Immunity? Scenario 1

Immunized | Susceptible | Contagious | Vaccinated but get the disease



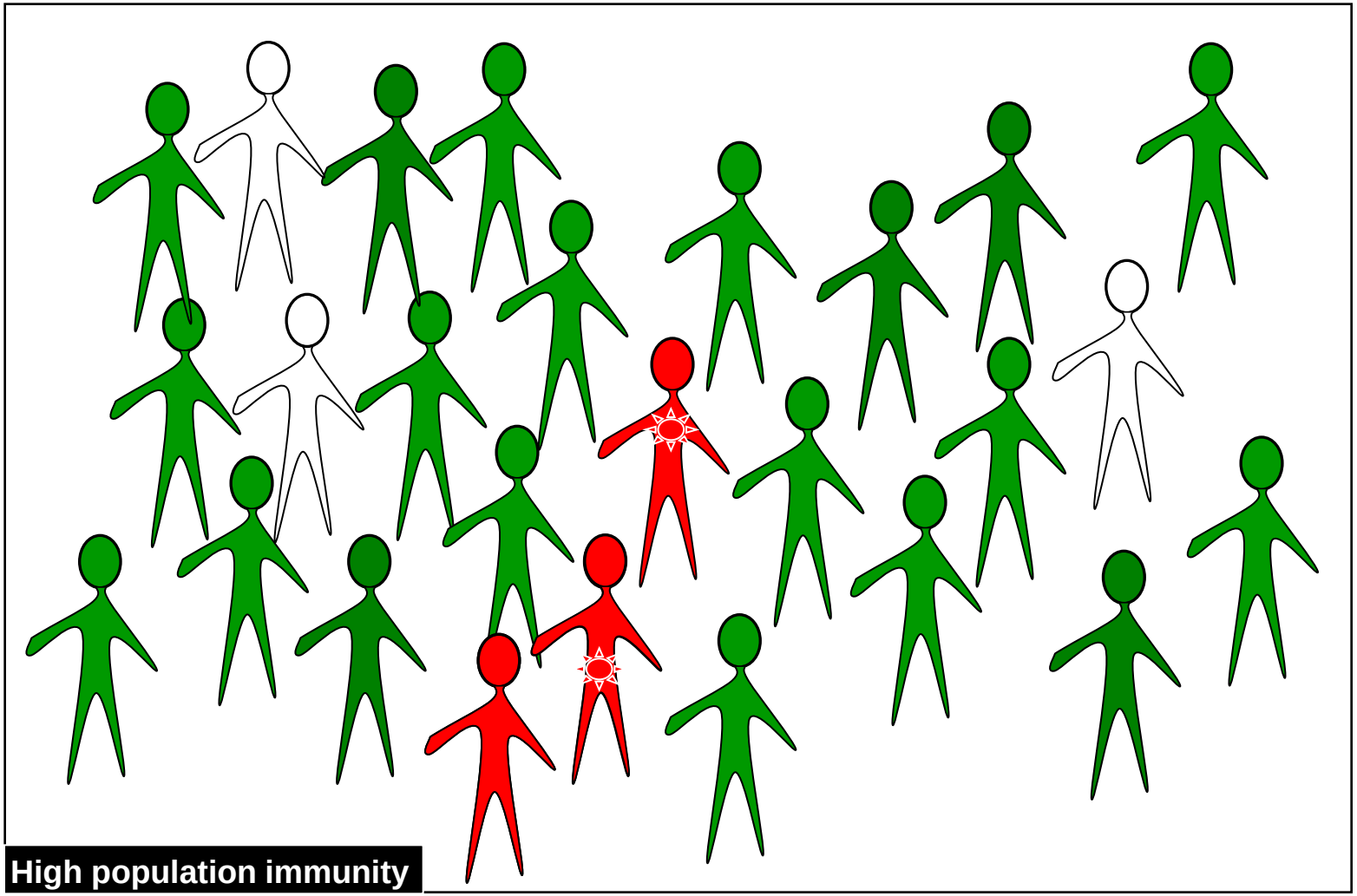
Low population immunity

Chance for contagious to meet susceptible is high

Disease spreads fast. Transmission is sustained. Outbreaks are frequent

What is Herd Immunity?: Scenario 2

Immunized | Susceptible | Contagious



High population immunity

Above a certain threshold of population immunity (95% for measles), chance for contagious to come into contact with susceptible is low

Disease spread is limited. Outbreaks are small. This population has Herd immunity

