JCVI statement on the routine pneumococcal vaccination programme for adults aged 65 years and older

20 July 2011

1. Following a review of the available evidence, in March 2011 JCVI issued a statement on the routine pneumococcal vaccination programme for those aged 65 years and older advising that it be discontinued, with the vaccine continued to be offered to those aged 65 year and over in clinical risk groups, based on clinical judgement (Annex A).

2. Following the issuing of that advice, the Department of Health asked for views from interested parties. Submissions were received from: Sanofi Pasteur MSD, Professor Andrew Pollard of the Oxford Vaccine Group, the British Medical Association, the Meningitis Trust and Diabetes UK.1 JCVI also received new as yet unpublished analyses of epidemiological data from the Health Protection Agency (HPA), Health Protection Scotland (HPS) and Dr Caroline Trotter of the University of Bristol. The JCVI pneumococcal sub-committee considered the submissions and the new analyses. JCVI subsequently considered the submissions, the new analyses and the views of the sub-committee.

3. JCVI concluded that the submission from Sanofi Pasteur MSD provided a selective interpretation of the evidence. No new persuasive evidence had been provided by Sanofi Pasteur MSD to alter the conclusions reached previously by JCVI nor further evidence to explain the lack of observable impact of PPV23 on invasive pneumococcal disease (IPD) in the population aged 65 years and older in the UK. Whilst many data had been provided on the immunogenicity of PPV23, these cannot be used to predict clinical outcome reliably, due to a lack of an established correlate of immune response with protection. The other four submissions provided little substantially new, or no new evidence.

4. JCVI noted that a newly extended analysis by the HPA of data on the incidence of IPD in England and Wales between epidemiological years 1998/99 and 2007/082 continued to show no observable overall impact of PPV23 at the population level in the age group 65 years and older. Neither did data on the incidence of IPD in Scotland.3 Nor did an analysis of English hospital episode statistics of admissions for pneumococcal meningitis, pneumococcal septicaemia, pneumococcal pneumonia or pneumonia between 2002/3 and 2008/9 in the 65 years and older age group.4 While there may be a number of

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1 Submissions at [http://www.dh.gov.uk/ab/JCVI/DH_123529](http://www.dh.gov.uk/ab/JCVI/DH_123529)
reasons for the lack of observable population level impact, indirect protection of this age group arising from the introduction of the pneumococcal conjugate vaccine (PCV) into the childhood vaccination programme is observed in analysis of IPD data for England and Wales.\(^5\) One possible reason may be the staggered introduction of the pneumococcal vaccination programme for those aged 65 years and older in England and Wales that began with vaccination of the oldest catch-up cohorts in 2003, moving to younger cohorts with the vaccination of routine cohorts beginning in 2005.\(^6\) However, no sustained impact on IPD was seen in Scotland where the routine and catch-up cohort vaccinations were introduced simultaneously in 2003.

5. JCVI considered that a newly extended analysis of the effectiveness of PPV23 in the population aged 65 years and older in England and Wales\(^7\) shows individual benefit from the vaccine greater than was suggested by the previous analysis (see Annex A). The new analysis, based on a substantially larger number of data on IPD in England and Wales, provided estimates of vaccine effectiveness in different age groups and between the healthy population and that with clinical risk factors. The analysis suggests that PPV23 is moderately effective against IPD for two years in the population aged 65 years and older taken as a whole (VE 48%, 95% CI 32-60 below two years post-vaccination) with effectiveness then waning rapidly (VE 21%, 95% CI 3-36 between two and five years and 15%, 95% CI -3-30 more than five years post-vaccination). In addition, there are indications that the vaccine may be less effective in some clinical risk groups compared with the healthy population and in older compared with younger age cohorts in the population aged 65 years and older.

6. However, JCVI noted that the new analysis suggests that the effectiveness of PPV23 may be higher and maintained for longer in the group aged 65 to 74 years without clinical risk factors for pneumococcal disease (VE 65%, 95% CI 23-84 below two years post-vaccination; 62%, 95% CI 21-82 between two and five years post-vaccination and 28%, 95% CI -72-70 more than five years post-vaccination).

7. JCVI considered that taken together these findings suggest that the vaccine may be more effective against IPD than had been assumed previously by JCVI and the sub-committee.\(^8\) In addition, the findings of this analysis, and also an analysis providing


\(^6\) CMO letter on adult immunisation update August 2003.


