Research Review
PRODUCT REVIEW

23-valent pneumococcal polysaccharide vaccine [PNEUMOVAX® 23]

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This review discusses the use of the 23-valent pneumococcal polysaccharide vaccine PNEUMOVAX® 23 (PPV-23), which protects against 23 different types of pneumococcal bacteria responsible for an estimated 90% of cases of life-threatening invasive pneumococcal disease (IPD).[1] In New Zealand, PPV-23 is funded as part of the Immunisation Schedule for adults and children from two years of age at very high risk of pneumococcal disease, and is recommended for all adults with chronic medical conditions and for those 65 years or older. It is well recognised that older adults disproportionately sustain morbidity and mortality due to vaccine-preventable illnesses, such as IPD. Healthcare professionals can play a key role in improving vaccine coverage and awareness of such illnesses.

PPV-23 may be administered concurrently with the influenza vaccine [FLUVAX® or FLUARIX®] and should be offered to adults attending vaccination clinics for seasonal influenza. For those patients not meeting the PNEUMOVAX® 23 funding criteria, the cost of the vaccine is approximately $55–$75.

Pneumococcal disease

Pneumococcal disease is a significant public health problem, with approximately 1.6 million cases of fatal pneumococcal disease occurring annually worldwide.[1] Most of these fatalities are in young children in developing countries, and in the elderly and individuals with chronic underlying diseases in developed countries.[1–4]

Pneumococcal disease is caused by the bacteria *Streptococcus pneumoniae* (pneumococcus), of which there are >90 identifiable serotypes.[3] Some of these serotypes are more prevalent in adults while others are more prevalent in children. *S. pneumoniae* is ubiquitous, and many individuals (up to 60% of unvaccinated children) carry the organism asymptomatically in their upper respiratory tract.[5] This bacteria, which is spread by respiratory droplet contact, is responsible for a range of pneumococcal diseases including non-invasive pneumonia, otitis media, sinusitis and bronchitis. More serious illness can occur when the bacteria invades normally sterile tissue, leading to severe and life-threatening invasive pneumococcal disease (IPD).[3,5] IPD includes bacteraemia, meningitis, infective arthritis, osteomyelitis, peritonitis and bacteraemic pneumonia.[3] The incubation period of the infection can be as short as one to three days.[5]

Of the >90 serotypes of *S. pneumoniae,* approximately 20 are responsible for >70% of cases of IPD.[3]

Individuals at high-risk

The following conditions are associated with increased risk of developing pneumococcal disease: immune deficiencies (including HIV infection, asplenia, organ transplantation and immunosuppressive therapy); anatomic abnormalities (skull fracture/cerebrospinal fluid leak, cochlear implant, congenital heart disease and splenectomy); chronic disease (chronic pulmonary, hepatic or neurological disease, Hodgkin's disease, sickle cell anaemia, diabetes mellitus, nephrotic syndrome and renal insufficiency); perinatal conditions (low birth weight and prematurity).[6] Also identified as IPD risk factors are young and old age (<2 years and >65 years), male sex, Māori and Pacific Island ethnicity, living in the most deprived areas, season (autumn and winter months), crowding and daycare attendance.[7]

Incidence of pneumococcal disease

According to World Health Organization (WHO) estimates, *S. pneumoniae* causes approximately 1-2 cases of meningitis, 15-19 cases of febrile bacteraemia and 100 cases of pneumonia per 100 000 population per year.[8] In New Zealand, IPD is a notifiable disease and is closely monitored by the Institute of Environmental Science and Research (ESR). While pneumococcal disease occurs throughout the year, it is more common in autumn and winter.[9]

According to the most recent ESR report for the 12-month period ending 30th September 2011, there were 527 notified cases of IPD (12.1/100 000 population).[10] During that period, the highest rates of IPD were reported in the ≥65 age group (39/100 000 population) and in the under 2 year old age group (23.7/100 000).[10]

