PCV Working Group Recommendations

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SAGE PCV Working Group

- Three questions of interest
  - Dosing schedule
  - Product Choice
  - Catch Up Immunization

- Please review SAGE Yellow Book for full recommendations

PICO Question 1: Schedule Choice

How does PCV administered to healthy children in a 2p+1 schedule compare with the vaccine administered in a 3p+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?

Schedule Choice **Policy**: Recommendation #1

- For infants, at least 3 doses of vaccine, administered **either** as 2 primary doses plus booster (2p+1) or 3 primary doses without a booster (3p+0), are recommended.

  - Consider **operational and programmatic issues**
  - **Low population vaccine coverage may warrant the use of a 3p+0 schedule.**
  - **Schedule switching is not necessary** unless one or more factors changes substantially

Schedule Choice **Policy**: Recommendation #2

- A dosing interval of **8 weeks between the first two doses of a 2p+1** schedule

- The dosing interval between primary doses within each schedule should **not be shorter than 4 weeks**

Schedule Choice **Policy**: Recommendation #3

In a 2+1 schedule……

- The timing of the booster dose should be selected to **maximize coverage**
- Booster at **9, 12, 15 or 18 months**
- **Optimal timing** of the booster dose not known

Schedule Choice **Research**: Recommendation #1

- Additional data from head-to-head studies of schedules are needed:

Schedule Choice **Research**: Recommendation #2

- Coverage achieved by different PCV schedules, including:
  - Timeliness of vaccination
  - Age of vaccination

Schedule Choice **Research**: Recommendation #3

- **Serotype specific quantitative immune correlates of protection** against invasive pneumococcal disease

Schedule Choice **Research**: Recommendation #4

- Studies to evaluate the **serotype specific duration of protection** from different schedules

Schedule Choice **Research**: Recommendation #5

- Modeling studies to systematically evaluate key drivers of the relative benefits of 2p+1 vs 3p+0 schedules

- Drivers may include:
  - Local epidemiology of carriage and disease
  - Demographic structure
  - Vaccine efficacy
  - Timeliness
  - Booster dose coverage

PICO Question 2: Product Choice

Is the impact or effectiveness of PCV10 and PCV13 (using either WHO recommended dosing schedules) 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?

Product Choice **Policy**: Recommendation #1

- Both vaccines have impact against overall vaccine-type disease and carriage
- PCV13 **may have additional benefit in settings where disease attributable to ST19A or ST6C constitutes a significant public health problem**
- However, there is at present **no supportive evidence of different net impact on overall disease burden** between the two products

Product Choice **Policy**: Recommendation #2

- Country-level product choice should consider:
  - Programmatic characteristics
  - Vaccine supply
  - Vaccine price
  - Local/regional vaccine serotype prevalence
  - Antimicrobial resistance patterns among vaccine serotypes

Product Choice **Policy**: Recommendation #3

- **Once a program has been initiated product switching is not recommended** unless one or more factors that led to the original choice of product changes substantially (see Recommendations 1 and 2)

Product Choice **Policy**: Recommendations #4

- Interchangeability between PCV10 and PCV13 has not been studied in the 2 or 3-dose ***primary*** series
- Limited evidence suggests that products confer comparable immunogenicity for the ***booster*** **dose** regardless of product used in primary series
- When a 2- or 3-dose primary immunization series is initiated, ideally the remaining doses needed to **complete the primary series** should be administered with the same product.
- If it is not possible to complete the primary series with the same product, the other vaccine should be used**, rather than miss a primary or booster dose**
- There is **no evidence to suggest that restarting the vaccination series** is necessary if a product switch occurs

Product Choice **Research**: Recommendation #1

- Field data and modeling are needed
  - Better understand the **drivers and predictors of pneumococcal serotype replacement in disease**

Product Choice **Research**: Recommendation #2

- **Head to head studies** are needed comparing immunological and carriage **impact of future and existing PCV products**
- Assessment of PCV impact on carriage has additional value in predicting herd effects and pneumococcal circulation
- Measuring immunogenicity is important for establishing correlates of protection against IPD and carriage

Product Choice **Research**: Recommendation #3

- Data are needed on PCV product interchangeability

Product Choice **Research**: Recommendation #4

- Further studies are needed to understand the **effects of maternal antibodies and maternal immunization**

PICO Question 3: 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?

