*The advice of JCVI is made with reference to the UK immunisation programme and may not necessarily transfer to other epidemiological circumstances*

**JCVI statement on the wider use of pneumococcal conjugate vaccines in the UK July 2013**

**Background**

1. In 2012, JCVI considered the impact and cost effectiveness of a routine immunisation programme to offer pneumococcal conjugate vaccine to older children and adults in clinical risk groups for invasive pneumococcal disease (IPD) in addition to young children as part of the routine childhood immunisation programme.

2. A seven-valent pneumococcal conjugate vaccine (PCV7) was introduced into the UK routine childhood immunisation programme in 2006 and replaced by a 13-valent pneumococcal conjugate vaccine (PCV13) in April 2010. PCV13 is authorised by the European Medicines Agency for use in children aged six weeks to 17 years to prevent invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* and in adults aged 50 years and older to prevent invasive disease caused by *Streptococcus pneumoniae*[1].

3. Following considerations about the wider use of PCV in clinical risk groups in 2010 and 2011, JCVI asked the Health Protection Agency (HPA) in 2011 to conduct a study of the impact and cost effectiveness of use of PCV in clinical risk groups and for both manufacturers of authorised PCV to be approached for data to inform the study[2]. In May 2012, the JCVI pneumococcal sub-committee augmented by additional experts in pneumococcal disease reviewed a pre-publication version of a cost effectiveness study by the HPA and the London School of Hygiene and Tropical Medicine (LSHTM) that was published subsequently[3]. This study followed the methodology and criteria of the National Institute of Health and Clinical Excellence to assess cost effectiveness. It was reviewed independently by an expert in health economics before consideration by the sub-committee. The sub-committee and additional experts also reviewed an unpublished cost effectiveness study provided by one, and reports provided by both, manufacturers of PCVs as well as data on the epidemiology of IPD in England and Wales and a number of other studies[4]. In June 2012, JCVI considered the cost effectiveness studies and the advice from the sub-committee[5] and considered iterations of this statement at its meetings in October 2012 and February 2013.

---

[1] Prevenar13® Summary of Product Characteristics http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001104/WC500057247.pdf

[2] JCVI June 2011 meeting minute: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_131104.pdf

[3] Rozenbaum *et al.* (2012) Vaccination of risk groups in England using the 13 valent pneumococcal conjugate vaccine: economic analysis. *BMJ* 345:e6879 doi: 10.1136/bmj.e6879.

[4] JCVI pneumococcal sub-committee May 2012 meeting minute: http://transparency.dh.gov.uk/2012/07/27/jcvi-pneumococcal-sub-committee-meeting-may-2012/

[5] JCVI June 2012 meeting minute: http://transparency.dh.gov.uk/2012/07/25/jcvi-meeting-june-2012/

**Assessment**

4. JCVI noted that data on the epidemiology of IPD in England and Wales from mid-2005 into 2012 showed evidence of appreciable direct protection and indirect population protection with a large decline in IPD from PCV7-serotypes across the population following the introduction of PCV7 into the routine childhood immunisation programme in 2006[6]. Direct protection and accumulating indirect population protection following the replacement of PCV7 with PCV13 in 2010 was evident with IPD from the seven serotypes common to PCV13 and PCV7 remaining at a low level and IPD from serotypes in PCV13 but not in PCV7 decreasing by about one half in those aged under five years and by about one third in those aged five years and older since April 2010[7]. Studies on the effectiveness of PCV7 and PCV13 against the common vaccine-type serotypes in the UK[8,9] suggest that this decline in IPD from vaccine-type serotypes can be expected to continue in a similar manner to that seen following the introduction of PCV7.

5. JCVI noted that whilst there had been a very significant decline in IPD from serotypes in PCV7 following the introduction of PCV7, this had been partially offset by increases in IPD from other non-PCV7 serotypes in the general population. However, following the introduction of PCV13, an increase in IPD due to non-PCV13 serotypes has not yet been observed in the general population, particularly those less than 65 years of age. Despite this, unpublished preliminary analyses by the HPA suggest that clinical risk groups may be at greater risk of IPD and non-bacteraemic pneumococcal pneumonia (NBPP) from non-PCV13 replacement serotypes compared with the general population. Whilst these preliminary findings need to be confirmed before firm conclusions can be drawn, the implication is that PCV13 may have a lesser impact on overall pneumococcal disease in clinical risk groups compared with the general population.

6. JCVI noted that the studies on the cost effectiveness of the wider use of PCV13 in the UK population from HPA-LSHTM and a vaccine manufacturer were similar in construction and in many of the assumptions made. Both relied on expert judgement about PCV13 effectiveness against IPD and NBPP as direct data are lacking. The results of both studies are highly uncertain and are sensitive to a number of assumptions. They also differ between the studies principally due to differing judgements about the likely overall impact of PCV13 on NBPP and the assumed rate at which indirect protection from the use of PCV13 in the routine

---

[6]Miller *et al.* (2011) Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study. *Lancet Infect. Dis.* 2011 11:760-768.

[7]Current Epidemiology of Invasive Pneumococcal Disease (IPD) http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Pneumococcal/EpidemiologicalDataPneumococcal/CurrentEpidemiologyPneumococcal/ (accessed January 2013)

[8]Andrews *et al*. (2011) Using the indirect cohort design to estimate the effectiveness of the seven valent pneumococcal conjugate vaccine in England and Wales *PLoS One*. 6:e28435.

