Current Status of PCV Use and WHO Recommendations

SAGE

18 October 2017

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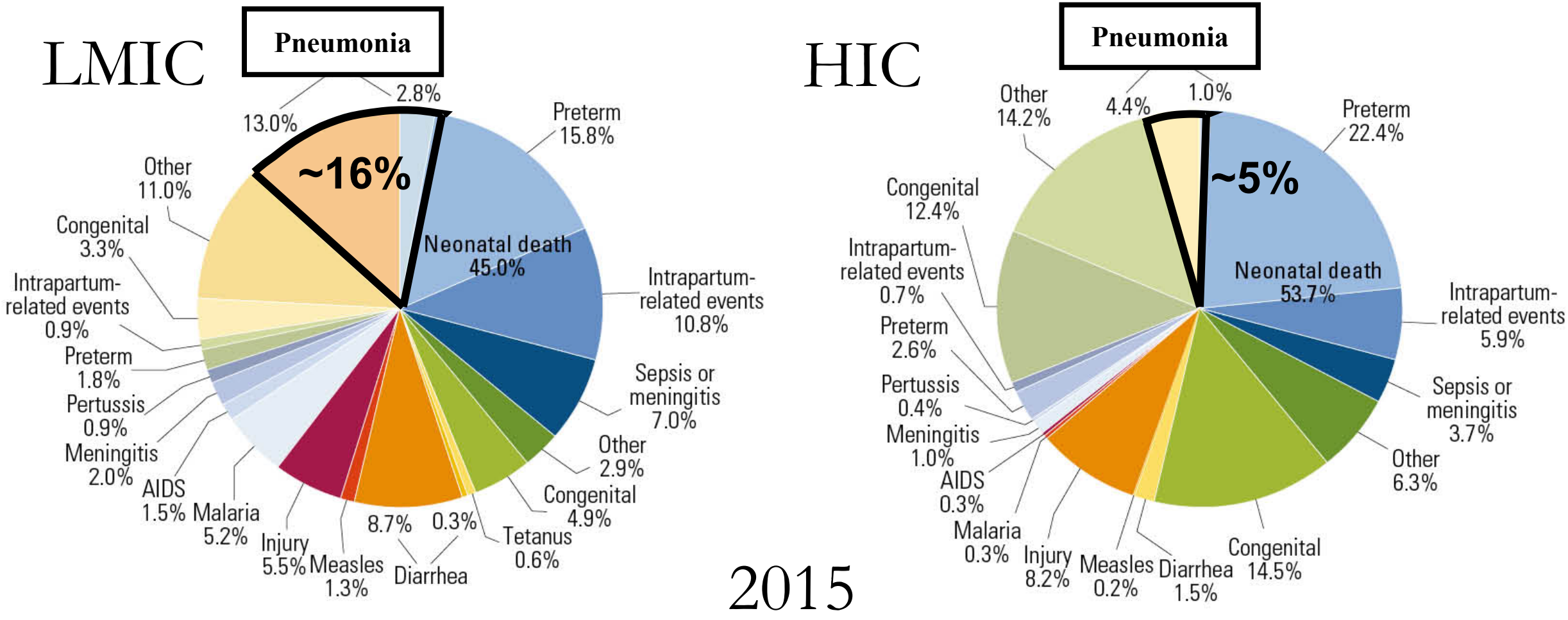
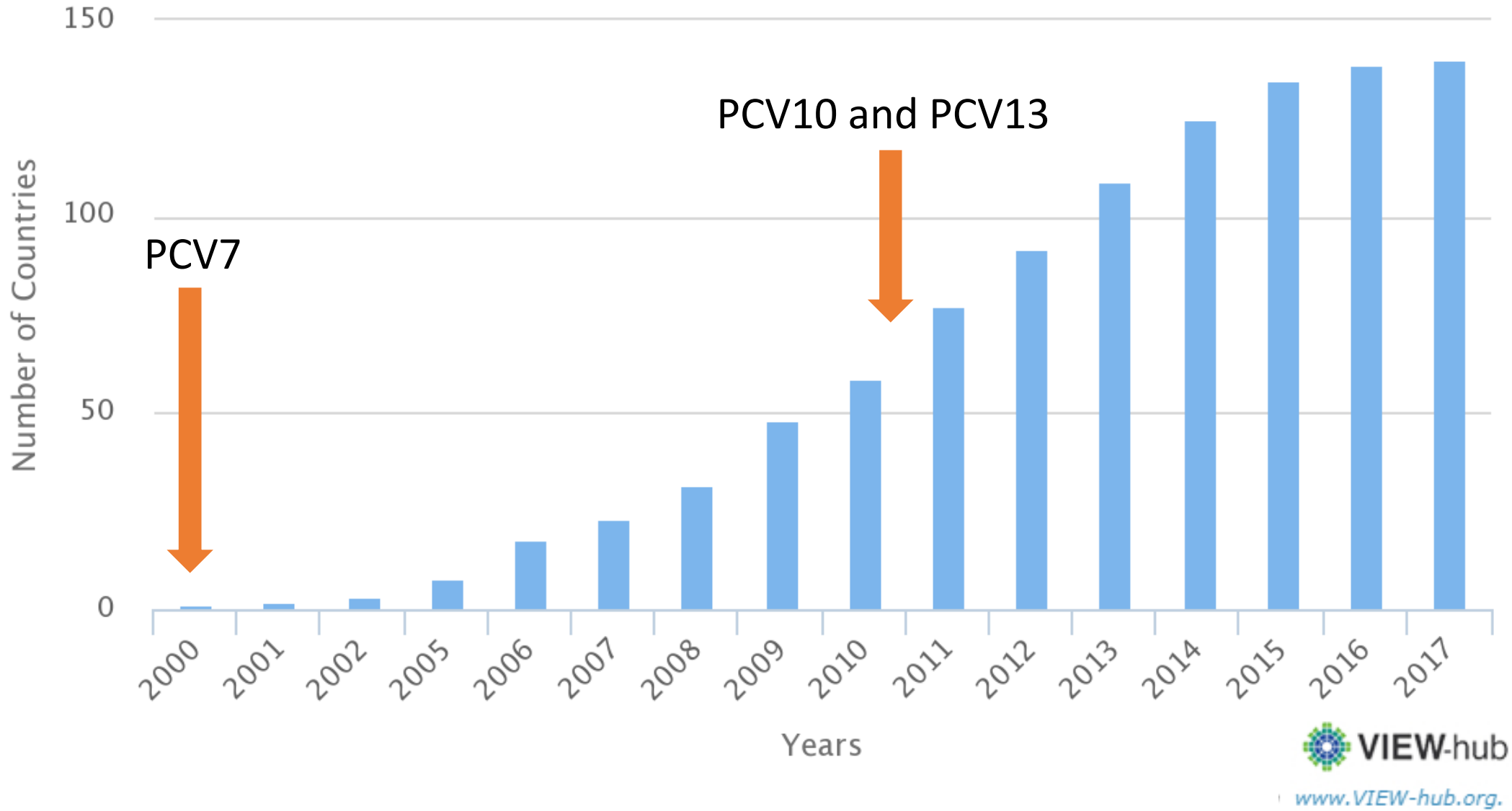
Pneumonia remains a major cause of child deaths