The incidence of IPD in children <2 years of age has shown a steady decline since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV-7) into the childhood immunisation schedule in 2008.[11] At this stage there has only been a small decline detected in IPD in those aged ≥65 years, with a fall from 43.6 to 39.4/100,000 in 2009 and 2010, respectively.[10,11]

It is evident that the risk of pneumococcal disease is higher in infants (especially Māori and Pacific Islanders), the elderly, and in individuals with viral upper respiratory tract infections or an immune deficiency status.[9] A national active surveillance study of pneumococcal meningitis during 2005 to 2007 revealed an annual incidence of 17.7/100 000 in children <2 years of age.[5]

Pneumococcal disease burden

While the true burden of pneumococcal disease is difficult to assess, it is recognised that IPD is a major cause of morbidity and mortality, resulting in a substantial clinical and economic burden worldwide.[12] The WHO estimates that every year approximately one million children younger than 5 years of age die from pneumococcal diseases.[4] In NZ, in the 10 years between 1996 and 2006, there were 2367 hospital admissions for IPD/pneumococcal pneumonia in children and young people aged 0-24 years.[7] Another NZ study estimated that in 2003 there were 26 826 episodes of community-acquired pneumonia in adults, with an estimated annual cost of $63 million (direct medical costs of $29 million, direct non-medical costs of $1 million and lost productivity $33 million).[13]

In NZ in 2010, the overall IPD case-fatality rate was 5.3% for all ages, with a rate of 8.9% in those aged 65 years and over.[11] The higher fatality rate in the elderly in NZ is consistent with that seen in the US, with the elderly representing one-third of the IPD cases, but accounting for 48.9% of all deaths due to IPD.[12] With the elderly comprising a significant at-risk population, the burden of IPD is set to increase with the aging population.

A recent North American study looking at the burden of community-acquired pneumonia (CAP), of which *S. pneumoniae* is the most frequently identified pathogen, revealed an all-cause mortality rate for CAP patients of 28% within 1 year.[14] The study also showed a substantial economic burden associated with the illness.[14]

Every year in NZ, otitis media in children <5 years results in 5000 hospital admissions, constituting a significant burden on NZ's health system.[15] This disease may leave an individual with permanent hearing loss and it is estimated that the cost to the Ministry of Education for a child who is profoundly deaf can be as much as $25 000 per year for up to 15 years.[16] The cost of residential care for an adult survivor of meningococcal disease left with severe intellectual and/or physical disability may be as high as $50 000 per year.[16]

As mentioned earlier, a NZ survey undertaken between 2005 and 2007 revealed an annual incidence of pneumococcal meningitis of 17.7/100 000 in children <2 years of age.[5] During that period, the case fatality rate was 10%, with 18% of surviving children suffering persisting neurological disability.[5] The survey also revealed that Māori and Pacific Island children were affected considerably more often (23.6/100 000 and 39.2/100,000) than other ethnicities (13.6/100,000).[5]

Vaccination against pneumococcal disease

NZ has a high rate of antibiotic resistance among *S. pneumoniae,* with erythromycin, penicillin and cefotaxime-resistant strains present.[17] Vaccination is considered to be the only public-health measure likely to reduce the burden of pneumococcal diseases.[3] The different pneumococcal vaccines target different virus strains.

S. pneumonia vaccines approved by Medsafe and currently funded by Pharmac as part of the Schedule are the 10-valent protein conjugate vaccine PCV-10 (Synflorix®) which replaces PCV-7 (Prevenar 7®), the 13-valent protein conjugate vaccine PCV-13 (Prevenar 13®) and the 23-valent pneumococcal polysaccharide vaccine PPV-23. The conjugate vaccines are suitable for use in children from 6 weeks of age. However, PPV-23 which was developed for use in adults in the mid 1980s, is a capsular polysaccharide vaccine and is not suitable for use in young children (<2 years) as it induces antibodies via a mechanism that immature immune systems are unable to respond consistently to.[5] So far, data is limited on the efficacy of the conjugate vaccines in adults.[5] The efficacy of PPV-23 in adults is discussed below.