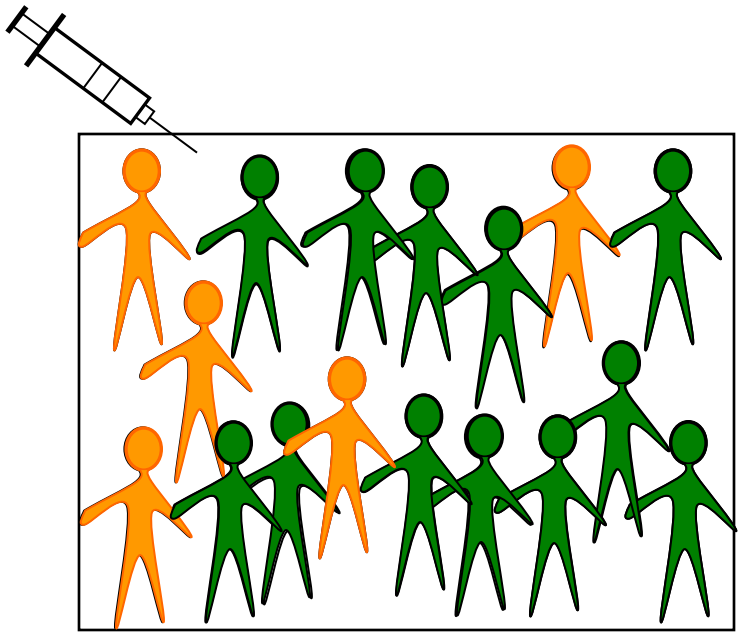
Summary: Herd immunity for measles

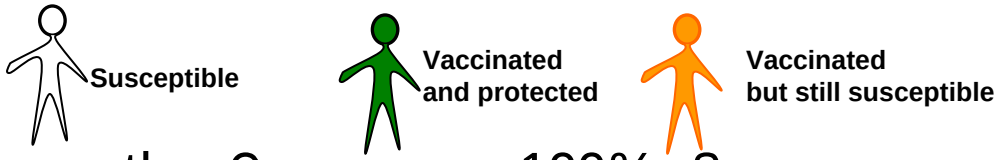
When ≈ **95%** of the population is immunized against measles:

- Measles virus circulation can be interrupted
- Disease spread is limited (outbreaks are small)
- Non immune individuals remain susceptible

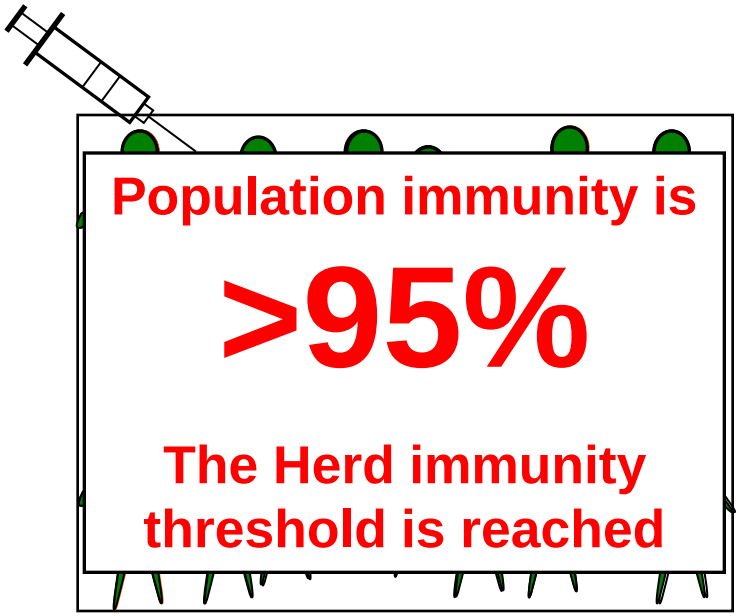
The goal of the vaccination program is to reach and maintain a population immunity > 95%

Vaccinated versus immunized





9 months: Coverage = 100% Sero-conversion rate = 85%. This population has not reached the **95% population immunity threshold (Herd immunity)** necessary to stop measles virus circulation. A second opportunity is necessary



Second opportunity vaccination will protect those who did not sero-convert with the 1st dose:

>95% of this cohort is now protected: the Herd immunity threshold for measles is reached

