

# Measles and Rubella

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# Measles



# Lessons from History

- Measles in Africa –
  - Prior to the 1980s child mortality in sub-Saharan Africa close to 50%
  - Measles was a major cause of mortality
- Measles in Fiji –
  - 1880 infected ship docks in Suva
  - Grand Council of Chiefs meeting underway
  - Massive mortality
- Measles most severe with –
  - Crowding
  - Malnutrition
  - Outbreaks in fully susceptible communities









# Measles and magic – stories from Ethiopia

- Measles seen as a form of possession
- “Possessed” children:
  - Do not like the shadows of grown-ups to cross them
  - Do not like injections
  - Do not like to be spoken to as if a child
  - Like pop-corn and candy

# Measles and magic – stories from Ethiopia

- Measles seen as a form of possession
- “Possessed” children:
  - Do not like the shadows of grown-ups to cross them
  - Do not like injections
  - Do not like to be spoken to as if a child
  - Like pop-corn and candy
- 10<sup>th</sup> century Iranian physician – Zakariya al-Razi (865-925)
  - Distinguished between measles and small pox
  - Described the rash of fatal measles

# Measles.....

- As a cause of death
  - Immediate
  - Delayed
- As a cause of blindness (with Vitamin A deficiency)
- As a cause of malnutrition
- As a cause of immune suppression



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*Fig. 9 Case 5. Left eye of a 2-year-old girl with measles. There are areas of epithelial staining in the mid-nasal and temporal areas, with peripheral punctate keratitis.*

# The true mortality burden of measles

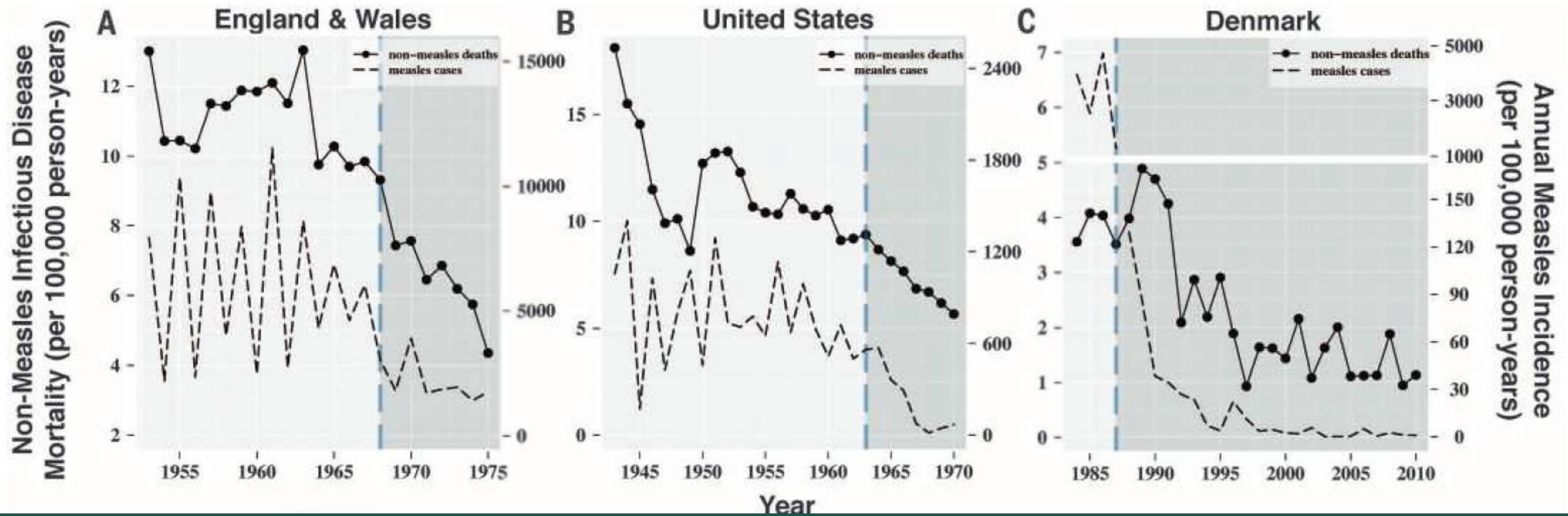
- Bangladesh trial – much greater than could be explained on the basis of measles prevention alone
- Two explanations:
  - Non-specific mortality benefit attributable to the vaccine
  - Long term effects of measles increase mortality
- Recent randomized trials of measles vaccine:
  - 4 + 9 mths versus 9 mths
  - Mortality outcome
  - Burkina Faso, Guinea Bissau
  - No impact on mortality (may be due to effect of OPV)

# Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality

Michael J. Mina,<sup>1,2\*</sup> C. Jessica E. Metcalf,<sup>1,3</sup> Rik L. de Swart,<sup>4</sup>  
A. D. M. E. Osterhaus,<sup>4</sup> Bryan T. Grenfell<sup>1,3</sup>

Immunosuppression after measles is known to predispose people to opportunistic infections for a period of several weeks to months. Using population-level data, we show that measles has a more prolonged effect on host resistance, extending over 2 to 3 years. We find that nonmeasles infectious disease mortality in high-income countries is tightly coupled to measles incidence at this lag, in both the pre- and post-vaccine eras. We conclude that long-term immunologic sequelae of measles drive interannual fluctuations in nonmeasles deaths. This is consistent with recent experimental work that attributes the immunosuppressive effects of measles to depletion of B and T lymphocytes. Our data provide an explanation for the long-term benefits of measles vaccination in preventing all-cause infectious disease. By preventing measles-associated immune memory loss, vaccination protects polymicrobial herd immunity.

