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VACCINOLOGY 2018

Immunization schedules in the Americas: looking to the future

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XI International Symposium for Latin American experts
Organized by: Fondation Mérieux and the Latin American Society for Pediatric Infectious Diseases (SLIPE)

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Definition of immunization schedule

"An immunization schedule is a schematic of the ideal timing of administration of one or more vaccines, based on the best opportunity to provide protection and minimize risk in the prevention of vaccine preventable diseases."

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- **Individual-based schedules**
- **Community-protection based schedule**

Why are schedules important?

- **Programmatic:** framework for delivery of vaccines to target population
- **Evaluation of coverage**
- **Research and development:** Parameters for vaccine studies (harmonization with existing vaccine schedules…)
- **Public guidance and confidence**

Immunization Schedules in the United States and Great Britain -1967-68

TABLE 1. Recommended schedules for routine immunization

United States*					England and Wales†					
Age	DTP	OPV	M	SP	Age	DTP	OPV	M	SP	BCG
2–3 months	X	X			3–6 months	X	X			
3–4 months	X									
4–5 months	X	X			5–8 months	X	X			
12–18 months	X	X	X		9–14 months	X	X			
12–24 months				X	12–24 months			X	X	
School entry (3–6 years)	X	X		X	School entry (3–6 years)	Td	X		X	
					10–13 years					X
Every 10 years	Td			X‡	School leaving	Td	X		X	

DTP, Diphtheria–tetanus–pertussis vaccine; OPV, oral poliovaccine; M, measles vaccine; SP, smallpox vaccine; Td, tetanus-diphtheria toxoid, adult type.

* Adopted from United States Public Health Service (1967): *Immunization Against Disease* 1966–67 (National Communicable Disease Center publication).

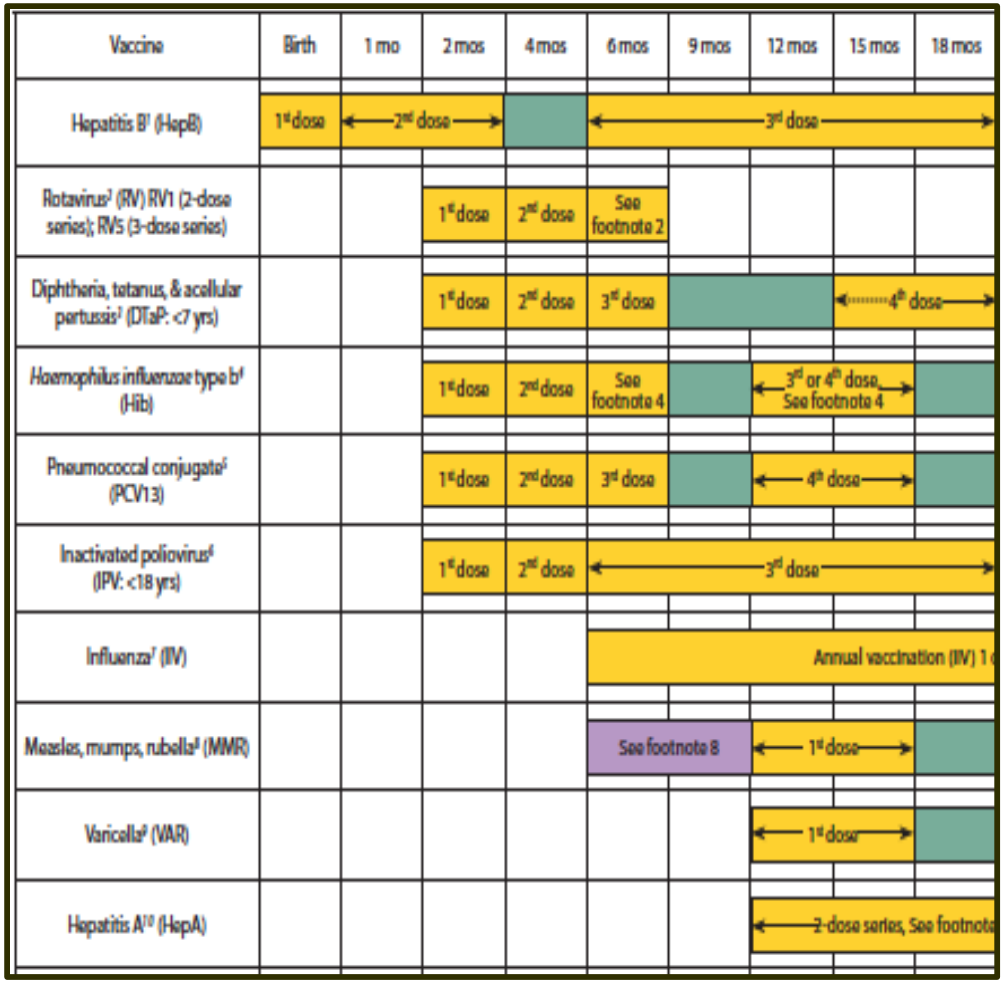
† Adopted from Ministry of Health (1968a,b).

‡ For high risk groups, i.e. health personnel and overseas travel—every 3 years.

Karzon, DT. *Postgrad Med J* 45; 147: 1969

Childhood (0-18 months) Immunization schedules in the USA and UK 2018

United States 2018



United Kingdom 2018

Age due	Vaccine given	How it is given[1]
Eight weeks old **(2m)**	Diphtheria, tetanus, pertussis, polio and *Haemophilus influenza type b* (Hib) (DTaP/IPV/Hib)	One injection
	Pneumococcal conjugate vaccine (PCV)	One injection
	Meningococcal B (MenB)[2]	One injection
	Rotavirus	One oral applica
Twelve weeks old[3] **(3m)**	Diphtheria, tetanus, pertussis, polio and Hib (DTaP/IPV/Hib)	One injection
	Rotavirus	One oral applica
Sixteen weeks old **(4m)**	Diphtheria, tetanus, pertussis, polio and Hib (DTaP/IPV/Hib)	One injection
	Meningococcal B (MenB)[2]	One injection
	Pneumococcal conjugate vaccine (PCV)	One injection
One year old (i.e. within a month of the first birthday)[4] **(12m)**	Hib/MenC booster	One injection
	Pneumococcal conjugate vaccine (PCV) booster	One injection
	Measles, mumps and rubella (MMR)	One injection
	Meningococcal B (MenB) booster[2]	One injection

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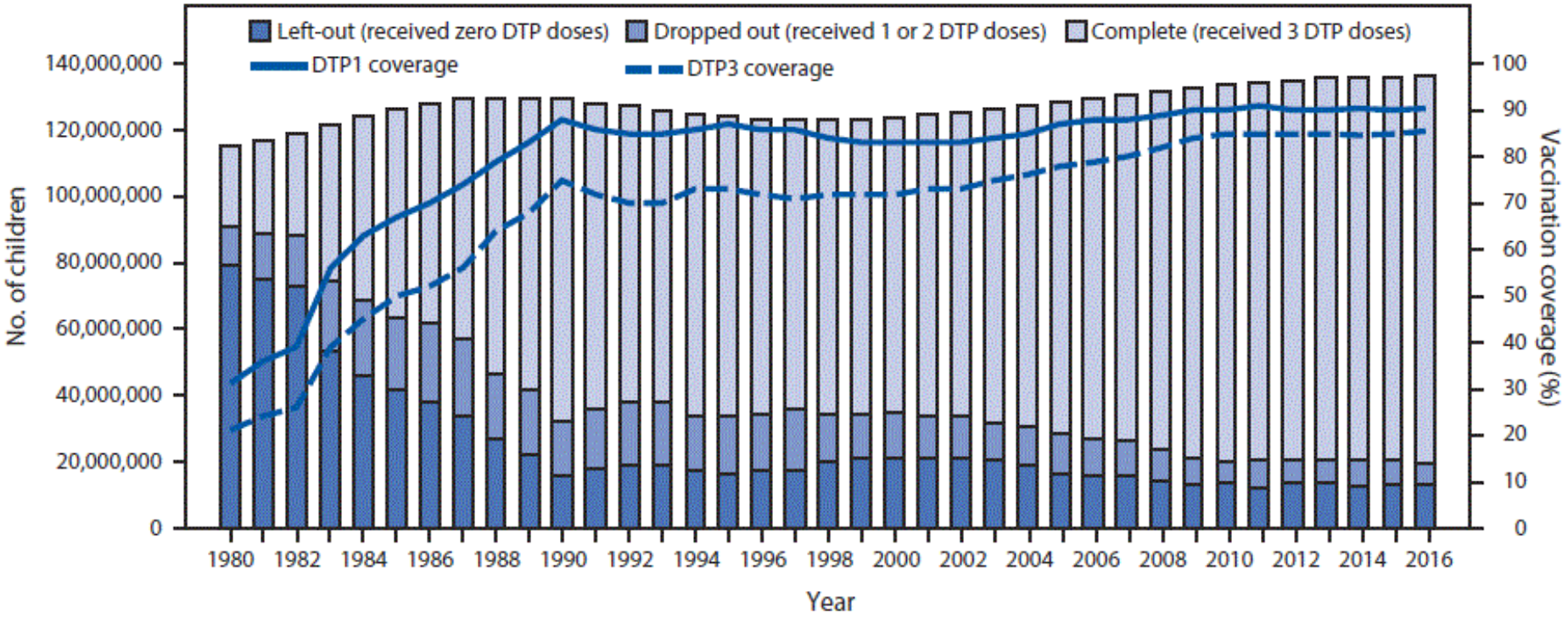
Global vaccine coverage estimates 1980-2016

DPT-1 and DPT-3 by completion



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The Impact of Vaccines in the Americas

OPS - OMS
PAHO - WHO

	1980		2015
All Vaccine Preventable Diseases	392,178	→	31,254
Measles	257,826	→	613*
Rubella	158,638	→	3
Pertussis	123,138	→	11,432
Diphtheria	5,834	→	0

http://ais.paho.org/phip/viz/im_vaccinepreventablediseases.asp

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* All from imported cases

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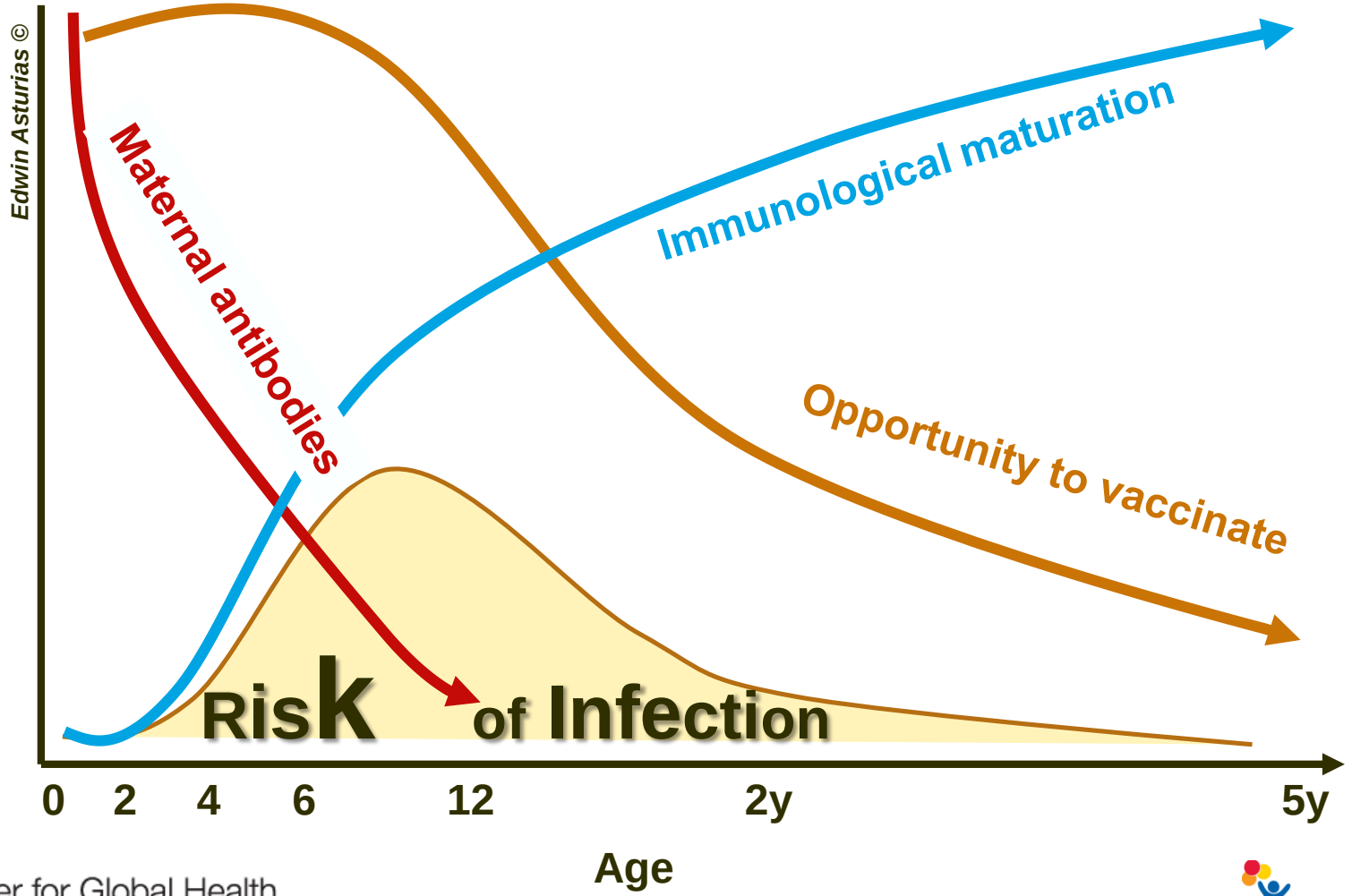
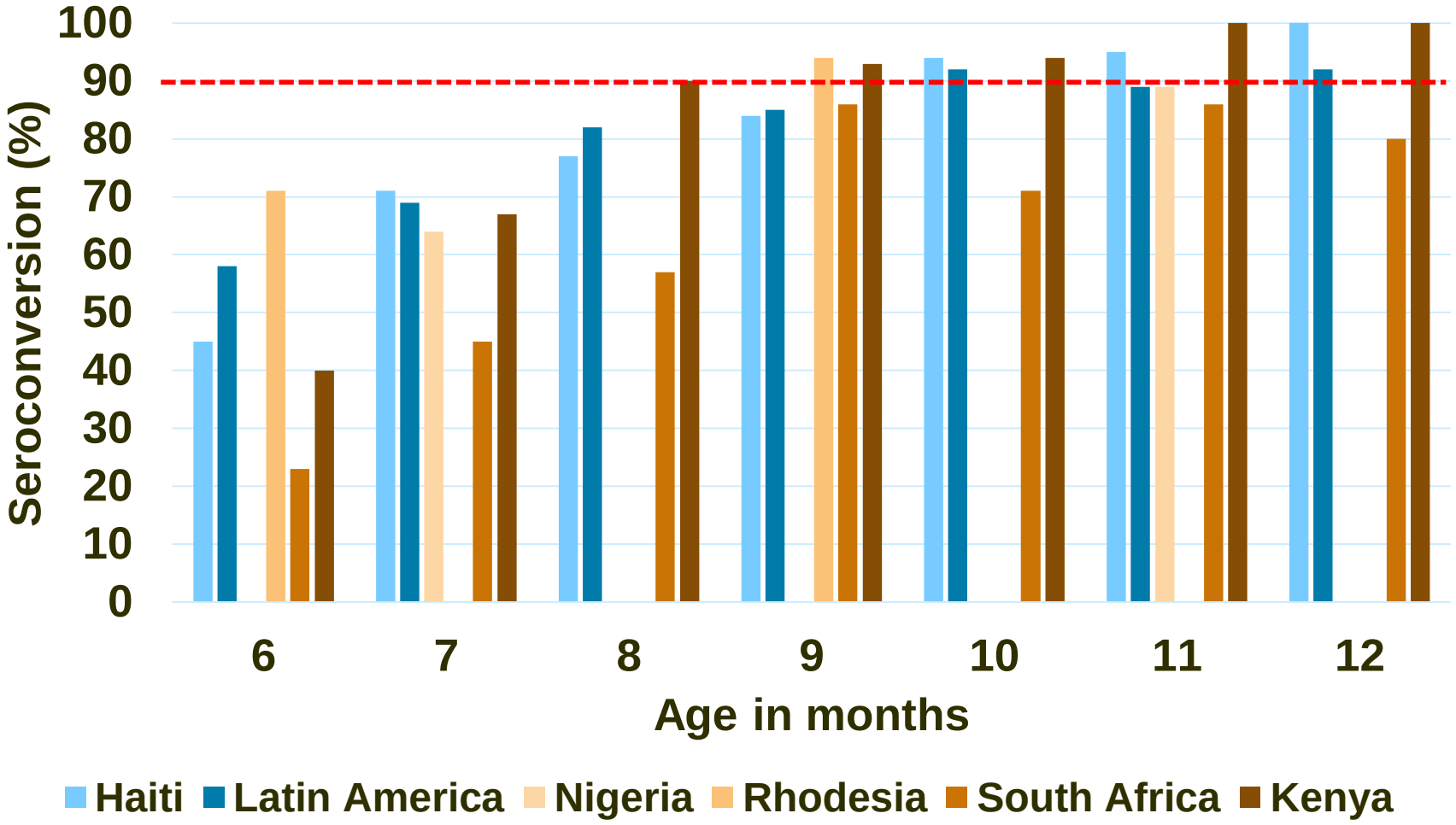
Elements used to design an optimal schedule for the primary series in infants