NZ MOH pneumococcal vaccination recommendations[5]

Group	Vaccine recommendations	Funding
Children <5 years of age (and born from 1st Jan 2008) not identified as high-risk of pneumococcal disease.*	Synflorix®	Funded
Children 0-5 years who meet the high-risk pneumococcal immunisation criteria.*	Prevenar 13® followed by PPV-23 (after age two years and ≥8 weeks after last PCV dose). Previously unvaccinated children aged 2-5 years require 2 doses of Prevenar 13®, 8 weeks apart. Revaccinate once with PPV-23, 3 years after the first PPV-23.	Funded
Children 0-16 years pre- and post-splenectomy (including those with functional asplenia)	Prevenar 13® followed by PPV-23 (administered after 2 years of age and ≥8 weeks after last PCV dose). Revaccinate once with PPV-23, after 5 years if first dose at >10 years of age and after 3 years if first dose at <10 years of age.	Funded
Children 5-16 years with high-risk conditions*	Prevenar 13® followed by PPV-23	Not funded
Adults ≥16 years pre- and post-splenectomy	PPV-23 (possibly after receiving Prevenar 13®) and revaccination 5 years after first vaccination and at age 65 years to complete three doses.	Funded
Adults ≥16 years with high-risk conditions*	PPV-23 and revaccination 5 years after first vaccination and at age 65 years to complete three doses.	Not funded
Adults ≥65 years	PPV-23 with revaccination after 5 years.	Not funded

*see MOH Immunisation handbook 2011 for definition of high-risk[5]

About PPV-23

PPV-23 is an unconjugated pneumococcal polysaccharide vaccine approved by Medsafe and available for intramuscular or subcutaneous injection. A 0.5 mL dose of the vaccine contains 25 µg of each of the following pneumococcal capsular polysaccharide antigens; 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F. These 23 specific bacterial subtypes are responsible for an estimated 90% of cases of IPD in developed countries.[1] Several of the *S. pneumoniae* subtypes covered by the PPV-23 vaccine are associated with high IPD case-fatality rates.[18]

Who should receive PPV-23?

New Zealand Best Practice Advocacy Centre (BPAC) recommends that the use of PPV-23 be considered for individuals fitting the following criteria:[19]

- Aged 65 years or older
- Chronic cardiovascular disease, e.g. congestive heart failure, cardiomyopathies
- Chronic pulmonary disease, e.g. chronic obstructive pulmonary disease, asthma
- Diabetes, alcoholism, chronic liver disease (cirrhosis), or cerebrospinal fluid leaks
- Chronic renal failure or nephrotic syndrome
- Functional or anatomic asplenia, e.g. sickle cell disease, splenectomy*
- Immunocompromising conditions or immunosuppressive treatment, e.g. HIV infection, congenital immunodeficiency, haematologic and solid tumors, treatment with alkylating agents, anti-metabolites, long-term systemic corticosteroids, radiation therapy, and organ or bone marrow transplantation
- Candidate for, or recipient of, cochlear implant or intracranial shunts
- Pre-term infants, born at under 28 weeks gestation
- Down's syndrome

*PPV-23 should be administered at least 2 weeks before elective splenectomy.

Concurrent administration with influenza vaccine advised

PPV-23 can be administered at the same time as the influenza vaccine, by separate injection in the other arm.[20] Such co-administration does not increase the risk of adverse events and does not decrease the antibody response of either vaccine.[20] A large prospective cohort study undertaken in Hong Kong has shown dual vaccination with PPV-23 and influenza vaccine to be more effective in protecting elderly persons with chronic illness from developing complications from respiratory, cardiovascular and cerebrovascular diseases than administration of either of the vaccines alone.[21] New Zealand best practice guidelines support the concurrent administration of PPV-23 and the influenza vaccine.[19]

Revaccination

While revaccination of immunocompetent individuals who have previously received PPV-23 is not routinely recommended, revaccination is recommended for those at high risk (see MOH vaccine recommendation in Table).[20] The minimum recommended time from first vaccination to revaccination is 5 years.

