
# Pneumococcal and Meningococcal Vaccine Recommendation in the Philippines

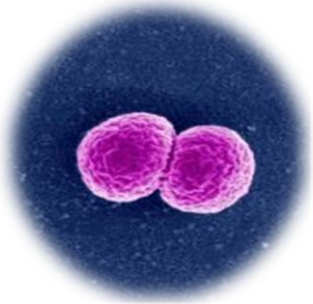
Rontgene M. Solante, MD, FPCP, FPSMID

# Rontgene Solante, MD

- PSMID, Past President
- Member, MEDSCAPE Steering Committee on Global Pneumococcal Disease Education
- Chairman, Adult Infectious Diseases and Tropical Medicine Section, San Lazaro Hospital
- Assistant Professor, UERMMMC
- Fellow/Diplomate PCP and PSMID

No Filipino, regardless of age, place of birth, or social status should die from a vaccine preventable disease.

# Invasive Meningococcal Disease (IMD)



- Neisseria meningitides
- 13 serogroups about 6 are the usual cause of IMD
- Nasopharyngeal carriage: 25% of adolescents

  5%–11% of adults
- Disease: IMD Meningitis or Meningococcemia
- Transmitted: droplet nuclei from carriers (sx/asx)
- Vaccine:
  - Meningococcal (ACWY) polysaccharide
  - Meningococcal (ACWY) conjugate

**Reference: 1.Weichselbaum A (1887)** Ueber die Aetiologie der akuten Meningitis cerebrospinalis. Fortschr Med 5:573 2. **Van Deuren M et al (2000)** Update on meningococcal disease with emphasis on pathogenesis and clinical management. Clin Microbiol Rev 13:144-66 3. **Granoff DM et al (2008)** Meningococcal vaccines. In: Plotkin (ed). Vaccines: Elsevier **Stephens DS et al (2007a)** Epidemic meningitis, meningococcemia, and *Neisseria meningitidis*. Lancet 369:2196-210 **ECDC (2014)** Surveillance of invasive bacterial diseases in Europe in 2012, Stockholm.

# Risk of Developing Invasive Meningococcal Disease[1]

- IMD is unpredictable in terms of outbreaks, epidemics, and geographic and temporal variations[1]
- Risk factors and behaviors that increase the risk of IMD disease include[2]:

## Social Factors

- Sharing of drinks and food[3]
- Smoking (active and passive)[4-6]
- Intimacy/kissing/close contact[5-7]
- Frequent visits to crowded places[4-6]

## Environmental Factors

- Close living quarters[4,5,8]
- Climate[5]

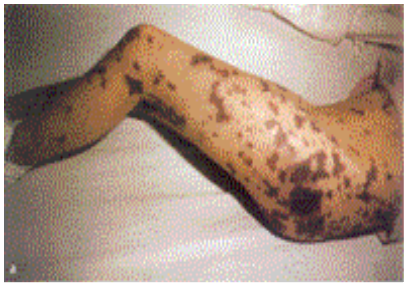
## Individual Factors

- Complement component deficiencies[4,5,9]
- Anatomic or functional asplenia[4,5,9]
- Genetic polymorphisms[5]
- Respiratory illnesses[4,5]

**The collective impact of these risk factors in determining disease susceptibility is not well understood; the disease is unpredictable**

1. Harrison LH et al. *Vaccine.* 2009;27(suppl 2):B51-B63. 2. Cohn AC et al. *MMWR Recomm Rep*. 2013;62(RR-2):1-28. 3. WHO Meningococcal meningitis fact sheet. 2012. 4. Bilukha OO, Rosenstein N. *MMWR Recomm Rep*. 2005;54(RR-7):1-21. 5. Harrison LH et al. *Vaccine*. 2009;27(suppl 2):B51-B63. 6. MacLennan J et al. *Emerg Infect Dis.* 2006;12(6):950-957. 7. Tully J et al. *BMJ*. 2006;332(7539):445-450. 8. Imrey PB et al. *Am J Epidemiol*. 1996;143(6):624-630. 9. MacNeil J. Epidemiology of serogroup B meningococcal disease, United States. Advisory Committee for Immunization Practices; 2014.

# Most Common Clinical Presentations of IMD

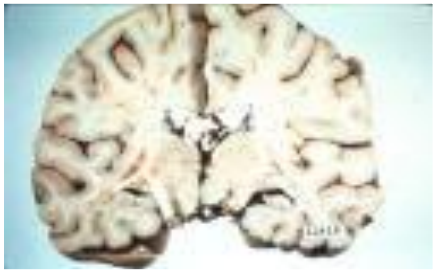


Bacteria in blood lead to increased permeability of blood vessels and inflammation associated

## Meningococcemia

- Rash
- Vascular damage
- Disseminated intravascular coagulation
- Multi-organ failure
- Shock
- Death can occur within 24 hours

**~5% to 20%of cases Up to 40% fatality rate**



Bacteria in cerebrospinal fluid lead to inflammation of meninges

## Meningitis

- Fever and headache (flu-like symptoms)
- Stiff neck
- Nausea
- Altered mental status
- Seizures

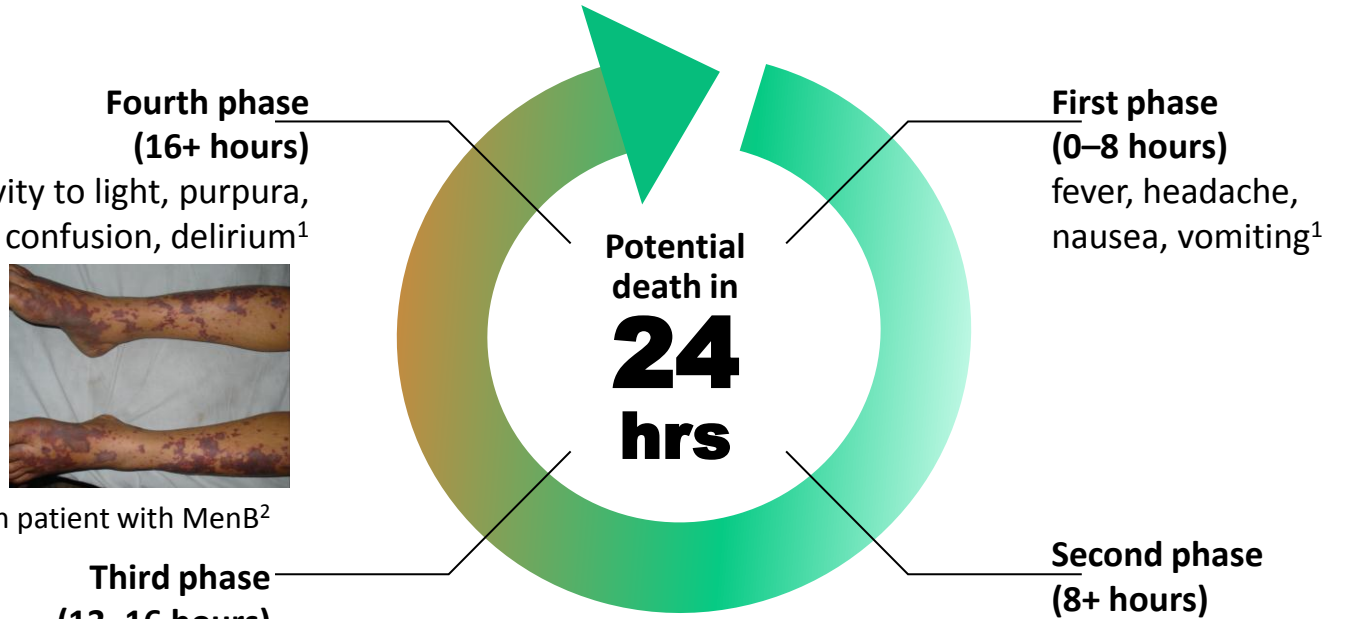
**~50% of cases**

**3%–10% fatality rate**

**1**. Rosenstein NE, et al. *N Engl J Med.* 2001;344:1378.

# Meningococcal Disease Has a Rapid Onset and Disease Course

- **Meningococcal disease can progress from nonspecific initial symptoms that can mimic the flu to death within 24 hours[1]**




Men ACWY serogroup A C W Y meningococcal disease.

Reported in Thompson study, patients ages 15 to 16.


1. Thompson MJ et al. *Lancet.* 2006;367(9508):397-403.
2. Agarwal MP et al. *CMAJ*. 2010;182:E18.

# Outbreaks of IMD

## In the last decade, outbreaks of IMD have occurred globally[1]

| | |
|---|---|
| **Africa** | • 1 Jan–15 Mar 2009: large-scale outbreak affecting countries of the African Meningitis Belt[2]<br>– 24,868 suspected cases, including 1,513 deaths[2]<br>– 85% of cases centred on one epidemic location in northern Nigeria and Niger[2] |
| **Asia** | • India (2005): 444 cases, 62 deaths[3]<br>• Philippines (2005): 78 cases, 30 deaths[4] |
| **South America** | • Brazil (2009): 194 cases, 50 deaths[5]<br>• Chile (2012): 60 cases, 16 deaths[6] |
| **Oceania** | • New Zealand (2001): 650 cases[7]<br>• New Zealand (2010): 96 cases, 6 deaths[7] |
| **USA** | • Princeton University (2013): year-long outbreak of MenB; 8 cases[8]<br>• University of California, Santa Barbara (2013): 4 cases in 2 weeks[8] |

**(1) Cohn A, MacNeil JR. (2013)** CDC Travelers' Health – Yellow book 2013. **(2) WHO. Meningococcal Disease: situation in the African Meningitis Belt. 2009**. **(3) Singhal S, et al. (2007)** *Emerg Infect Dis*;13:1614–16; **(4) WHO. (2005)** Meningococcal disease in the Philippines - update **5. Cardoso CW, et al. (2012)** *Vaccine* 2012;30:5541–6; **(6) Chilean Ministry of Health. Plan of action W-135. 2013. (7) Lopez LK, et al. (2011)** ESR: Wellington, New Zealand; **(8) National Foundation for Infectious Diseases**. Addressing the Challenges of Serogroup B Meningococcal Disease Outbreaks on Campuses. May 2014.