Seroconversion rates by age in developing countries after measles immunization (1 dose)



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Adapted from *Halsey NA.* Pan Am Health Org 1983; 4-13.

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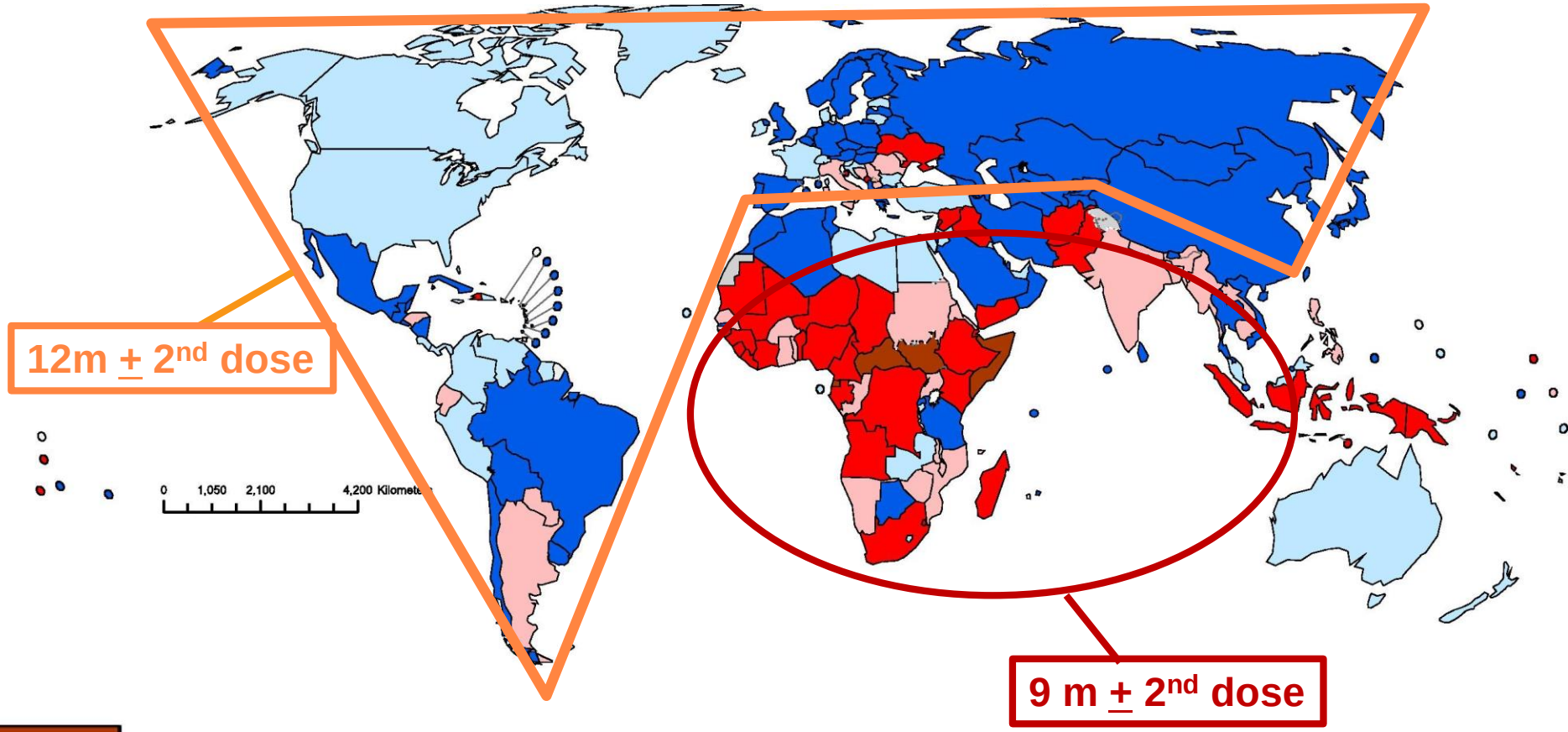
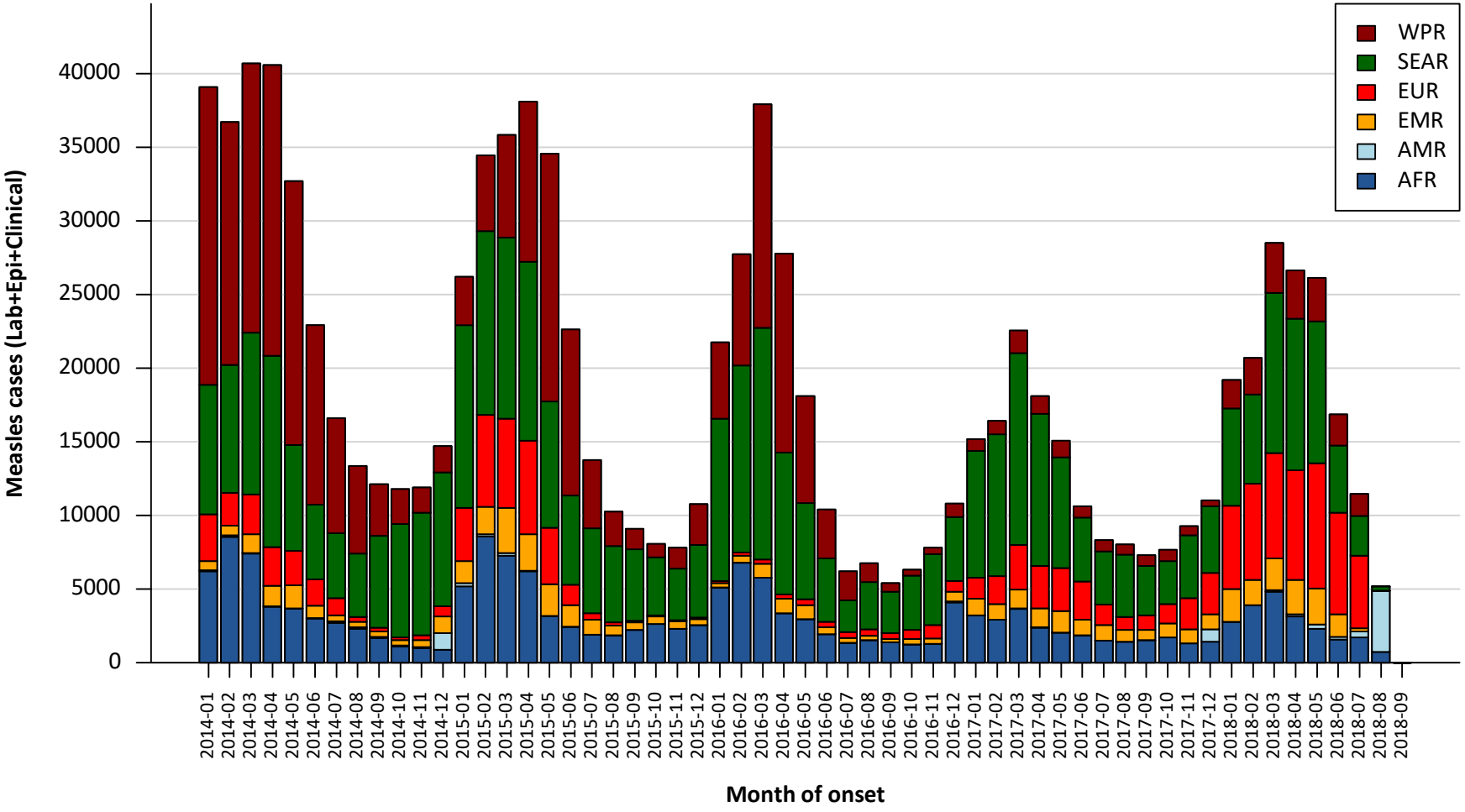
Global coverage and schedules of measles containing vaccines – June 2016



<50%	(4 countries or 2%)
50–79%	(38 countries or 20%)
80–89%	(33 countries or 17%)
90–94%	(40 countries or 21%)
≥95%	(79 countries or 40%)

Measles case distribution by month and WHO Region (2014-2018)



Notes: Based on data received 2018-09 - Data Source: IVB Database - This is surveillance data, hence for the last month(s), the data may be incomplete.

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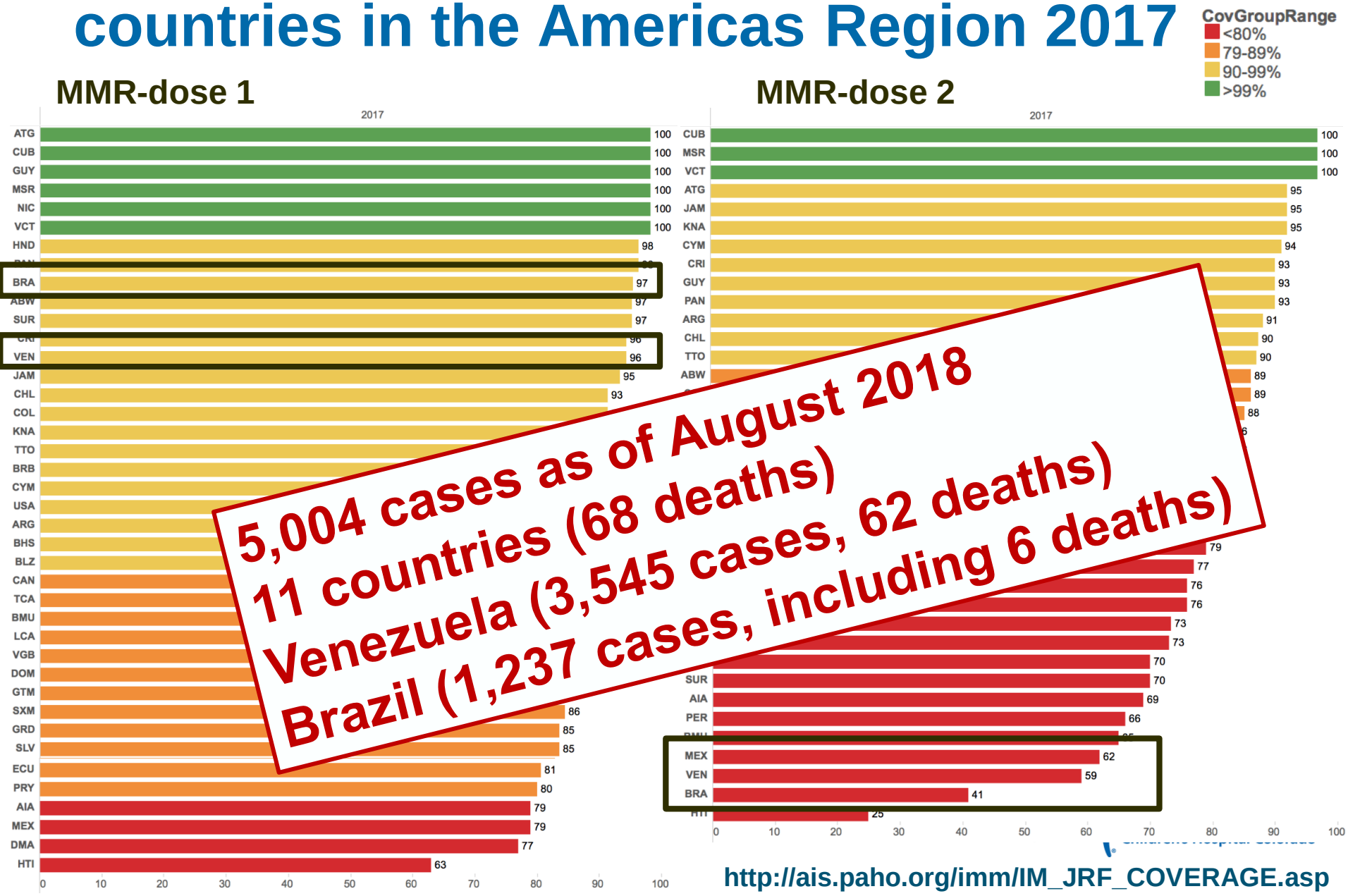
Coverage of MMR1 and MMR2 vaccines in countries in the Americas Region 2017