# Decline in non-measles infectious diseases deaths following measles vaccine introduction





# Strategies for measles control

- Isolation of cases – useless
- Effective treatment
  - Vitamin A and antibiotics can reduce mortality, but not transmission
- Vaccination and immunity
  - Maternally derived immunity 6-9 months, declining
  - Second dose needed to pick up primary vaccine failures (about 10%)
- During 90s plans developed for eradication of measles based on polio strategy
  - Routine immunization + regular campaigns

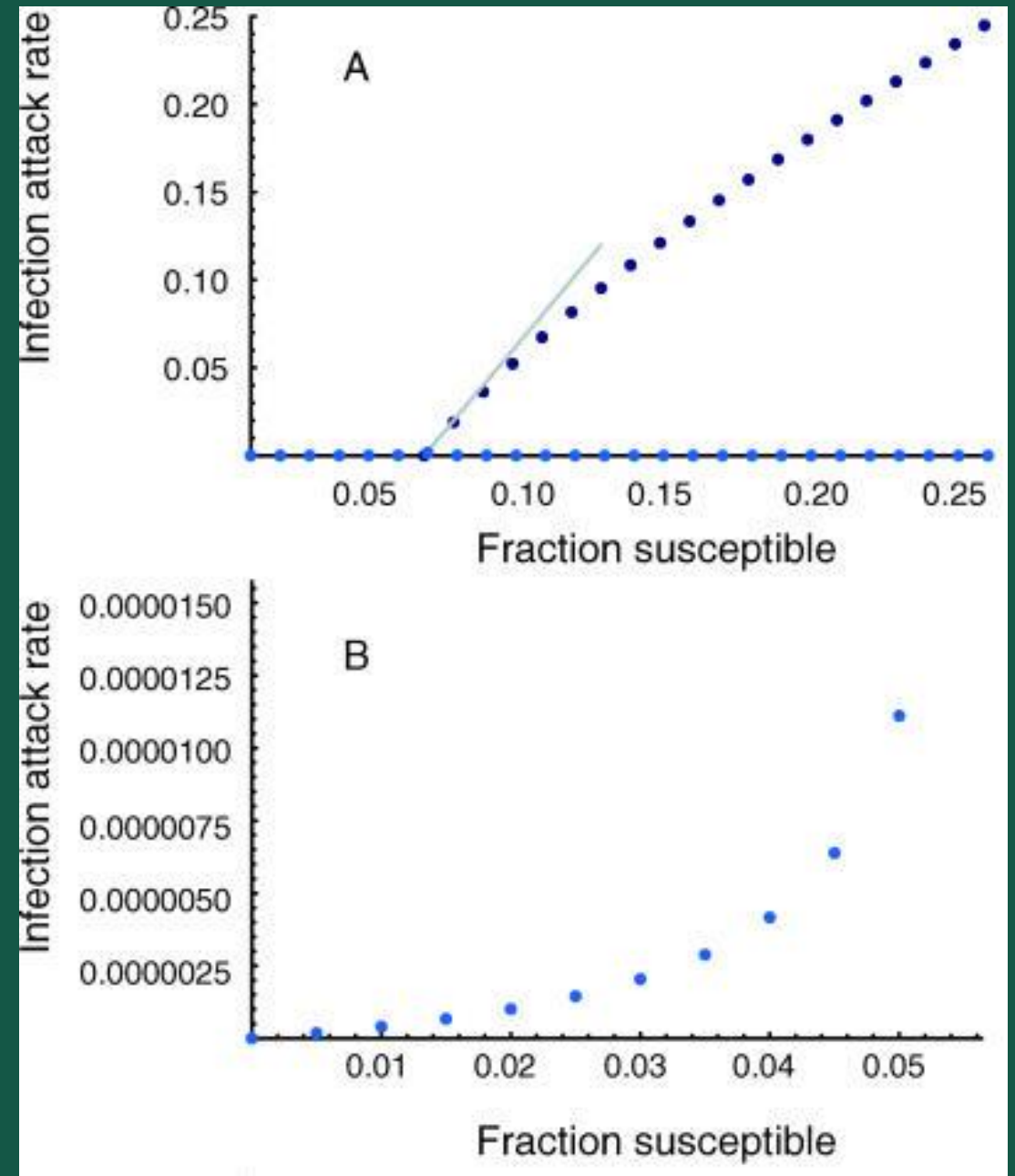


# Epidemiologic Basis for Eradication of Measles (1967)

- Virtually universal infection
- Reservoir is humans, no non-human reservoirs
- Chronic carriers do not exist
- Transmission dependent on balance between immunes and susceptibles
- Transmission dies off before all susceptibles exhausted
- Herd immunity threshold – estimated to be 55% based on data from Baltimore

† Sencer DJ, Dull HB, Langmuir AD. Epidemiologic Basis for the Eradication of Measles in 1967. Public Health Reports 1967; 82:253-256

What fraction of the population must be vaccinated to eliminate measles?

