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A Model to Estimate the Cost Benefit of an Occupational Vaccination Programme for Influenza with Influvac® in the UK[1]

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Abstract

Objectives: To model the economic impact of introducing an occupational vaccination programme for influenza with an inactivated influenza subunit vaccine (Influvac®) in the UK.

Design and setting: Using published sources, a decision tree was constructed which modelled the costs and benefits of introducing an influenza vaccine in a business in the UK from the perspective of an employer.

Study participants and interventions: The model considered the implementation of an occupational vaccination programme with Influvac® in a business employing 1000 normal healthy adults earning the national average wage in the UK. The model assumed that 95% of employees would be absent from work after contracting influenza for a mean of 5 days and that the level of productivity would be reduced by 60% for one day by 85% of sick employees returning to work.

Main outcome measures and results: The expected probability of an employee being absent from work following an influenza vaccination would be reduced from 5.7 to 1.8% when the incidence of influenza in the community is 6%. Accordingly, if all 1000 employees were vaccinated, a business would be expected to reduce absenteeism from work attributable to an influenza outbreak by 220 days. Moreover, the expected return on every pound invested by an employer would be £1.03, £3.09 and £5.15 (2000 values) when the annual incidence of influenza in the community is 2, 6 and 10%, respectively.

Conclusions: Implementation of an occupational vaccination programme with Influvac® would be expected to reduce the incidence of influenza among a workforce leading to less absenteeism from work and averted lost productivity. Even if the incidence of influenza was as low as 2% it may be a worthwhile investment for UK employers to vaccinate their employees with Influvac®.

1 Use of the tradename is for product identification purposes only and does not imply endorsement.

Influenza is a common respiratory illness that has been estimated to affect up to 20% of the population annually.[1] In a non-epidemic year in the UK, influenza results in approximately 9000 hospitalisations in people aged over 65 years[2] and between 3000 and 4000 deaths.[3] In a serious epidemic year, such as 1989/1990, mortality can be as high as 30 000 deaths.[4] Additionally, influenza has a substantial impact on direct and indirect costs.[5-9] In 1982/1983, there were an estimated 6.4 million working days lost in the UK associated with certified influenza illness.[10] These data clearly demonstrate that influenza is a serious public health problem, which requires all possible prevention and control measures to minimise its impact.

The efficacy and effectiveness of currently available inactivated influenza vaccines have been proven beyond doubt. Influenza vaccines have been shown to be effective in reducing the incidence of infection and associated morbidity and mortality,[11-13] and most European countries have a governmentally-sponsored programme for vaccinating high-risk groups.[14] A recent review on 15 years of experience with an inactivated influenza subunit vaccine (Influvac®) showed safety and efficacy data derived from marketing experience and clinical studies.[15] During the period 1982 to 1996, 87.5 million doses of the subunit vaccine were distributed and only 273 adverse events were reported and filed in the post-marketing surveillance database. Of these 273 adverse events, 121 were rated as serious, but in most cases no cause-effect relationship with the vaccine was established. The data from clinical studies showed that 56% of vaccinees reported no reactions at all after vaccination. From 3000 subjects, 95% reported no or only slight inconvenience and 4% reported moderate inconvenience after vaccination. Serological protection rates of 65 to 78% were reported in a meta-analysis of clinical data in the above-mentioned review.

Influenza vaccination among people over 60 years of age is both clinically effective and cost effective in reducing the incidence of infection and associated illness, hospitalisation and mortality when the infectious and vaccine strains are closely related.[11-13,16-19] Present UK guidance on influenza immunisation recommends that it should be provided for those of any age with chronic respiratory disease, heart disease, renal disease, diabetes mellitus and immunosuppression due to disease or treatment. It is also recommended for those over 74 years of age and all those living in long-stay residential accommodation.[20] However, little emphasis is given to working age adults receiving the vaccine. Moreover, while it may be clinically beneficial to vaccinate healthy adults under 65 years of age, it has been reported that there are few economic benefits to the healthcare system and society.[21] Against this background, this study aimed to model the economic impact of introducing an occupational vaccination programme in terms of the net costs to an employer in the UK.