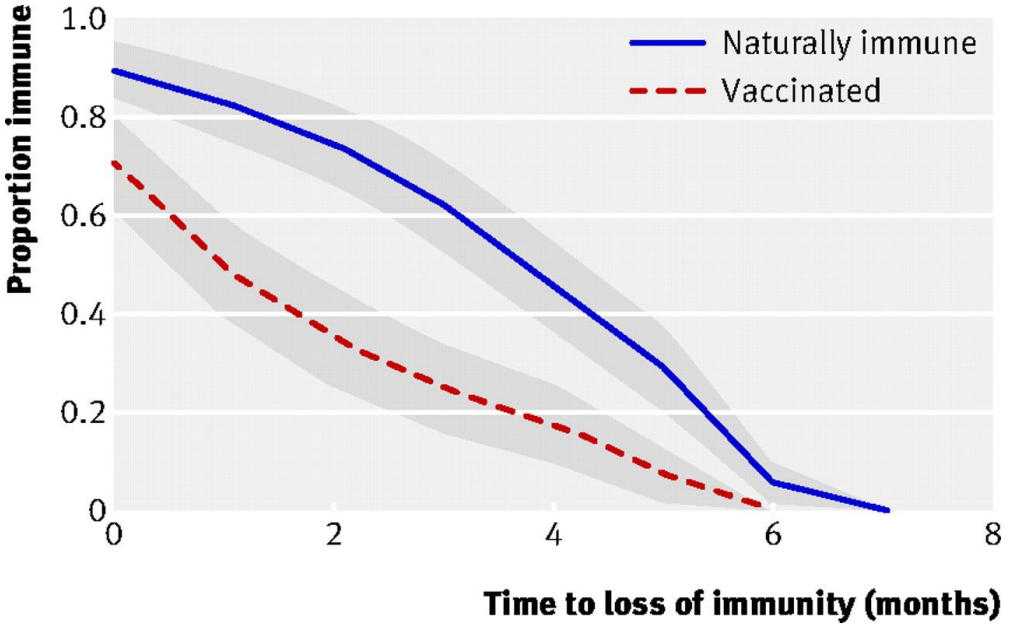


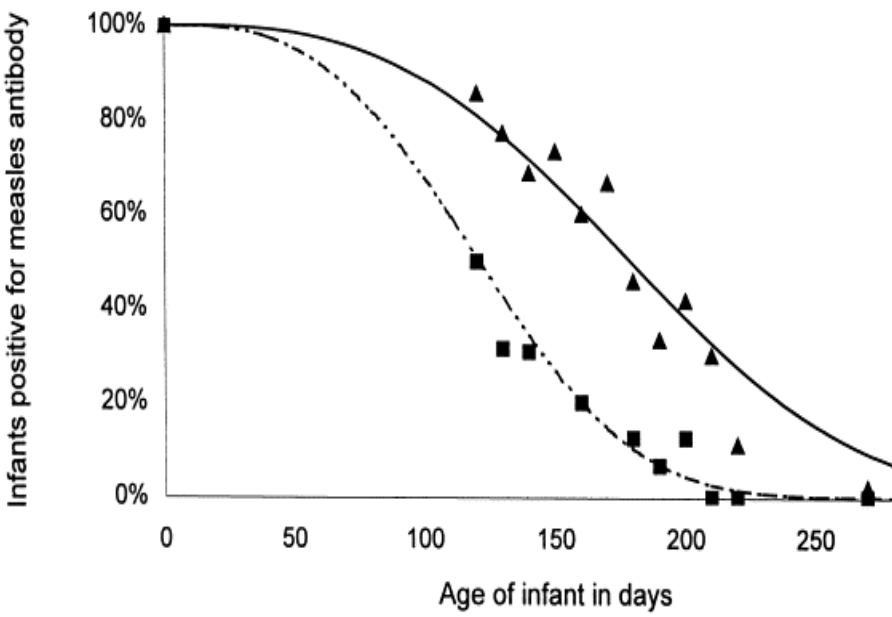
http://ais.paho.org/imm/IM_JRF_COVERAGE.asp

Proportion of infants of vaccinated and naturally immune women still immune as a function of time to loss of immunity

Belgium

Canada





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E Leuridan et al. BMJ 2010;340:bmj.c1626
H.F Pabst. Vaccine 1999; 17:182

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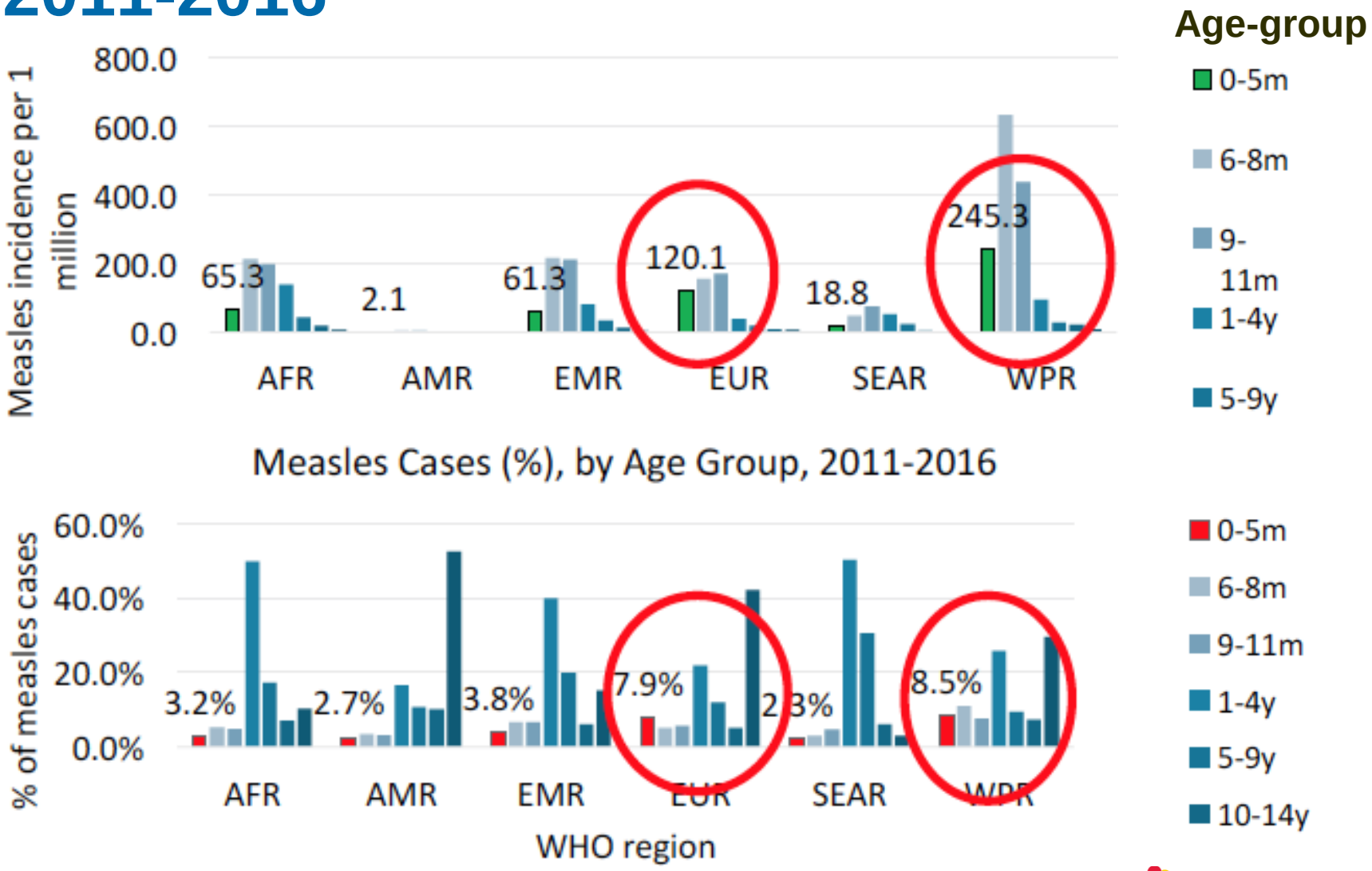
Measles age-specific incidence by Region 2011-2016



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From N.S. Crowcroft SAGE Measles WG 2017

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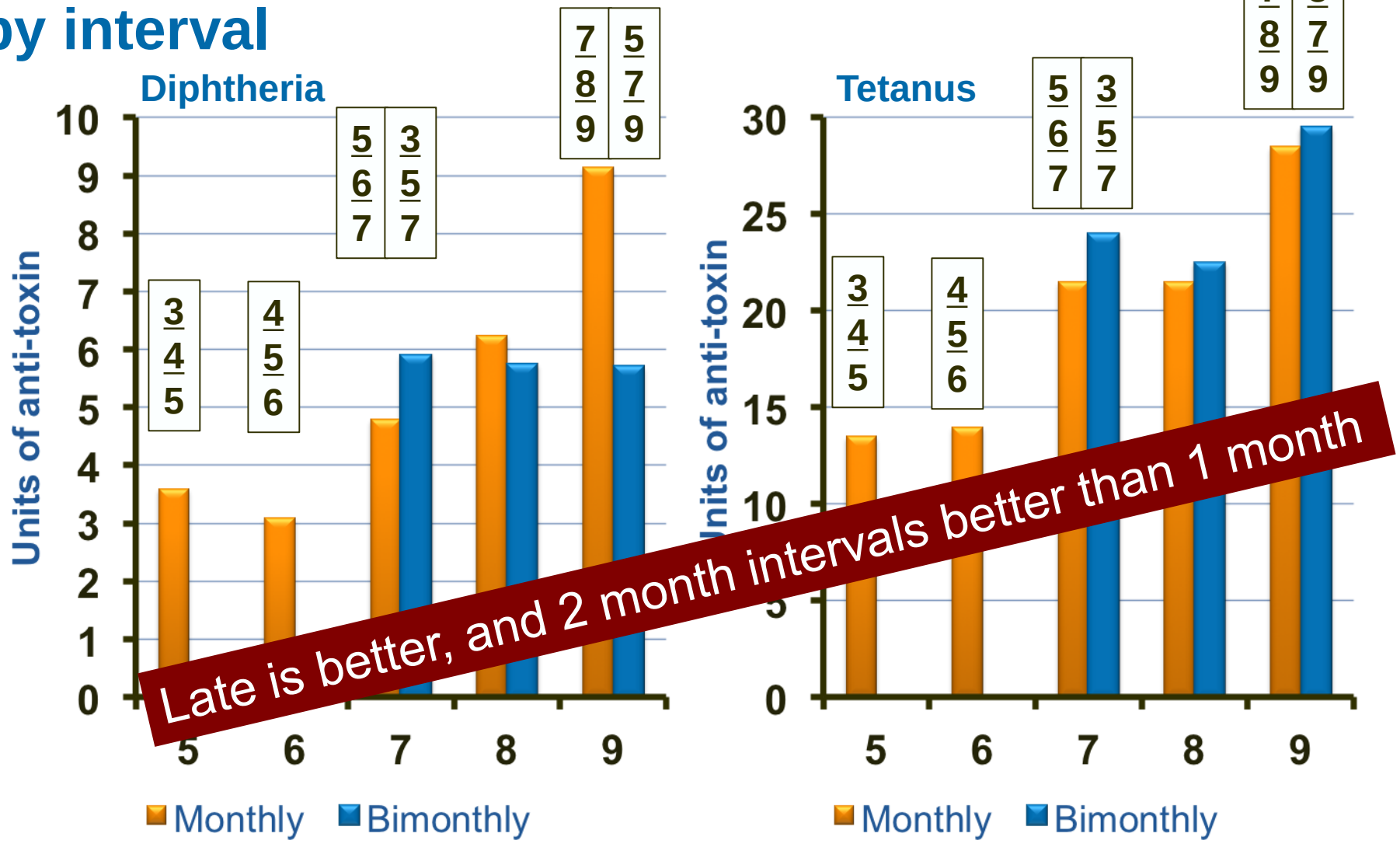
GMC responses to diphtheria and tetanus in children receiving 3 doses of DTwP-IPV by interval



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Modified from
Brown GC et al AJPH 1964;79 (7):585

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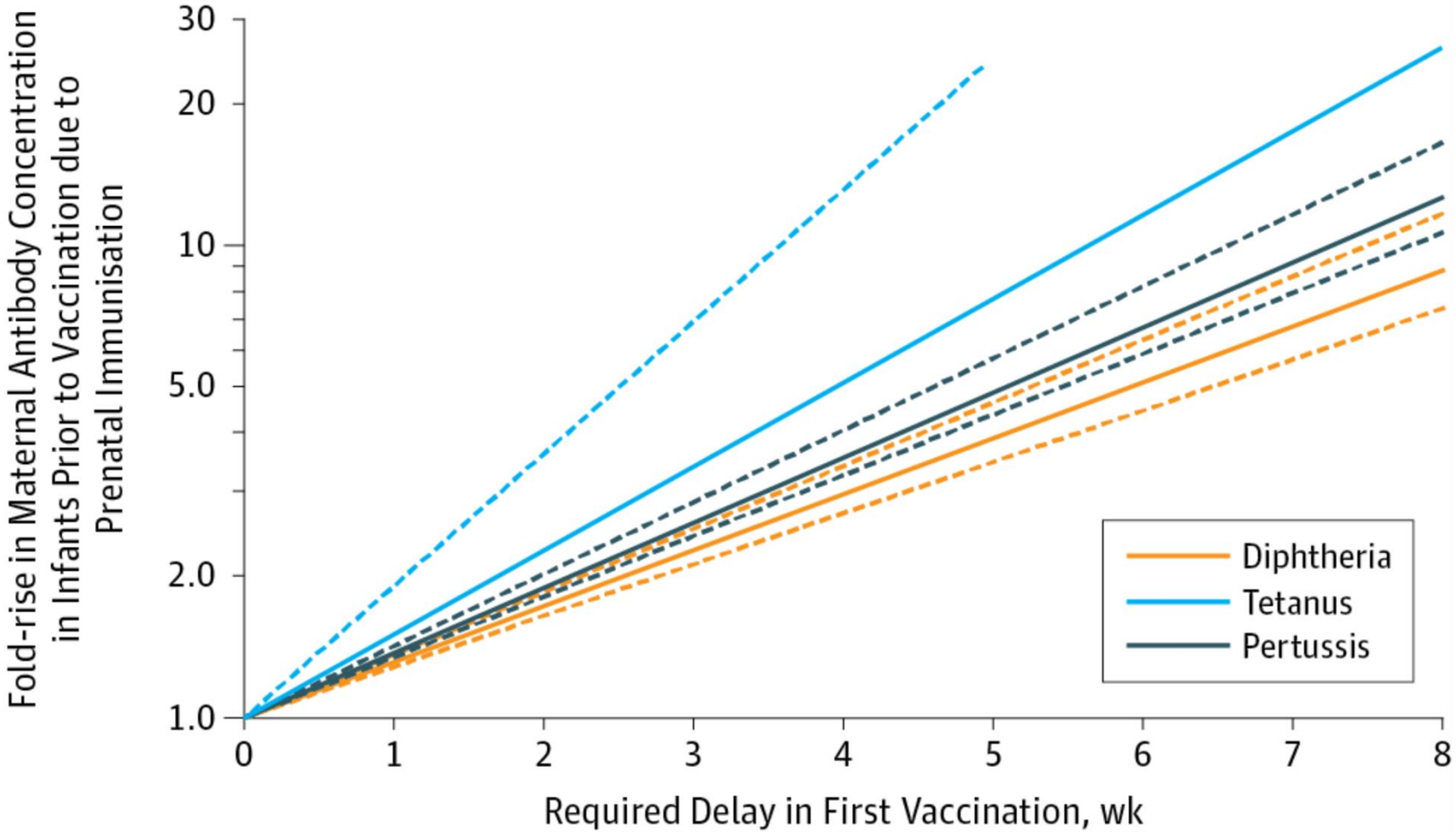
Meta-analysis of Influence of Maternally Derived Antibody and Infant Age at Vaccination on Infant Vaccine Responses