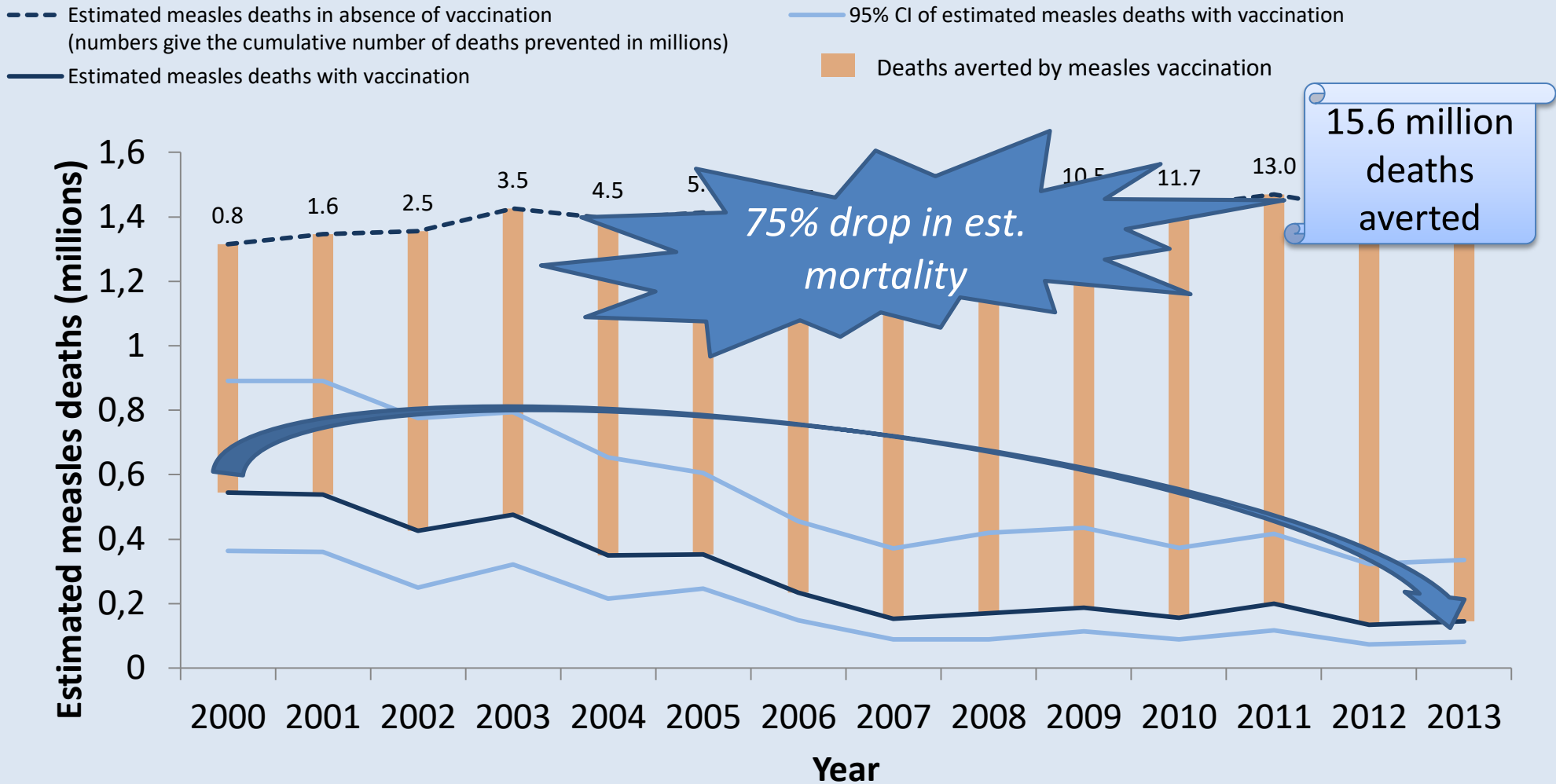




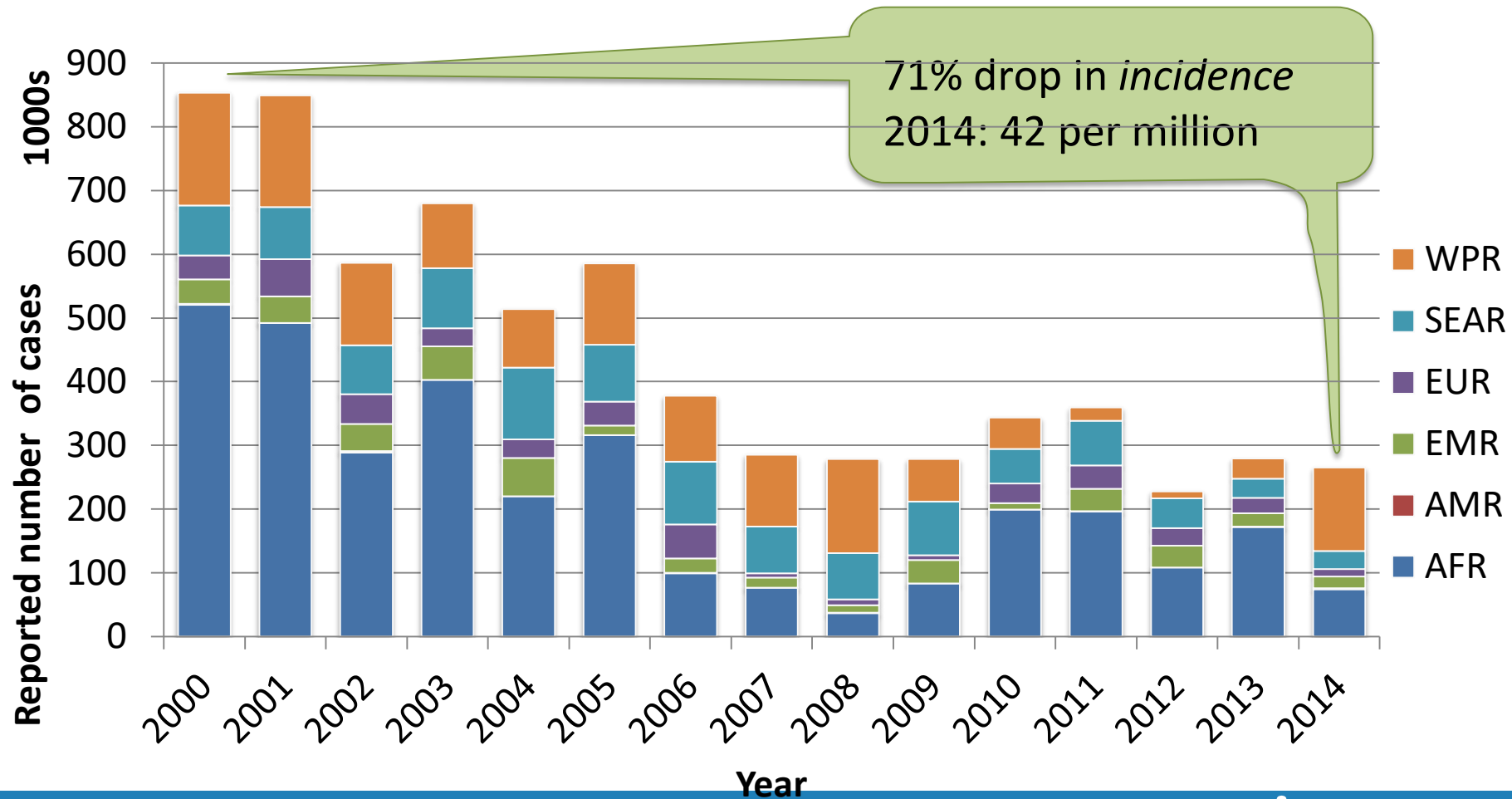
# 2000 – The measles burden dilemma

- Measles mortality estimates ranged from 770,000 deaths (WHO) to 55,000 (M Garenne)
- All estimates based on models
  - Assume 10% primary vaccine failure
  - Assume all non-immunes will get measles
  - Derive **case fatality rate** from reports (mainly outbreaks)
- WHO locked into high estimates
  - Deaths  $\propto$  money for measles control
- High throughput hospitals in Africa not reporting many cases

# Global estimated measles mortality and measles deaths averted, 2000 - 2013

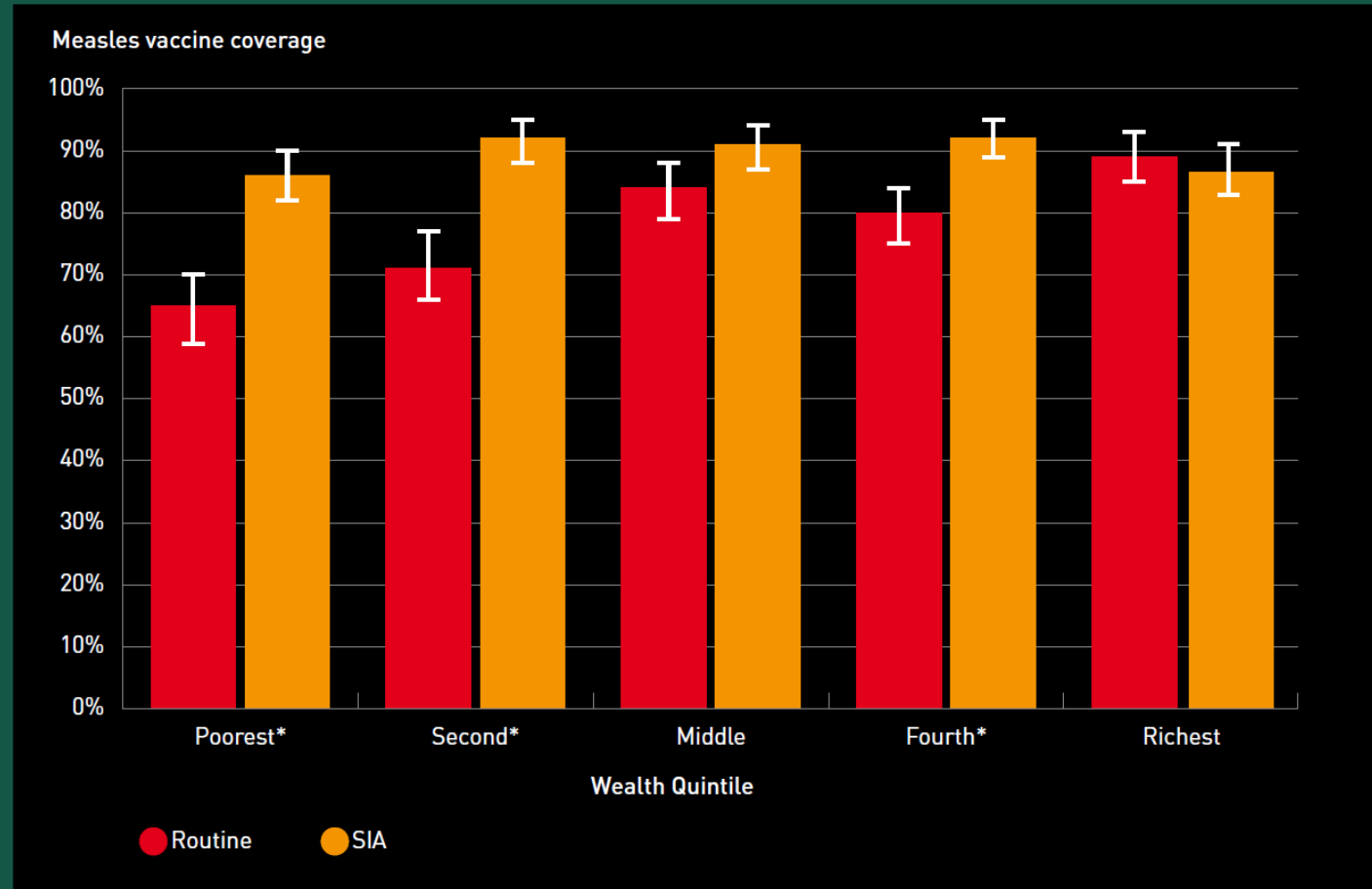


# Reported measles cases by WHO Region, 2000-2014



Data as of 27 May 2015. 148 / 194 Member States reporting data for 2014

# Measles vaccine coverage, Kenya 2002





# Progress in measles reduction since 2008

- In Africa, 172,000 reported cases in 2010 (from 37,000 in 2008)
  - Declining funding
  - Problems with some religious groups
- Many cases in Europe (esp. France)
- Major outbreak in UK in 2013
  - Areas with poor coverage
  - Related to spurious, but ongoing argument about autism
- Outbreaks in countries certified measles free
  - Brazil
  - Mongolia
- Many groups in UK and US choosing not to be vaccinated