Contraindications

Hypersensitivity to any component of the vaccine in a contraindication to its administration.[20] PPV-23 should not be given concurrently with ZOSTAVAX® because of possible reduced immunogenicity of ZOSTAVAX®.[20] For other contraindications, warnings and precautions refer to the PPV-23 Medsafe Data Sheet.[20]

Clinical efficacy of PPV-23 in adults

It is clear that individual's aged ≥65 years of age and those with chronic illnesses are a high-risk group for developing IPD. While evaluations of the efficacy of PPV-23 have yielded contradictory conclusions for the prevention of pneumococcal pneumonia in recommended target groups, most studies have demonstrated consistent findings for the prevention of IPD among the general population of elderly and healthy young adults.[22] The large differences in effectiveness estimates seen in recent meta-analyses are thought to be due to inclusion of different patient groups in the trials, with some studies including immune-compromised individuals, a group that generally has a lower than normal response to vaccination.[5,22] Furthermore, the impact of PPV-23 vaccine on IPD in a population is highly dependent on vaccine coverage and, as with other vaccines, low vaccination effectiveness may reflect poor vaccine uptake, not poor vaccine performance.[23]

One of the most recent systematic reviews, conducted by the Cochrane Collaboration has shown that PPV-23 is effective in preventing IPD in adults, with a pooled estimate of vaccine efficacy from 10 prospective clinical trials of 74%, and from five observational studies or 68%.[24] Furthermore, almost all of the case-control, retrospective and indirect cohort studies have shown that PPV-23 provides substantial protection against IPD.[3] A recent review by Fedson et al concluded that in elderly adults, PPV-23 vaccination prevents 50–80% of cases of IPD requiring hospitalisation and prevents 20–25% of cases of CAP.[3] Prior pneumococcal vaccination also appears to be associated with reduced morbidity, mortality and length of hospital stay among hospitalised adults with CAP.[25]

Primary vaccination and revaccination with PPV-23 induces robust immune responses in elderly adults that last for at least 5–10 years.[3,26,27] Studies have shown that antibody levels decline substantially within 1–2 years of primary vaccination, but persist at levels approximately 2-fold higher than baseline for ≥5 years.[3] Revaccination with PPV-23 3 to 6 years after the prior dose has been shown to be immunogenic and generally well tolerated.[27-29]

Is PPV-23 cost-effective?

During the past 10 years there have been numerous studies demonstrating the cost-effectiveness of PPV-23 vaccination in the elderly, with some studies showing that such vaccination may be cost-saving.[12,30] A two-year retrospective cohort study of elderly individuals with chronic lung disease showed that vaccination prevented 43% of hospitalisations due to pneumonia and 31% of pneumonia-related deaths, thus providing significant health and economic benefits.[31]

Safety of PPV-23

On the basis of decades of use, PPV-23 is considered safe.[1] Minor local reactions including transient redness and pain at the injection site occur in 30-50% of those vaccinated, while low-grade fever occurs infrequently.[1] Inadvertent intradermal administration may cause severe local reactions.[20] The rate of local reactions appears to be higher following revaccination,[32] but the risk of systemic events does not appear to be increased.[33]

A large study investigating the safety of PPV-23 in adults ≥65 years of age and in those 50-64 years of age did not show an increased rate of severity of adverse effects in the older age group.[27] However, there have been post-marketing reports of frail elderly patients with multiple comorbid conditions experiencing severe adverse events.[20] Adverse events requiring consultation with a GP occur at a rate of 8/1000 vaccinations and more severe side-effects occur at a rate of 1/100 000.[5] Anaphylactoid reactions have been infrequently reported and revaccination must not be undertaken in these individuals.[20]

Specialist commentary on the clinical efficacy, safety and cost-effectiveness of PPV-23

Prevention of acute myocardial infarction and stroke among elderly persons by dual pneumococcal and influenza vaccination: a prospecitve cohort study[21]