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Voysey M. JAMA Pediatr. 2017;171(7):637-646.
doi:10.1001/jamapediatrics.2017.0638

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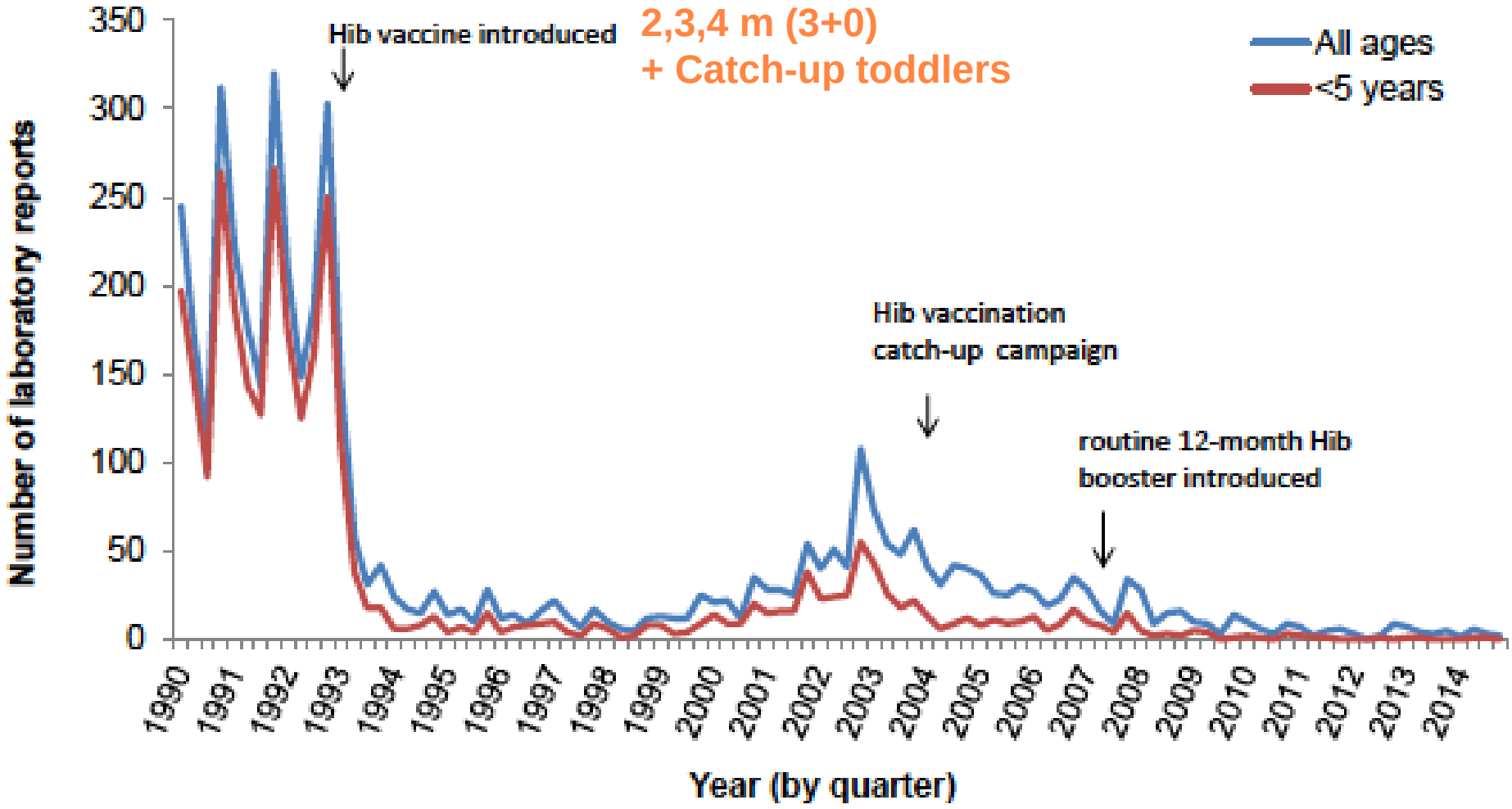
Hib invasive disease incidence in UK 1990-2015



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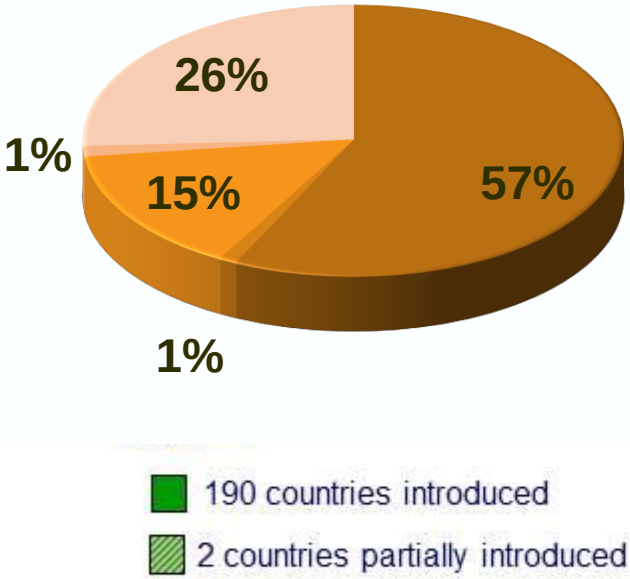
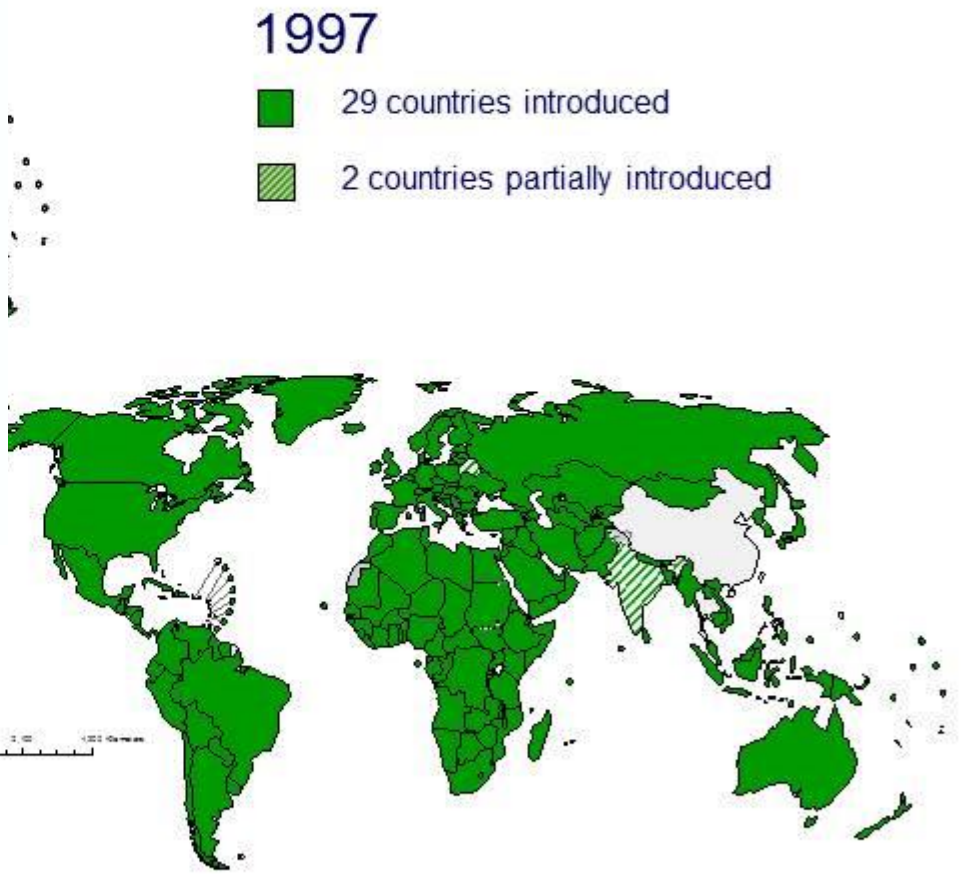
Countries having introduced Hib vaccine in 1997 and 2014

Percent of children by schedule globally

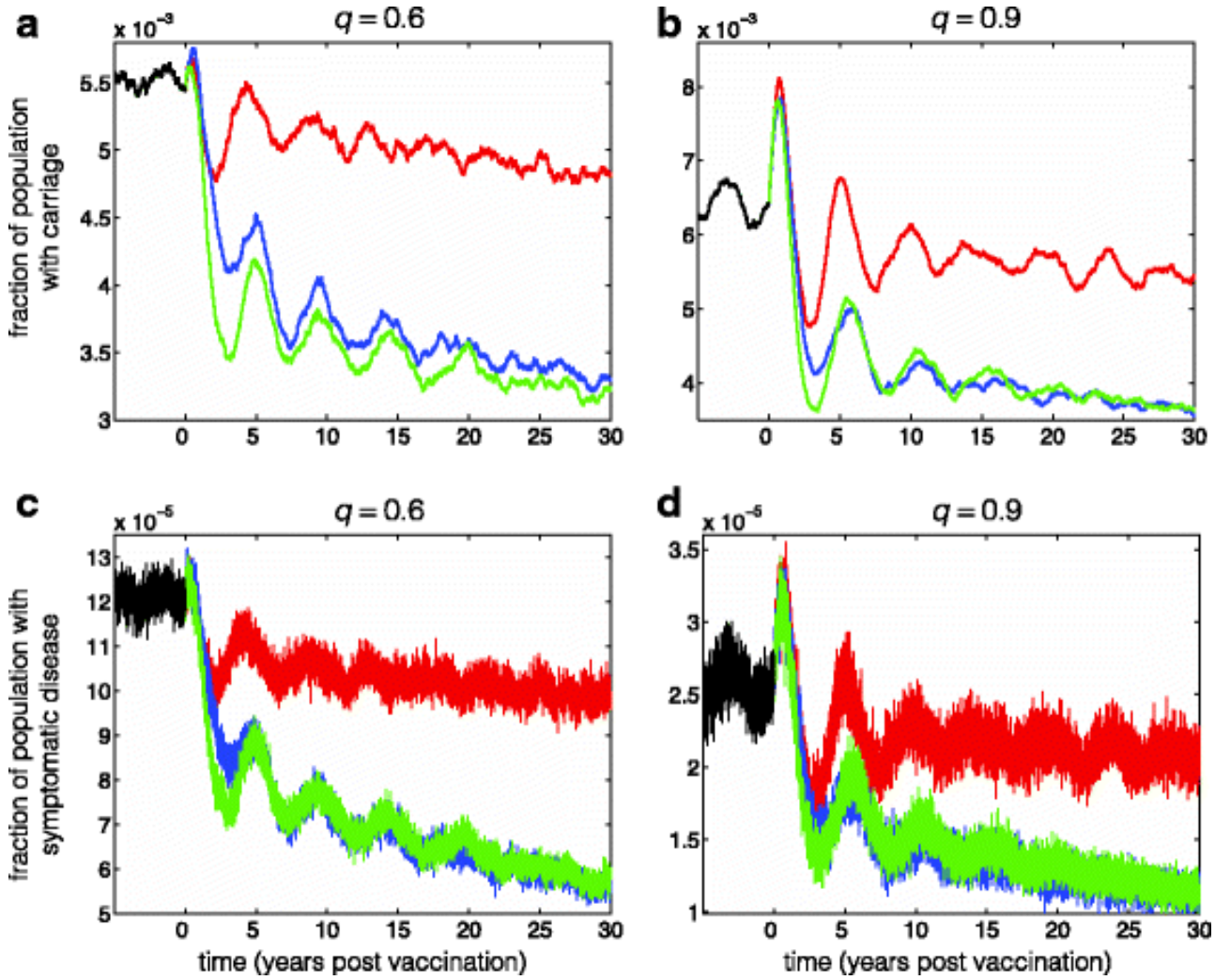




Source: WHO/IVB Database as at 24 July 2015.
Map production: Immunization Vaccines and Biologicals, (IVB), World Health Organization.
194 WHO Member States. Date of slide: 28 July 2014

WHO

Modelling the effects of booster dose Hib schedules for public health immunization



Assuming 90% coverage

Primary series only

Primary series + booster 1 year

Primary series + booster 2-4 years

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Charania N. BMC Pub Health *2017; 17:705*

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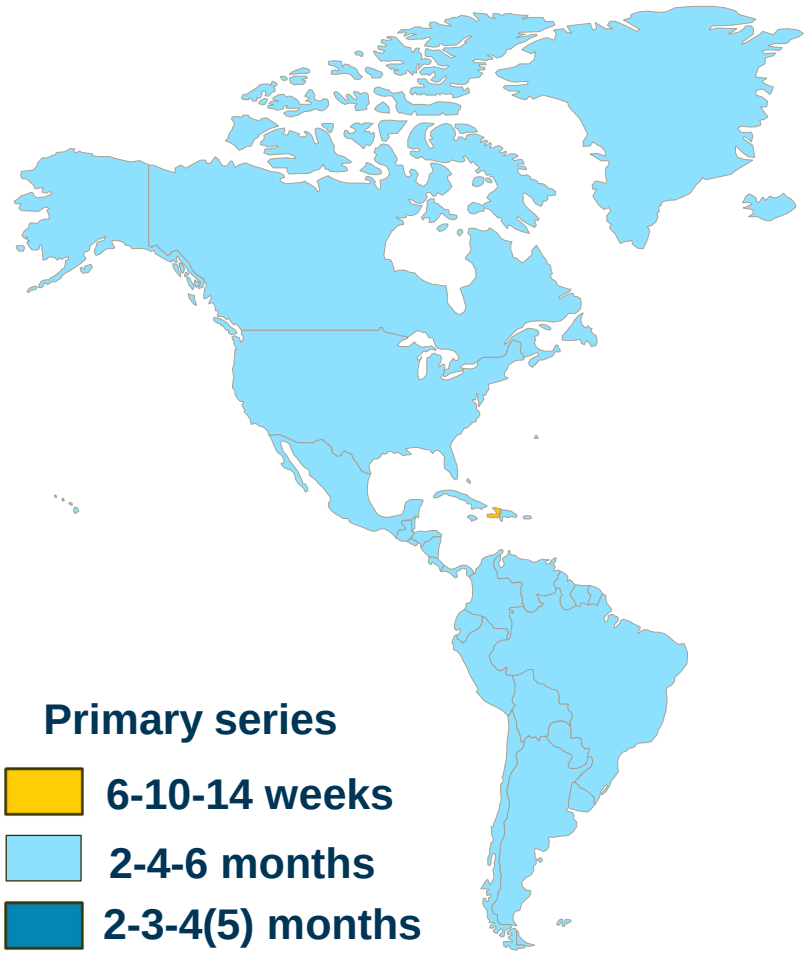
Current DPT-Hib Series Schedules in the Region of the Americas 2018