# WHO Measles Targets

## Global milestones by 2015:

1. Measles dose 1 coverage  $\geq 90\%$  national and  $\geq 80\%$  in every district
2. Measles reported incidence  $<5$  cases per million
3. Measles mortality reduction of 95% vs. 2000

## Regional targets:

### Measles Elimination goals:

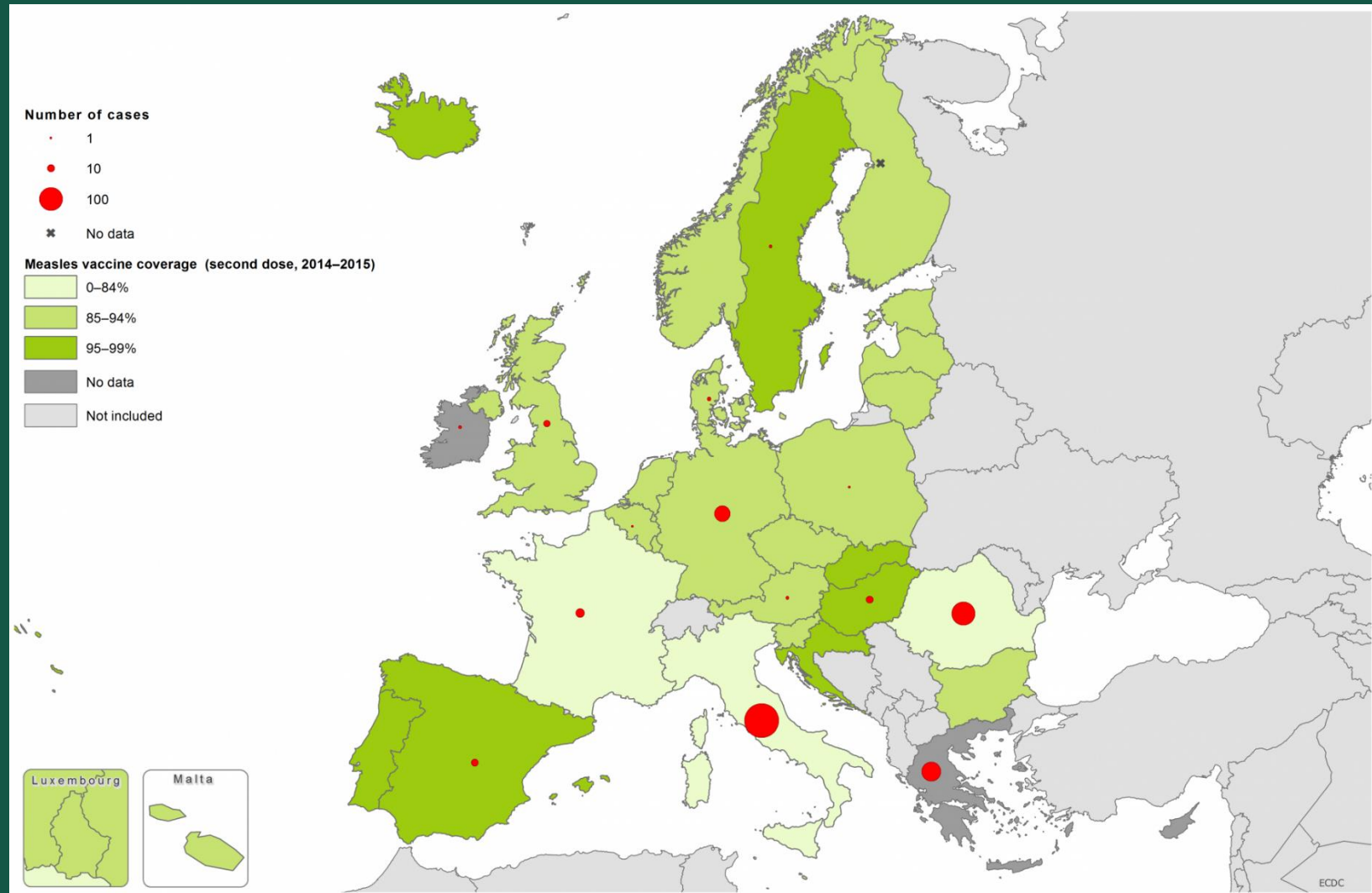
2000 PAHO

2012 WPRO

2015 EURO, EMRO

2020 AFRO, SEARO

# Measles in Europe – 1/9/16 – 31/8/17



Data: European CDC, Oct 2017

News › World › Europe

# France to make vaccination mandatory from 2018 as it is 'unacceptable children are still dying of measles'

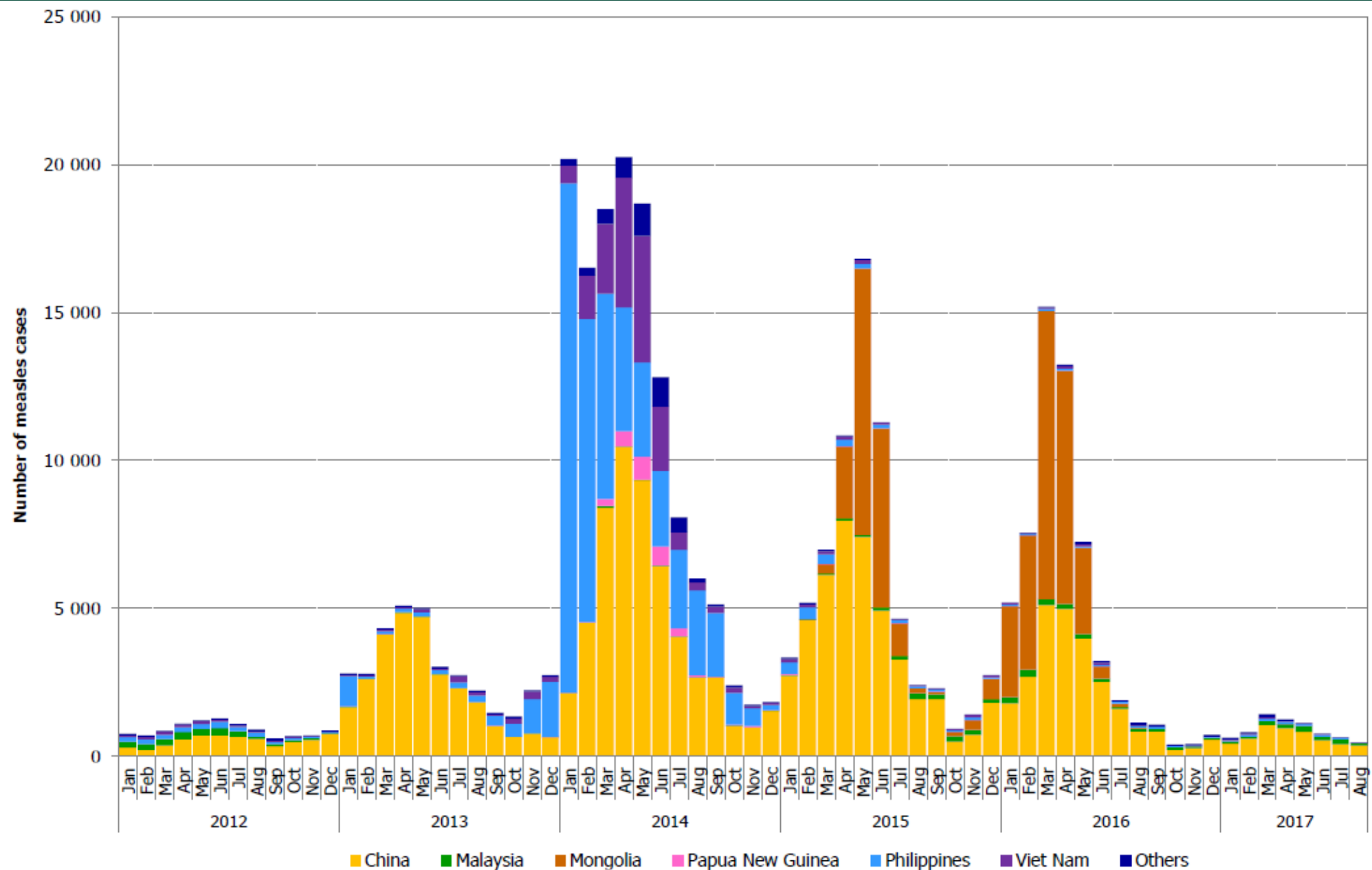
Move follows similar initiative in Italy, where non-vaccinated children cannot attend state schools

Katie Forster Health Correspondent | [@katieforster](#) | Wednesday 5 July 2017 09:52 BST | [Comment](#)



There were 79 cases of measles reported in France in the first two months of 2017 PA





Source: Measles and rubella monthly country reports to WHO by 20 September 2017  
Includes laboratory confirmed, epi-linked and clinically confirmed cases for 2012

**Table 5.1. Reported MCV Coverage by Country in the Western Pacific Region, 2010–2016**

Country	MCV-1 Coverage							MCV-2 Coverage						
	2010	2011	2012	2013	2014	2015	2016	2010	2011	2012	2013	2014	2015	2016
Australia	94	94	94	94	94 *	95 *	ND	88	90	91	92	93 *	93	94
Brunei Darussalam	94	91	99	96	97	96	98	93	93	96	92	96	98	97
Cambodia	93	93	93	90	94	73	123	ND	ND	82	64	95	72	105
China	99	100	100	100	99	99	100	99	100	100	100	100	99	99
China, Hong Kong SAR	95	95	95	95	95	95	95	95	95	95	95	95	95	95
China, Macao SAR	ND	93	93	99	93	91	94	ND	90	89	96	93	91	92
Japan	94	94	96	95	98	94	96	97	92	92	93	96	93	93