Black, R. E., R. Laxminarayan, M. Temmerman, and N. Walker, editors. 2016.
Reproductive, Maternal, Newborn, and Child Health. Disease Control Priorities, third edition, volume 2. Washington, DC: World Bank.
doi:10.1596/978-1-4648-0348-2. License: Creative Commons Attribution CC BY 3.0 IG)

Global PCV use has rapidly increased



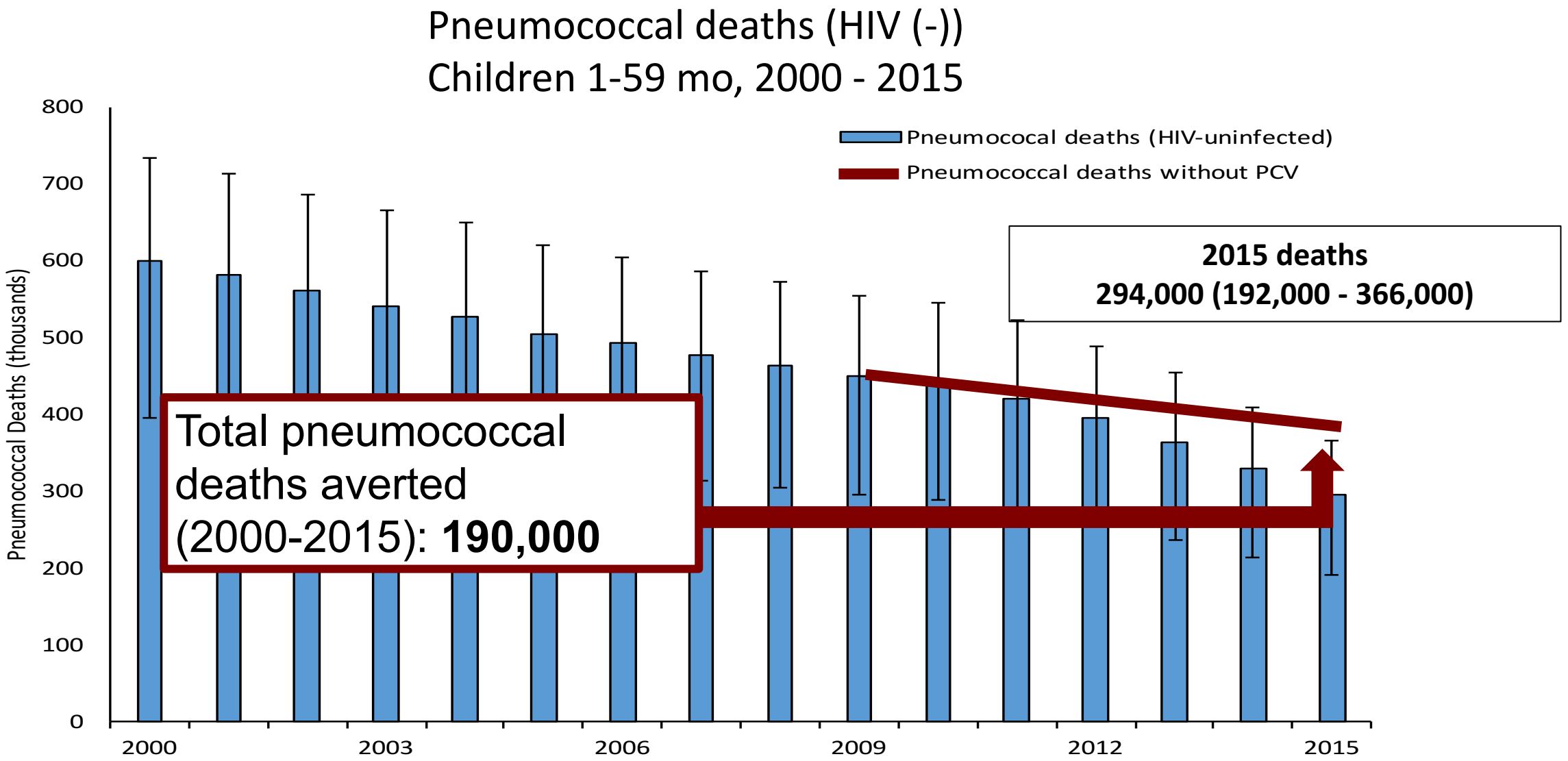
VIEW-hub

www.VIEW-hub.org.

World Health Organization

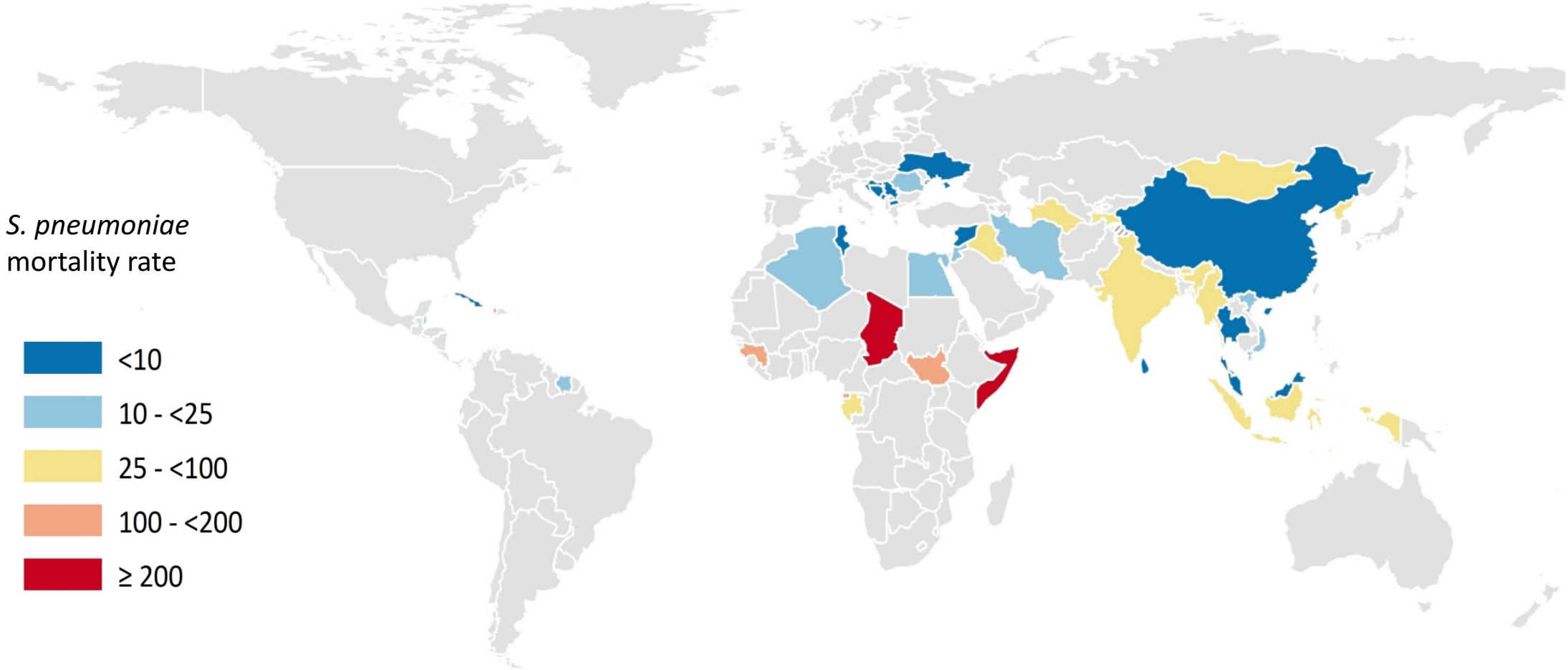
IVAC International Vaccine Access Center