# IMD in the Philippines

- Between 17 and 35 cases of meningococcal disease were reported annually to the Department of Health between 2004 and 2008, with the exception of 2005 when 115 cases were reported.
- ***Incidence per population in the nonoutbreak years:***
  - Between 0.0 and 0.04/100,000 with marked variability between regions
  - Between 34% and 50% of cases were reported in children **aged <5 years**.
  - In 2005, most cases (88/115) were reported in the **5–49 years age group**
- ***Meningococcal serogroup A outbreak:***
  - *Regions of Baguio City, Mt Province and Ifugao (between 2004 and 2005)*
    - 98 cases (**33% mortality**) reported to the WHO up to January 2005
  - *San Jose, Sipalay, Negros Occidental (1989)*
    - Probably due to serogroup A
    - 10 cases, incidence 65/100 000 population
    - All but one case had meningococcaemia
    - **Mortality was 50%**
    - Seven of 10 cases occurred in individuals aged **less than or equal to 19 years**

Vyse, et al. Epidemiol. Meningococcal disease in Asia: an under-recognized public health burden. Infect. (2011), 139, 967–985

# San Lazaro Hospital Census Jan-Aug 2017

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| B | 118 | 117 | 753 | 464 | 1217 | 1233*^ | 1 | 74*^ | 1308 |
| histosomiasis | 1756 | 792 | 97 | 1434 | 1531 | 1048*^ | 1 | 463*^ | 1512 |
| akebite | 23 | 2 | - | 8 | 8 | 4 | - | 1 | 5 |
| tanus Non-Neo | 325 | - | 67 | 191 | 258 | 160 | 1 | 1 | 162 |
| Meningitis | 180 | 50 | 30 | 101 | 131 | 109* | - | 25* | 134 |
| phoid Fever | 53 | 16 | 5 | 3 | 8 | 11^ | - | 7 | 18 |
| ricella | 56 | 1 | 24 | 26 | 50 | 65*^ | - | - | 65 |
| | 220 | 8 | 192 | 82 | 274 | 259* | - | 2 | 261 |

#Admission DX • Confirmed cases^includes revised dx*2016 admissions, discharges 2017°revised to PCAP, Lower GI bleeding, sepsis$revised to SVI,CAP-MR

**Special Disease Surveillance under PIDSR (Jan-Aug.1,2017)**

| ITDs (No. Tested) | Isolates/ Serotypes | No. (%) | ITDs (No. Tested) | Isolates/ Serotypes | No. (%) |
|---|---|---|---|---|---|
| Dengue (N=200) | Dengue 1 | 31 | Diphtheria (N=56) * | | |
| | Dengue 2 | 9 | | | |
| | Dengue 3 | 45 | | C. Diphtheria (Culture + PCR) | 31(55%) Δ |
| | Dengue 4 | 6 | | | |
| | TOTAL | 91(45%) | | | |
| HFMD (N=68) | Enterovirus | 26(38%) | Japanese Encephalitis (N=7) | Japanese enceph<br>4- Negative<br>2- Pending Result | 1(14%) |
| SARI (N=166) | Influenza B<br>Influenza A(H1N1)<br>Influenza A(H3)<br>Influenza A(No sub-type) | 1 (1%)<br>13(9%)<br>1(1%)<br>7(4%) | Measles (N=123) | Rubella IgM °<br>Measles IgM<br>28- Pending result | 2 (2%)<br>2(2%) |
| Meningococcemia (N=23) | N. Meningitidis-PCR | 14(60%) | Rotavirus Disease (N=204) | Rotavirus | 77 (38%) |

* w/ admitting dx as ATP (N=6), Parotitis (N=2), PCAP (N=1) °1 Pregn

FM-SS-EPI-002
Date Effective: March 18, 2016, Rev.

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# Meningococcal Vaccine Development and Conjugation

## Plain polysaccharide vaccines

- The first meningococcal vaccines developed were plain polysaccharide vaccines[1]
- *MPSV 4 (Menomune*™[2]) was the first quadrivalent meningococcal vaccine approved for use (USA)
- *MPSV2 (Mencevax*™ AC), MPSV3 (*Mencevax*™ ACW,) and MPSV4 (*Mencevax*™ ACWY) then was made available[1]

**1981**

## Conjugate vaccines

**1999** — **MenC conjugate vaccines**[3]

**Quadrivalent conjugate vaccines:**

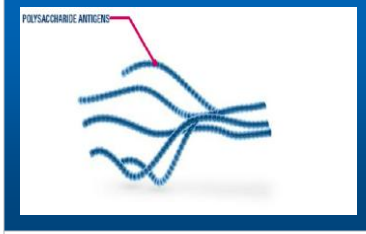
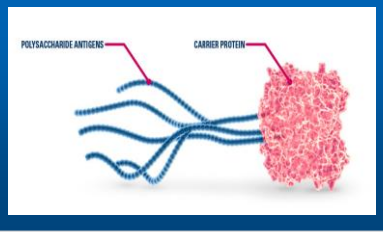
**2005** — *MCV4 DT (Menactra*™) USA[4]

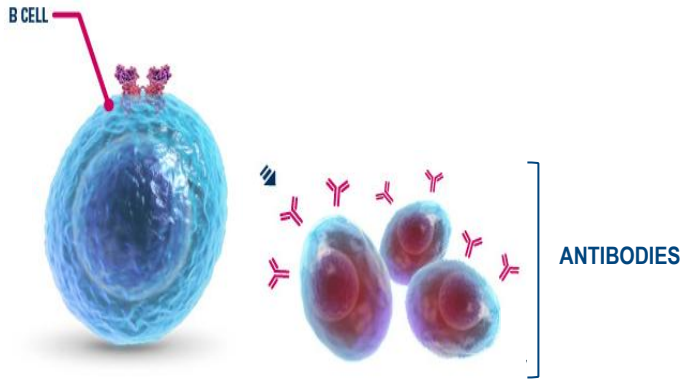
**2010** — *MCV4 CRM (Menveo*™) USA and EU[5,6]

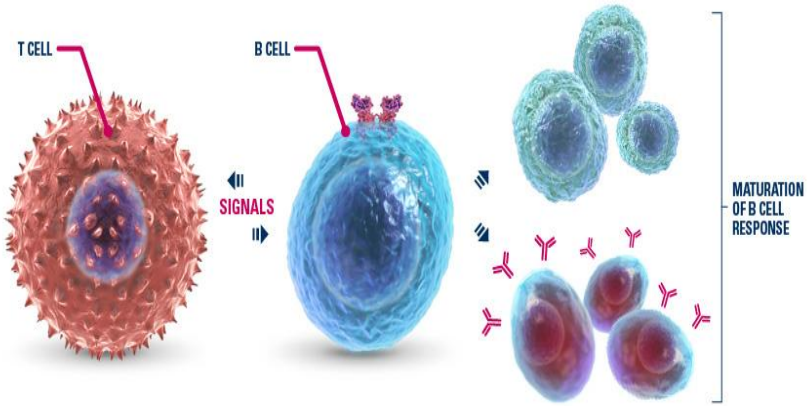
**2012** — *MCV4 TT (Nimenrix*™*)* EU[7]

1. Miller J, *et al. Adv Prev Med* 2011; Article ID 846756; 2. FDA. Menomune PI 2013;
3. Gasparini R, *et al*. *Hum Vaccin* 2011;7:1–13; 4. FDA. Menactra PI 2014; 5. FDA. Menveo PI 2013;
6. EMA. Menveo SmPC 2015; 7. EMA. Nimenrix SmPC 2015.

# Vaccine Conjugation and Immune memory

|  **Polysaccharide Vaccines[1–3]** |  **Conjugate Vaccines[1–4]** |
|---|---|
| Contain polysaccharide antigens | Contain polysaccharide antigens covalently linked to a carrier protein |
| T cell–*independent* immune response | T cell–*dependent* immune response |
| Stimulate B cells to produce antibodies | Stimulate T cells to help B cells produce antibodies and generate immune memory |




**1.** Siegrist CA. In: Plotkin et al, eds. *Vaccines.* 5th ed. Philadelphia, PA: Saunders Elsevier; 2008:17-36. **2.** de Roux A, et al. *Clin Infect Dis.* 2008;46:1015-1023. **3.** Clutterbuck EA, et al. *Immunology.* 2006;119:328-337. **4.** Pollard AJ, et al. *Nat Rev Immunol*. 2009;9:213-220.

# Quadrivalent (ACWY) meningococcal conjugate vaccine formulations

| Vaccine composition | *MCV4 TT (Nimenrix™)*[1, 5] | *MCV4 CRM (Menveo™)*[2,3] | *MCV4 DT (Menactra™)*[4] |
|---|---|---|---|
| **Carbohydrates** | MenA PS (5 µg)<br>MenC PS (5 µg)<br>MenW PS (5 µg)<br>MenY PS (5 µg) | MenA OS (10 µg)<br>MenC OS (5 µg)<br>MenW OS (5 µg)<br>MenY OS (5 µg) | MenA PS (4 µg)<br>MenC PS (4 µg)<br>MenW PS (4 µg)<br>MenY PS (4 µg) |
| **Carrier protein** | TT (44 µg) | $CRM_{197}$ (32.7–64.1 µg) | DT (48 µg) |
| **Excipients** | Sodium chloride, water | Sodium dihydrogen phosphate monohydrate, disodium phosphate dihydrate, sodium chloride, water | Sodium chloride, water |

**The compositions of the available quadrivalent conjugate vaccines are different, with different carrier proteins utilised for each vaccine**

DT, diphtheria toxoid; OS, oligosaccharide; PS, polysaccharide; TT, tetanus toxoid.
*Based on EU and US product labels.
1. EMA. Nimenrix SmPC 2015; 2. EMA. Menveo SmPC 2015; 3. FDA. Menveo PI 2013;
4. FDA. Menactra PI 2014. 5 Nimenrix LPD Rev 0 dated 17 December 2015

# Quadrivalent meningococcal conjugate vaccine indications*

| | *MCV4 TT (Nimenrix™)*[1, 5] | *MCV4 CRM (Menveo™)*[2,3] | *MCV4 DT (Menactra™)*[4] |
|---|---|---|---|
| **Age groups** | **EU/ PH**: Individuals from 12 months of age. No upper age limit | **USA**:[2] Individuals 2months–55 years of age **EU**:[3] ≥2 years | **USA**: Individuals 9 months to 55 years of age |
| **Indications** | Active immunisation against invasive disease caused by *Neisseria meningitidis* groups A, C, W and Y | Active immunisation of individuals at risk of exposure to *N. meningitidis* groups A, C, W and Y | Active immunisation to prevent invasive meningococcal disease caused by *N. meningitidis* serogroups A, C, W and Y |

*MCV4 TT (Nimenrix™)* is licensed from 1 year of age and can be given as a single dose schedule starting 12 months of age [5]

*Based on EU and US product labels.

1. EMA. Nimenrix SmPC 2015; 2. FDA. Menveo PI 2013; 3. EMA. Menveo SmPC 2015;
4. FDA. Menactra PI 2014. 5 Nimenrix LPD Rev 0 dated 17 December 2015

# Vaccine Presentation

| Presentation | Storage | Administration |
|---|---|---|

- Powder and solvent for solution for injection in a pre-filled syringe
- After reconstitution, a single 0.5-mL dose
- The solvent is clear and colorless.