Catch Up Vaccination **Policy**: Recommendation #1

- Catch-up vaccination as part of PCV introduction will accelerate:
  - Direct and indirect protection
  - PCV impact on disease

Catch Up Vaccination **Policy**: Recommendation #2

- Catch-up vaccination with PCV can be done:
  - **24 months and older**
    - **1 dose** of vaccine
  - **12-23 months**
    - **some programs have used 2 PCV doses separated by at least 8 weeks, and others have used 1 dose**
  - **7-11 months**
    - **some programmes have used 2 doses, and others have used 3 doses**
  - **6 months or under**
    - **a 3 dose regimen** should be offered
- If limited availability/capacity, the youngest children should be prioritized

Catch Up Vaccination **Policy**: Recommendation #3

- Unvaccinated children up to 5 years of age at high risk for pneumococcal infection based on a medical condition:
  - Receive at **least 2 PCV doses separated by at least 8 weeks** to assure immunogenicity.

Catch Up Vaccination **Policy**: Recommendation #4

- In areas/communities where **low vaccination coverage has permitted sustained vaccine serotype pneumococcal transmission** (or disease), especially those with coverage below 50%:
  - Catch up campaigns (also termed **periodic intensification of routine immunization**) can be used

Catch Up Vaccination **Policy**: Recommendation #5

- Catch-up vaccination **to replace missed doses among individual children** should be encouraged
  - Particular focus on **children at highest risk of pneumococcal disease**

Catch Up Vaccination **Policy**: Recommendation #6

- In **humanitarian or emergency situations**, age-appropriate schedules of PCV vaccination should be implemented
  - Certainly for children under 1 year of age
  - Usually for children up to 5 years of age as indicated by the situation

- Through use of the framework for vaccination in humanitarian emergencies

- Immunization of children over age 5 may be indicated in certain situations

Catch Up Vaccination **Policy:** Recommendation #7

- Vaccination may be considered in response to outbreaks of confirmed VT pneumococcal disease, based on the characteristics of the outbreak:
  - Outbreak size
  - Duration
  - Age group affected

Catch Up Vaccination **Research**: Recommendation #1

- Further assessment is needed of **pneumococcal epidemiology in outbreaks, and outbreak response** opportunities with PCV
  - Especially ST1

Catch Up Vaccination **Research**: Recommendation #2

- Further assessment of the benefits/limitations of developing and using PCV products **containing single or a limited number of outbreak-associated serotypes**
  - For use as a tool for controlling pneumococcal outbreaks.

Catch Up Vaccination **Research**: Recommendation #3

- Studies should be conducted in **settings where outbreaks or humanitarian emergencies have recently occurred** to
  - Evaluate risk of pneumococcal disease, including pneumonia
  - Assess impact of PCV use in these settings

Catch Up Vaccination **Research**: Recommendation #4

- A systematic **analysis of evidence comparing 1-dose versus 2-dose catch-up vaccination**

Catch Up Vaccination **Research**: Recommendation #5

- Additional data are needed, through modeling or impact studies, on the relative benefit and cost of catch-up vaccination at:
  - Time of PCV introduction
  - Switch to PCVs containing different serotypes or valencies

SAGE PCV WG:
Surveillance Recommendations

- Need high quality long term surveillance in a range of settings
- Sentinel, routine and NP surveillance, aspiration for global surveillance
- Surveillance should assess NP carriage, pneumonia, meningitis, sepsis, IPD
- For at least 5 years but long term observation will be needed to inform long term changes in replacement

Acknowledgements

- SAGE PCV WG members
- WHO Secretariat
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To review complete draft recommendations, please view the SAGE PCV WG executive summary on the SAGE website: http://www.who.int/immunization/sage/meetings/2017/october/presentations_background_docs/en/