\(^8\) JCVI minute of February 2009.


estimated case fatality ratios\textsuperscript{9} are consistent with assumptions made in a study that suggests an age-based programme for those aged 65 years and older in England and Wales is cost effective and may be more cost effective than a risk group-based programme.\textsuperscript{10} Previous assumptions about the effectiveness of the vaccine had suggested that the age-based programme may not be cost effective.\textsuperscript{11} Nevertheless, JCVI recognised that the cost effectiveness of the programme is due primarily to the relative low cost of the vaccination programme (provided the vaccine is administered routinely with seasonal influenza vaccine) rather than because the vaccine is highly effective clinically. Revaccination with PPV23 is precluded by a paucity of evidence on the effectiveness of repeat doses of PPV23 and evidence of possible immune hyporesponsiveness and increased reactogenicity.\textsuperscript{12,13,14,15}

8. JCVI noted that experience from the seasonal influenza vaccination programme suggested that universal aged-based recommendations may result in higher vaccination coverage than risk group-based recommendations\textsuperscript{16} as they may be implemented more easily. As the age of routine PPV23 vaccination is aligned currently with seasonal influenza vaccination, a risk group-based programme may be more difficult for health professionals to implement, and thus, may lead to lower coverage and may incur greater opportunity costs compared with an age-based programme for those aged 65 years and older.

9. JCVI concluded that uncertainty remains about the effectiveness of PPV23 against IPD and whether it also lowers morbidity from IPD. There is also a lack of UK data on the effectiveness of PPV23 against pneumococcal pneumonia and mortality. The paucity of reliable data makes the formulation of evidence-based advice more challenging. However, the new analysis on the effectiveness of PPV23 based on the UK experience of


\textsuperscript{14} Clatterbuck et al. Pneumococcal conjugate and plain polysaccharide vaccines have divergent effects on antigen-specific B-cells. Unpublished.

\textsuperscript{15} Lazarus et al. (2011) A Randomized Study Comparing Combined Pneumococcal Conjugate and Polysaccharide Vaccination Schedules in Adults. CID. 52, 736-742.

the vaccine provides better evidence that suggests the vaccine provides at least some short-term individual protection against IPD in those 65 years and older, although protection may be less and wane faster in older age groups and for some clinical risk groups. In addition, the new data are consistent with assumptions made in a study that suggests the current programme is cost effective and would be more cost effective than a risk group-based programme.

10. JCVI concluded that (i) PPV23 may provide some short term protection against IPD to those aged 65 years and older with possibly longer lasting protection in the youngest age cohorts, (ii) routine universal vaccination of all those aged 65 years and older is likely to be cost effective and (iii) an alternative risk group-based programme may be more difficult to implement, be less effective and less cost effective. The committee advised that, based on these observations, the existing routine universal programme for those aged 65 years and older should continue. PPV23 should also continue to be offered to children aged two years or older and adults in the specified clinical risk groups for pneumococcal disease.\(^\text{17}\)

11. However, JCVI considered that the epidemiology of pneumococcal disease and the effectiveness and cost effectiveness of the PPV23 vaccination programme should be kept under review and be reviewed again within two years, in light of the indirect protection arising from the introduction of PCV13 into the childhood vaccination programme and the findings of ongoing studies on the effectiveness of PCV in adults.\(^\text{18}\) In addition, better data and further studies are required on the effectiveness of PPV23, particularly on the impact on pneumococcal pneumonia, morbidity and mortality.


Annex A

JCVI statement on discontinuation of the routine pneumococcal vaccination programme for adults aged 65 years and older

16 March 2011

1. A programme to offer pneumococcal vaccination to all those aged 65 years and older was introduced in 2003 in the UK following advice from JCVI. It was acknowledged by the committee at the time that estimates of the likely effectiveness and duration of protection of the available vaccine – a 23-valent pneumococcal polysaccharide vaccine (PPV23) – were uncertain. However, given the published evidence, high burden of invasive pneumococcal disease in the population aged 65 years and older, the established safety profile of PPV23 and the broad coverage against pneumococcal serotypes provided by the vaccine, the committee agreed that a vaccination programme should be introduced. Under this programme, a single dose of PPV23 has been offered to all those aged 65 years and older.

2. JCVI and its pneumococcal sub-committee recently reviewed cumulative data on the incidence of invasive pneumococcal disease in England and Wales from 1996 to 2010 and recent data on the immunogenicity and effectiveness of the 23-valent pneumococcal polysaccharide vaccine in older age groups.