Methodology

Literature Review

An electronic search of Medline, NHSEED and Cochrane databases was carried out. The search term for the Cochrane and NHSEED databases was 'influenza' and no date limit was included. The Medline database was searched between 1 January 1995 and the 31st of August 2000. The abstracts of the publications identified by this search strategy were assessed to identify those studies that related to the data items that were needed to construct the model. This was supplemented with information obtained from relevant National Health Service (NHS) databases.

Decision Model

Using information derived from published studies and NHS databases, a decision tree modelling the costs and benefits of introducing an influenza vaccination programme into a business was developed from the perspective of an employer in the UK (figure 1).

The inputs of the model comprised:

- the initial decision to vaccinate
- the incidence of influenza in the community
- the efficacy of vaccination/probability of an employee contracting influenza

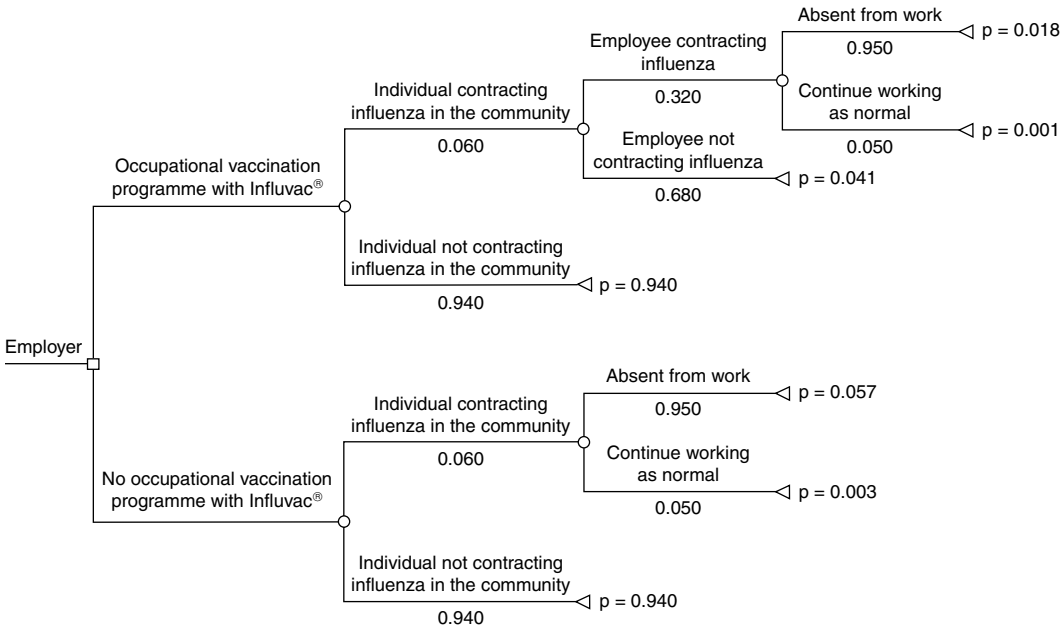

Fig. 1. Decision tree modelling the consequences of an occupational influenza vaccination programme. Numbers denote the probability of an employee following a particular path.

- the probability of an infected employee being absent from work
- the length of time off work
- the probability of reduced productivity after an infected employee returns to work.

The base case model assumed that in the absence of an occupational vaccination programme the probability of employees contracting influenza would be the same as that among 15- to 64-year-old individuals in the UK as a whole. Additionally, it was assumed that 95% of employees in a UK business employing 1000 people earning an average wage of £84 per day at 2000 prices[22] would be absent from work after contracting influenza for a mean of 5 days.[23] This was based on an assumption that influenza is a disease severe enough to result in almost all employees who contract this illness to take sick leave. The base case model also assumed that the level of productivity would be reduced by 60% for one day by 85% of employees with influenza returning to work[24] and that none of the absent employees would be replaced by agency staff or overtime by another employee. The efficacy of the vaccine was estimated to be 68% (95% lower and upper confidence limits: 49%; 79%).[25]