Coverage and Immunity

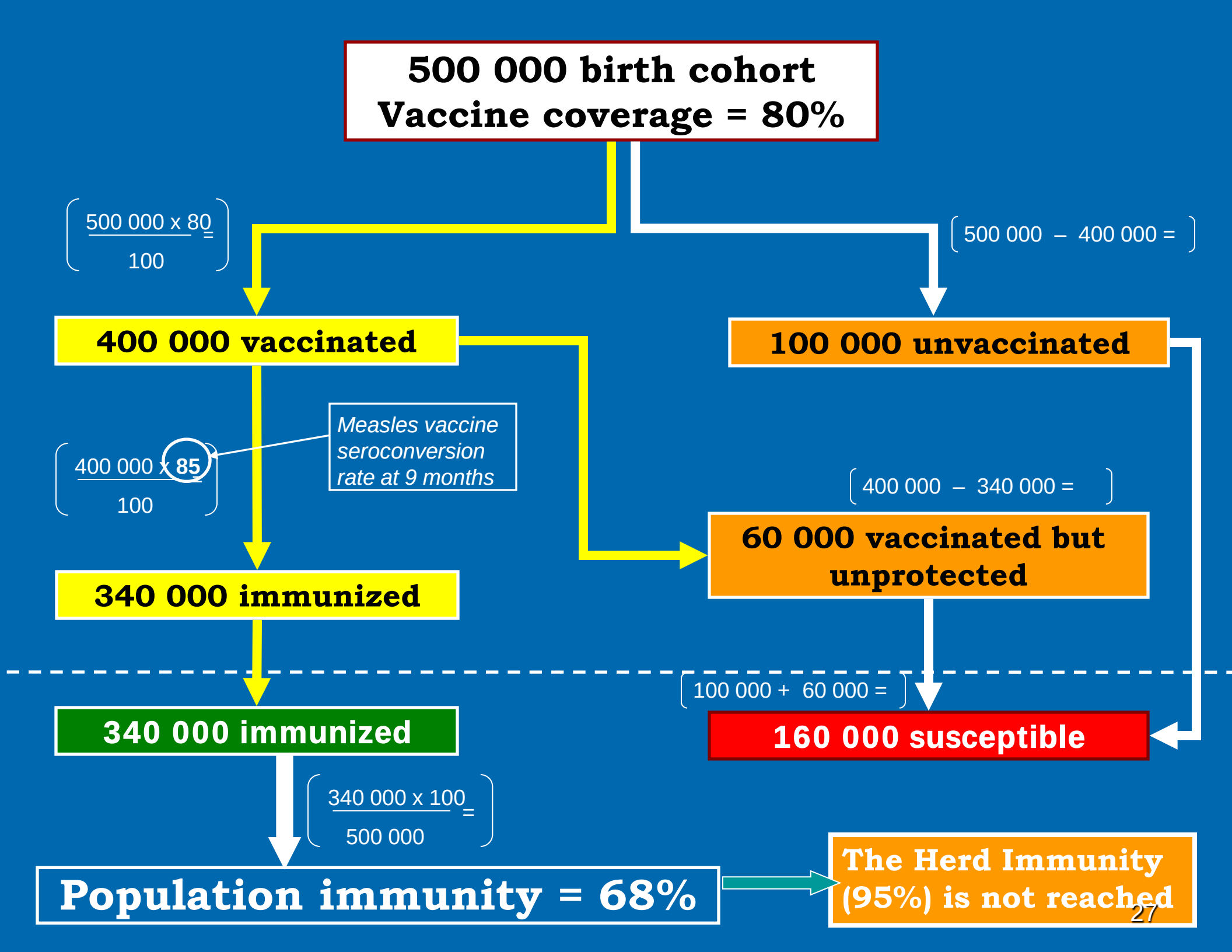
- Vaccination coverage not the same as population immunity
- At least 95% population immunity required to stop transmission
- 95% population immunity not achievable with only 1 dose (routine) even at high coverage
- Accumulation of susceptible over time. High risk of outbreak when number of susceptibles (primary vaccine failure + unvaccinated) ≥ birth cohort

Second opportunity for vaccination against measles require to rapidly raise population immunity