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# Storage

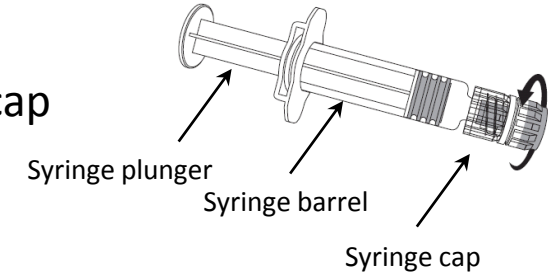
Presentation | **Storage & Handling** | Administration

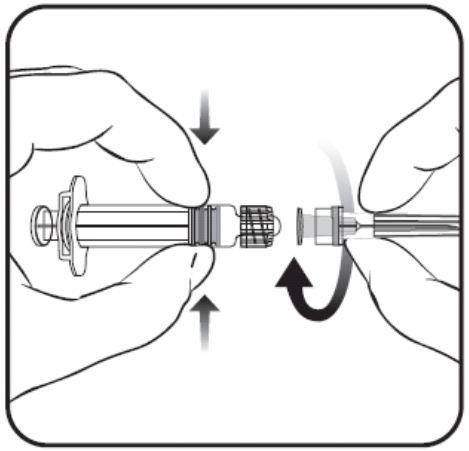
- Refrigerate at 2–8°C for up to 3 years
- NOT to be frozen
- After reconstitution, the vaccine should be used immediately
  - However, chemical and physical in-use stability has been demonstrated for 8 hours at 30°C

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# Vaccine Handling

- Holding the syringe barrel in one hand unscrew the syringe cap (anticlockwise)
- Twist the needle clockwise into the syringe until locked – remove the needle protector
- Add the solvent to the powder. Shake well until the powder is completely dissolved
- Reconstituted vaccine is a clear colourless solution
- After reconstitution, the vaccine should be used immediately
- Any unused product or waste material should be disposed of in accordance with local requirements



**_MCV4 TT (Nimenrix™ )_must be reconstituted by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder**

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# Administration

Presentation | Storage | **Administration**

- Intramuscular injection only, preferably in the deltoid muscle
  - In toddlers aged 12–23 months, the vaccine may also be administered in the anterolateral part of the thigh
- Should never be administered intravascularly, intradermally or subcutaneously

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# Safety and Tolerability

- The safety of MCV4 TT (*Nimenrix™)* was evaluated using a pooled analysis of 9,621 individuals aged 12 months to 55 years who had received one dose of *the vaccine* in clinical studies[1]

Side effects observed across all age groups:

*Very common (≥1/10)*: swelling, pain and redness at injection site, fatigue, irritability, drowsiness, headache, fever, loss of appetite

*Common (≥1/100 to <1/10):* gastrointestinal symptoms (including diarrhoea, vomiting and nausea), injection site haematoma

*Uncommon (≥1/1,000 to <1/100):* insomnia, hypoaesthesia, dizziness, crying, pruritus, rash, myalgia, pain in extremity, malaise, injection site reactions including induration, pruritus, warmth, anaesthesia

*Rare (≥1/10,000 to <1/1,000):* large swelling of the vaccinated limb associated with redness

Click below for the safety data from each age group:


Toddlers


Children


Adolescents


Adults


Elderly

Safety overview

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# Co-administration with other vaccines

*MCV4 TT* can be co-administered with one or more of the following vaccines:

- Hepatitis A and B vaccines (HAV; HBV)
- Inactivated polio vaccine (IPV)
- *Haemophilus influenzae* type b vaccine (Hib)
- Measles–mumps–rubella (MMR) M
- Measles–mumps–rubella–varicella (MMRV) vaccines
- Unadjuvanted seasonal influenza vaccine
- 10-valent pneumococcal conjugate vaccine
- Combined diphtheria–tetanus–acellular pertussis–hepatitis B–inactivated polio–*Haemophilus influenzae* type b vaccine (DTaP-HBV-IPV/Hib)

**If MCV4TT (*Nimenrix™*) is to be given at the same time as another injectable vaccine, different injection sites should be used**

Reference: EMA. Nimenrix SmPC 2015 .2,. Nimenrix LPD Rev 0 dated 17 December 2015

# The safety and immunogenicity of *MCV4 TT* has been evaluated across multiple age groups

## Toddlers[1]
12–23 months

- Immunogenicity comparable with MenC-$CRM_{197}$
- Can be co-administered with MMR, MMRV, DTaP-HBV-IPV/Hib and PCV10
- Persistence of immune response has been evaluated up to 5 years post-vaccination

## Children[1]
2–10 years

- Immunogenicity comparable with MPSV4 and MenC-$CRM_{197}$
- Persistence of immune response has been evaluated up to 44 months post-vaccination
- Booster response observed after priming 4 years earlier

## Adolescents[1,2]
11–17 years

- Immunogenicity comparable with MPSV4 and MenACWY-DT[1]
- Can be co-administered with HAV/HBV vaccine[1]
- Persistence of immune response has been evaluated up to 5 years post-vaccination[2]

## Adults[1]
18–55 years

- Immunogenicity comparable with MPSV4
- Persistence of immune response has been evaluated up to 3 years post-vaccination
- Can be co-administered with seasonal influenza vaccine

## Elderly[1]
≥56 years

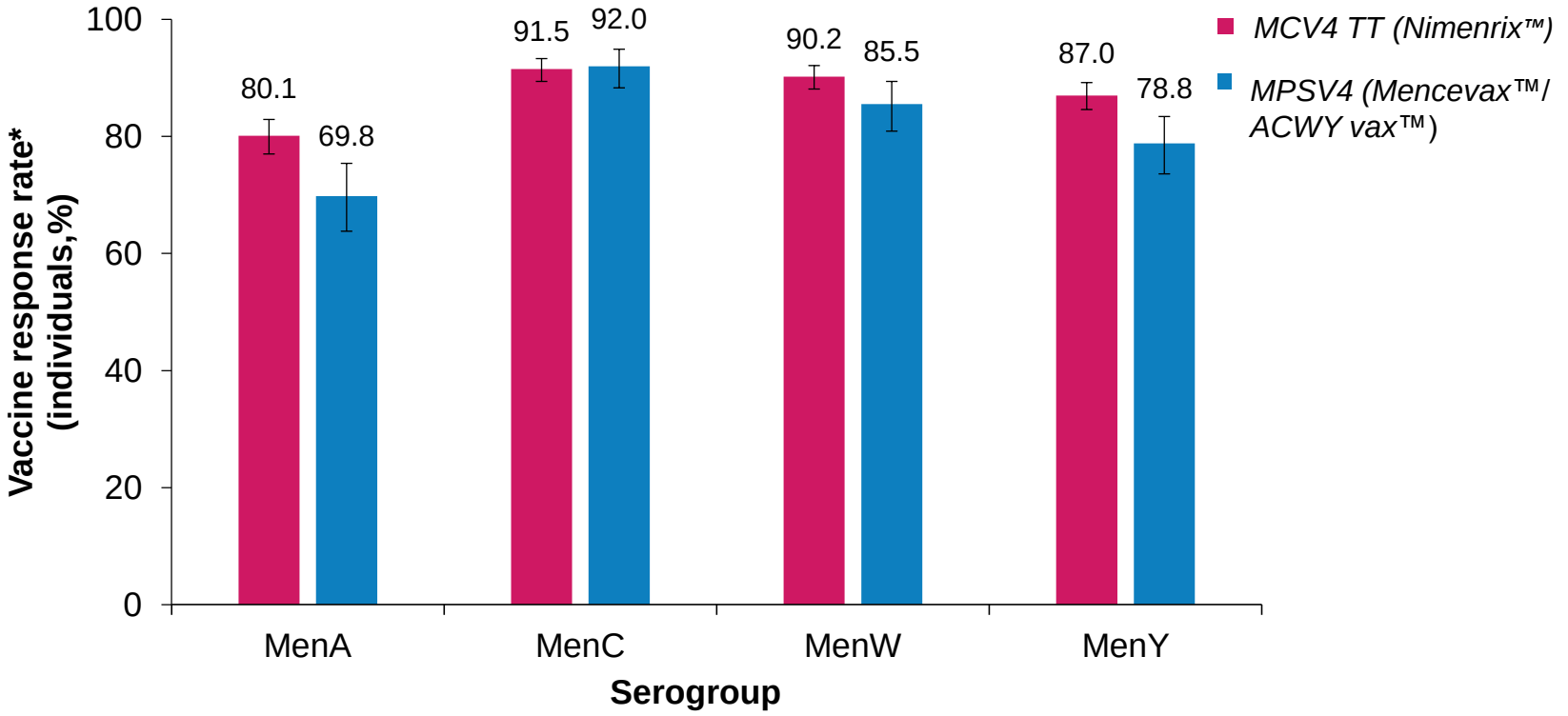
- Immunogenicity comparable with MPSV4

DTaP, diphtheria-tetanus-acellular pertussis; HAV, hepatitis A virus; HBV, hepatitis B virus; Hib, *Haemophilus influenzae* type b; IPV, inactivated polio vaccine; MMR, measles–mumps–rubella; MMRV, measles–mumps–rubella–varicella; PCV10, 10-valent pneumococcal conjugate vaccine.

1. EMA. Nimenrix SmPC 2015; 2. Pfizer Data on file (Study MenACWY-TT-059 [111670]) 2014.

# Adults: non-inferior vaccine response rates* with MCV4 TT compared with MPSV4

**Age 18–55 years**




*MCV4 TT* was non-inferior to MPSV4 in terms of vaccine response 1 month post-vaccination

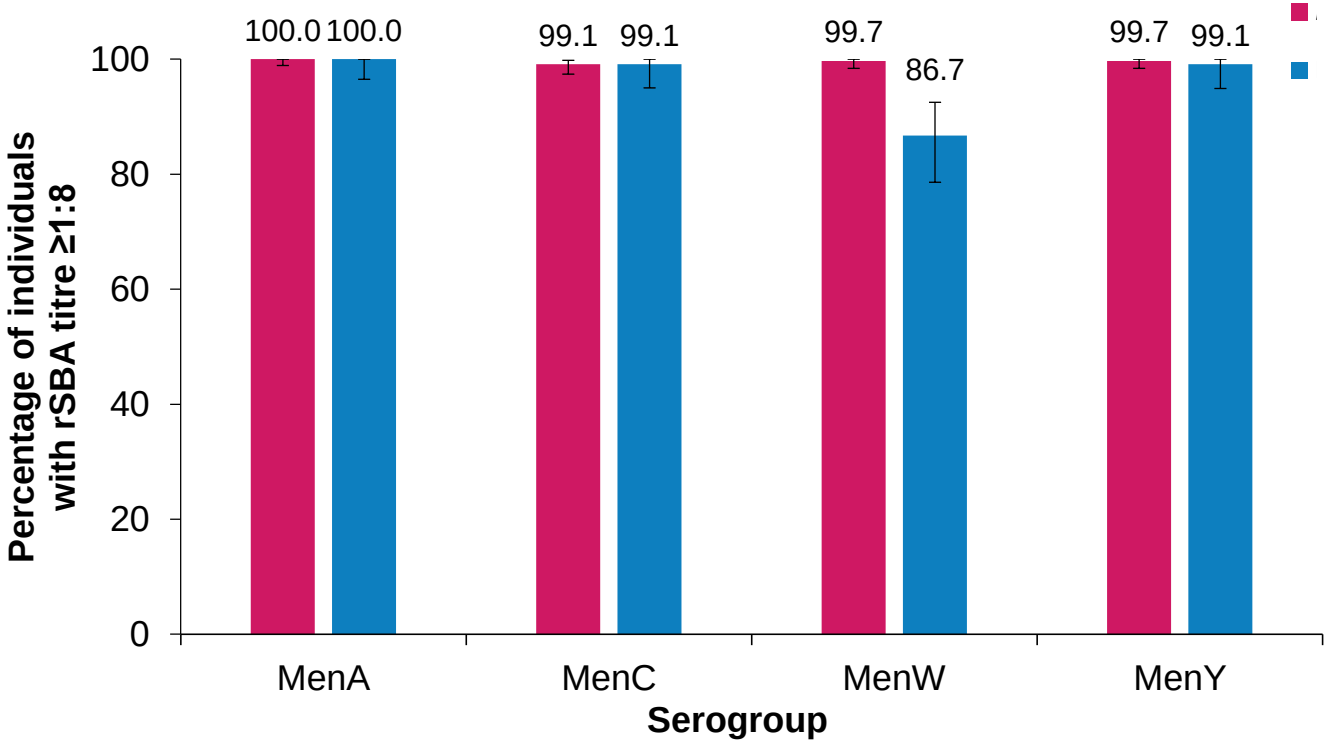
*Vaccine response was defined as rabbit complement serum bactericidal antibody (rSBA) titre ≥1:32 in initially seronegative (rSBA titre <1:8) subjects and rSBA titre ≥4-fold the pre-vaccination titre in initially seropositive (rSBA titre ≥1:8) subjects. According-to-protocol cohort for persistence. Error bars represent 95% CI.

