

WHO position paper on pneumococcal vaccines

Geneva, Switzerland

Published in the Weekly

Epidemiological Record on 6 Apr 2012

WHO position paper on pneumococcal vaccines, April 2012

- The current position paper focuses on the 10-valent and 13-valent pneumococcal conjugate vaccines (PCVs) and replaces the 2007 position paper on 7-valent PCV
- The position paper on 23-valent pneumococcal polysaccharide vaccine published in 2008 remains valid but its key conclusions and recommendations are integrated in this updated position paper

WHO position paper on pneumococcal vaccines, April 2012

-pathogen and transmission-

- *Streptococcus pneumoniae* (the pneumococcus) includes >90 serotypes of varying clinical significance. The serotypes most commonly causing disease vary by age, disease, region, and time
- In the pre-immunization era, 6 - 11 serotypes accounted for $\geq 70\%$ of all invasive pneumococcal disease occurring in children worldwide
- Some serotypes such as 6B, 9V, 14, 19A, 19F, and 23F are frequently associated with antimicrobial drug resistance
- Temporary pneumococcal colonization of human nasopharynx is common (27%-85%), especially in infants and young children (main reservoir)
- Pneumococci are usually transmitted through respiratory droplets

Pneumococcal disease

Pneumococcal infections include

- asymptomatic nasopharyngeal colonization
- less severe illnesses such as sinusitis and otitis media
- serious diseases such as meningitis, bacteremia, and pneumonia

Invasive pneumococcal disease (IPD) is commonly defined as morbidity associated with the isolation of pneumococci from the sterile body site, but mainly from blood or cerebrospinal fluid

Case fatality rates among young infants in developing countries may reach 20% for pneumococcal septicemia and 50% for pneumococcal meningitis

Epidemiology of pneumococcal disease

- WHO estimates that in 2008, of the estimated 8.8 million global annual deaths amongst children <5 years of age, 476 000 (333 000 – 529 000) were caused by pneumococcal infections
- Most pneumococcal diseases are sporadic, outbreaks are known to occur but are uncommon
- Disease rates and mortality are higher in low income countries with high child mortality; the majority of pneumococcal deaths occur in Africa and Asia
- Children with HIV infection are at substantially increased risk of serious pneumococcal disease

Pneumococcal vaccines

- Currently marketed pneumococcal vaccines include one polysaccharide vaccine (PPV23) and two conjugate vaccines (PCV10 and PCV13). The 7-valent conjugate vaccine (PCV7) is now gradually removed from the market
- Pneumococcal polysaccharide vaccines are safe, but poorly immunogenicity in infants <24 months of age and fail to induce an anamnestic antibody response
- PCVs contain selected polysaccharide serotype-antigens chemically bound to various protein carriers
- PCV10 is composed of serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F, whereas PCV13 in addition includes serotypes 3, 6A, and 19A

WHO position paper on pneumococcal vaccines, Apr 2012

PCV efficacy, duration of protection and safety

- PCV10/PCV13 are indicated for prevention of IPD, pneumonia and acute otitis media caused by vaccine serotypes in children aged 6 weeks - 5 years; PCV13 also for the prevention of pneumococcal disease in adults aged ≥ 50 years
- Randomized, controlled trials of PCV7 and PCV9 showed on average VEs of 71% and 93%, respectively, following 3 primary doses or 3 primary plus a booster dose, against IPD. For radiologically confirmed pneumonia, estimated VE of the 3 primary doses was 24%
- VE against IPD was still 78% 6.3 years post PCV immunization
- PCV10 and PCV13: comparable vaccine efficacy (VE) for respective vaccine serotypes, based on non-inferiority studies against PCV7
- PCVs are considered safe in all target groups, including immunocompromised individuals
- Immunogenicity and reactogenicity of the involved antigens are shown not to be significantly altered when PCVs are given concomitantly with other childhood vaccines

WHO position on pneumococcal vaccines (a)

- Currently available PCVs are safe and efficacious and represent significant progress in the fight against pneumococcal morbidity and mortality
- WHO recommends the inclusion of PCVs as a priority in childhood immunization programmes world-wide, in particular in countries with high childhood mortality
- The use of pneumococcal vaccine should be seen as complementary to the use of other pneumonia-control measures, such as appropriate case management, exclusive breast feeding for first six months of life, and reduction of risk factors including indoor pollutants and tobacco smoke
- Planning for national use of pneumococcal vaccines should include estimates of disease burden and of pneumococcal serotypes distribution in different age groups

WHO position on pneumococcal vaccines (b)

- PCV10 and PCV13 have comparable safety and efficacy profiles for serotypes contained in the vaccines
- The choice of PCV vaccine depends on factors such as the vaccine serotypes compared to serotypes prevalent in the locally identified target groups, vaccine presentation and supply, and cost-effectiveness considerations
- It is recommended that primary immunization is administered with the same product. However, if impossible to complete the series with the same type of vaccine, the other PCV-product should be used

WHO position on pneumococcal vaccines (C)

- For administration to infants, 3 primary doses (3p+0 schedule) or, as an alternative, 2 primary doses plus a booster (2p+1 schedule) are recommended
- If the 3p+0 schedule is used, vaccination can be initiated as early as 6 weeks of age with a minimum interval between doses of 4 weeks, i.e. scheduled for administration at ages 6, 10, and 14 weeks or 2, 4, and 6 months, depending on programmatic convenience
- If the 2p+1 schedule is selected, the 2 primary doses may be given as early as 6 weeks of age and at a minimum interval of 8 weeks or more for the youngest infants and 4-8 weeks or more for infants aged ≥ 7 months. One booster dose should be given between 9-15 months of age

WHO position on pneumococcal vaccines (d)

- If disease incidence peaks in young infants (<32 weeks of age), a 2p+1 schedule might not offer optimal individual protection for certain serotypes (e.g., 6B, 23F) compared to a 3p+0 schedule, particularly in the absence of herd protection
- Higher antibody levels are induced by the third (booster) dose in a 2p+1 schedule compared to the third dose in a 3p+0 schedule. This may be important for duration of protection or effectiveness against certain serotypes
- The magnitude of herd protection will depend i.a. on immunisation strategy, coverage, reduction in carriage of vaccine serotypes, proportion of pneumonia due to vaccine serotypes, and composition of the population

WHO position on pneumococcal vaccines (e)

- Unvaccinated/incompletely vaccinated children recovering from invasive pneumococcal disease should be vaccinated as appropriate for their age
- HIV positive infants and pre-term neonates who have completed their 3 first vaccine doses before reaching 12 months of age may benefit from a booster dose in the second year of life
- Interrupted schedules should be resumed without repeating the previous dose
- Catch-up vaccination at programme introduction accelerates herd protection and hence the impact on disease and carriage
- When injected at different sites, PCVs can be administered concurrently with any other vaccines in infant immunization programmes

WHO position on pneumococcal vaccines (f)

- PCVs are considered safe in all target groups for vaccination, also in immunocompromised individuals
- Except for very rare anaphylactic reactions, there are no contraindications to the use of these vaccines. However, vaccination should be deferred until after acute infections with high fever
- The impact of PCV should be carefully monitored as part of routine sentinel surveillance. Available evidence does not suggest that concerns about serotype replacement should be an impediment to PCV introduction
- The data on the potential use of such vaccines for immunization in pregnancy to protect newborn babies are currently not considered sufficient to make policy recommendations
- Further data are needed on the impact of large-scale PCV vaccination of individuals >50 years of age. However, given the herd protection in adults following routine infant immunization with PCV7, high PCV-coverage of infants should normally be given priority