Authors: Hung IF et al

Summary: Researchers from Hong Kong undertook a prospective cohort study involving outpatients aged ≥65 years with chronic illness who participated in a PPV and trivalent influenza vaccine (TIV) vaccination program; 7292 received both PPV and TIV, 2076 received TIV vaccine alone,1875 received PPV alone, and 25,393 were unvaccinated. At 64-weeks follow-up, dual-vaccinees experienced fewer deaths (hazard ratio [HR] 0.65; 95% CI 0.55–0.77) and fewer cases of pneumonia (HR 0.57; 95% CI 0.51–0.64), ischemic stroke (HR 0.67; 95% CI 0.54–0.83) and acute myocardial infarction (HR 0.52; 95% CI 0.38–0.71) compared with unvaccinated subjects. Furthermore, compared with no vaccination, dual vaccination resulted in fewer intensive care and coronary admissions (HR 0.45; 95% CI 0.22–0.94 and HR 0.59; 95% CI 0.44–0.79, respectively).

Comment: This paper is interesting because the subjects were invited to join one of three groups; hardly the stuff of randomisation, but at least the design reflects the real world of patient choice. One has to assume that they all received the same advice and recommendations, so that the investigators did not push them into one group or another. I also like the way the paper allows one to see the absolute reduction in endpoints, not just odds ratios (ORs) or percentage reductions. In the real world patients want to know how likely they are to get sick if they get vaccinated, or if they are not vaccinated. The Kaplan-Meier graphs show that there is around a 3% absolute reduction in admission and 1.5% reduction in admissions after 500 days of follow up, comparing those getting both influenza and PPV with those unvaccinated. This on its own may not sound so great, but when taken with the reductions in stroke, myocardial infarction and pneumonia, makes for a fairly convincing body of evidence to support double vaccination in over 65 year olds. These data were sufficient to form the basis of fully funded double vaccination in Hong Kong.

Antibody persistence 10 years after first and second doses of 23-valent pneumococcal vaccine, and immunogenicity and safety of second and third doses in older adults[34]

Authors: Musher DM et al

Summary: This study assessed antibody levels 10 years after first or second doses of PPV-23 and assessed safety and immunogenicity 30 days after revaccination at 10 years, in 133 subjects aged ≥60 years. Mean IgG concentrations exceeded vaccine-naïve levels for 7 of 8 serotypes tested 10 years after first or second doses. Second and third doses administered at this time were immunogenic and were generally well tolerated.

Comment: This article is discussed as an example of a truly tedious, but very important group of studies trying to provide data that underpins recommendations regarding when to revaccinate! An issue with polysaccharide vaccines is that they are not regarded as inducing T cell memory, and the best correlation of protection is antibody levels. Another feature is that there is concern that polysaccharide vaccines may induce hyporesponsiveness to subsequent doses. This study provides reassurance that antibody levels persist and revaccination does not result in too many local reactions. There remains a huge lack of clinical data describing benefit of second and third doses, meaning that few authorities recommend more than two doses in a lifetime. The concern regarding increased reactogenicity is not offset by clinical benefit data. Immunogenicity studies such as this would, however, suggest that for selected high-risk patients it would not be unreasonable to give up to three doses of PPV.

Vaccines for preventing pneumococcal infection in adults (review)[24]

Authors: Moberley SA et al

Summary: This Cochrane review was undertaken in order to assess the effectiveness of PPV in preventing disease or death in adults. An extensive literature search was undertaken for randomised controlled trials (RCTs) comparing PPV with placebo, control vaccines or no intervention, and for non-RCTs assessing PPV effectiveness against IPD. Twenty-two eligible studies were identified involving a total of 48 656 subjects in 15 RCTs and 62 294 subjects in 7 non-RCTs. Analysis of 10 RCTs involving a total of 35 483 subjects, revealed that PPV reduced the risk of all IPD, with a protective vaccine efficacy of 74% (95% CI 56–85). Likewise, analysis of the non-RCTs revealed evidence for protection against IPD in populations for whom the vaccine is currently utilised. However, efficacy against all cause pneumonia was inconclusive with substantial statistical heterogeneity (OR 0.71, 95% CI 0.52–0.97; random-effects model, I2 = 87.3%) and PPV was not found to be associated with substantial reductions in all-cause mortality (OR 0.87, 95% CI 0.69–1.10; random-effects model, I2 = 75.3%).