EMA Nimenrix SmPC 2015

# Adults/adolescents: persistence of immune response evaluated up to 3 years post-vaccination with MCV4 TT

**Age 11–55 years**

Up to **3** years persistence



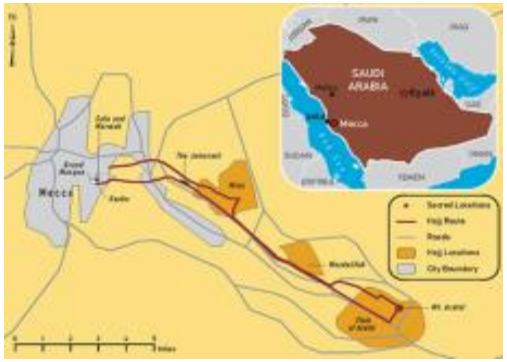

3 years after vaccination, ≥99.1% of adolescents and adults (11–25 years) vaccinated with *Nimenrix™* retained rSBA titres ≥1:8 for serogroups A, C, W and Y

rSBA, rabbit complement serum bactericidal antibody.

Borja-Tabora C, *et al. BMC Infect Dis* 2013;13:116.

# Hajj: Annual Pilgrimage to Mecca is the Largest annual mass gathering in the world

- Required at least once of all able-bodied adult Muslims who can afford to do so
- More than 2-3 million Muslims make Hajj each year
  - Due to Muslim (lunar-based) calendar, Hajj shifts approximately 10 days earlier every year, leading to seasonal variations in weather
- Because of the sheer number and crowding of people, panic can easily trigger stampedes




Feldman C, Abdulkarim E, Alattar F, et al. Pneumococcal disease in the Arabian Gulf: Recognizing the challenge and moving toward a solution. *J Infect Public Health*. 2013 Jul 31. pii: S1876-0341(13)00096-8. doi: 10.1016/j.jiph.2013.06.004. [Epub ahead of print]

# Potential Public Health Risks during mass gatherings

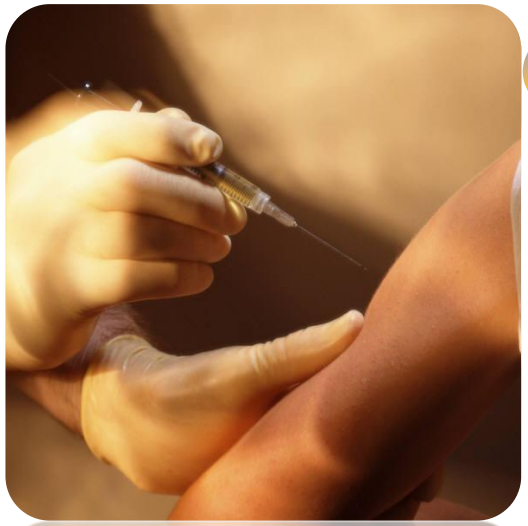
- **Risk of Importing Infectious disease** to the country hosting the gathering
- **Transmission of Infectious diseases** among the visitors and travellers during these events
- **National and International spread of Infectious** diseases as the visitors who have acquired an infectious disease return to their own country
- **Difficulty in implementing control measures** like contact tracing in cases of outbreaks due to mobility of people during the gatherings

Centers for Disease Control and Prevention. CDC Health Information for International Travel 2014. New York: Oxford University Press; 2014.

# Health regulations and guidelines: Hajj Vaccination

**Mass gatherings such as Hajj and Umrah can significantly increase the risk for infectious diseases**

**For example, outbreaks of meningococcal disease used to be a problem. We now require all pilgrims to receive the meningococcal vaccine**



| Required Vaccinations | Target group |
|---|---|
| **Meningococcal vaccination** (At least 10 days before Hajj – Compulsory for ALL) | All pilgrims and children over two, as well as pregnant women & all locals living in Hajj premises, in addition to HCWs and security staff protecting pilgrims |
| **Vaccination against yellow fever** (At least 10 days before Hajj) | Pilgrims hailing from places affected by the disease, such as African regions, and some South-American countries |
| **Polio vaccination** (At least 10 days before Hajj, another dose given upon arrival | Pilgrims of all age groups hailing from regions stricken by polio |

| Recommended Vaccinations | |
|---|---|
| **Vaccination against pneumococcal pneumonia** | Patients with such diseases as sickle cell anemia, renal failure, immunodeficiency, and splenectomy. It could be given, also, to the elders and those suffering from chronic liver, heart and lung diseases |
| **Vaccination against seasonal influenza** (Six weeks before Hajj) | All pilgrims, especially the elders, those suffering from chronic diseases, patients with immunodeficiency (natural and acquired alike), as well as patients with metabolic diseases, obese persons, and pregnant women beginning with the fourth month |

SOURCE: Health Regulations for Travellers to Hajj and Umrah, KSA Ministry of Health
http://www.moh.gov.sa/en

# PSMID Recommendation

***Meningococcal vaccination is recommended for high-risk groups.***

**PSMID recommends meningococcal vaccination for 2 years old and above belonging to the following high-risk groups:**

- People with functional or anatomic asplenia.
- People with terminal complement component or properdin deficiencies.
- People with HIV infection (**new recommendations 2016**)
- Microbiologist who is routinely exposed to N.meningitides.
- People who travel to or reside in areas where *N. meningitides* is hyperendemic or endemic or in outbreak areas caused by vaccine-preventable serogroups.
- **People who wish to decrease their risk of meningococcal infection**


1. PSMID and PFV HANDBOOK ON ADULT IMMUNIZATIONFOR FILIPINOS 2009 pages 39- 42 accessible at http://www.pcp.org.ph/documents/CPGs/PSMID/Handbook%20on%20Adult%20Immunization%202009.pdf
2. CDC Epidemiology and Prevention of Vaccine Preventable diseases 10th Edition January 2007 Meningococcal Disease Pages 271-282

# Meningococcal Vaccine Recommendation

***Current Risk Recommendation for IMD***

## SCHEDULE FOR ADULT IMMUNIZATION 2015

| VACCINE TYPE/ROUTE | TARGET INDIVIDUALS | SCHEDULE | PRECAUTIONS/CONTRAINDICATIONS |
|---|---|---|---|
| **MENINGOCOCCAL**<br>• Polysaccharide vaccine (MPSV) - Intramuscular or Subcutaneous<br>• Conjugate vaccine (MCV4) -Intramuscular | Recommended for:<br>• Those traveling to areas with meningococcal outbreaks<br>• Health workers with contacts of meningococcal patients<br>• Those with immunocompromised conditions and complement deficiency<br>• Functional or Anatomic Asplenia | • Single dose 0.5 ml. No revaccination.<br>• Single dose 0.5 ml. Revaccination after 5 years if there is risk of exposure | • For those with severe allergic reaction to the vaccine component. |

Reference: PSMID SCHEDULE FOR ADULT IMMUNIZATIONFOR FILIPINOS 2015 http://www.philvaccine.org/vaccination-schedules/adult-immunization-schedule accessed November 10, 2016

# Vaccines for High Risk / Special Groups

**Meningococcal Vaccine**

Given intramuscularly (IM) or subcutaneously (SC)

Tetravalent meningococcal (ACYW-135) conjugate vaccine MCV4-D, MCV4-TT, MCV4-CRM given intramuscularly

Tetravalent meningococcal polysaccharide vaccine (MPSV4) given intramuscularly (IM)/subcutaneously (SC)

Indicated for those at high risk for invasive disease: persistent complement deficiencies, anatomic/functional asplenia, HIV, travellers to or resident of areas where meningococcal disease is hyperendemic or epidemic or belonging to a defined risk group during a community or institutional meningococcal outbreak

Dosing schedule:

- MCV4-D: minimum age is 9 months . For children 9-23 months give 2 doses 3 months apart. For children 2 years and above give one dose.
- MCV4-TT given to children 12 months and above as a single dose
- MCV4-CRM given to children 2 years and above as a single dose

Revaccinate with a MCV4 vaccine every 5 years as long as the person remains at increased risk of infection

MPSV4 given to children 2 years and above as a single dose. If MPSV4 is used for high risk individuals as the 1st dose, a 2nd dose using MCV4 should be given 2 months later. Booster doses of MPSV4 are not recommended.

MCV4-D and PCV13 should be given at least 4 weeks apart

**HIGH RISK GROUPS: Persistent complement deficiency, asplenia, HIV, traveller or residing in hyperendemic area**

**Men ACWY- D ( Menactra)**

Minimum age 9 months

For 9-23 months: Give 2 doses, 3 months apart

**Men ACWY- TT ( Nimenrix)**

Minimum age 12 months as single dose

**Men ACWY-CRM ( Menveo)**

Minimum age 2 years as single dose

Revaccinate with MCV4 every 5 years if still at remains increased risk

MCV4 –D and PCV 13 should be given at least 4 weeks apart

Reference: http://www.philvaccine.org/vaccination-schedules/childhood-immunization-schedule accessed November 10, 2016


# Pneumococcal vaccine recommendation in the Philippines

Rontgene M. Solante, MD, FPCP, FPSMID

# Leading Causes of Adult Morbidity and Mortality

## MORBIDITY: TEN (10) LEADING CAUSES

| Diseases | 2010* | |
|---|---|---|
| | Number | Rate |
| 1. Acute Respiratory Infection ** | 1,289,168 | 1371.3 |
| 2. **Acute Lower Respiratory Tract Infection & Pneumonia** | 586,186 | 623.5 |
| 3. Bronchitis/Bronchiolitis | 351,126 | 373.5 |
| 4. Hypertension | 345,412 | 367.4 |
| 5. Acute Watery Diarrhea | 326,551 | 347.3 |
| 6. Influenza | 272,001 | 289.3 |
| 7. Urinary Tract Infection** | 83,569 | 88.9 |
| 8. TB Respiratory | 72,516 | 77.1 |
| 9. Injuries | 51,201 | 54.5 |
| 10. Disease of the Heart | 37,589 | 40.0 |

*Philippine Health Statistics; Mortality table last updated 26 April 2013; Morbidity table last updated 05 May 2014