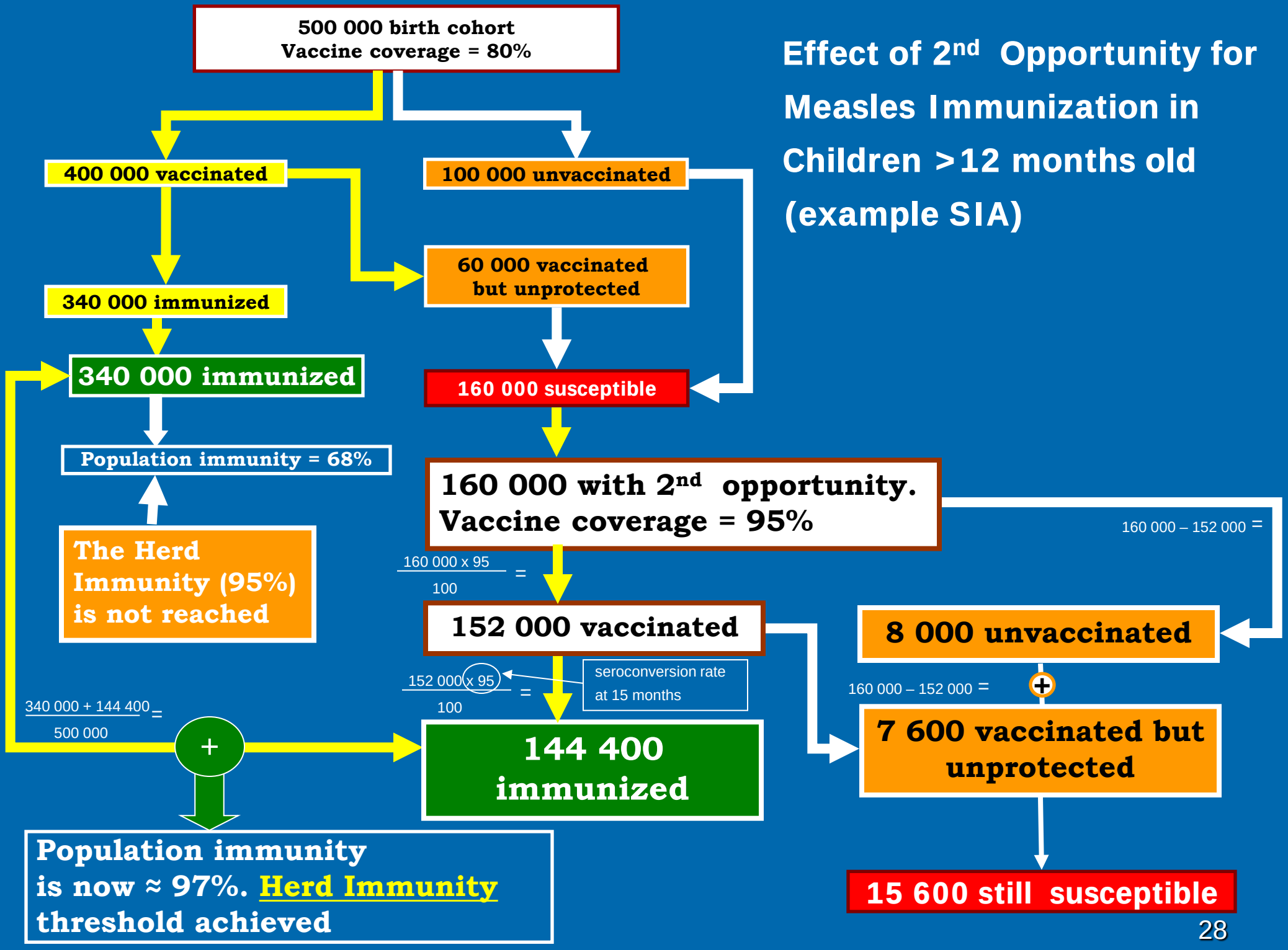
How the second opportunity works: scenario 1

A country with a birth cohort of 500 000 reports 80% coverage for measles vaccine.

- What is the population immunity?
- Is Herd immunity for measles (**95% of the population immune**) achieved?


500 000 birth cohort
Vaccine coverage = 80%
500 000 x 80 =
100
500 000 – 400 000 =
400 000 vaccinated
100 000 unvaccinated
Measles vaccine seroconversion rate at 9 months
400 000 x 85
100
400 000 – 340 000 =
60 000 vaccinated but unprotected
340 000 immunized
100 000 + 60 000 =
160 000 susceptible
340 000 immunized
340 000 x 100 =
500 000
Population immunity = 68%
The Herd Immunity (95%) is not reached

Effect of 2nd Opportunity for Measles Immunization in Children >12 months old (example SIA)



Summary: effect of 2nd opportunity for measles immunization in children > 12 years old

- After RI dose at 9 months with 80 % coverage:

500K x 0.80 x 0.85 = **340K immune**

Coverage

Vaccine efficacy at 9 months

- After 2nd opportunity with 95 % coverage*:

Vaccine efficacy >12 months

160K x 0.95 x 0.95 = **144K immune**

Missed + primary vaccine failure at 1st dose

Coverage 2nd opportunity

- Routine 1st Dose + 2nd opp. = (340K + 144K) / 500K

≈ 97 (> 95% immunity)

→ **Herd immunity threshold achieved**

*Assume independent vaccinations – probably reasonable if 1st dose routine and 2nd dose SIA