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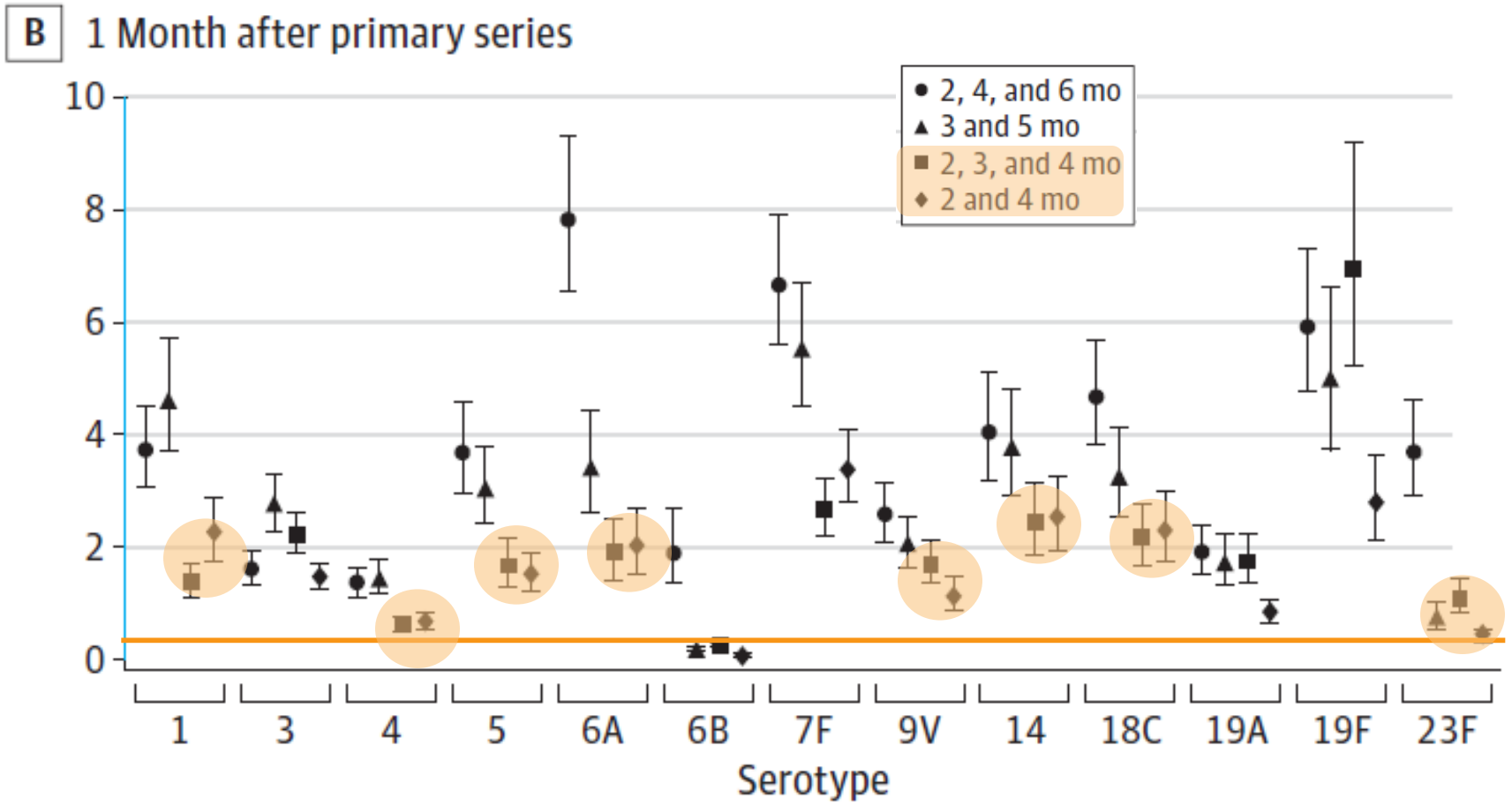
http://apps.who.int/immunization_monitoring/globalsummary/schedules

Pneumococcal Serotype-Specific Antibody GMCs Measured at 4 different Time Points (95% CI) in 4 different schedules in Netherlands



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Spijkerman et al JAMA. 2013;310(9):930-937.

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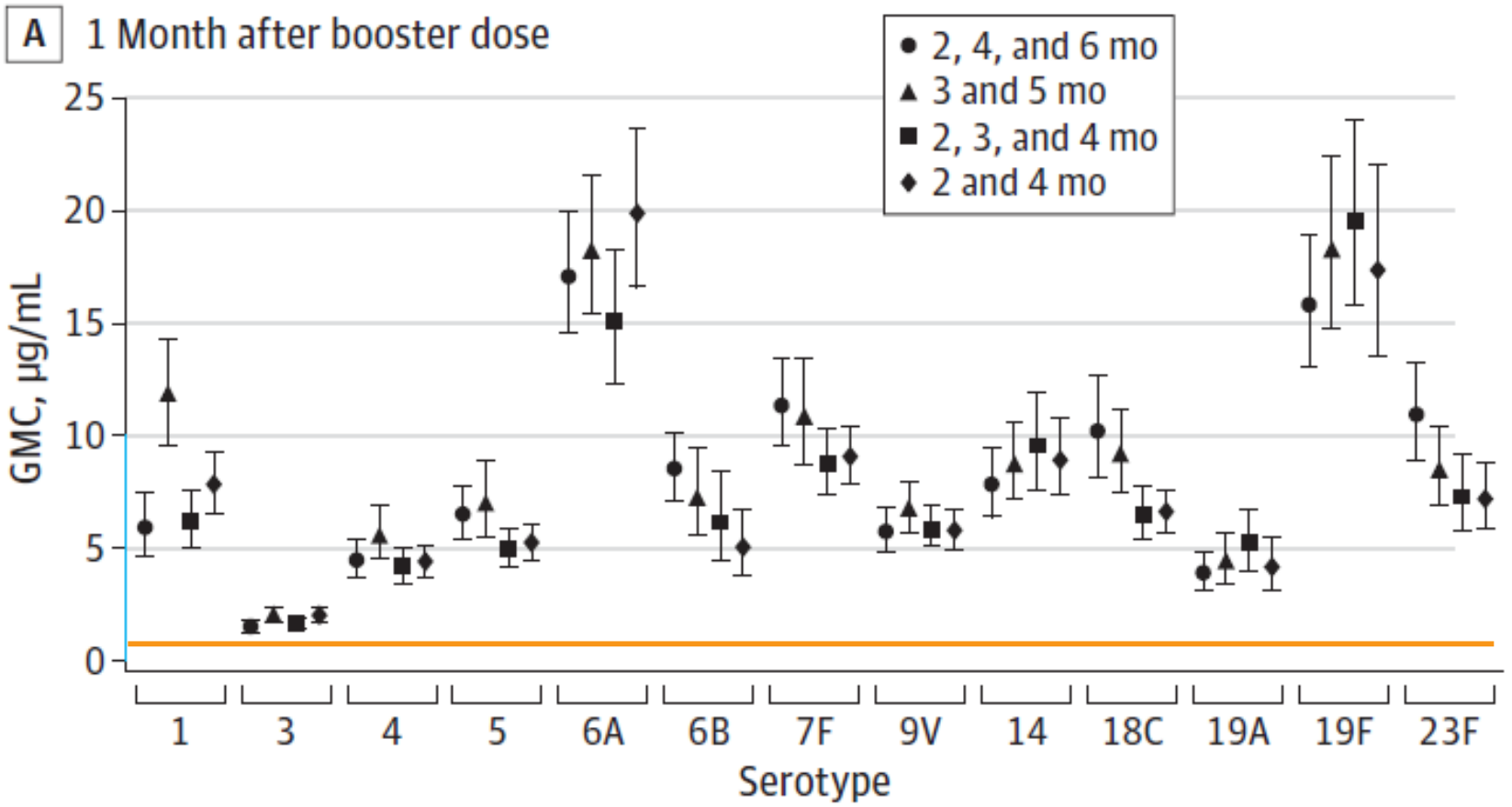
The JAMA Network

Pneumococcal Serotype-Specific Antibody GMCs Measured at 4 different Time Points (95% CI) in 4 different schedules in Netherlands



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Spijkerman et al JAMA. 2013;310(9):930-937.

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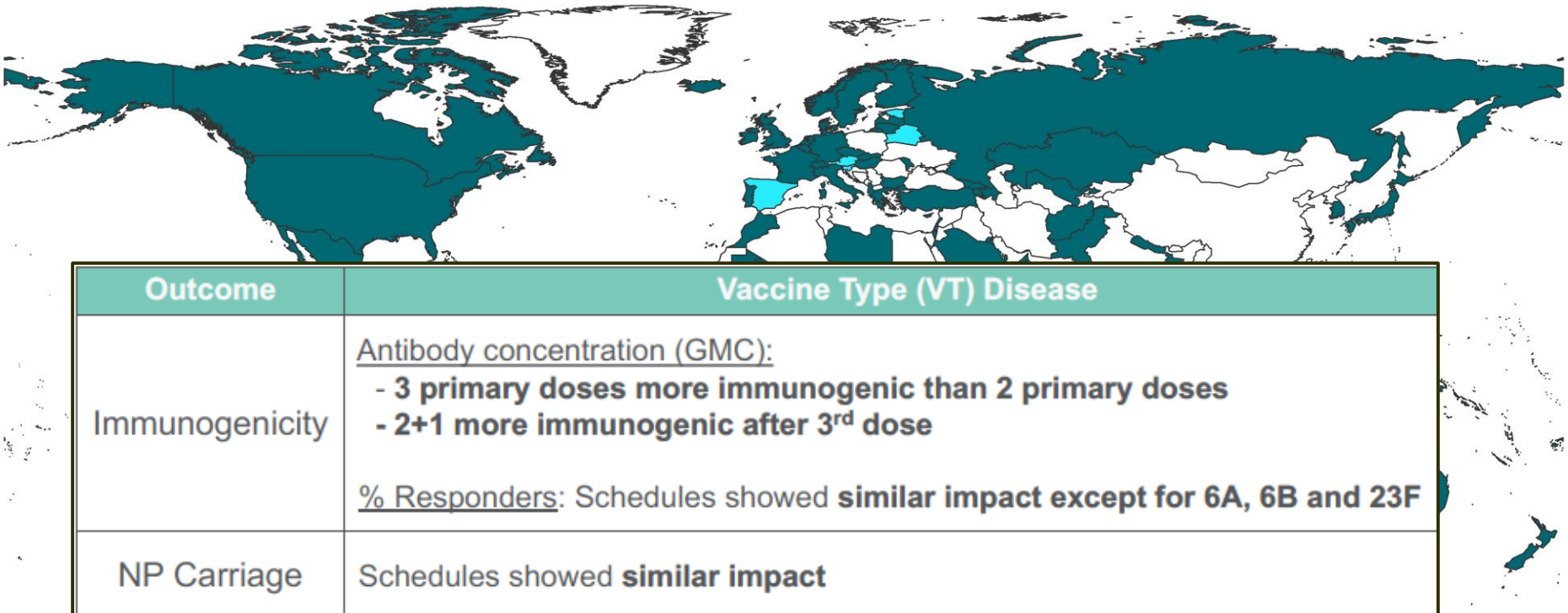
Pneumococcal vaccine introduction as of 2015 – 190,000 deaths averted



Outcome	Vaccine Type (VT) Disease
Immunogenicity	Antibody concentration (GMC): - **3 primary doses more immunogenic than 2 primary doses** - **2+1 more immunogenic after 3rd dose** % Responders: Schedules showed **similar impact except for 6A, 6B and 23F**
NP Carriage	Schedules showed **similar impact**
IPD	VT: Both schedules showed **similar impact**; Limited 3+0 data ST1: Clear evidence of 2+1 impact; evidence of 3+0 impact but limited data
Overall	**Both schedules are effective** in reducing VT Carriage and Disease

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Knoll M. Presented at SAGE Oct 2017

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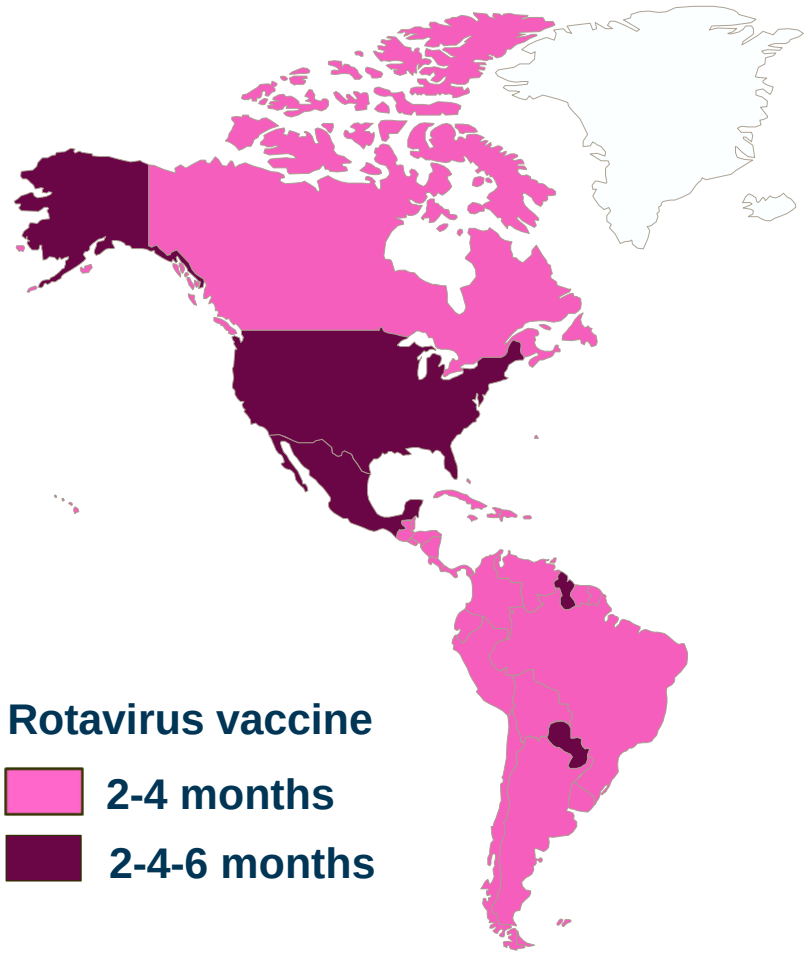
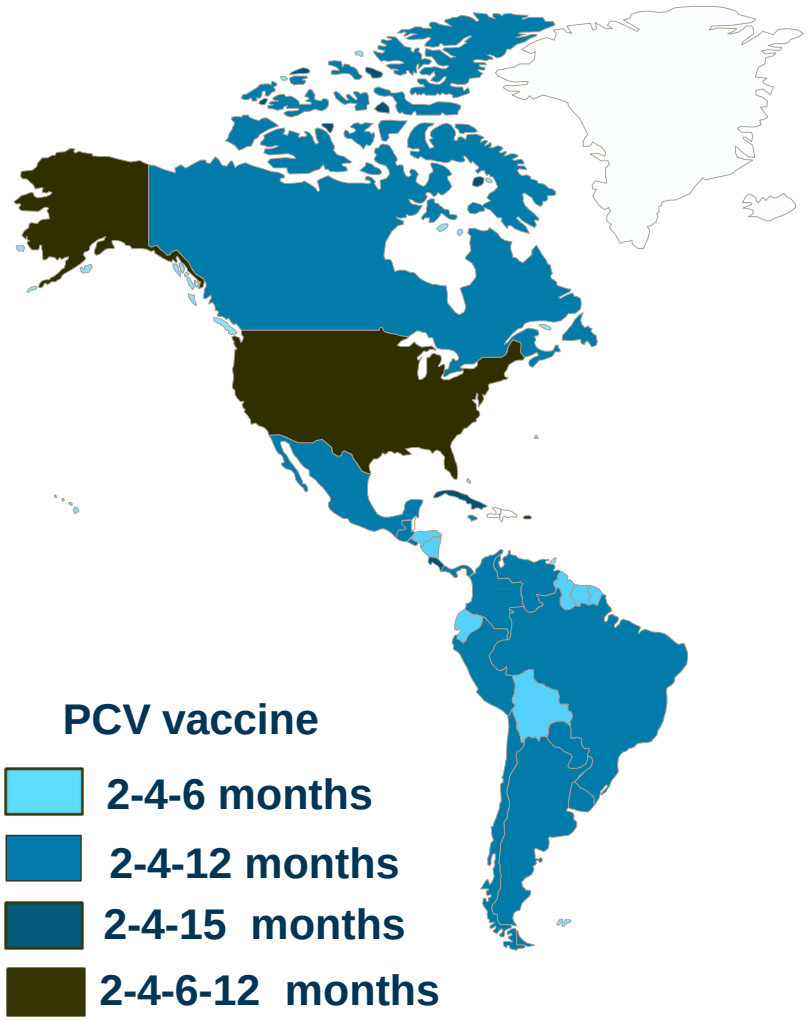
Current Rotavirus and PCV Schedules in the Region of the Americas 2018