## MORTALITY: TEN (10) LEADING CAUSES

NUMBER AND RATE/100,000 POPULATION

| CAUSES | 5-Year Average (2004-2008) | | 2009* | |
|---|---|---|---|---|
| | Number | Rate | Number | Rate |
| 1. Diseases of the Heart | 82,290 | 94.5 | 100,908 | 109.4 |
| 2. Diseases of the Vascular System | 55,999 | 64.3 | 65,489 | 71.0 |
| 3. Malignant Neoplasms | 43,185 | 49.6 | 47,732 | 51.8 |
| 4. **Pneumonia** | 35,756 | 41.1 | 42,642 | 46.2 |
| 5. Accidents** | 34,704 | 39.9 | 35,990 | 39.0 |
| 6. Tuberculosis, all forms | 25,376 | 29.2 | 25,470 | 27.6 |
| 7. Chronic lower respiratory diseases | 20,830 | 24.0 | 22,755 | 24.7 |
| 8. Diabetes Mellitus | 19,805 | 22.7 | 22,345 | 24.2 |
| 9.Nephritis, nephrotic syndrome and nephrosis | 11,612 | 13.4 | 13,799 | 15.0 |
| 10. Certain conditions originating in the perinatal period | 12,590 | 14.5 | 11,514 | 12.5 |

# Cost of Hospitalization for Pneumonia in the PH

| Parameter | Philippine Data |
|---|---|
| **All-cause pneumonia hospitalization rates in adults** [1] | • **No. 1 among top illnesses based on PHIC Claims in 2013**<br>• **519,000** insurance claims among patients hospitalized<br>• Cost: **PHP 7.9 B ( $160M)** |
| **- Proportion due to *S. pneumoniae*** | • Around **30%** of CAP isolates in Asia Pacific cases are due to Streptococcus pneumoniae |
| **Common serotypes** [3] | • 1, 5, 14, 4, 6B, 3, 20, 12, 2, 23F, **6A,** 25, 19A , 7F, 18C (PCV13/PPV23)<br>• 20, 12, 2, 15, 17, 10 (PPV23)<br>• 28,32,31,35,38,39,40,41 = nonPCV13/PPV23 |

**1**. Phil Health Insurance Corporation (PHIC 2 Philippine Health Statistics; Morbidity table last updated 05 May 2014 2. Song J-H et al. Int *J Antimicrob Agents*. 2008;31(2):107-114. 3. Laboratory-Based Surveillance of *S. pneumoniae* in Tertiary *Health Care Centers in the Philippines (2010-2012) .Dr. Ma. Rosario Capeding*

# Cost of Hospitalization for Pneumonia in the PH

| Parameter | Philippine Data |
|---|---|
| Cost of pneumonia hospitalization | **The estimated cost of hospitalization for CAP-MR( Moderate Risk)** was **PhP 36,153 - 113,633** (US$852 – 2,678)<br>1-week post-discharge cost was PhP 1,450 – 8,800 (US$ 34 – 207)<br><br>The post discharge cost for CAP-HR was PhP 1,716 – 10,529 (US$40 – 248).<br><br>In comparison, the present PhilHealth case rate payments for CAP-MR is PhP 15,000 (US$354) and PhP 32,000 (US$754) for CAP-HR. |

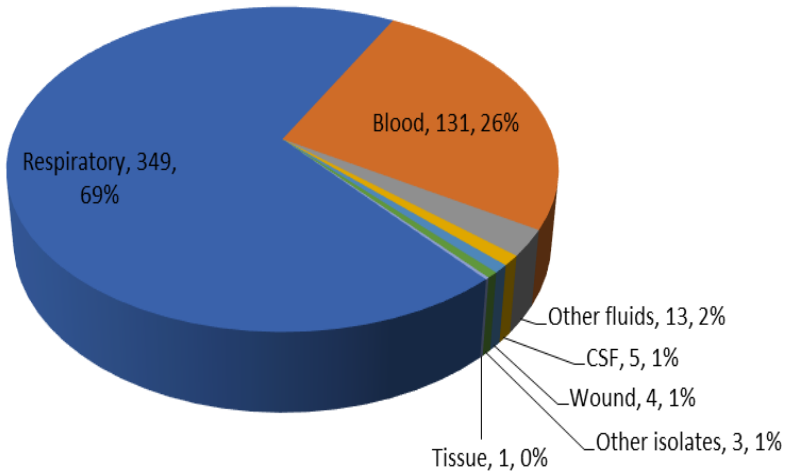
Conclusion :

- The estimated healthcare cost of hospitalization is markedly higher than the Phil Health case rate payments.
- As per the study results, the economic burden of pneumonia is, thus, significantly higher than PhilHealth estimates.

Tumanan Mendoza et al. Economic Burden of Community-Acquired Pneumonia Among Adults in the Philippines Its Equity and Policy Implications in the Case Rate Payments of the Philippine Health Insurance Corporation. Manuscript accepted in Value in Health Regional Issue soon to be published online at the Value in Health Regional Issues (ViHRI) website http://www.ispor.org/publications/VIHRI/About_VIHRI.asp

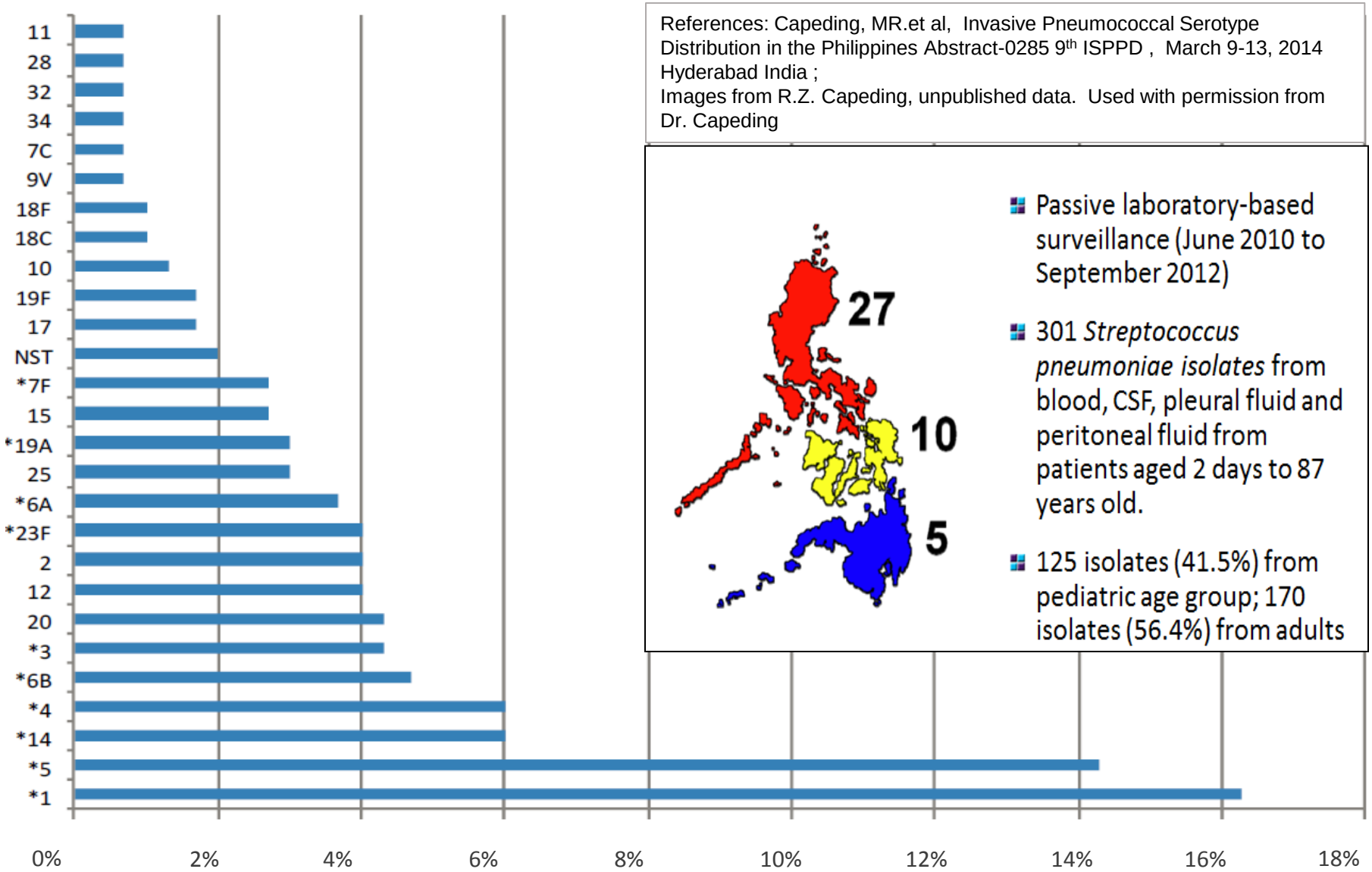
# Distribution of *Streptococcus pneumoniae* , DOH n=507

- This was 16% more than the 436 *S. pneumoniae* isolates reported for 2015.
- Major contributors making up 45% of the 2016 *S. pneumoniae* data were DMC (108 isolates), VSM (66 isolates) and PGH (54 isolates).
- Majority of the *S. pneumoniae* reported were respiratory isolates (69%) and invasive isolates (27%) from blood and cerebrospinal fluid cultures.
- The rest of the isolates were from wound, tissue and other body fluids