3. JCVI noted that there had been no discernable decrease in the incidence of invasive pneumococcal disease in those aged 65 years and older following the introduction of the vaccination programme despite widespread use of PPV23 in this age group. However, following the introduction of a seven-valent pneumococcal conjugate vaccine (PCV7) into the childhood vaccination programme in 2006, a significant decrease in invasive pneumococcal disease in older people has been observed but only in disease arising from the seven pneumococcal serotypes that this conjugate vaccine provides protection against. Whilst herd immunity has produced an overall reduction in the incidence of pneumococcal disease in older adults, this has been tempered by an increase in other pneumococcal serotypes as a consequence of replacement of vaccine serotypes with non-vaccine serotypes. However, early indications following the substitution in 2010 of PCV7 with a 13-valent pneumococcal conjugate vaccine (PCV13) in the childhood vaccination programme suggest that it would be reasonable to expect a further decline in invasive pneumococcal disease in older adults from some of the additional serotypes in PCV13.

4. An analysis of epidemiological data from England and Wales suggests that the effectiveness of PPV23 is poor in those aged 65 years and older (overall vaccine effectiveness of 23% (95% CI 3 – 36%) over six years post-vaccination). Furthermore, the effectiveness of PPV23 is short lived with no evidence of effectiveness beyond six years [estimated effectiveness of 1% (95% CI -31 – 35%)] Results from recent studies and meta-analyses conducted in other countries vary but overall the data suggest that the

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19 Pneumovax Summary of Product Characteristics.
26 Health Protection Agency unpublished data on the epidemiology of invasive pneumococcal disease 1996-2010
28 Health Protection Agency. Unpublished data.
effectiveness of the vaccine in those aged 65 years and older is poor\(^{29,30,31,32,33}\). An older study also suggests the effectiveness of PPV may not be long lasting and that it may also shorten with increasing age\(^{34}\). Furthermore, recent evidence suggests that revaccination with PPV23 may not induce an improved immune response\(^{35,36}\) and possibly a poorer response due to immune hyporesponsiveness\(^{37}\).

5. JCVI considered unpublished data on the use of PCV13 in adults\(^{38}\) and noted that there is no conclusive evidence currently that this vaccine would be more effective in older adults.

6. Given the cumulative evidence of (i) a lack of impact on invasive pneumococcal disease from the pneumococcal vaccination programme for those aged 65 years and older, (ii) the poor effectiveness and lack of long-lasting protection conferred by PPV23 in adults aged 65 years and older and (iii) a lack of an improved, and possibly an impaired, response to revaccination, JCVI considers the routine pneumococcal vaccination programme for those aged 65 years and older to be ineffective. As there is no licensed and demonstrably effective alternative vaccine currently, the committee concludes that there is little benefit from continuing the programme and advises that it be discontinued.

7. JCVI considers that PPV23 should continue to be offered to children aged two years or older and adults in the specified clinical risk groups for pneumococcal disease\(^{39}\) as evidence suggests the vaccine is more effective in younger and middle-aged groups\(^{16,40}\) and, although the evidence is not clear cut, may provide protection to those at increased risk of pneumococcal disease because of underlying health conditions\(^{22,41,42,43,44,45}\). However, for the reasons given above (paragraph 6), JCVI advises that clinicians should use clinical judgement when considering the benefits of vaccination in those in the seventh decade.

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\(^{33}\) Vila-Corcoles et al; EPIC Study Group (2010) Effectiveness of the 23-valent polysaccharide pneumococcal vaccine against invasive pneumococcal disease in people 60 years or older. *BMC Infect Dis* 10, 73


\(^{35}\) Mushet et al. (2010) Safety and antibody response, including antibody persistence for 5 years, after primary vaccination or revaccination with pneumococcal polysaccharide vaccine in middle-aged and older adults. *JID.* 201, 516-524.


\(^{38}\) Pfizer unpublished data.


of life and older taking into account patient age and the severity of the clinical risk factors for pneumococcal disease.

8. As adults receive herd immunity protection from the use of PCV7 and now PCV13 in the childhood vaccination programme, JCVI advises that any proposed change in the coverage against pneumococcal serotypes provided by the vaccine used in the childhood programme must consider the potential impact on herd immunity and pneumococcal disease in the wider population.

9. JCVI will keep the epidemiology of pneumococcal disease, the impact of pneumococcal vaccinations and the potential of new alternative vaccines under review.