Current Status of PCV Use and WHO Recommendations

SAGE
18 October 2017

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Pneumonia remains a major cause of child deaths

Global PCV use has rapidly increased

- PCV7
- PCV10
- PCV13

Years:
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011
- 2012
- 2013
- 2014
- 2015
- 2016
- 2017

Number of Countries:
- 0
- 50
- 100
- 150
PCV has substantial impact on childhood deaths

Pneumococcal deaths (HIV (-))
Children 1-59 mo, 2000 - 2015

Total pneumococcal deaths averted (2000-2015): 190,000

Few countries remain without nationwide PCV

S. pneumoniae mortality rate

- Blue: <10
- Light blue: 10 - <25
- Light yellow: 25 - <100
- Orange: 100 - <200
- Red: ≥ 200
PCV coverage remains disparate

WUENIC Coverage Rates
- Very Low (<60%)
- Low (60-69%)
- Medium (70-79%)
- High (80-89%)
- Very High (90-100%)

[Map showing PCV coverage rates worldwide]
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
PCV impact evaluations are widespread, all regions

...but gaps remain
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: dosing 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**
   - Immunogenic Response: Vaccine Type specific antibody (IgG)

2. **Direct Effect:**
   - Protection against Colonization
   - Protection against Disease

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)

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Global IPD Serotype Distribution: Top 20

10 types account for 70% of disease
95% CI: 9-12 types

Weighted by regional disease burden (cases)

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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