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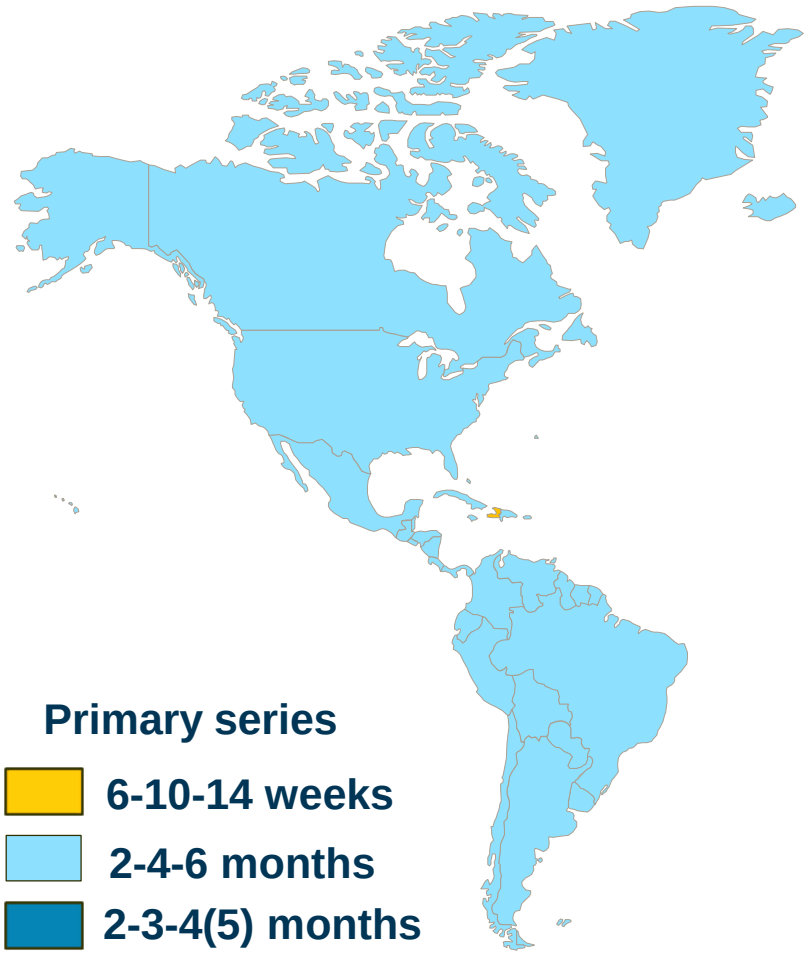
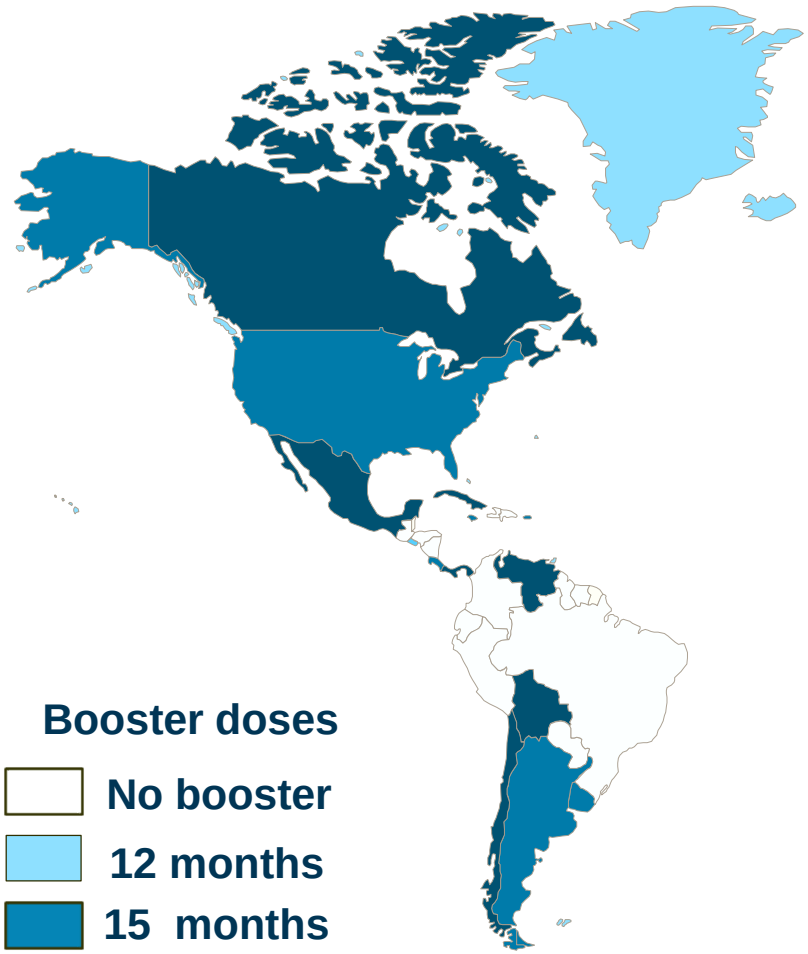
http://apps.who.int/immunization_monitoring/globalsummary/schedules

Current DPT-Hib Series Schedules in the Region of the Americas 2018



Primary series

- 6-10-14 weeks
- 2-4-6 months
- 2-3-4(5) months
- 3-5-12 months



Booster doses

- No booster
- 12 months
- 15 months
- 18 months

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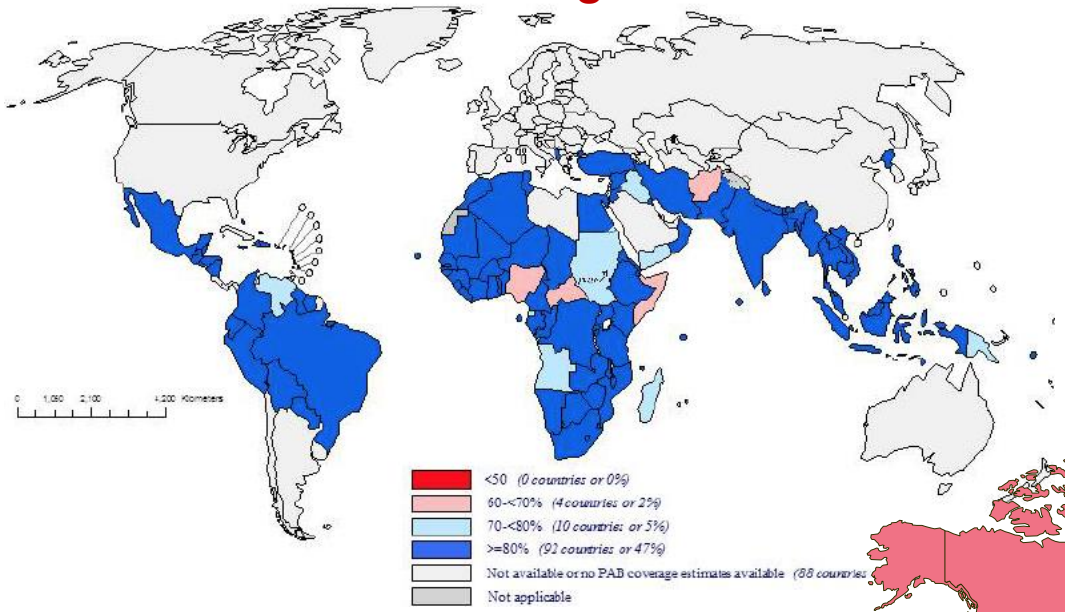
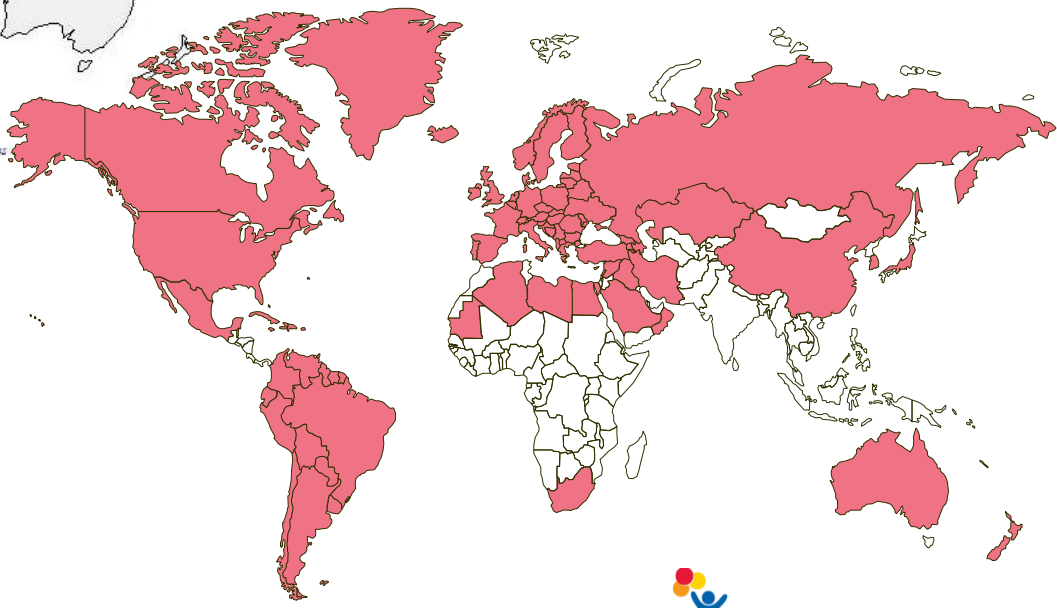
http://apps.who.int/immunization_monitoring/globalsummary/schedules

