Commentary: Pneumococcal immunization may not be cost-effective in the elderly in developed countries

Norman Waugh

Mangtani and colleagues\(^1\) have created a model to examine whether pneumococcal immunization in people \(\geq 64\) years in a developed country setting is cost-effective. The key elements in any such programme would be: effectiveness in preventing pneumococcal disease; the frequency of such events; the costs of the immunization programme—vaccine cost and payments to general practices (or others)—the costs avoided from reduction of disease and hence of events such as hospital admissions; and the net balance of costs and benefits. In their model, data on some of these elements are more certain than others.

The costs of such an immunization programme are reasonably well known, because it has already been introduced in Scotland. In the Grampian Health Board (population 530 000), 44 377 patients were immunized, in the year ended March 2004, at a vaccine cost of £574 088 and the cost of fees to practices of £312 855, at £7.05 per patient\(^2\) (Grampian Health Board, unpublished data). Mangtani and colleagues used a sophisticated method to estimate costs in general practice, by collecting cost data, but for the NHS, the fee is the actual cost. The observed cost in Grampian, based on experience, was £19.95 per person immunized, compared with the authors’ estimate of £9.30. The main differences are in the cost of the vaccine (£4 difference) and in its administration—Mangtani and colleagues estimate the cost in nurse clinics to be £1.91 but in reality the cost was the £7.05 fee paid to the general practices.

The costs of the events prevented by immunization were carefully ascertained, based in part on non-routinely collected data from a case series of patients with invasive disease. Production costs are over-estimated because the people in the age group \(\geq 64\) years were largely retired. The Department of Health has now advised that discount rates should be 3.5% for both costs and benefits,\(^2\) but the figures used by the authors were those recommended at the time of submission. The effect of applying the new figures would mainly impact on life years saved and future costs avoided, and would reduce cost-effectiveness. The frequency of adverse events—pneumonia and bacteraemia—was based on both practice and hospital data, supplemented by data from a case–control study. The practices came from the General Practice Research Framework, and can be considered ‘expert’ in data collection.

The key assumptions are on the effectiveness of immunization. This has long been an area of debate. Mangtani and colleagues use a figure of 50% efficacy against illness and death from pneumococcal bacteraemia. This figure seems to be a compromise between the results of meta-analyses of randomized controlled trials\(^3,4\) which show 38% protection (but with 95% confidence interval (CI) of −4 to 63% overlapping no benefit), whereas observational studies report mean benefit of 55% (44–64%) if only studies in the elderly and chronic diseased are used (i.e. excluding groups such as patients with HIV and US Navajos). It does not seem to fit with their previous review,\(^5\) which concluded that there was no evidence of a mortality reduction in developed countries.

As regards the much commoner manifestation of pneumonia, the authors note that three meta-analyses of the trials of the polysaccharide vaccine in elderly people in developed countries show no protection. Indeed, the latest and one of the better observational studies\(^6\) found a slight increase in pneumonia (hazard ratio 1.14, 95% CI 1.02–1.28). However they then assume some protection and hence cost savings from a reduction in non-bacteraemic pneumonia, using a figure of 37.5% reduction in both bacteraemia and pneumonia (Table 2). They do substantiate this with corresponding figures assuming no protection against pneumonia, which show a rather different picture.

Government advice in the UK takes an unjustifiably favourable view of the efficacy of the vaccine—'overall efficacy in preventing pneumonia is probably 60–70%'.\(^7\) Most (8 of 13) of the supporting references are epidemiological, and the only meta-analysis of evidence of efficacy cited\(^8\) failed to find evidence of efficacy in high-risk groups, being based on randomized controlled trials (RCTs). So in effect, the UK Government has based its advice on observational studies, while seeming to ignore the RCTs.

Previous economic evaluations have chosen to rely on efficacy data from observational studies rather than trials. Sisk and colleagues\(^9\) used a base case efficacy of 80% protection against pneumonia, which seems to have been based mainly on one observational, case–control study,\(^10\) which had a much wider age range than just the elderly, though mean age was 68 years. Ament and colleagues\(^11\) asserted that pneumococcal immunization would be cost-effective if it only reduced invasive disease, but assumed a reduction in pneumococcal bacteraemia of 60% and that immunization also gave some protection against pneumonia. The RCTs do not support these assumptions.

The model created by Mangtani and colleagues provides a useful contribution to the literature, because it can be used to test other assumptions. It would be interesting to re-run the model with the higher vaccine cost, the new discount rates, and
a lower efficacy rate, simultaneously. Perhaps more important would be to use the model for economic evaluation of the new conjugate vaccine which may be more effective. The problems of bias in economics research in the vaccines field, with specific reference to pneumococcal vaccines, have been recently highlighted by Beutels. The problem with pneumococcal immunization is that, for elderly people in developed countries, the evidence suggests some protection against the uncommon outcome of invasive disease (not quite statistically significant in the RTCs but more marked in the observational studies) but no protection against the commoner pneumonia.

References