PCV has substantial impact on childhood deaths



Wahl B, O'Brien KL, Greenbaum A, Liu L, Chu Y, Majumder A, Lukšić I, Nair H, McAllister D, Campbell H, Rudan I, Black R, Knoll MD. "Global, regional, and national burden of Streptococcus pneumoniae and Haemophilus influenzae type b in children in the era of conjugate vaccines: updated estimates from 2000-2015." Submitted (2017).

Few countries remain without nationwide PCV



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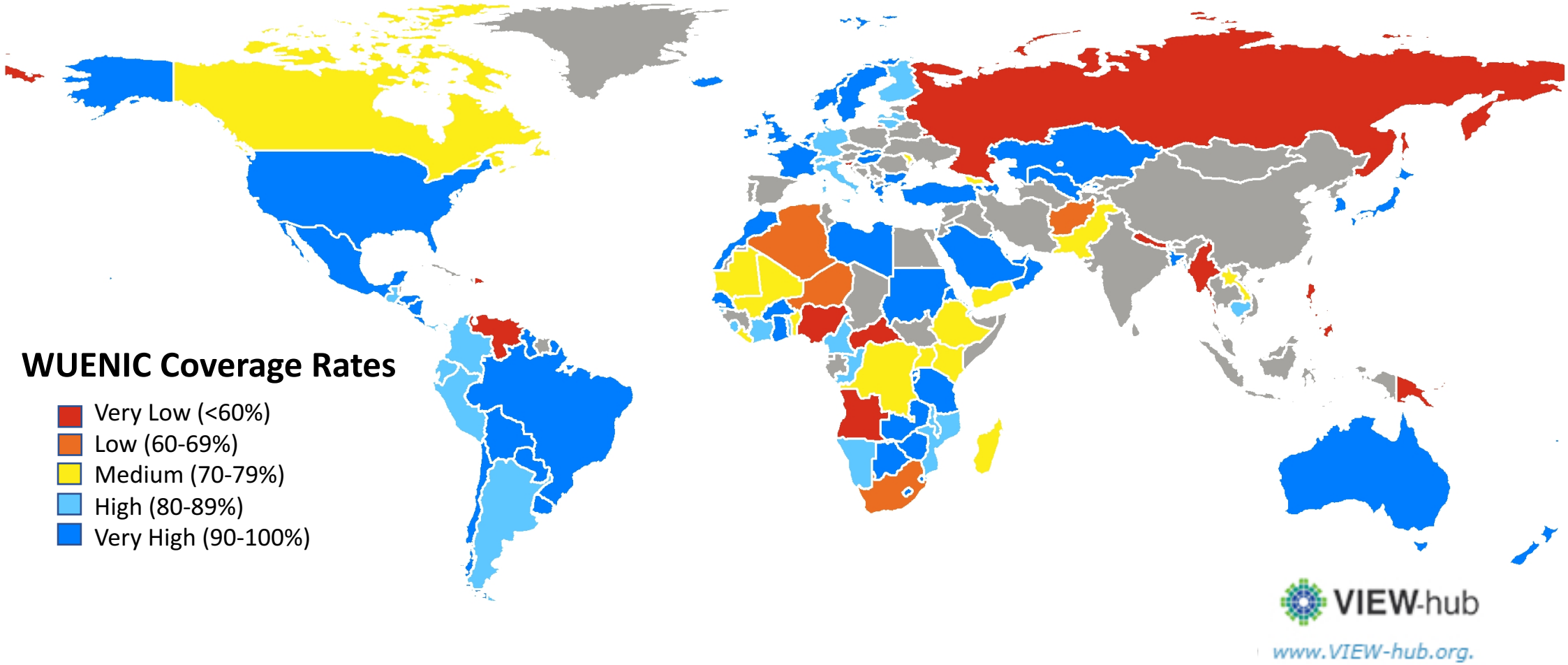
PCV coverage remains disparate