Comment: I couldn't leave the Cochrane review out, as it has been so oft-quoted. It is now the main source quoted to say that PPV is effective against invasive disease and bacteraemic pneumococcal pneumonia. The numbers of participants included in the studies meta-analysed are truly mind-boggling. These numbers certainly give confidence regarding safety, but the varying methods, heterogeneity of populations etc. conspire to leave doubt about how useful PPV is in preventing non-specified pneumonia. In other words, this review makes it harder for cost-conscious individuals or governments to justify spending money on PPV.

Effects of a large-scale introduction of the pneumococcal polysaccharide vaccine among elderly persons in Stockholm, Sweden[35]

Authors: Spindler C et al

Summary: The impact of a 3-year PPV-23 vaccination campaign in Stockholm on the incidence and serotype distribution of IPD was assessed in this study. The campaign, which was initiated in 1998 and directed towards the elderly, had a vaccine coverage of 36%. The findings were compared with those in Skåne County, where no vaccination campaign was performed. During 1997-2001, the incidence of vaccine-type IPD in Stockholm significantly declined in the elderly, but not in the other age groups (from 50 to 28.9/100 000). During that period, no decline in the incidence of the disease was seen in Skåne County.

Comment: This study is included in this review because in many ways it is my favourite paper. It is well written, pragmatic and uses methods that are appropriate for a NZ context. The PPV was made available at reduced costs to those receiving routine seasonal influenza vaccine. The effects on IPD were substantial in the over 65 year olds, but there are many factors that prevent over-detailed analysis, and to their credit, the authors do not try and look at soft data. In other words, it was observational, had no true control group and did not continue for long enough to look at sustained effects on disease. However, a study of a population of 2.7 million people, using a practical approach tied to influenza vaccination has a lot going for it! It is well worth reading the paper itself as a model of practical research.

Efficacy of 23-valent pneumococcal vaccine in preventing pneumonia and improving survival in nursing home residents: double blind, randomised and placebo controlled trial[36]

Authors: Maruyama T et al

Summary: The efficacy of PPV-23 in those at high risk of pneumococcal pneumonia was investigated in this RCT involving 1006 Japanese nursing home residents who were randomly allocated to PPV-23 (n = 502) or placebo (n = 504). Study participants were followed-up for at least 26 months. During follow-up, 63 (12.5%) participants in the vaccine group and 104 (20.6%) in the placebo group developed pneumonia. Pneumococcal pneumonia was diagnosed in 14 (2.8%) participants in the vaccine group and 37 (7.3%) in the placebo group (P<0.001). Death from pneumococcal pneumonia was significantly higher in the placebo group than in the vaccine group (35.1% vs 0%; P<0.01). The death rate from all-cause pneumonia (vaccine group 20.6% vs placebo group 25.0%) and from other causes (17.7% vs 15.9%) did not differ significantly between the two study groups.

Comment: This is a massive study and has the rare value of being randomised and placebo controlled. The study relied on obsessional follow-up and monitoring by the physicians caring for the patients, and has the unique feature of extensively using the pneumococcal urinary antigen. Despite impressive reductions in pneumococcal pneumonia, there was no statistically significant reduction in all-cause pneumonia related deaths. This paper then leaves us with further evidence for using the vaccine in elderly people living in residential care, although obviously immunosuppressed persons were excluded. The failure to reduce death rates from pneumonia in general leads to be one of recurrent obsessions: it may be that quite a few patients labelled with pneumonia in fact have aspiration pneumonitis (non antibiotic requiring) or heart failure. Such patients would not plausibly be protected by pneumococcal vaccination. This is one of the central difficult messages about vaccination: those vaccinated want to prevent pneumonia or respiratory illness or death, and are not impressed by arguments saying that the vaccine will only prevent a proportion of such cases. This issue makes it imperative to explain such nuances, just like explaining that influenza vaccine will only have limited benefit for preventing "head colds".