Countries with recommended for immunization of pregnant women 2018

TT/Td vaccine coverage 2016



Influenza vaccine recommended 2018



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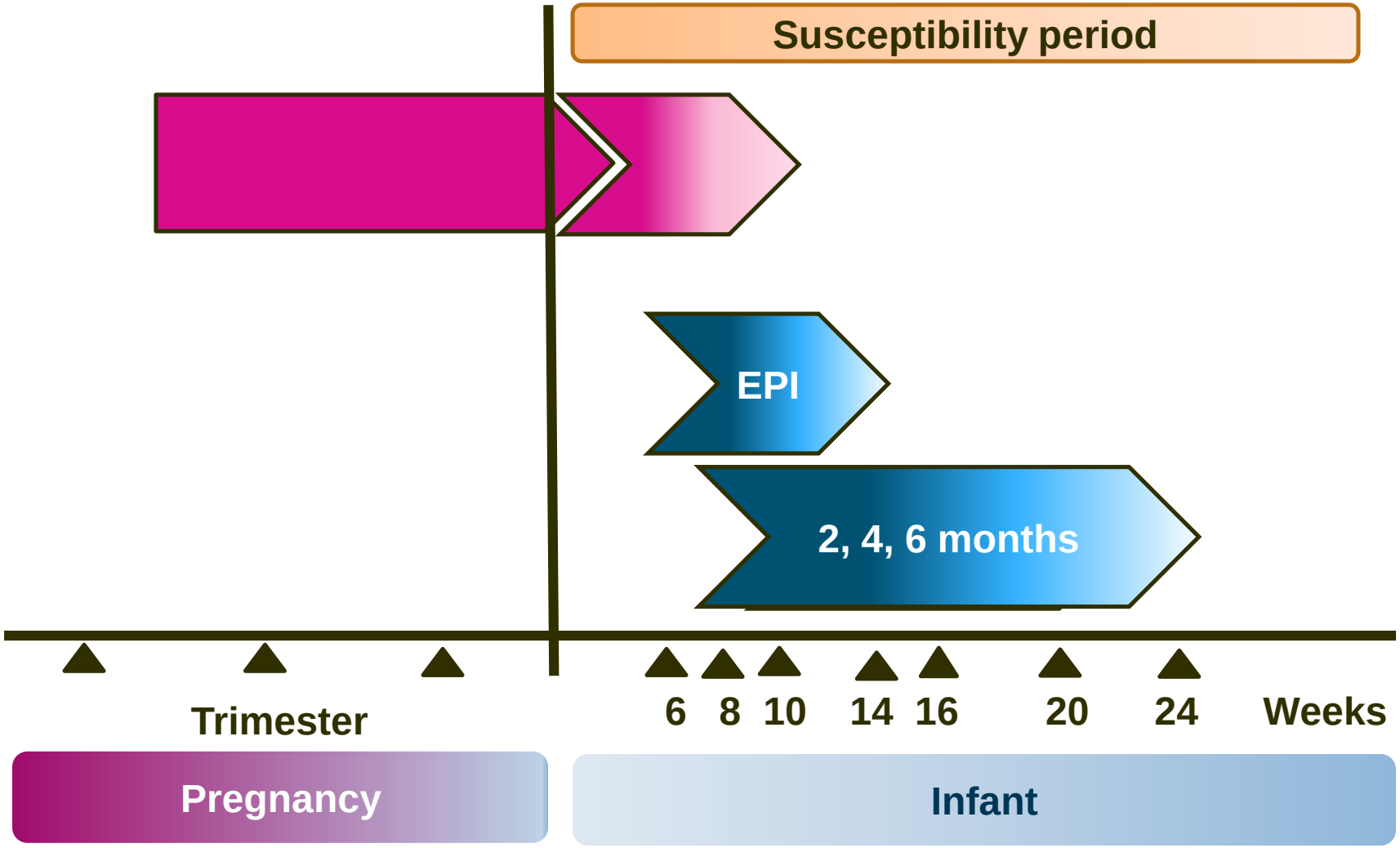
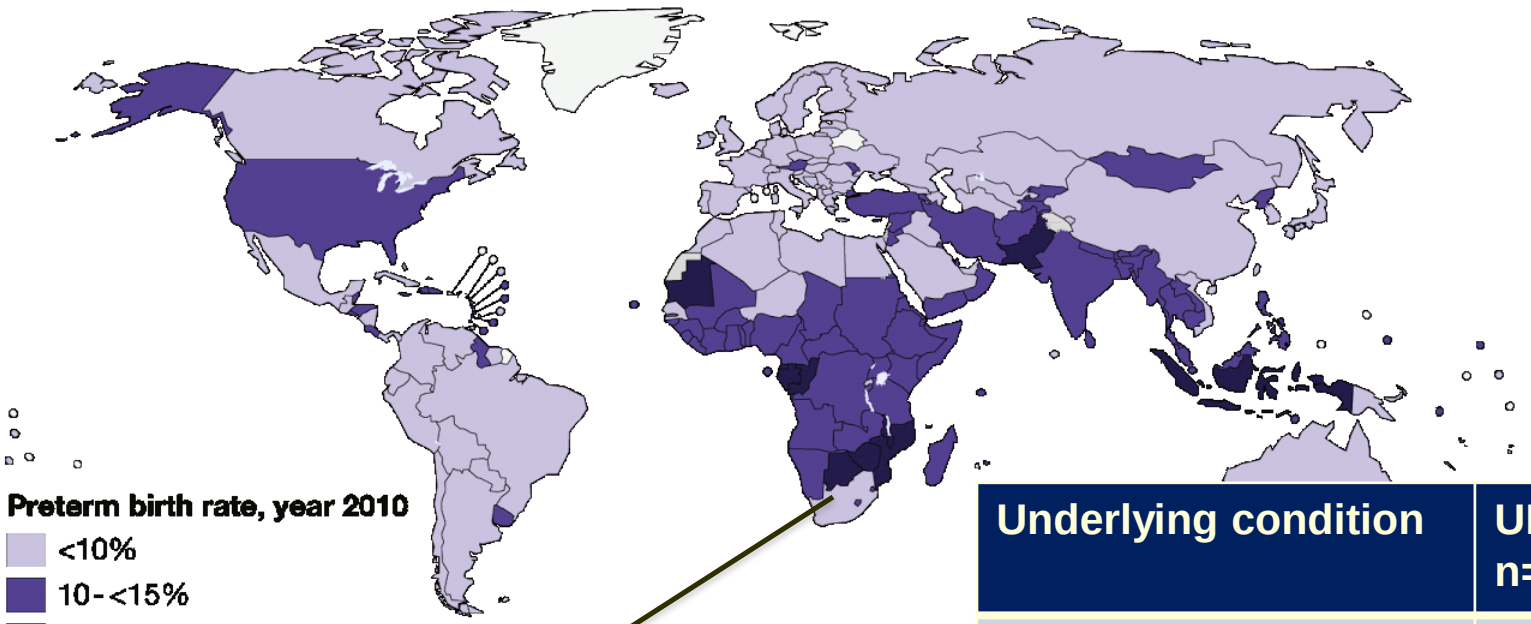
http://apps.who.int/immunization_monitoring/globalsummary/schedules

Integrating Maternal and Infant Schedules



Vaccine schedules and conjugate (Hib) vaccines in special populations (HIV, PTB)

Figure 2: Global burden of preterm birth in 2010



11 countries with preterm birth rates over 15% by rank:

1. Malawi
2. Congo
3. Comoros
4. Zimbabwe
5. Equatorial Guinea
6. Mozambique
7. Gabon
8. Pakistan

South Africa

Hib<5 years from 0.7 to 1.3/100,000 (2003 to 2009).

51% "vaccine failures"

HIV (+) in 34%

Underlying condition	UK n=220	Other n=38
Prematurity (<37wk)	6	18
Malignancy	4	4
Congenital	5	5
Other	3	8
Total	16	32

von Gottberg A (GERM-SA) Vaccine. 2012;30(3):565-71

Ladhani S. Clin Microbiol Infect. 2010;16(7):948-54

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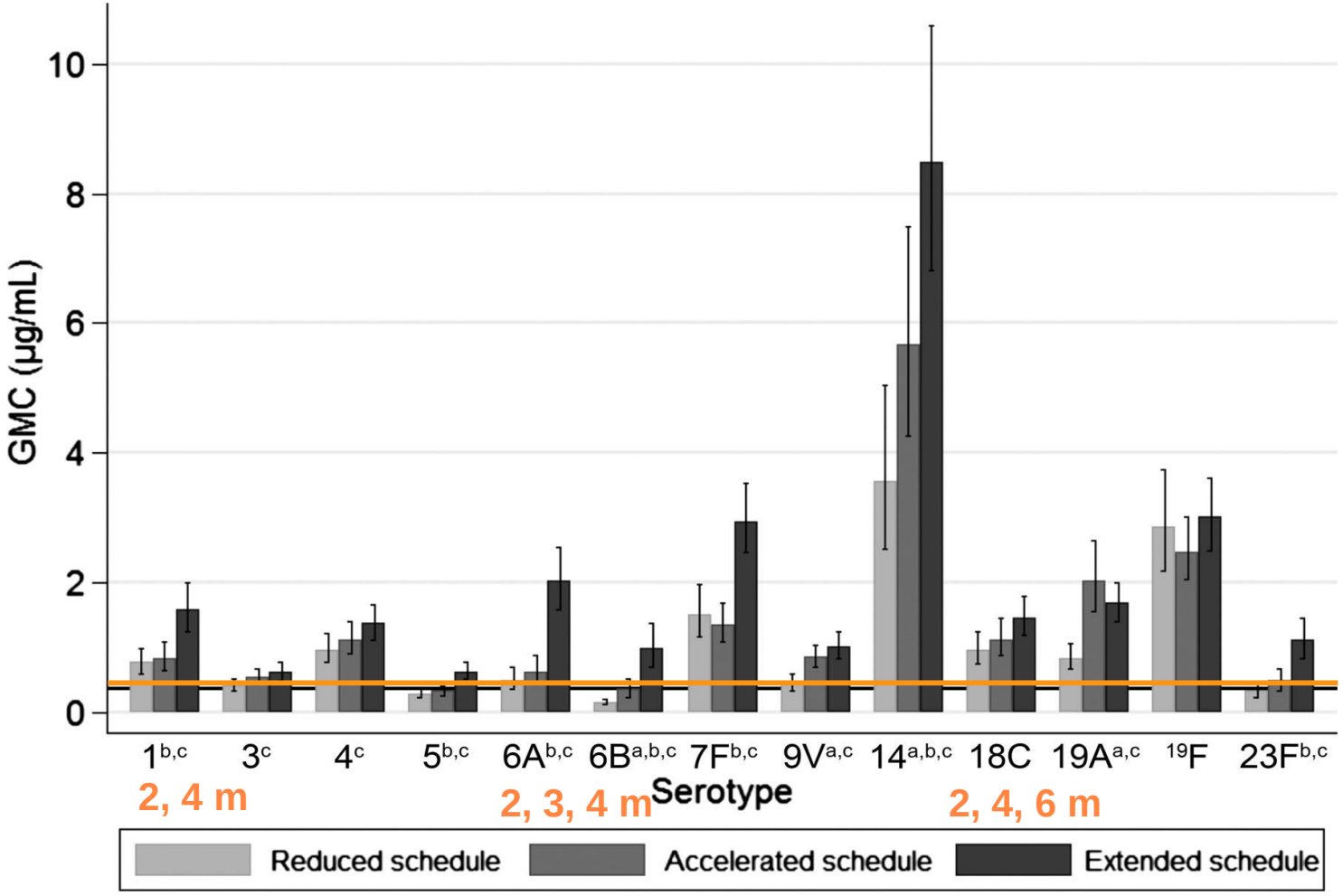
Pneumococcal (PCV13) IgG GMCs after primary vaccination for each serotype and group in premature infants in the UK



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Kent A. Pediatrics. 2016 Sep;138(3).

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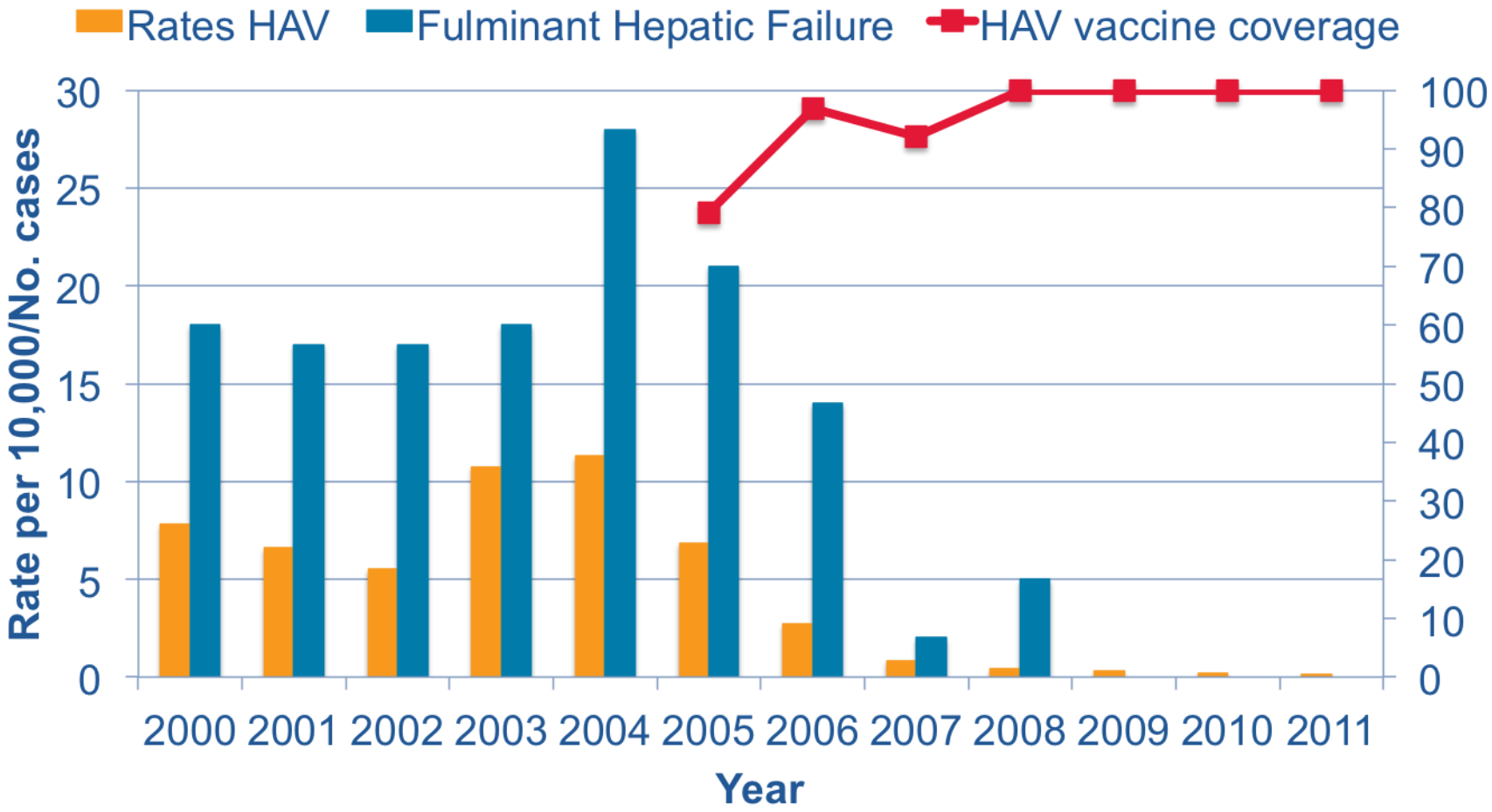
Vaccination schedules for Population Immunity (Community Protection)

- **HepA vaccine:** 2 vs. 1 dose
- **PCV:** UK 1+1 schedule?

- **IPV:** 1-2 doses – best timing and issues with silent transmission (more tomorrow)

Trend of Hepatitis A incidence rates and cases of hepatic failure due to HAV in Argentina pre and post 1 dose HAV program



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Adapted from Vizzotti C. PIDJ. 2014;33(1):84-8

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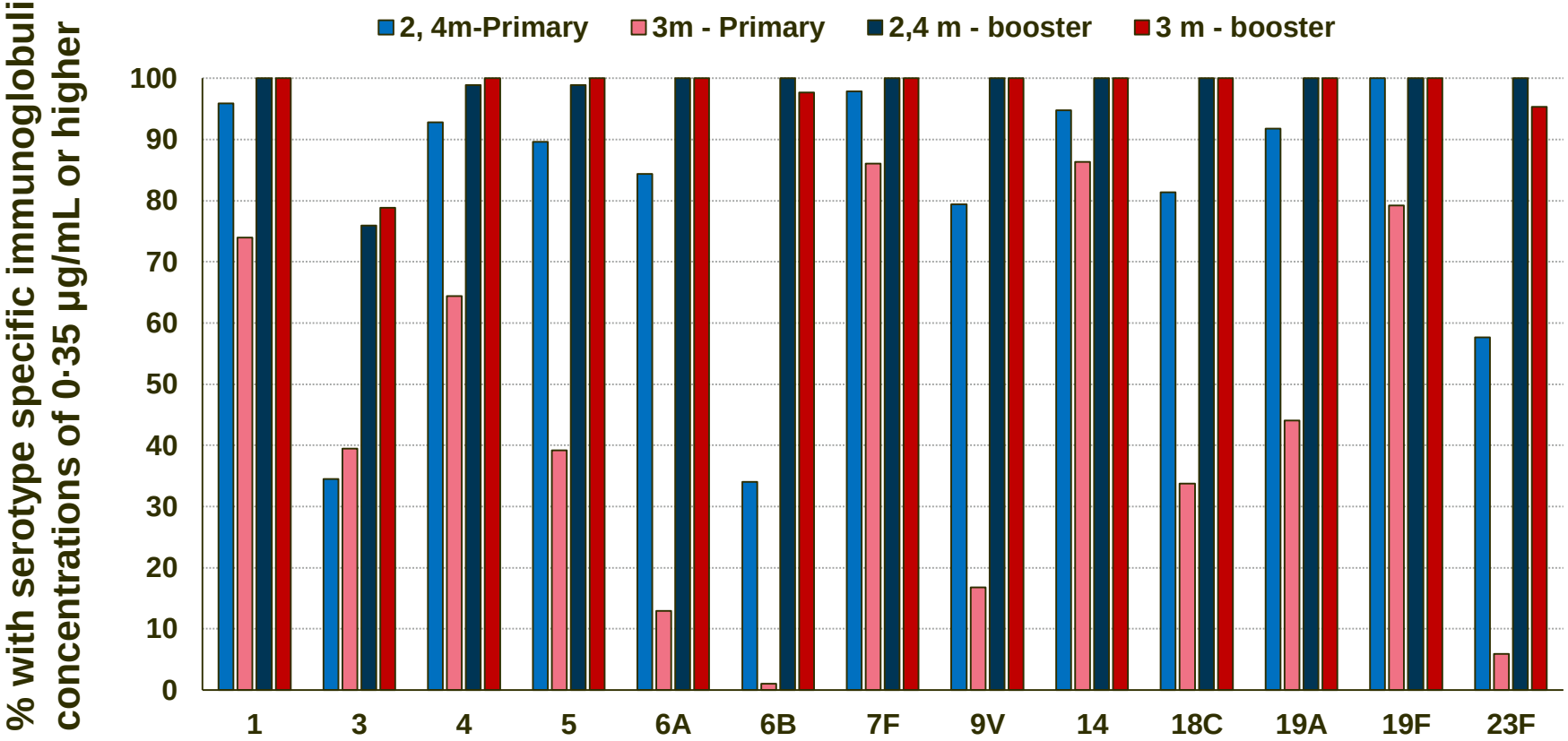
Pneumococcal conjugate vaccine 13 delivered as one primary and one booster dose (1 + 1) compared with two primary doses and a booster (2 + 1) in UK infants