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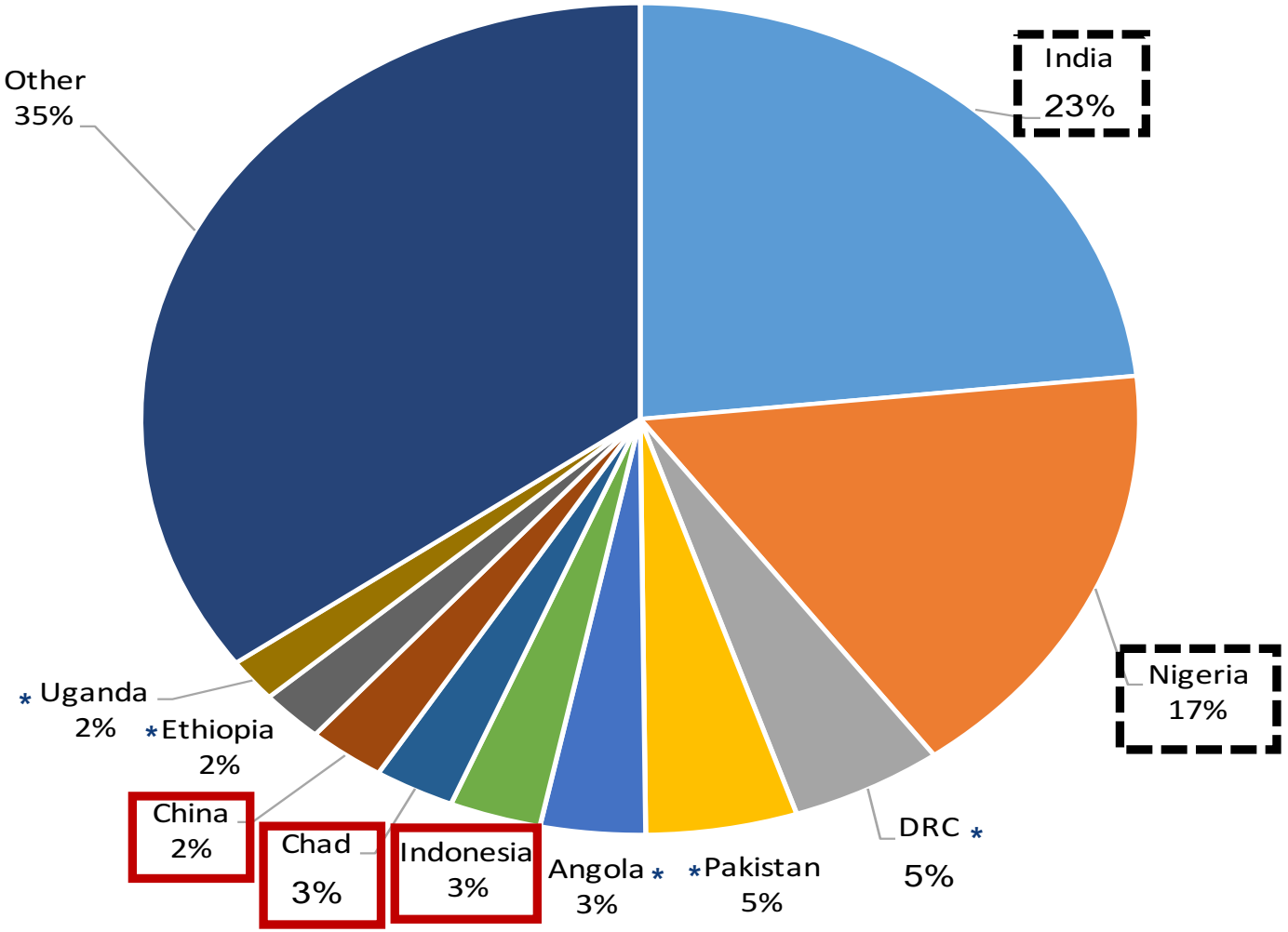
Remaining pneumococcal deaths: 2015