By assigning costs at 2000 prices to the influenza vaccine (Influvac®) and lost productivity, the decision model determined the cost benefit to a UK employer of introducing an occupational vaccination programme with Influvac®. The costs were defined as those costs attributable to implementing the vaccination programme (i.e. the cost of the vaccination). Lost productivity arising from vaccination has not been included in the base case model. We considered the period of vaccination to be in the order of 15 to 20 minutes and any lost productivity would be negligible and more than likely made up by the employee. Also excluded are the costs due to adverse effects of the vaccination. These are likely to be minimal due to the favourable adverse effect profile of the vaccination.[15]

The benefits to an employer of introducing such a programme were defined as the cost of averted lost productivity using the human capital approach (i.e. the salaries of staff who were absent from work plus the salaries of staff who were at work but not totally productive).[26] Hence, the cost benefit of a UK employer introducing a vaccination programme with Influvac® for influenza was estimated by evaluating the ratio of benefits to costs in order to determine the monetary return on every pound invested by an employer. When the ratio is greater than unity, there would be a net saving to an employer. When the ratio is less than unity, there would be a net additional cost to an employer. The cost benefit of the vaccination programme was calculated for varying incidences of influenza in the community and varying percentages of the workforce that were vaccinated.

Incidence of Influenza

Between 1989 and 1998 there were a mean 421 872 general practitioner (GP) consultations annually in England and Wales attributable to influenza and influenza-like illness.[2] It was assumed that one-third of influenza sufferers in the UK would consult a primary care physician based on a UK study which reported that 29% of employees who were absent from work due to influenza and influenza-like illness visited their GP.[24] Hence, it was calculated that there were a mean 1.27 million cases of influenza annually over this ten year period in England and Wales. This corresponds to 278 400 consultations among those aged between 15 and 64 years and 0.84 million cases in the community, equivalent to a mean annual incidence of 2% over the 10-year period.

In the 1972/1973 and 1975/1976 winter periods, the mean weekly GP consultation rates due to influenza and influenza-like illness were 265 and 311 per 100 000 population, respectively, in those parts of England and Wales most severely effected by the illness.[27] These epidemics lasted for 11 weeks and thus the estimated total number of GP consultations was 2915 and 3421 per 100 000 population for the most severely affected regions for 1972/1973 and 1975/1976, respectively. In 1996/1997 there was a 5% incidence of influenza and the GP consultation rate among the 15- to 64-year-old age group was about 1840 per 100 000 population,[2] which is about 54 and 63% of the highest rates observed in England and Wales in 1972/1973

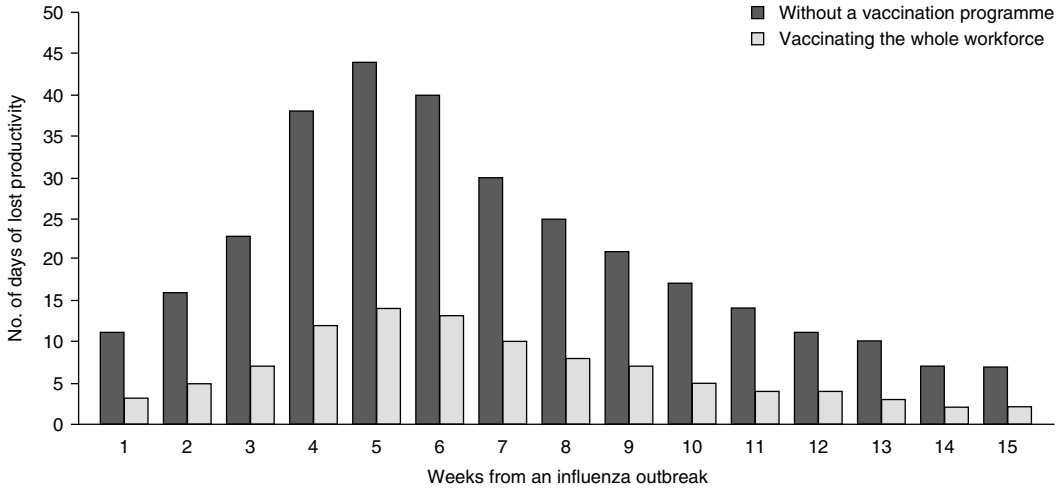

Fig. 2. Number of days of lost productivity due to influenza in a UK business employing 1000 people with and without a vaccination programme. The incidence of influenza in the community is assumed to be 6%.