Antimicrobial Resistance Surveillance Program 2016
Department of Health

# Serotype Distribution of Pneumococcal Isolates (n=301)

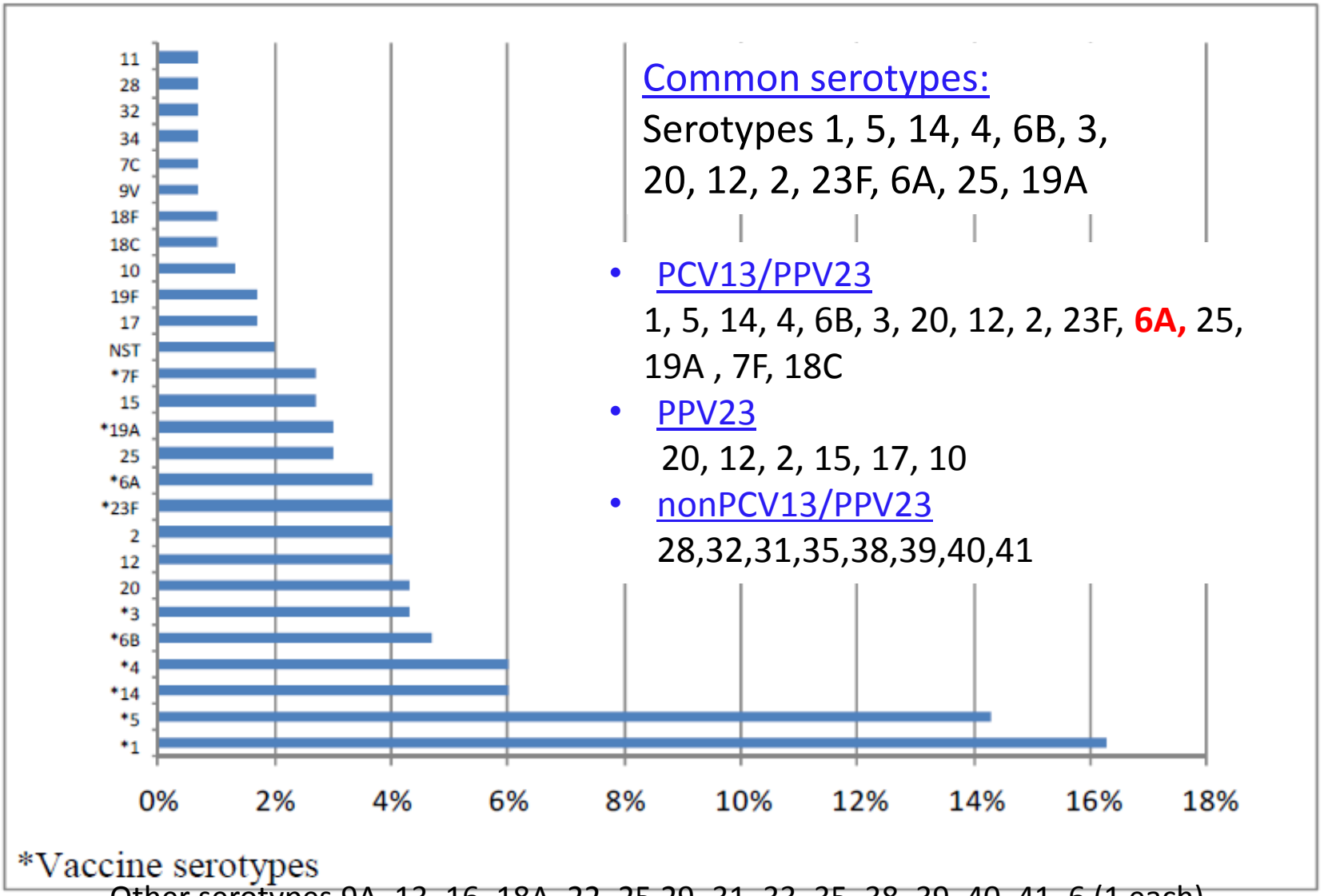



References: Capeding, MR.et al, Invasive Pneumococcal Serotype Distribution in the Philippines Abstract-0285 9th ISPPD , March 9-13, 2014 Hyderabad India ;
Images from R.Z. Capeding, unpublished data. Used with permission from Dr. Capeding




- Passive laboratory-based surveillance (June 2010 to September 2012)
- 301 *Streptococcus pneumoniae isolates* from blood, CSF, pleural fluid and peritoneal fluid from patients aged 2 days to 87 years old.
- 125 isolates (41.5%) from pediatric age group; 170 isolates (56.4%) from adults

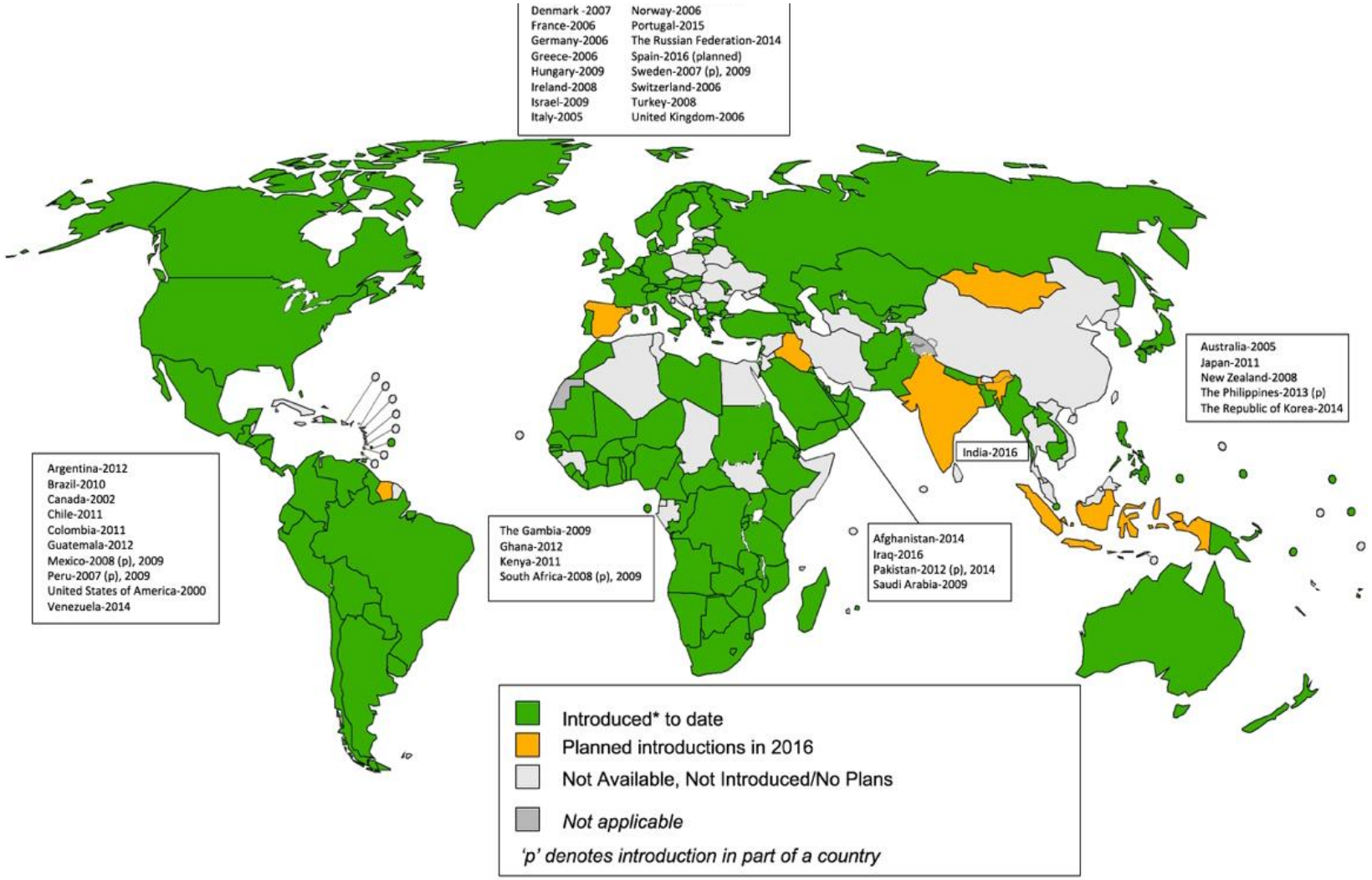
# Pneumococcal serotype distribution in the Phils (N=301)




Other serotypes 9A, 13, 16, 18A, 22, 25,29, 31, 33, 35, 38, 39, 40, 41, 6 (1 each)

R.Z. Capeding, Laboratory-Based Surveillance of *Streptococcus pneumoniae* in Tertiary *Health Care Centers in the Philippines* Research Institute for Tropical Medicine June 2010 to September 2012 (unpublished)

# Countries with Pneumococcal Conjugate vaccine (PCV) in the national immunization program (NIP) and planned introductions in 2016, organized by WHO region



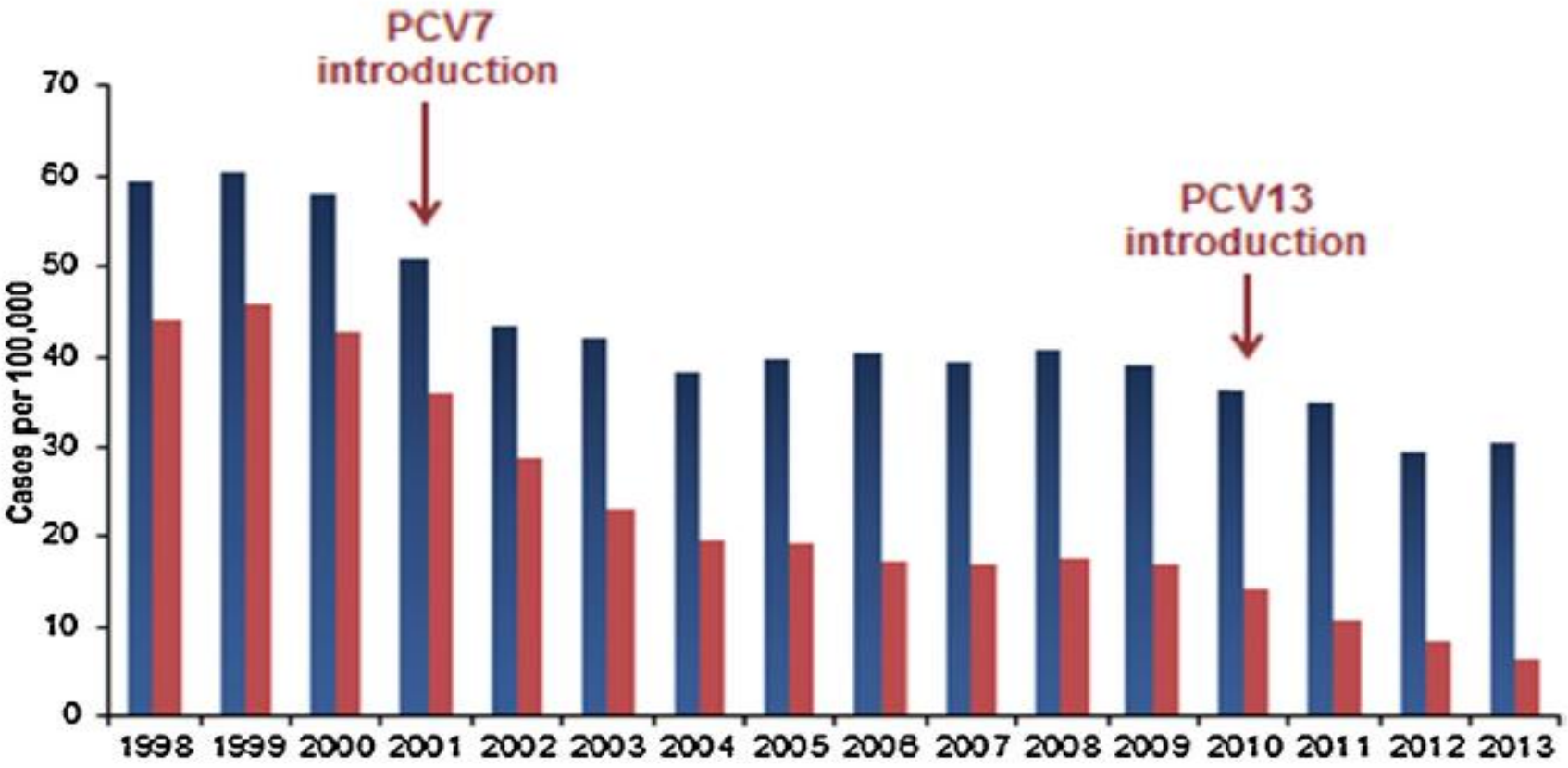

http://www.who.int/immunization/monitoring_surveillance/data/en
Accessed 7 December 2016

# Effects of PCV on IPD in children and adults

- associated with **significant reduction in IPD** in children post PCV 7/13
- Active Bacterial Core Surveillance (ABCs) of the CDC (USA)[1]
  - 156.1 cases/100,000 in ’98-’99 to 33.6/100,000 in 2001 < 2 y
  - 93% reduction in < 5 y ; 75% reduction in 5-17 y
  - 72% reduction in 18-49 y ; 62% reduction in 50-64 y ; 58% reduction in 65+ y
- Calgary Area Streptococcus pneumoniae Epidemiology Research (CASPER) program (Canada) [2]
  - 33% reduction 0–5 mos; 86% reduction 6–23 mos
  - 67% reduction 2–4 y ; 26% reduction 5–17 y
  - 22% reduction 18–64 y, 36% reduction 65–84 y, 42% (≥85 years)