*** Countries that have introduced are still in early stages of introduction.**

Countries with the highest burden and have recently introduced PCV

Countries with high mortality that have not introduced PCV



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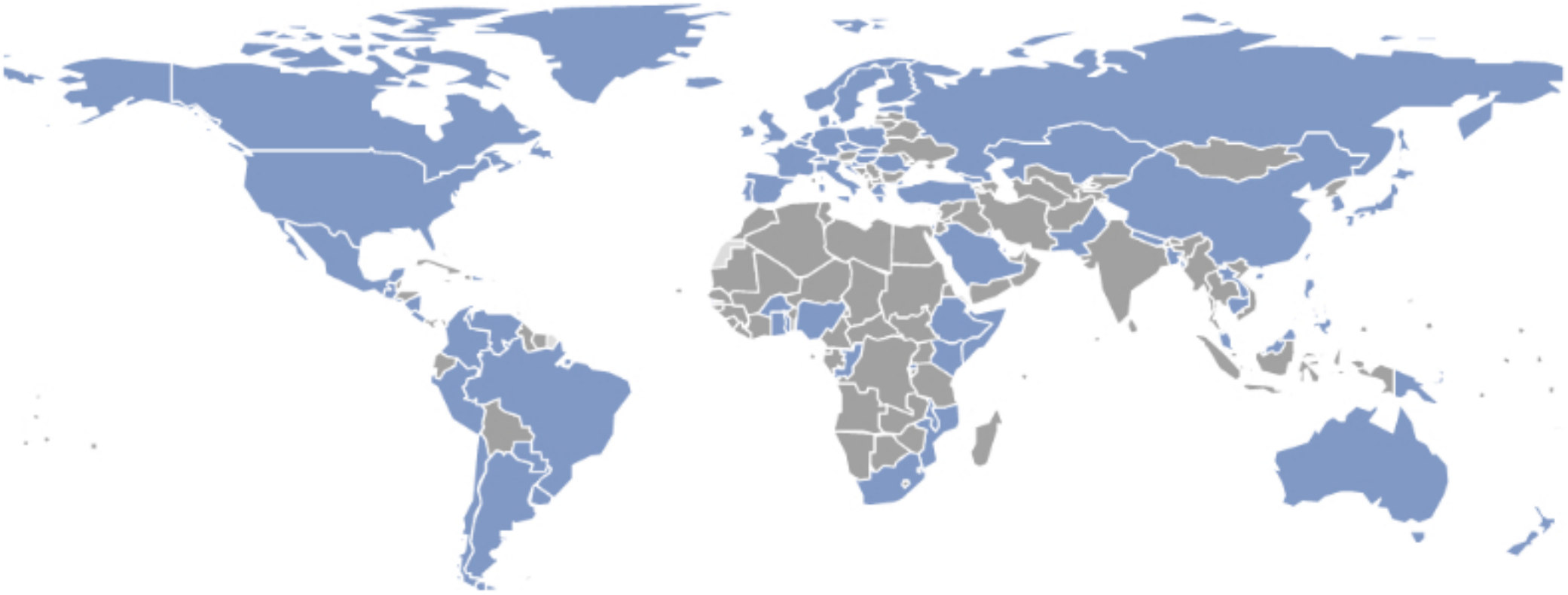
PCV impact evaluations are widespread, all regions



…but gaps remain

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Programmatic considerations for PCV optimization

- **Dosing timing** and disease burden in infants and toddlers
- PCV **coverage and timeliness**
- Crowded vaccination schedules in infancy
- Programmatic challenges of **switch in schedule or product**
- **Financial** and **sustainability** issues
  - Gavi transitioning
  - Changes in vaccine price and supply
  - New presentations
  - Sustainability in resource constrained countries