Prof David Goldblatt, MBChB, Jo Southern, PhD, Nick J Andrews, PhD, Polly Burbidge, BSc, Jo Partington, BSc, Lucy Roalfe, BSc, Marta Valente Pinto, MD, Vasilli Thalasselis, Emma Plested, Hayley Richardson, BSc, Matthew D Snape, MBChB, Prof Elizabeth Miller, FRCPath



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Lancet Infectious Diseases 2018
Volume 18, Issue 2, Pages 171-179

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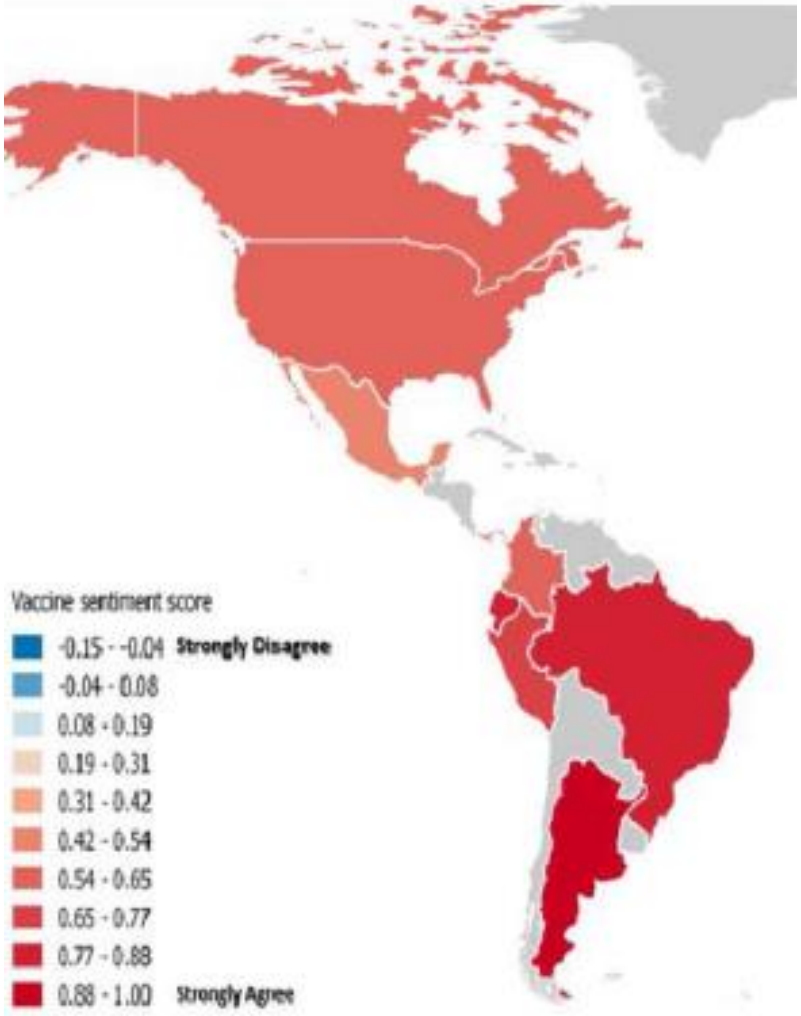
Trends in vaccine hesitancy and the importance of safety in the Americas Region

"Overall, I think vaccines are safe…"



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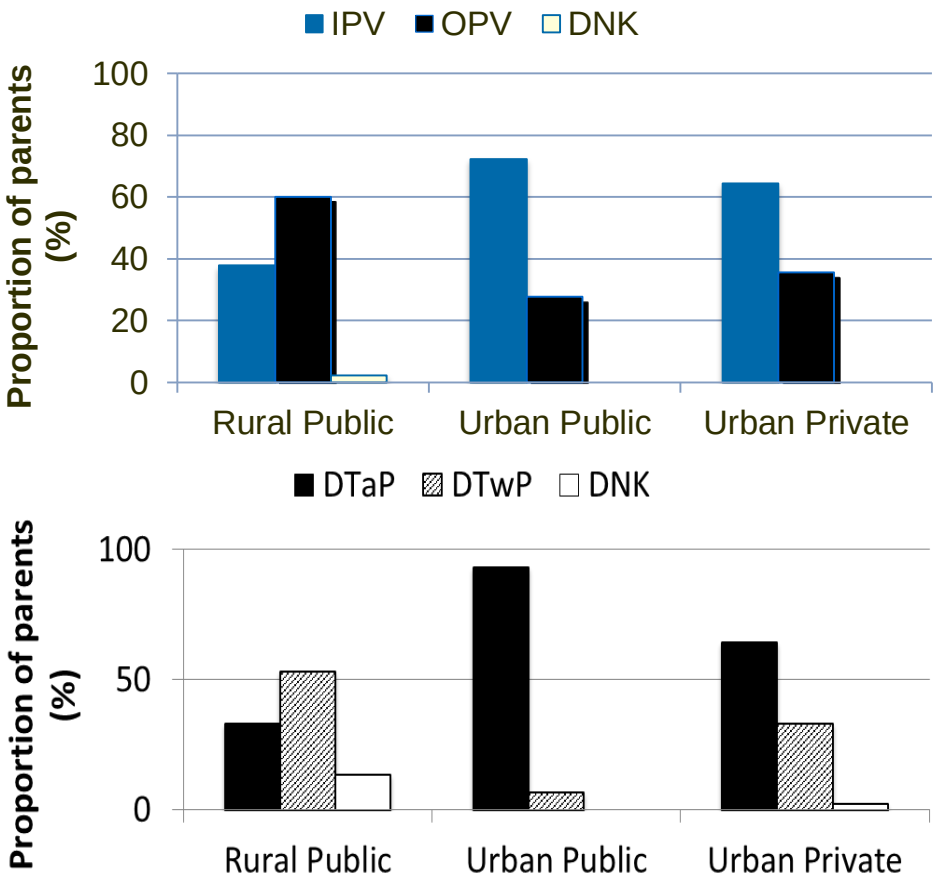
Vaccine preferences by antigen and safety in different populations Guatemala



Data: Desiree Pastor, PAHO

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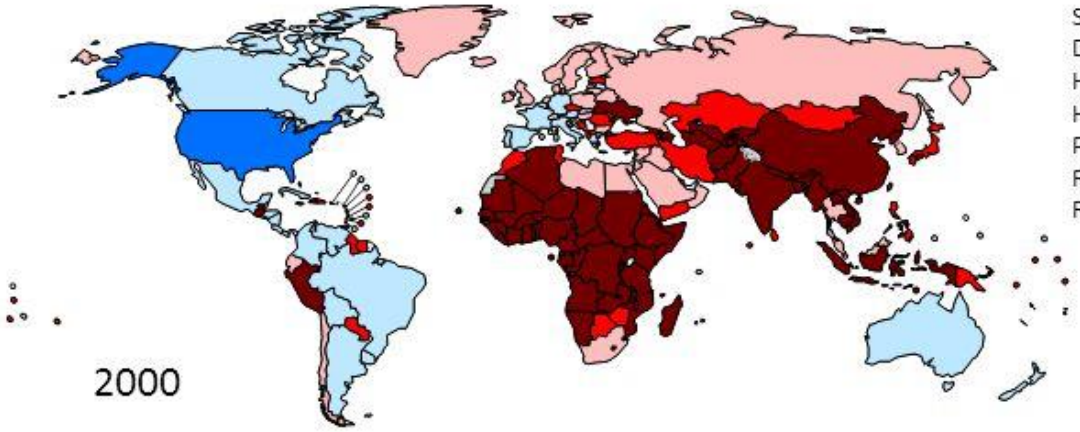
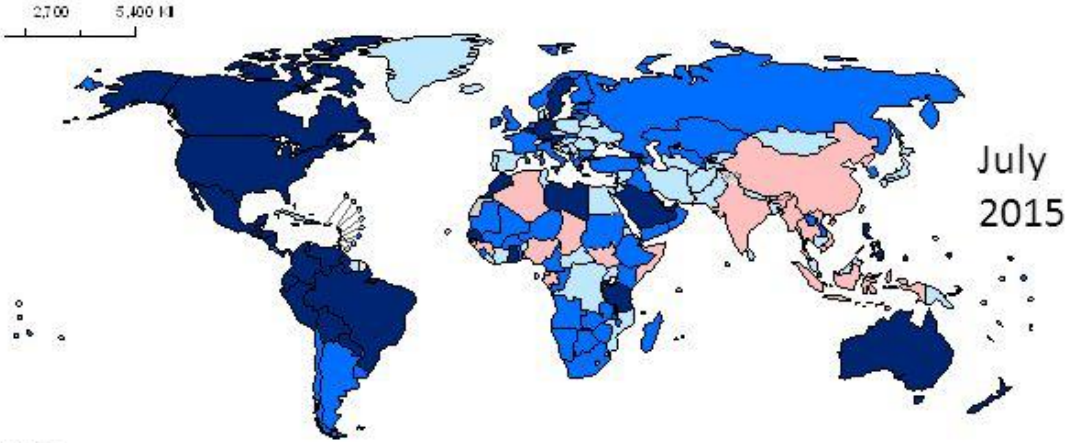
Dela Fuente Paediatr Child Health. 2016 Mar;21(2):e15-6

Number of Vaccines/Antigens Introduced Nationwide in Immunization Schedules - 2000 compared to date



Selected antigens are :
Diphtheria, Tetanus, Pertussis, Measles, Polio - universal use
Hepatitis B,
Heamophilius Influenza type B,
Pneumococcal conjugate
Rotavirus
Rubella



- 5 antigens (DTP, Measles and Polio)
- 6 antigens
- 7 antigens
- 8 antigens
- 9 antigens
- 10 antigens
- Not applicable
- Not available

Data Source: WHO/IVB Database, as at 20 July 2015

Map production: Immunization Vaccines and Biologicals, (IVB), World Health Organization

Date of slide: 20 July 2015

WHO

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NITAG strengthening in the Americas 2011-2017 and country decision

ACIP

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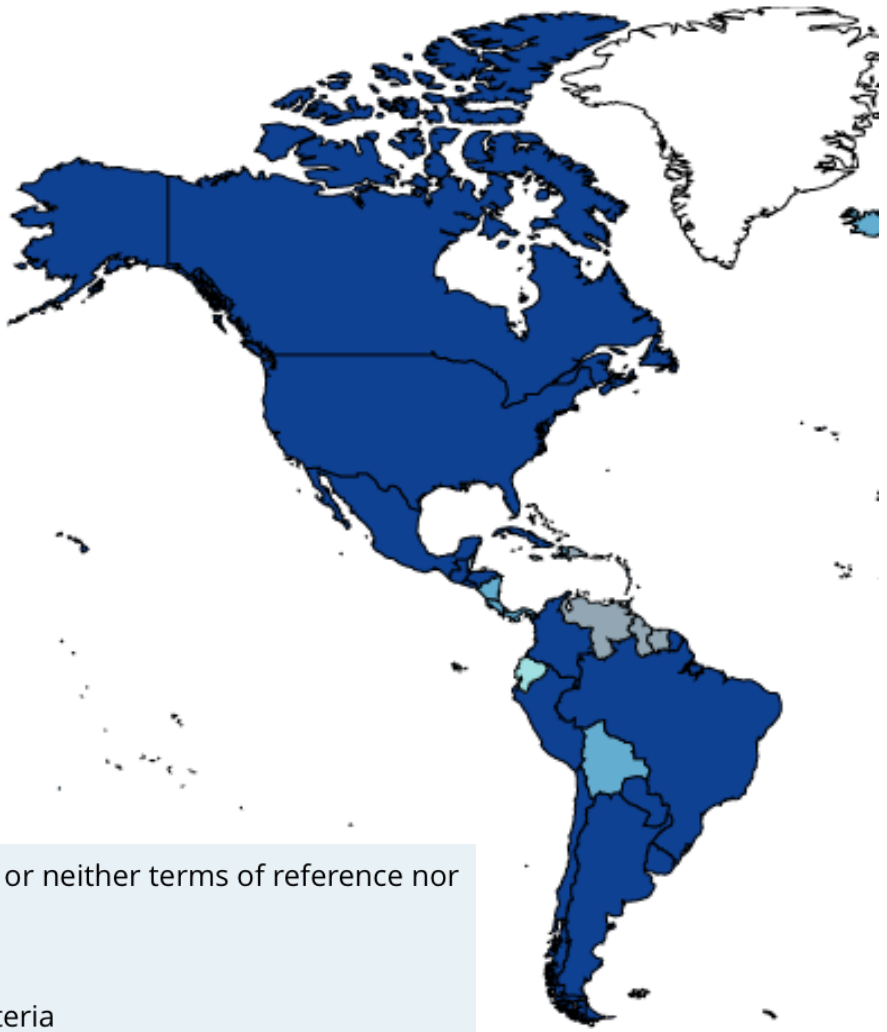
Regional Technical Advisory Group

CAPIs

NITAGs



Center for Global Health
COLORADO SCHOOL OF PUBLIC HEALTH

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Comparison of challenges for immunization schedules in HIC and Latin America

Issue	Latin America	Europe	USA
Alignment with best immunogenicity	++	+++	++
Booster doses	+	+++	+++
Crowding of injections	+/++	+++	+++
Vaccine hesitancy/spacers	+/-	++	+++
Maternal immunization	+/-	++	++
Programmatic flexibility	+	++	+/-

Summary

- **Immunization schedules in the Americas have fostered development and introduction of life-saving vaccines**
- **Boosters ≥ 12 months** crucial for long term and indirect protection
- **Primary series could be modified**
  - Ages for best immunological fit and delivery
  - **2 doses in the first year** probably sufficient
- Schedules will need to address **safety and crowding** for upcoming vaccines and confidence