[9]Andrews *et al.* Effectiveness of the 13 valent pneumococcal conjugate vaccine against IPD in England and Wales poster 148 ISPPD March 2012.

childhood immunisation programme is accumulating. In the HPA-LSHTM study, no impact on NBPP was assumed, consistent with the lack of any overall impact of PCV7 on NBPP in high risk children targeted for PCV7[10]. The studies produced contrasting findings about the cost effectiveness of a routine programme to offer PCV13 to clinical risk groups. JCVI concluded that the findings of the HPA-LSHTM study suggested that a routine programme would not be cost effective to introduce.

**Advice**

7. In light of the evidence of accumulating indirect population protection against PCV13 serotypes across the UK population from the use of PCV13 in the routine childhood immunisation programme (which is based on the experience with PCV7 and can be expected to extend to those in high risk groups including HIV infected individuals), JCVI concluded that the additional benefit of the direct protection provided by wider use of PCV13 in clinical risk groups in the UK is declining and is likely to diminish further within a few years. Given the uncertain effectiveness and cost effectiveness of a programme to offer PCV13 to all clinical risk groups in the UK (and high financial cost), and the evidence that the impact and cost effectiveness of such a programme is diminishing, JCVI advised against the introduction of such a programme in the UK.

8. Furthermore, given the evidence of accumulating indirect protection against PCV13 serotypes across the UK population and the current absence of data on the effectiveness of PCV13 in older adults, JCVI also advised against the introduction of a routine immunisation programme to offer PCV13 to older adults in the UK.

9. Nevertheless, JCVI considered that some clinical risk groups with a particularly elevated risk of, and high mortality from, IPD may benefit from immunisation with PCV13 in the short-term (while PCV13 serotypes continue to circulate). Those indicated for PCV13 would include individuals who are clinically severely immunocompromised, for example: bone marrow transplant patients or those with acute and chronic leukaemias, multiple myeloma, or genetic disorders severely affecting the immune system (e.g. IRAK-4, NEMO, complement deficiency).

10. For these patients it is suggested that one dose of PCV13 should be offered even if the routine childhood immunisations with PCV have been received. For leukaemia patients, PCV13 should be offered six months following completion of therapy[11,12] and for bone marrow transplant patients PCV13 should be offered

[10] Rozenbaum *et al.* (2012) Vaccination of risk groups in England using the 13 valent pneumococcal conjugate vaccine: economic analysis. *BMJ* 345:e6879 doi: 10.1136/bmj.e6879. Appendix 1.
[11] Patel *et al.* (2012) Serotype-specific pneumococcal antibody concentrations in children treated for acute leukaemia. *Arch. Dis. Child.* 97, 46-48.
[12] Royal College of Paediatrics and Child Health (2002) Immunisation of the immunocompromised child. Best practice statement.

nine to 12 months following transplantation[13]. Revaccination(s) with PCV13 at suitable interval(s) may be considered for some patients that could benefit from more than one dose of PCV13 (for example bone marrow transplant patients[13]) possibly following an assessment of serotype-specific immune responses. The 23-valent pneumococcal polysaccharide vaccine (PPV23) may also be considered for patients two years and older (with the exception of leukaemia patients following therapy as it is judged that there is no ongoing immunosuppression). This is in order to provide some protection against non-PCV13 serotypes, although evidence is limited or lacking about the immune response of this vaccine in severely immunocompromised patients. In these circumstances, PPV23 should be offered at least six months following the last dose of PCV13 and patients who have already received PPV23 should be offered PCV13 with an interval of at least six months following the dose of PPV23 that has already been received.

11. Whilst the effectiveness and cost effectiveness of PCV13 immunisation of severely immunocompromised individuals are uncertain, the offer of immunisation is warranted given the high increased risk of complications from infection and the likely high cost of treatment of complications in these patients. Decisions about the pneumococcal immunisations and testing of serotype-specific immune responses of these patients should be made by a clinician in secondary or tertiary care based on clinical judgement. Clinicians may also wish to consider the joint guidance from the Paediatric European Network for Treatment of AIDS Vaccines Group and the Children's HIV Association when considering the pneumococcal immunisation of children with HIV infection[14]. Nevertheless, as the benefit of PCV13 immunisation for all these individuals is expected to diminish over time as PCV13 serotypes no longer circulate, clinicians should consider the likely benefit when contemplating PCV13 immunisation in severely immunocompromised patients over the forthcoming years.

12. As with all immunisation programmes, JCVI will keep its advice under review in light of new information that may emerge. JCVI plans to review the effectiveness and cost effectiveness of pneumococcal immunisations within the next two years in light of the changing epidemiology of IPD and data from new studies on the effectiveness of pneumococcal immunisations. In the meantime, those aged two to less than 65 years in the other clinical risk groups[15] and all those aged 65 years and older should continue to be offered PPV23 as currently advised.

---

**13** Tomblyn *et al.* (2009) Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biol Blood Marrow Transplant 15, 1143-1238.

14 Menson *et al.* (2012) Guidance on vaccination of HIV-infected children in Europe. *HIV medicine.* 13, 333-336.

15 Patients with asplenia / splenic dysfunction; chronic respiratory disease; chronic heart disease; chronic kidney disease; chronic liver disease; cerebrospinal fluid leaks; cochlear implants; and immunocompromise with the exception of clinically severely immunocompromised patients.