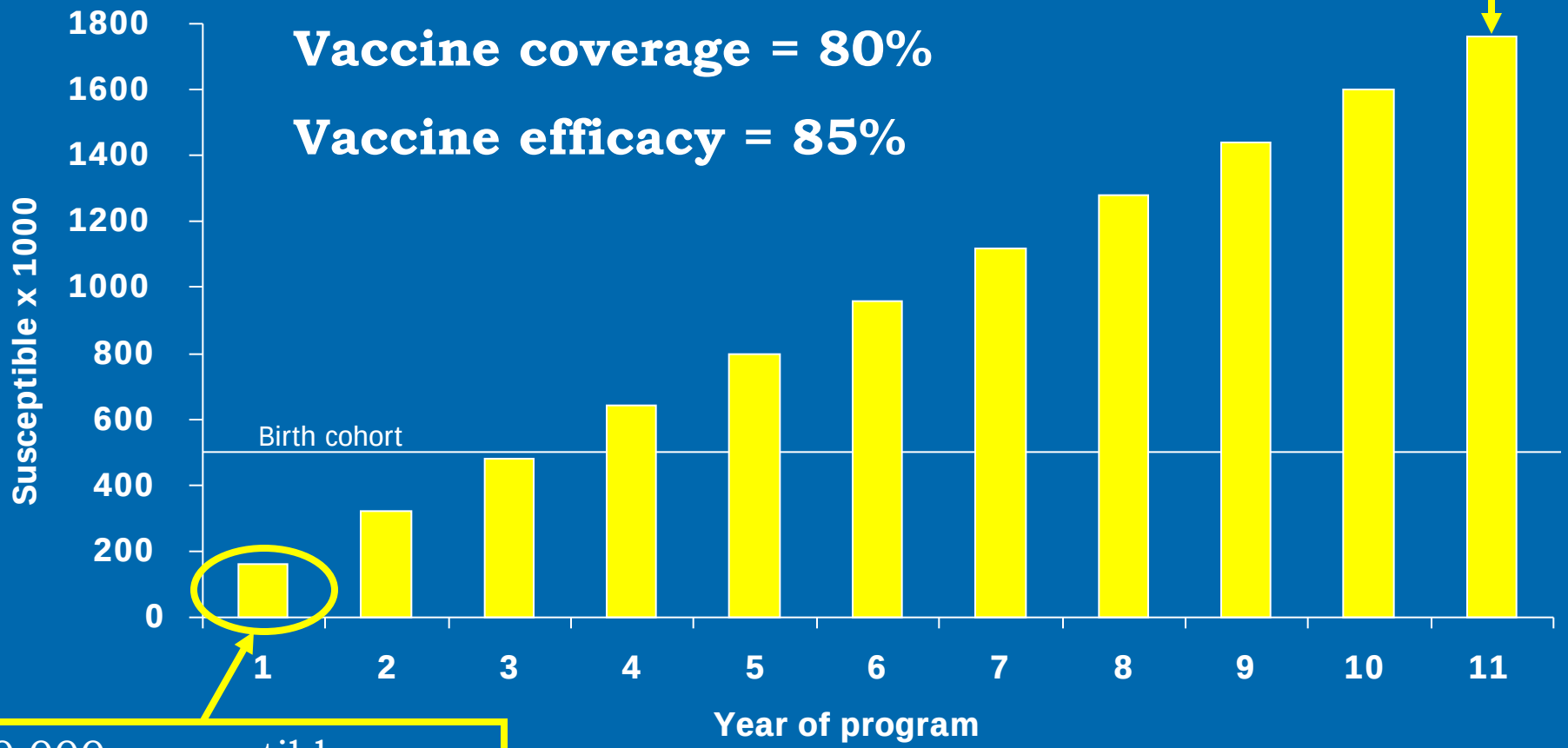
Accumulation of susceptible Routine 1 dose

500 000 newborns

Vaccine coverage = 80%

Vaccine efficacy = 85%

1 760 000 susceptibles accumulated on the 11th year of the program



160 000 susceptibles accumulated the 1st year

Adapted from: de Quadros CA, et al. JAMA 1996;275(3):224-9.