Summary of 2012 WHO Recommendations:
Schedule Choice

- WHO recommends **3p+0 or as an alternative 2p+1.**
- If disease peaks in **infants < 8 months of age, a 2p+1 schedule might not offer optimal individual protection** for certain serotypes
- Higher antibody levels are induced by the 3rd dose in a 2p+1 schedule.
- For 2p+1: d**osing intervals between the two primary doses** should be
  - **8 weeks or more** for infants ≤ 6 months
  - **4-8 weeks or more** for infants ≥ 7 months
  - **One booster dose** between 9-15 months of age

Summary of 2012 WHO Recommendations:
Product Choice

- **PCV10 and PCV13 have comparable safety and efficacy** profiles for VT serotypes
- The **choice of PCV** depends on:
  - Vaccine serotypes prevalent
  - Vaccine supply
  - Cost-effectiveness
- When primary immunization is initiated, it is **recommended that remaining doses are administered with the same product**

Summary of 2012 WHO Recommendations:
Catch Up

- Catch up vaccination as part of introduction **will accelerate herd protection**

- 2 catch up doses at interval at least 2 months apart at time of introduction to children:
  - **12-24 months of age**
  - **2-5 years of age at high risk** for pneumococcal infection.

Limitations of data supporting the 2012 WHO Recommendations:

- Largely data from
  - PCV7 using studies
  - High income settings
  - 3p+1 and 3p+0 settings
  - Studies insufficient to analyze serotype specific effects

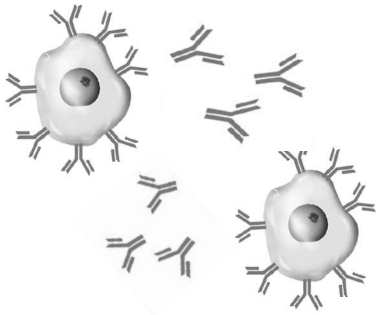
PCV Use in 2017

- PCV has proven impact in vaccinated and unvaccinated age groups
- Most countries use PCV; key countries have recently introduced
- Despite progress, pneumococcal disease burden significant
- Gaps remain in evidence of impact
- PCV WG reviewed available effectiveness and impact evidence on disease and non-disease outcomes
  - Dosing schedule
  - Product choice
  - Catch up vaccination
- How to optimize PCV impact?

PCV Modes of Action

1

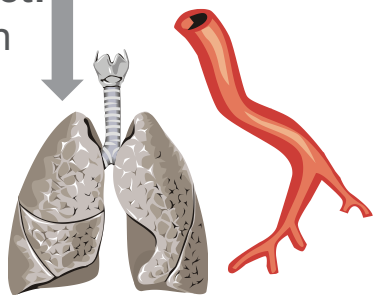
Immunization



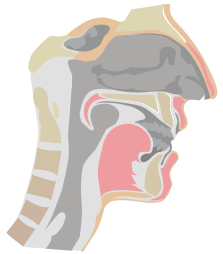
2

Immunogenic Response:
Vaccine Type specific antibody (IgG)

Direct Effect:
Protection Against Disease



Direct Effect:
Protection against Colonization



3

Indirect Effect:
Reduced Disease Transmission and Colonization of Susceptible Contacts

PICO Question I:

Schedule Comparison

How does PCV administered to **healthy children in a 2+1 schedule compare with a 3+0 schedule**, with respect to **immune response** in vaccinated children and impact on **clinical outcomes** (IPD, pneumonia, and mortality), and **nasopharyngeal carriage** in the vaccinated children as well as unvaccinated age groups through indirect protection?

PICO II Question: Product Comparison

Both products were licensed and pre-qualified on the basis of immunogenicity and non-inferiority to PCV7, which was licensed on the basis of demonstrated efficacy against invasive pneumococcal disease

PCV10 – Synflorix:

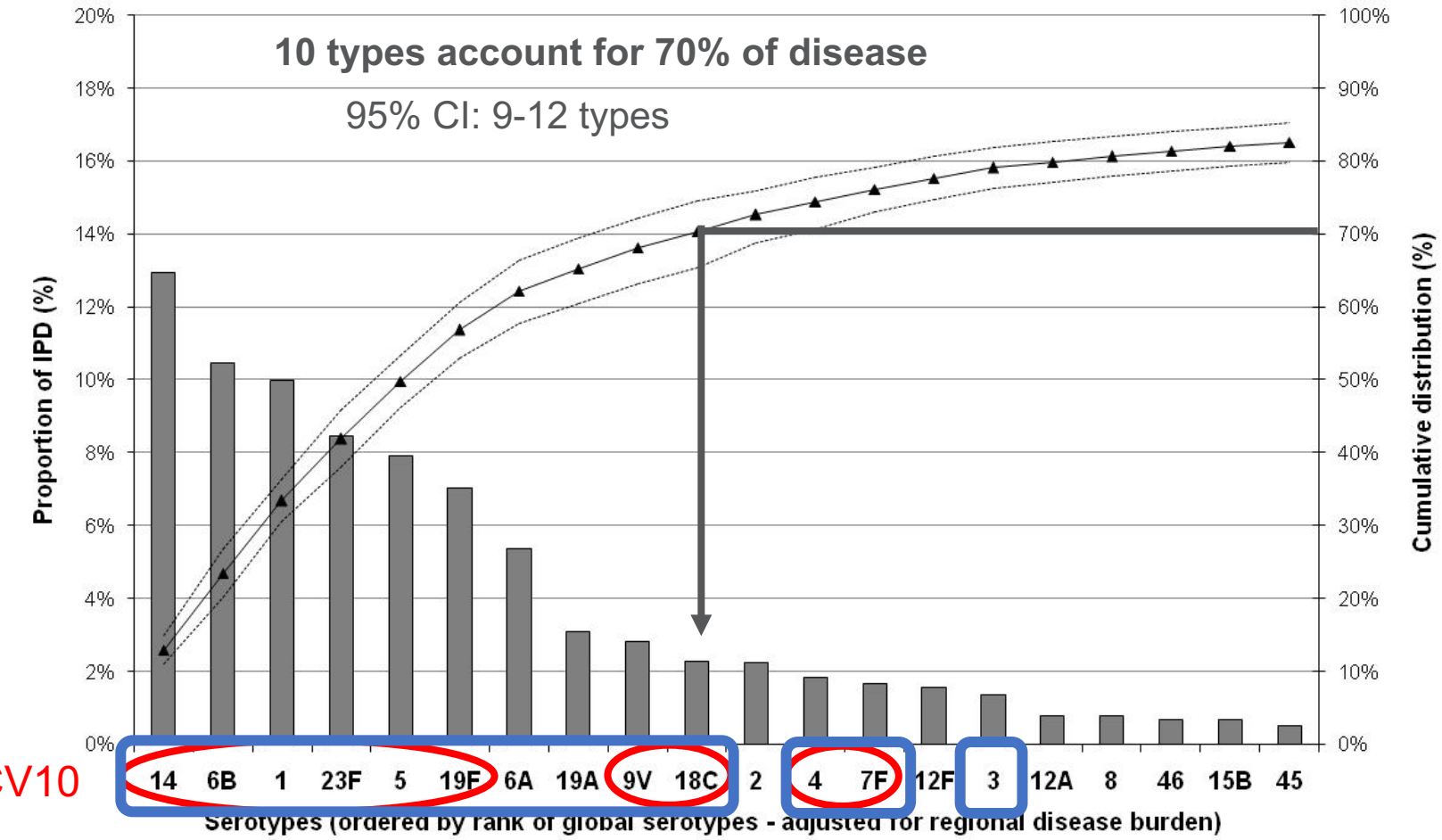
- Carrier Proteins: protein D from non-typeable Haemophilus influenzae (PD) (NTHi), Tetanus Toxoid (TT), Diphtheria Toxoid (DT)

PCV13 – Prevenar-13:

- Carrier Protein: CRM197 a non-toxic mutant of diphtheria toxin (CRM)

Product	Serotype & Carrier Protein												
	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
PCV10	1µg PD		3µg PD	1µg PD		1µg PD	1µg PD	1µg PD	1µg PD	3µg TT		3µg DT	1µg PD
PCV13	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	4.4 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM	2.2 µg CRM

Global IPD Serotype Distribution: Top 20



PCV13 PCV10

Source: GSP Version 2 Dec 5, 2008 AMC/TPP analysis

Weighted by regional disease burden (cases)

Reference: Johnson HL, *PLoS Med.*, 2010

PICO Question II:
Product Comparison

Is the impact or effectiveness of PCV10 and PCV13 (using either WHO recommended dosing schedule) different, based on data reporting **immune response** following vaccination, and impact **on NP Carriage and clinical outcomes** (IPD, pneumonia and mortality) in vaccinated children as well as unvaccinated age groups through indirect protection?

PICO Question III:

Catch-up Vaccination

*What additional value does **catch-up vaccination with 1 or 2 doses of** PCV in vaccine-naïve healthy children offer **as compared with vaccination of only age eligible children** (as per the vaccination schedule in the country) in relation to the overall impact on **pneumococcal disease**?*

Thank you

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For questions, please contact:
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