1 *Matthew R Moore et al. Lancet Infect Dis* 2015; 15: 301–09;
[2] Icabaj J et al Clinical Infectious Diseases 2016;62(12):1521–6

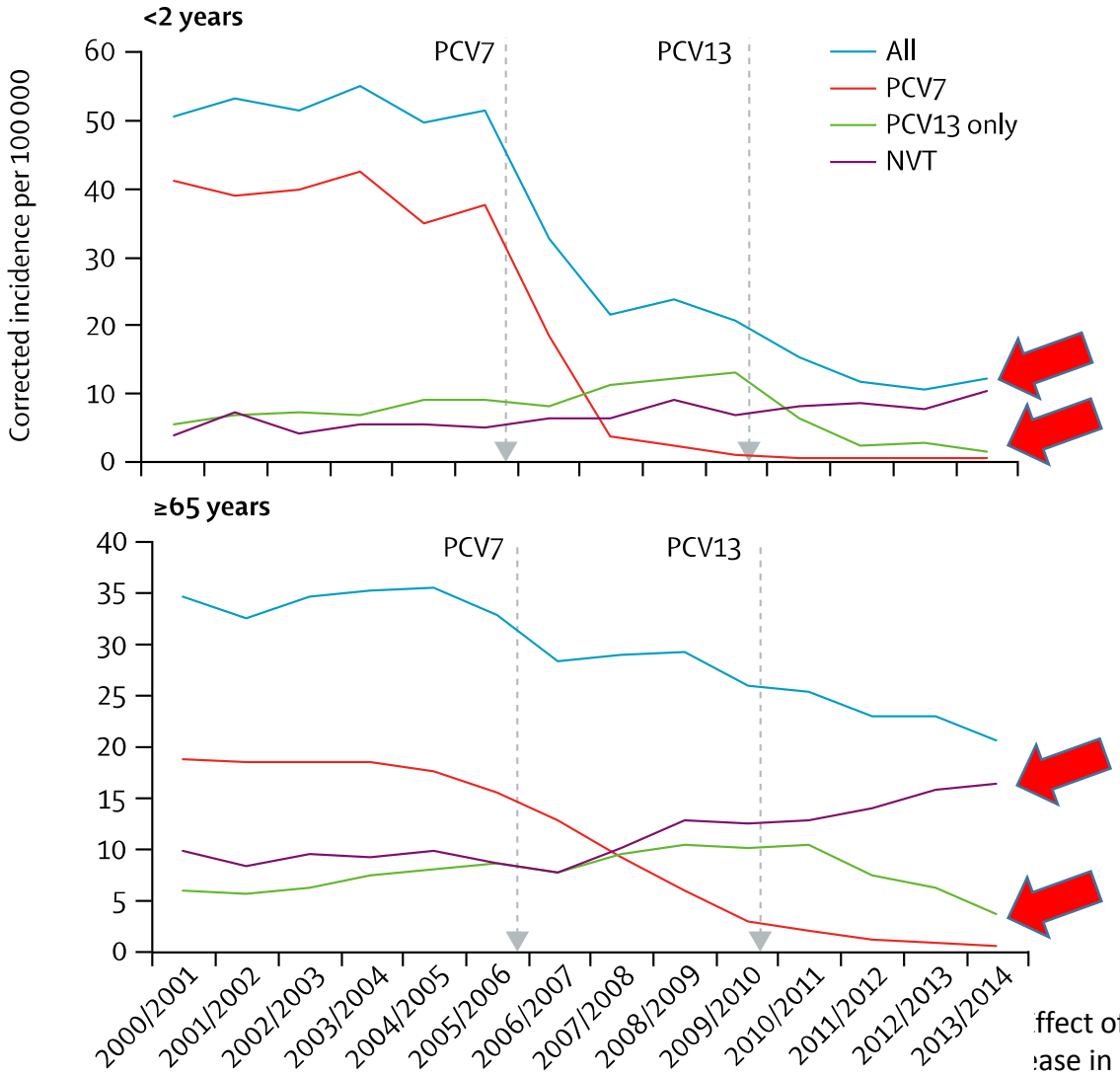
# Incidence of IPD among Adults ≥ 65 years in the US: 1998–2013




**PCV13-serotype IPD shown in red**

Pilishvili et al. *Vaccine* 2015; 33 (Suppl 4): D60-D65.

# Effect of the 13-valent pneumococcal conjugate vaccine on IPD in children and adults England and Wales 4 years after its introduction



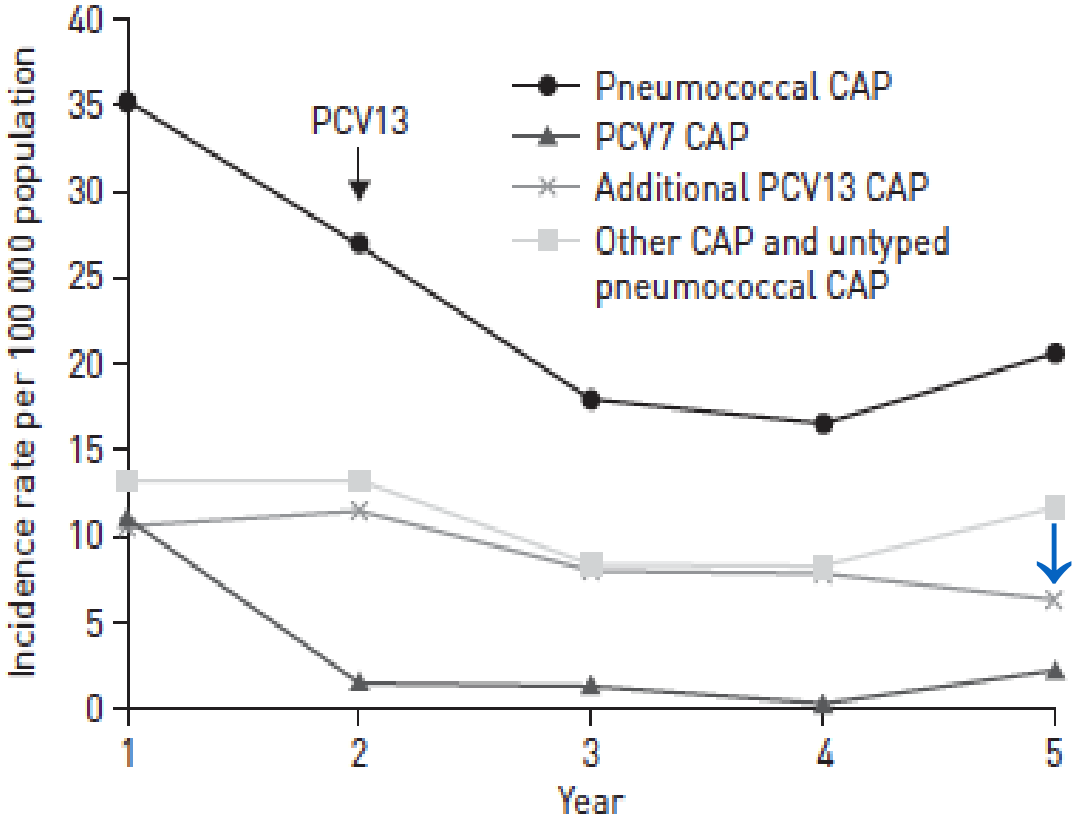

- 8 years of PCV use in England and Wales has reduced the overall incidence of invasive pneumococcal disease by **more than 50%**

- **Non-PCV13 serotypes** 8, 10A, 12F, 15A, and 24F increased significantly in 2013/14

ffect of the 13-valent pneumococcal conjugate vaccine
ease in England and Wales 4 years after its introduction
Lancet Infect Dis 2015; 15: 535–43

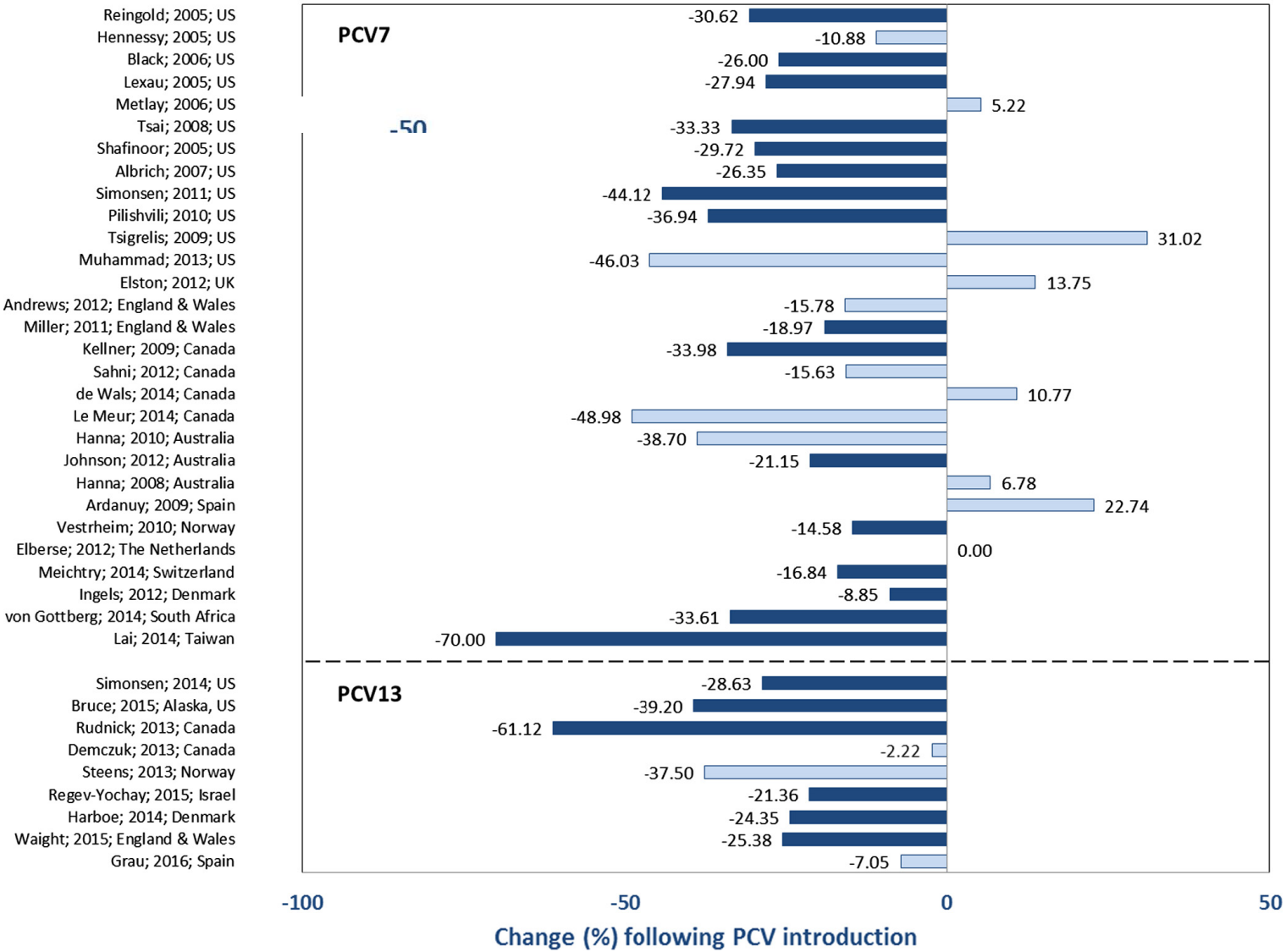
# PCV13 Vaccination of Children Reduces PCV13 serotype-*unique* NBPP in Adults: Nottingham

- **PCV7 began in 2006; PCV13 in 2010**
- **Incidence of hospitalised NBPP in adults ≥ 16 yrs decreased over 5-year period (2008-2009 to 2012-2013)**
- **Incidence of adult NBPP due to *unique* PCV13 serotypes fell 30% in 2 yrs following introduction of PCV13**




Rodrigo C et al. *Eur Respir J* 2015; 45: 1632-41.