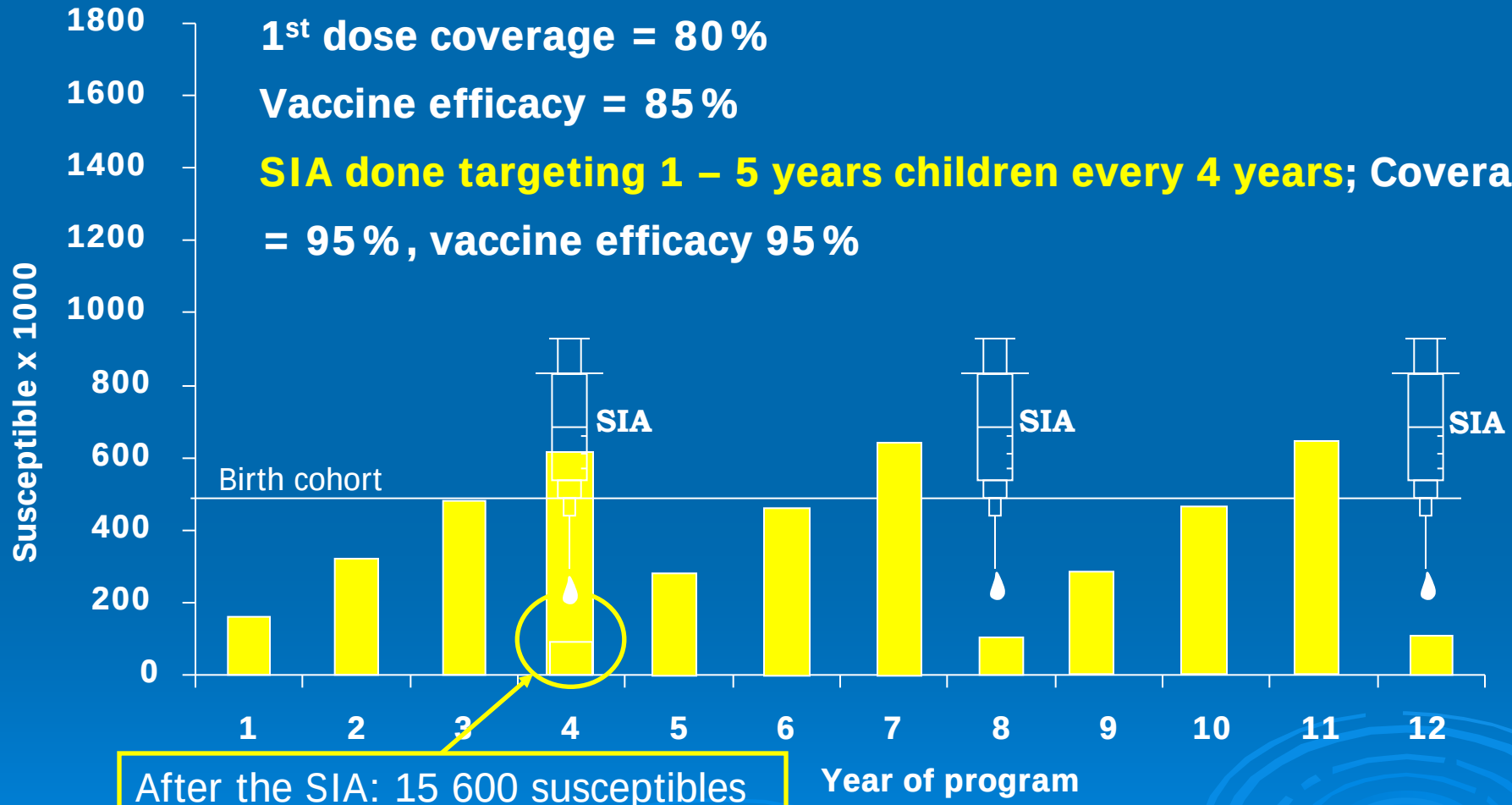
Accumulation of susceptible with second opportunity

500,000 newborns

1st dose coverage = 80%

Vaccine efficacy = 85%

SIA done targeting 1 – 5 years children every 4 years; Coverage = 95%, vaccine efficacy 95%