Lao PDR	64	69	72	82	87	88	76	ND	ND	ND	ND	88	ND	ND
Malaysia	95	95	86	97	94	99	ND	95	ND	99	99	93	99	99
Mongolia	97	98	99	97	98	98	99	95	98	98	97	98	98	90
New Zealand	95 *	95 *	95 *	95 *	95 *	86	92	90 *	91 *	na *	na *	na *	87	89
Papua New Guinea	59	60	67	70	65	60	51	ND	ND	ND	ND	60	ND	ND
Philippines	80	79	85	90	88	59	80	10	28	38	53	77	63	66
Republic of Korea	98	99	99	100	100	96	98	98	98	97	95	98	97	97
Singapore	95	95	95	95	95	88	ND	94	94	95	ND	95	90	ND
Viet Nam	98	97	96	98	97	94	99	98	93	83	86	97	92	95
Pacific Island Countries and Areas	75	79	84	87	87	95	86	74	78	84	91	85	90	ND

Source: WHO/UNICEF Joint Reporting From (JRF)

# Mongolia

- Territory – 1.6 million sq kilometers
- Population – 3.1 million, 32% living in poverty
- Extremely isolated, extreme climate
- Very significant indoor and outdoor air pollution, especially in winter



# Measles in Mongolia

- Political upheaval 1991 – breakdown of public health
- High vaccine coverage since early 90s
- Declared measles free by WHO 2014
- March – October 2015
  - Over 20,000 suspected measles cases, many 15-24 years
  - 1,434 lab confirmed
  - 50% under 5 years old, half under 9 months
- 2 main groups
  - Young adults
  - Young infants

# Barriers to measles eradication

- The global political situation is worse than 20 years ago
  - Large areas of the middle-east now no-go areas
  - Polio workers targeted thanks to US military activities
- Global travel much more accessible
- Stepwise country by country; region by region will not work
- Global control in all areas with high coverage of MCV2 needed, followed by co-ordinated “final push”
  - Perhaps this will be achieved by 2020, what then?