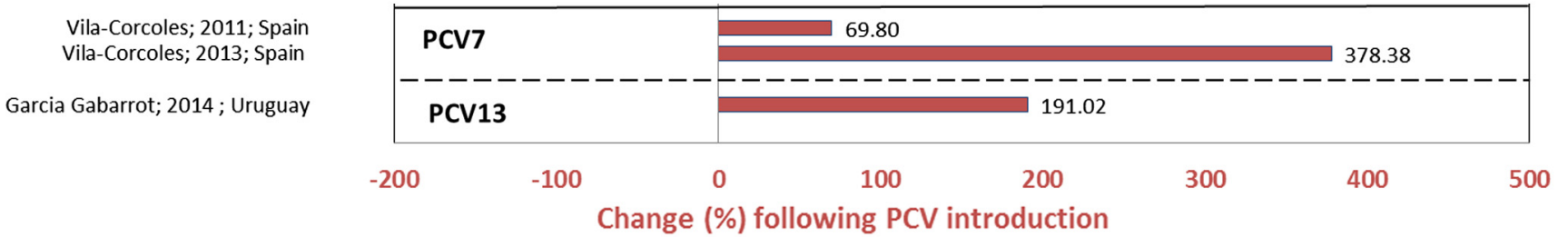
# Systematic Review:
# Adult IPD change (%) of incidence following the introduction of PCV



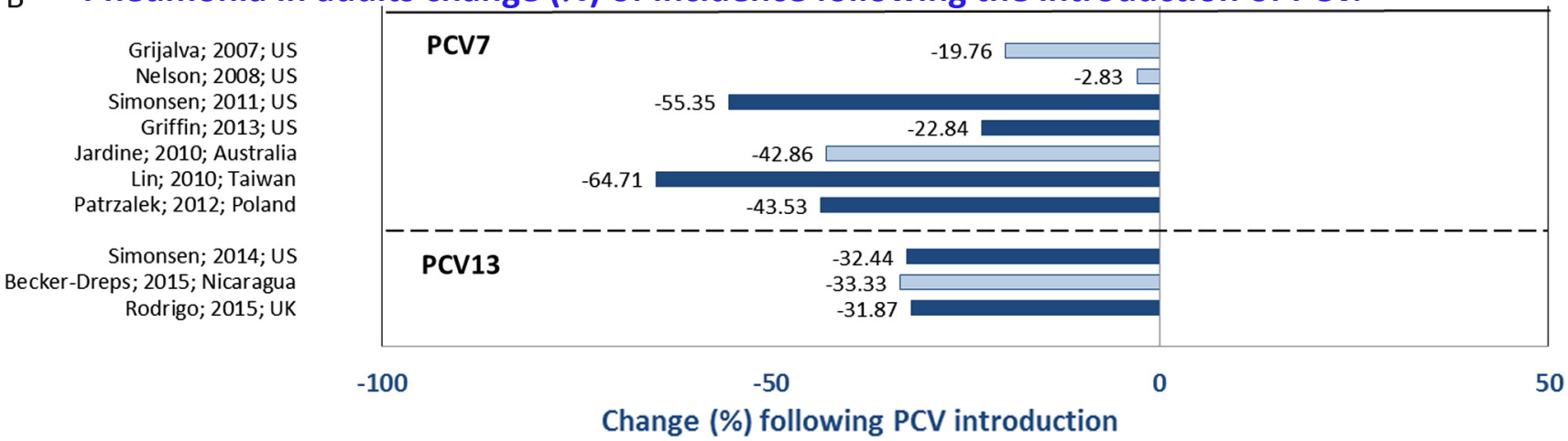

Tsaban G et al. Indirect protection, following pneumococcal conjugated vaccines introduction: A systematic review of the literature. Vaccine 35 (2017) 2882–2891

# Systematic Review:
# Decline in both adult IPD and CAP following the introduction of PCV

A **Invasive pneumococcal disease in adults change (%) of incidence following the introduction of PCV – outliers studies**




B **Pneumonia in adults change (%) of incidence following the introduction of PCV.**




Tsaban G et al. Indirect protection, following pneumococcal conjugated vaccines introduction: A systematic review of the literature. Vaccine 35 (2017) 2882–2891

# PCV13 Adult National Recommendations Worldwide (as of August 2016)

| Age-Based Recommendation | | | Risk-Based Recommendation | |
|---|---|---|---|---|
| **Age + Risk + High Risk(N = 19)** | | | **At Risk + High Risk (n = 7)** | |
| Austria | Hungary | Hong Kong | Germany | Sweden (Regional) |
| Belgium | Italy (Regional) | New Zealand | Iceland | Switzerland* |
| Czech Rep | Turkey | Panama | Portugal | Indonesia |
| Greece | Lithuania | Bahrain | Spain (Regional) | |
| Estonia | Poland | Kuwait | **High-risk (n = 13)** | |
| Finland | Denmark (COPD) | Qatar | UK | Norway |
| United Arab Emirates | | | France | Israel |
| **Age + High Risk (n = 5)** | | | Russia | Croatia |
| USA | Canada | Taiwan | Ireland | Slovenia |
| El Salvador | Australia | | Netherlands | Korea |
| **Age** | | | Argentina | Oman |
| Bulgaria | | | Uruguay | |

Sings HL. Pneumococcal conjugate vaccine use in adults – Addressing an unmet medical need for non-bacteremic pneumococcal pneumonia. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.05.075

# Expanded Program on Immunization
# Estimated Immunization Coverage 2014

| Year of Introduction EPI | Infant Vaccine | Estimated Immunization Coverage |
|---|---|---|
| 1979 | BCG | 87 % |
| 1979 | DPT 1 | 86% |
| | DPT 3 | 79% |
| 1979 | OPV3 | 84 % |
| 1982 | Hepa B 3 | 79 % |
| 2007 | Hepa B at Birth | 54% |
| 1992 | MCV 1 | 88 % |
| | MCV2 | 64% |
| 2010 | HiB 3 | 79% |
| 2010 | PCV | **30%** |

* Rotavirus has no report on Estimated Immunization Coverage as of July 2015

Reference: WHO and UNICEF estimates of national immunization coverage - next revision available July 15, 2016 data as of July 7, 2015

# Changing epidemiology and implications for use of pneumococcal vaccines among adults

- Despite clear evidence of a herd effect from , there remains a significant burden of disease in adults
- PCV13 serotypes currently account for approximately one fourth of IPD among adults aged 65 years and older
- The 11 serotypes that account for 38% of IPD in adults aged 65 years and older are included in PPSV23
- Current recommendations **PCV13 and PPSV23** use among adults 65 years or older is cost-effective
    - Potentially prevent 230 cases of IPD and approximately 12,000 cases of CAP, over the lifetime
    - assuming 60% vaccination coverage among adults aged ≥65 years

1 Lancet Infect Dis 2015;15(Mar (3)):301–9
2 MMWR Morb Mortal Wkly Rep 2014;63(Sep (37)):822–5.

# 2017 Adult Immunization Guideline (as of June 2017)

| PNEUMOCOCCAL Vaccination | Target Individuals | Schedule |
|---|---|---|
| **Conjugate (PCV13)**<br>• **Intramuscular**<br><br>**Polysaccharide (PPSV23)**<br>• **Intramuscular or Subcutaneous** | Recommended for all susceptible adults particularly:<br>• Age 50 years and older without history of pneumococcal vaccination<br>• Adults <50 years old with:<br>  ○ Chronic lung disease (including bronchial asthma, tuberculosis)<br>  ○ Chronic cardiovascular/renal/liver diseases<br>  ○ Diabetes mellitus<br>  ○ Alcoholism<br>  ○ Cochlear implants<br>  ○ CSF fluid leaks<br>  ○ Immunocompromised conditions:<br>  – Functional and anatomic asplenia<br>  – Leukemia and lymphomas<br>  – Generalized malignancy<br>  – Transplants<br>  – Chemo/radiation therapy<br>  – HIV/AIDS<br>• Residents of nursing homes or long-term care facilities<br>• Smokers | **No previous vaccination:**<br>• **PCV 13 first, followed by PPSV23 at least 1 year after the PCV13 dose**<br><br>**Previously received PPSV23:**<br>• **should receive PCV13 to be given at least 1 year after the dose of PPSV23**<br><br>**Previously received PPSV23 at less than 50 years old, but who are now 50 years old or more:**<br>• **1 dose of PCV13 at least 1 year after the most recent dose of PPSV23, then 1 dose of PPSV23 after 1 year of the PCV13 dose**<br><br>**Revaccination**<br>• **1 dose PPV23 maybe given 5 years after last dose of PPV23** |

Reference: Schedule for Adult Immunization 2017 , Philippine Society for Microbiology and Infectious Diseases (PSMID), and Philippine Foundation for Vaccination (PFV) Updated as of April 2017

# 2016 Senior citizens pneumococcal vaccination program of the Department of Health

- 1 dose of PPV23 at 60 years old

- 1 dose of PPV3 65 years old

# Opportunities for Public-Private partnership

- Disease Awareness campaign
- Capability Enhancement Vaccinator Workshops/ Immunization Conferences
- Socio Civic Mobilization
- Shared Patient Care



# Current strategies for adult pneumococcal vaccination

1. **Expand advocacy** and awareness on the importance of vaccination thru dissemination of adult immunization guideline and recommendations to private practitioners such as general practitioners specialty practitioners nephrology, oncology, endocrinology, rheumatology,

# Current strategies for adult pneumococcal vaccination

2. Prioritize pneumococcal and influenza vaccination of emerging **at-risk** population particularly the **elderly**, those with **HIV**, **chronic cardiovascular conditions**, **malignancy** and **diabetes**.

# Current strategies for adult pneumococcal vaccination

3. Engage and partner with government sector such as Department of Health to encourage them to adopt the adult vaccination guideline to local government unit/hospitals, and Philippine Health Insurance Corporation (PhilHealth) for their OPD package services

# Challenges

1. Financial constraints in the private sector and funding in the public sector,
2. Operational Challenges: geographic and logistic difficulties
   - Cold Chain Support,
   - Training of Vaccinators
   - Vaccination Schedule & Dosing Compliance
   - Vaccine Supply
3. Measures of Impact and gaps in epidemiologic data
   - Burden of Disease, Circulating Serotypes
   - Active Surveillance
   - Impact Studies for Full birth cohort Coverage
5. EPI transition to a Comprehensive National Immunization Program

No Filipino, regardless of age, place of birth, or social status should die from a vaccine preventable disease.