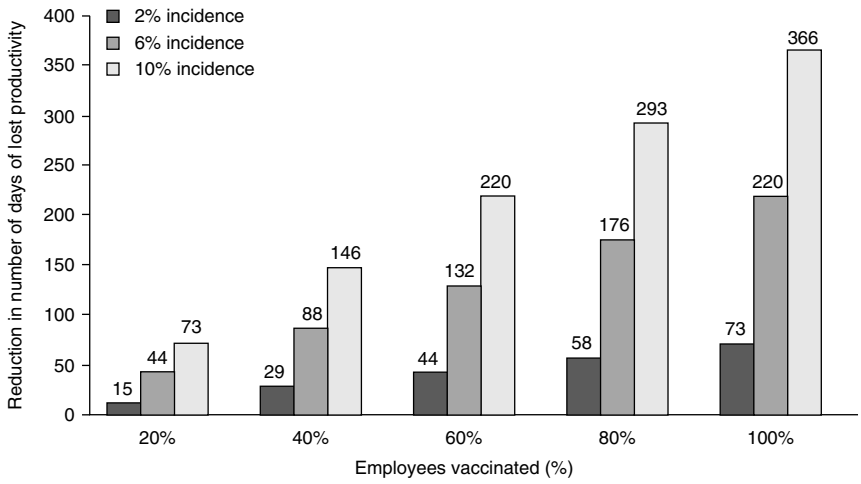

Fig. 3. Reduction in number of days of lost productivity in a UK business employing 1000 people, stratified by incidence of influenza and percentage of employees vaccinated.

and 1975/1976 respectively. Hence, the incidence of influenza in the community on these two occasions in the 1970s for the 15- to 64-year-old age group was estimated to be about twice that of the highest rate observed in the 1990s at 10% of the total population.

Thus, over the last 30 years the annual incidence of influenza in the community has varied between 2 and 10%. Hence the cost benefit of providing an occupational influenza vaccination programme was estimated for an incidence of influenza of 2 and 10% and a midpoint of 6%.

The estimated incidence of influenza among 15- to 64-year-old individuals in the community was used as a proxy for the expected incidence of influenza in an occupational setting in the absence of a vaccination programme.

Sensitivity Analyses

Sensitivity analyses determined how the cost benefit of an occupational vaccination programme with Influvac® changes in accordance with changes in the:

- efficacy of influenza vaccination (50 to 90%)
- incidence of influenza (2 to 10%)
- cost of implementing a vaccination programme with an inactivated influenza subunit vaccination (£5.97 to £10.71 per vaccination)
- average daily wage of employees (£20 to £200 per day)
- percentage of absent employees being replaced by agency staff and other employees working overtime (0 to 100%)
- length of time-off work after contracting influenza (0 to 5 days)
- number of days of reduced productivity by 85% of staff returning to work (0 to 2 days).

Results

Lost Productivity

According to the decision model, the expected probability of an employee being absent from work following an influenza vaccination would be reduced from 5.7 to 1.8% when the incidence of influenza in the community is 6%. The weekly number of days of lost productivity following an influenza outbreak for a business employing 1000 people where the annual incidence of influenza is 6% in the population is shown in figure 2.

The expected reduction in the number of days of lost productivity as a result of introducing a vac-

cination programme in the workplace, stratified by the incidence of influenza and the percentage of employees vaccinated is shown in figure 3.