# Verification of Elimination

## 2014 GVAP Report:

*"After consulting with their respective Regional Technical Advisory Group, every region establish a regional verification commission, and after consulting with their respective National Immunization Technical Advisory Group, every country explore options for establishing a national verification commission, to scrutinize and monitor progress towards the measles and rubella elimination targets."*

## Progress:

- Global Verification Framework published in 2013
  - Definitions
  - Criteria for elimination
  - 5 lines of evidence
- 4 Regions have developed their verification guidelines
- AMR, EUR, WPR have fully functional Regional Commissions
- Differences in definitions and surveillance indicators

# Issues

- Do complex regional and national targets really help?
- Are new vaccines needed?
- Dogmatic approach to schedules seems outdated
- Models help, but most conclusions are self evident
- New research, fresh thinking

# Rubella

- Mild febrile illness with fever, rash, some arthralgia, etc
- Main public health importance is Congenital Rubella Syndrome (CRS)
  - Eyes – cataracts, microphthalmia, retinitis, etc
  - Ears – sensorineural deafness
  - Heart – pulmonary stenosis, Patent Ductus Arteriosus, VSD
  - Others – microcephaly, hepatosplenomegaly, bone problems
- Incidence prior to vaccine introduction:
  - 0.1 – 0.2/1000 live births
  - 0.8 – 4.0/1000 live births during epidemics

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# Congenital Rubella Syndrome (CRS)

- True burden of CRS unknown
- Depends on the proportion of women becoming pregnant who are susceptible at a time when rubella is circulating



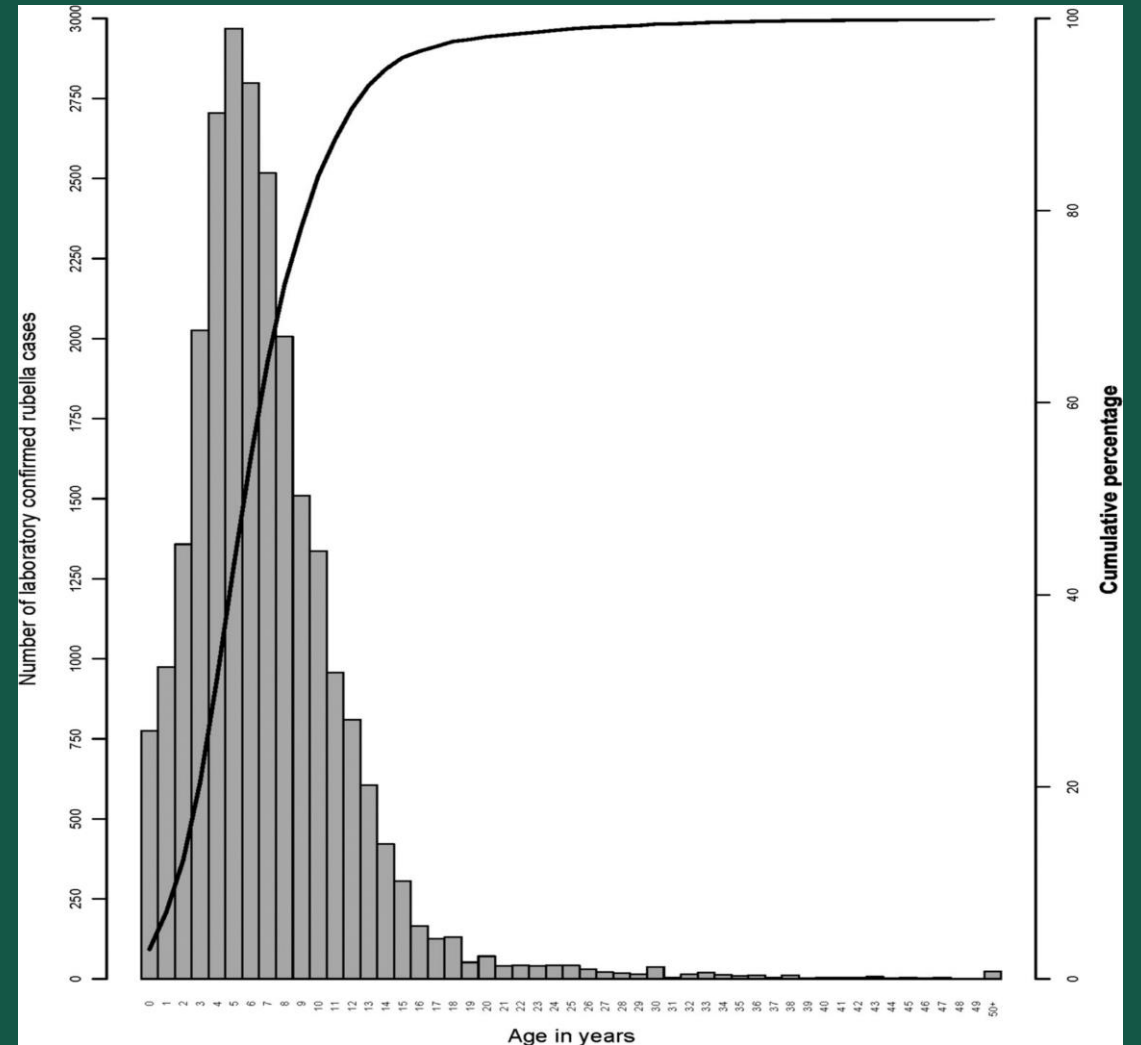
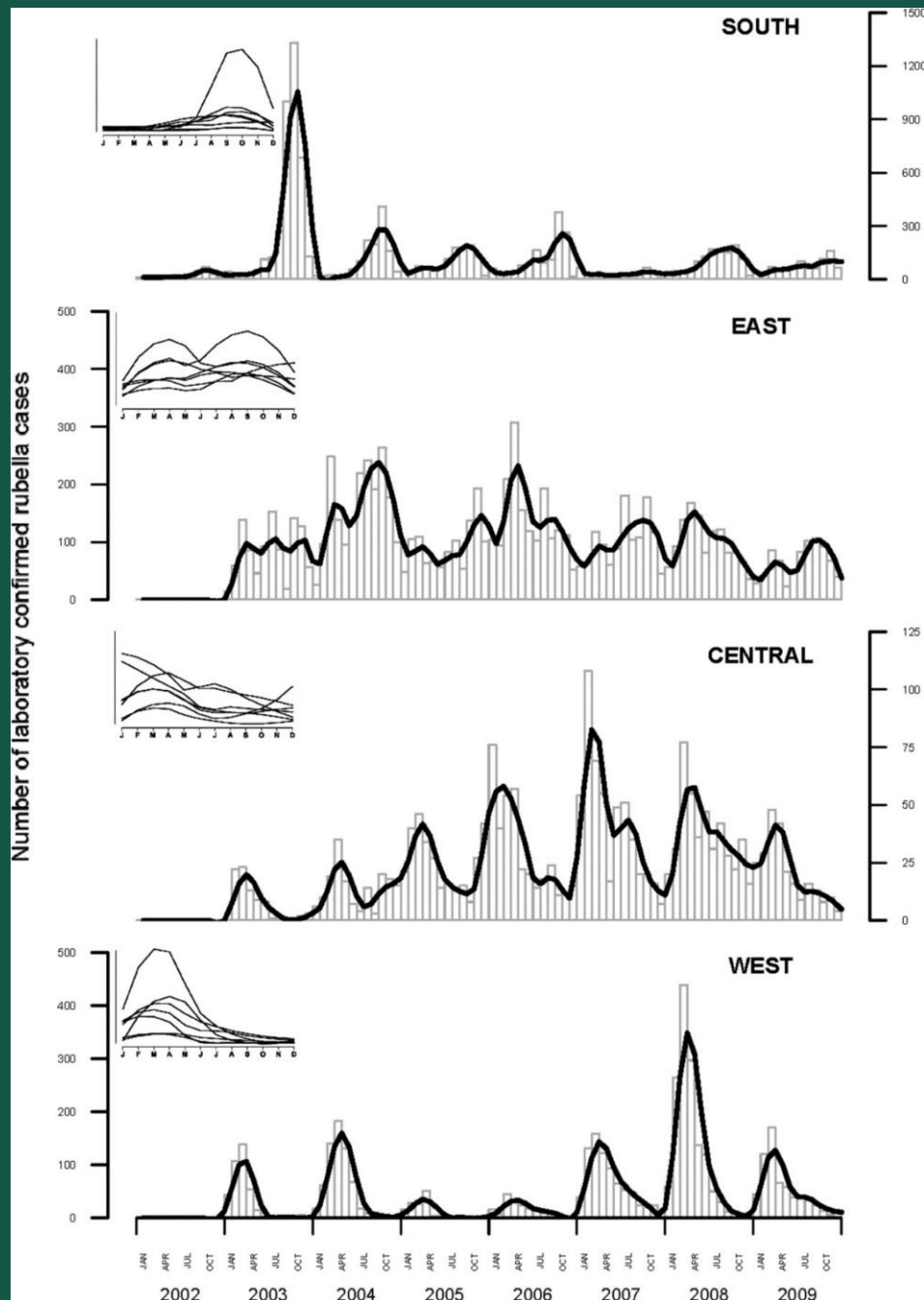
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**Table 1.1. Estimated Number of Congenital Rubella Syndrome (CRS) Cases by WHO in 1996 and 2010**