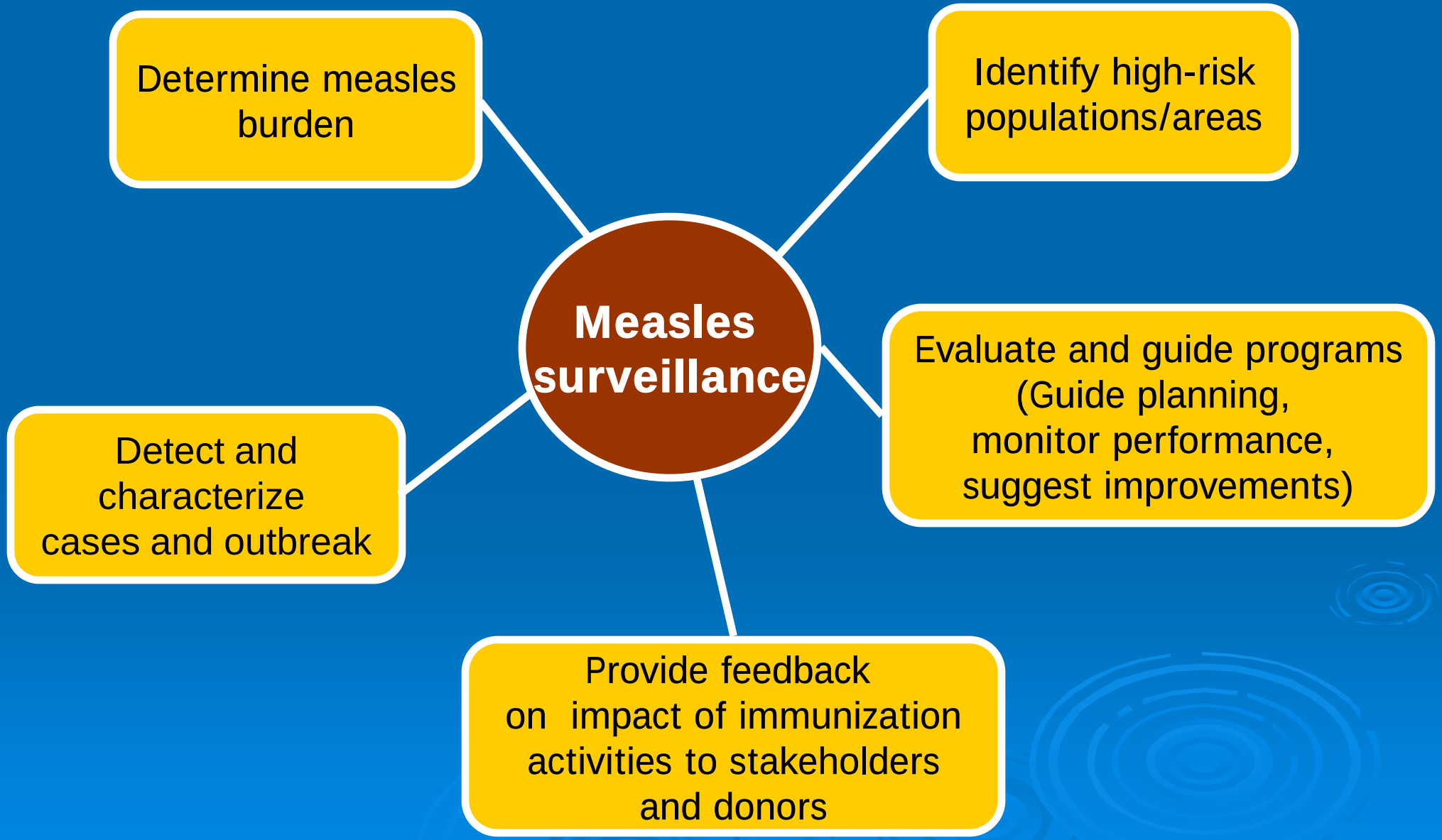


After the SIA: 15 600 susceptibles remaining at the end of year , compare to 640 000 expected without SIA..

4 – Measles surveillance

Systematic and ongoing, collection, analysis, interpretation, dissemination, of data to reduce measles morbidity and mortality

Goals of Measles Surveillance



Case based and aggregate surveillance

Case based

- Collection and storage of data on cases
- A case investigation form for each case
- In the database or line listing, each record represent a case with clinical and lab data
- Date collected same as in outbreak (see outbreak section)

Aggregate

- A summary count of cases is provided by one or more attributes (place, age group, vaccination status)
- Example: Districts reporting the number of cases of measles by age group, or by vaccination status, by gender

Measles case definitions

Clinical measles = suspected case:

- Fever + rash + cough or conjunctivitis or coryza (the **3C**)

  – or –

- Clinician suspect measles

Confirmed measles case:

- Lab confirmed: measles **IgM positive**
- Epidemiological linkage

Measles "lay" case definition

to assist communities in notifying health facilities

ANY PERSON

with

FEVER **and** **RASH**

Laboratory confirmation of suspected measles

Why laboratory confirmation is important?

The predictive value of clinical case definition falls as the incidence of the disease falls. Rule out other causes of rash and fever.

What to collect ?

Blood sample for serum, to test for measles **IgM**

When to collect ?