Costs and Benefits of an Occupational Influenza Vaccination Programme with Influvac®

The expected cost of lost productivity in the absence of an occupational vaccination programme was estimated to be £9072, £27 132 and £45 192 when the incidence of influenza is 2, 6 and 10%, respectively. The cost and benefits of introducing Influvac® in the workplace for a business employing 1000 people earning the average UK national wage are shown in table I.

Table I illustrates that an occupational vaccination programme with Influvac® is a worthwhile investment for a UK employer, even if the incidence of influenza is as low as 2%, since the ratio of benefits to costs is greater than unity.

Sensitivity Analyses

In the base case model, it was assumed that the cost of vaccination is due solely to the unit cost of Influvac®, with the administration of the vaccine being carried out by employed occupational health nurses at no additional cost to the employer. Sensitivity analysis assessed the impact of including an administrative cost for implementing the vaccination programme by assuming a G grade (a staffing grade used in the UK) nurse (working 7 hours per day) vaccinates 25 people a day at a cost (including vaccine acquisition cost) of £10.71 per vaccination (table II).

This analysis showed that providing the cost of implementing a vaccination programme (including vaccine acquisition cost) was no more than £6.20, then introducing an occupational vaccination programme would lead to net savings for an employer (table II). If the cost of implementing the programme was more than £6.20, then an employer would incur a net additional cost when the influenza incidence is 2%. Nevertheless, if the cost of implementing the programme was as high as £10.71, introducing an occupational vaccination programme would lead to net savings for an employer when the incidence of influenza is 3.5% or above.

Table II also illustrates that introducing an occupational vaccination programme in the workplace would be a cost-beneficial investment for an employer even when the incidence of influenza was 2% providing the following:

- the efficacy of Influvac® was at least 65%
- the average wage of an employee was at least £80 per day (£27 per day if the incidence of influenza in the community was 6%)
- employees took more than 4.8 days off work after contracting influenza (1.3 days if the incidence of influenza in the community was 6%)
- there was at least 0.5 days of reduced productivity when employees returned to work after sick leave.

The sensitivity analyses also demonstrated that even if none of the employees who are absent from work were replaced by agency or overtime staff, in-

Table I. Costs (£; 2000 values) and benefits of an occupational influenza vaccination programme with Influvac® for a UK business employing 1000 people

Percentage of the workforce vaccinated	Estimated cost to an employer of vaccinating employees	Estimated cost of averted lost productivity following the implementation of an occupational vaccination programme when the incidence of influenza is:		
		2%	6%	10%
25	1492	1542	4613	7683
50	2985	3085	9225	15366
75	4477	4627	13838	23048
100	5970	6169	18450	30731
		1.03[a]	3.09[a]	5.15[a]

a Return on investment for every £ spent by an employer on vaccinating employees with Influvac® (cost-benefit ratio).

Table II. Sensitivity analyses (all costs are in 2000 values)

Scenario	Lower and upper values applied	Base case	The range of the cost benefit ratio for upper and lower values of the scenarios at varying incidences of influenza (threshold values[a])		
			2%	6%	10%
Efficacy of influenza vaccine (%)	50-90	68	0.76-1.37 (65)	2.27-4.09	3.79-6.82
Cost of implementing the vaccination programme (£)	5.97-10.71	5.97	1.03-0.58 (6.20)	3.09-1.72	5.15-2.87
Average daily wage of an employee (£)	20-200	84	0.25-2.46 (80)	0.74-7.36 (27)	1.23-12.26
Percentage of employees absent from work being replaced by agency and overtime staff	0-100	0	1.03-1.55	3.09-4.64	5.15-7.72
Number of days absent from work after contracting influenza	0-5	5	0.11-1.03 (4.8)	0.30-3.09 (1.3)	0.49-5.15
Number of days of reduced productivity by 85% of staff returning to work	0-2	1	0.94-1.13 (0.5)	2.80-3.38	4.67-5.63

a The threshold values at which an occupational influenza vaccination programme breaks-even from the perspective of an employer.

troducing an occupational vaccination programme in the workplace would be a cost-beneficial investment for an employer even when the incidence of influenza is 2%.