WHO region	1996		2010	
	Number	Range	Number	Range
Africa	29,692	6,535–70,996	40,680	8,923–97,483
Americas	9,683	2,577–19,081	3	0–394
East Mediterranean	9,251	3,007–22,297	5,720	73–19,537
European	9,749	5,986–13,367	12	1–983
Southeast Asia	47,621	3,651–138,674	47,527	3,317–139,760
Western Pacific	11,707	6,617–15,676	9,127	4,831–11,066
GLOBAL	117,703	28,372–280,090	103,068	17,146–269,223

\*Unpublished data, Adams E, Vynnycky E. 2012.  
WHO, World Health Organization.



From: Rubella Epidemiology in Africa in the Prevacine Era, 2002–2009

J Infect Dis. 2011;204(suppl\_1):S215-S225.

doi:10.1093/infdis/jir108

# Rubella vaccine – key points

- Highly effective after 1 dose, with long lasting immunity
- Epidemiological paradox:
  - In a partially immunized community, more pregnant women may be susceptible
  - Led to increase in CRS cases in Greece, Costa Rica
  - Private sector use may encourage this in Asia
- Often delivered as 2 doses due to presentation with measles
- General approaches:
  - Vaccinate young women prior to pregnancy  
(Not recommended during pregnancy, but no evidence of ill effects)
  - Include with measles for all children
  - Campaigns to eliminate transmission

# WHO Resolution WPR/R68.R1 (Oct 11, 2017)

- “... Deeply concerned that CRS has been increasing significantly in several countries in the Region;”
- “... Sustained low coverage of rubella immunization in infants and young children (eg. when rubella vaccine is used only in the **private sector**) can result in an increase in susceptibility among women of childbearing age that may increase the risk of CRS (WPR/RC68/4)”
- 17/21 PIC countries now have RCVs in the national immunization program
- All non-PIC countries have RCVs in the national immunization program
  - 2012 – Laos
  - 2013 – Cambodia
  - 2015 – Papua New Guinea, Vietnam

# Conclusions - measles

- Remains a global public health problem
- Extraordinarily infectious
- Regional elimination is not meaningful
- Global approach relies on 2-dose strategy supplemented by SIAs where appropriate
- Maternal immunity waning in most countries
  - MCV1 should be earlier
- Growing global insecurity makes the outlook bleak



# Conclusions - Rubella

- Global control has been poor
- CRS should be virtually eliminated by vaccination
- Strong, co-ordinated national programs needed
- Partial immunization of a community is potentially dangerous