Collect a blood specimen at 1st contact with the health care system

Between 4 to 28 days after rash onset (high sensitivity)

Day of rash onset plus the next 3 days (70 – 80% of samples will be IgM+)

Measles final classification

- **Laboratory-confirmed**
- **Epidemiologically confirmed**

  Meet clinical case definition, reported from same district/HF, rash onset after lab-confirmed cases (link to laboratory-confirmed case)
- **Clinically confirmed**

  Meet clinical case definition but without adequate blood specimen taken
- **Discarded**

  Suspected case, not meet clinical or laboratory definition

Supplements: measles outbreak

- **WHO Draft Guidelines**
  - 3 or more suspected cases by district by month
  - 1 or more confirmed (**IgM+**) case by district by month
  - 1 or more suspected case in a refugee or internally displaced person camp
- **PAHO Measles Elimination Guidelines**
  - " ... a single laboratory-confirmed measles case is considered to be a confirmed measles outbreak."
- **AFRO Measles Surveillance Guidelines**
  - 5 or more suspected cases by district or health facility by month
  - 3 or more confirmed cases by district or health facility by month

Common sources of susceptibles for measles outbreaks

- **Failure to vaccinate**
  - Low routine coverage
  - Low campaign coverage (<95%)
- **Vaccine failure**
  - Expected (15% failure at 9 months)
  - Unexpected (cold chain problems)
- **Policy or schedule failure**
  - Wrong age group targeted during SIA
  - Missed birth cohorts (complicated SIA schedule)
- **Migration**
  - Massive influx of susceptible populations
  - Importation of cases
- **Other**
  - Children born to HIV+ women

Rational for measles outbreak investigation

- Important source of surveillance data
- Important source of information for program evaluation and research
- High visibility – political and ethical issues force an investigation and a response. Chance to advocate and remind about need to improve vaccination programs

Important background information to collect

- **What is already being done with this outbreak?**
- **Previous surveillance data**
  - What type of surveillance: case-based or aggregate?
  - When were the last epidemics?
  - When is the measles season?
  - What does the analysis of surveillance data show?
- **Routine vaccination age and coverage**
- **Date, age range and coverage of recent SIAs**
- **Known population movements**

Key data to collect from cases

Use line list. Collect same information as in the case report

- **Person**
  - Age
  - Vaccination status (+ date of last vaccination)
  - Outcome – alive or dead
- **Place**
  - Residence at time of rash onset
- **Time**
  - Date of rash onset = “Date of Onset”

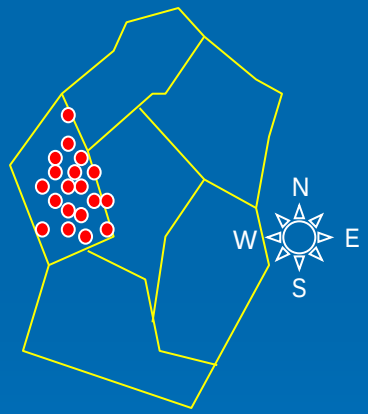
Remember: only take blood from 5 – 10 cases, then stop

Other information sometimes collected during investigations

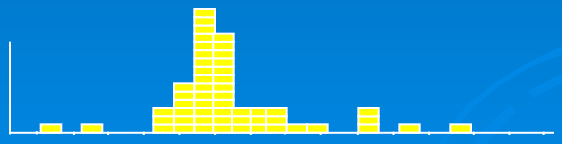
- **Reasons for non-vaccination**
- **Contact information**
  - Where was case 7 – 18 days ago?
  - Where was case in past 4 days?
- **Basic clinical information**
  - Measles symptoms (fever, rash, 3Cs)
  - Complications (diarrhea, pneumonia, encephalitis, otitis media, others)
  - Hospitalized?

Analysis of measles outbreak data

- **Confirm the outbreak**
  - Is the number greater than expected?
  - Does the definition of an applies



- **Define the extent of the outbreak**
  - Time: epidemic curve
  - Place: map
  - Person: age, immunization status
  - Calculate incidence if population data available



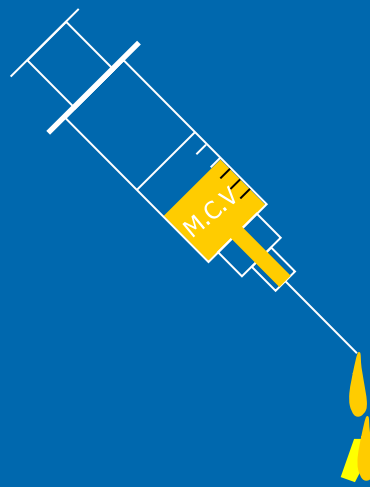
Additional data analysis

- **Measure severity**
  - Proportion of cases hospitalized
  - Proportion of cases with complications
  - Deaths (case fatality rate)

- **If possible, measure effectiveness of vaccination**
  - Attack rate method
  - Proportion of cases vaccinated versus proportion of population vaccinated

Measles: Key points

- Leading cause of vaccine-preventable mortality
- Sustainable measles mortality reduction requires 2nd opportunity for immunization
- Effective surveillance is needed to direct control strategies
- Control strategies are working!



Thank you