Cost-effectiveness of pneumococcal polysaccharide vaccination in adults: A systematic review of conclusions and assumptions[12]

Authors: Ogilvie I et al

Summary: This US review identified 11 economic evaluations of PPV-23 in adults from an extensive literature search. In general, all of the studies found vaccination with PPV-23 to be a cost-effective, and in some cases a cost-saving strategy for the prevention of IPD.

Comment: A study of this type has to be included in this review, but I am afraid that despite being a good summary, I remain confused. Essentially, the lack of clear data around PPV's efficacy makes economic analysis very imprecise. This means that whilst there is a general body of data indicating that PPV is cost effective when judged against the US $50,000 per quality adjusted life year gained threshold, there is a range of estimates including cost saving. Points of interest for me were that it appears likely that PPV in the >65yr olds will be most cost effective early in the phases of PCV programmes for children; and reducing the cost of administration by tagging to influenza vaccine has significant cost benefits. There was not time for this review to compare the cost effectiveness data for elderly PPV vs childhood PCV, but I suspect that adults are actually hard done by relatively speaking! NZ desperately needs clearer thinking on adult vaccination, because the messages are confused by who pays, personal autonomy and lack of clear information around risk. The low rates of private healthcare insurance in NZ means that cost effectiveness means that the person pays the cost of vaccination, and the state yields the financial benefit of avoiding hospital admission. This of course is not true for influenza vaccination, and the thrust of several of the papers selected leads to the suggestion that PPV and influenza go together nicely. Like influenza it is actually very hard to give very precise information to a person contemplating vaccination about what illness they are actually likely to avoid by being vaccinated. Unless fully or partially funded, most people will baulk at the cost without getting to potential benefit in their considerations.

Pneumococcal vaccines in adults: Assessing the evolving evidence[26]

Authors: Grabenstein JD and Manoff SB

Summary: This review assessed the evolving clinical evidence on the use of pneumococcal vaccines in adults. The authors reported that the literature contains many studies demonstrating the efficacy of PPVs against pneumococcal disease. They concluded that the published studies demonstrate the following: PPV helps prevent pneumococcal disease; antibody responses of adults to PPV-23 and PCV-13 are generally similar 6–12 months after vaccination; antibody concentrations after PPV-23 persist above baseline in ambulatory adults for many years; ambulatory adults respond to PPV-23 vaccination several times; the gap between pneumococcal vaccines in serotype coverage is approximately 20% and in the future this could increase.

Comment: This review article was written by Merck employees, and so must be considered in that light, although of course it was published in a reputable journal. My main reason for including it in this review is that it discusses the use of PCV in adults. The theoretical advantage of PCV is that it induces T cell based memory, although the fewer number of serotypes makes it less attractive than PPV. The authors conclude that both vaccines appear equally immunogenic in adults, and at this stage there appears to be insufficient data to recommend the use of PCV prior to PPV.

Experts' concluding remarks

Reviewing the literature for this review reminded me that the evidence for the use of PPV is actually very strong for the over 65 year olds, especially for the prevention of invasive disease. The strongest data and the most compelling opportunity coincide when PPV is given with seasonal influenza vaccine. In this setting, there appears to be evidence even for the prevention of myocardial infarction and stroke, in keeping with other observations linking an inflammatory response with these events.

Linking influenza and pneumococcal vaccine administration together would tie in nicely with a population-based approach to disease prevention, at a time when it is on peoples' minds. This would presumably better target those who are inclined to accept vaccination, because until publically funded, the costs of the visit to the GP and for the vaccine itself will be a barrier to many. The important difference of course is that PPV is only recommended for at most two doses in those aged 65 and above, and so it not a cost that will be oft-repeated.

Hopefully the herd benefits of PCV vaccination to infants will accrue in the elderly, but until then it makes sense to give PPV at the time of influenza vaccination.

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