Discussion

The model shows, as expected, that the cost savings associated with providing a vaccination programme in the workplace are sensitive to the incidence of influenza. Community estimates of the incidence of influenza are limited in number. The two largest studies are US-based, one of which estimated an annual incidence of 8% among the whole population between 1976 and 1980.[28] The corresponding figures for the 15- to 24-year-old and 25- to 59-year-old age groups were 4.2 to 4.4% and 2.0 to 2.1%, respectively.[28] Another US-based study had a much higher incidence of 21%.[29] Two smaller studies showed the incidence of influenza to be 1.6 and 4.5%.[23,30] This compares with our estimate of 2 to 10% over the last 30 years in the UK. Thus, over the last ten years, an occupational vaccination programme for influenza would have been at least a cost neutral strategy and in 3 of the 4 years which had an influenza outbreak (during which we estimated that annual influenza rates were between 3 and 5%) it would have resulted in an estimated cost saving of between £3341 and £9510 for a business with 1000 employees. This equates to an annual reduction in absenteeism from work as a result of influenza of between 111 and 184 days.

The incidence of influenza below which an occupational vaccination programme would not be cost neutral was found to be sensitive to the cost of implementing the programme. Thus, if the cost of administering the vaccination was to form part of the costs of implementing the programme, assuming a vaccination rate of one person every 10 minutes (£8.79 per vaccination) at a baseline efficacy rate of 68%, the threshold incidence of influenza would be expected to increase from 2 to 3%. The confidence intervals associated with the vaccine's efficacy varied between 49 to 79%, resulting in threshold incidence rates of 2.8 to 1.7% assuming all other variables were as described for the base case model. This reflects the differences in efficacy between the rare years when the vaccine's virus differed from the predominant circulating virus and the majority of years when they were well matched – which have been shown in one recent study to be 50 and 83%, respectively.[21] Notwithstanding this, even if employers implemented a vaccination programme, it is unlikely that all employees would receive the vaccination; some employees may not present for vaccination or some may refuse to be vaccinated.

Many economic evaluations have used the human capital approach to value productivity using earnings data.[26] However, this approach is not without controversy.[31] In particular, wage rates reflect the marginal productivity of a worker and there are often imperfections in the labour market and ineq-

uities such as discrimination by race or gender.[26] Also, on return to work following a short-term absence, production may be made up. Furthermore, employers usually have excess capacity in the work force to cover absenteeism.

The exact relationship between short-term absence and production loss depends on the type of work and organisation in which an individual is employed. Thus, in certain cases, absence from work reduces the effective labour time less than proportionally. Estimations of the extent to which productivity and absence from work vary from direct proportionality have been made.[32] For the Netherlands, this 'elasticity' has been estimated to be 0.8 i.e. a 10% reduction in labour time results in an 8% decrease in production. Nevertheless, using this approach, we found that the threshold incidence of influenza, below which an occupational vaccination programme is not cost neutral, is sensitive to the average wage of a company's employees. Thus, at an average daily wage of £100 and £130 per day, equivalent to the highest decile and upper quartile of national wages for full-time employees in the UK,[33] the threshold incidence rates would be reduced to 1.7 and 1.3%, assuming all other variables were as described for the base case model. The average wage of those employed in managerial and administrative positions in the UK is about £126 per day. Thus, for those on higher rates of paid employment, vaccinating employees would be a cost beneficial investment for an employer, when the incidence of influenza is 2% or above. However, one study has found that fewer days per illness were taken by managers than by administrative staff[15] so the cost benefit of the vaccination programme may not necessarily increase with increasing pay rates.

An average wage of £126 per day is about 1.5 times that of the average daily wage in the UK, which may equate to the overtime costs paid to employees who cover for other employees who are absent from work or the rate paid to agency staff. Thus, in those organisations which implement such strategies to cover for absent staff, vaccinating employees would be a cost beneficial strategy. These organisations would include work locations such as nursing homes and hospital wards where there is a need to maintain nurse to patient ratios as part of national and local practice standards.

Our study has been limited to a consideration of the costs borne by an employer associated with influenza. Consequently, we have not included other direct and indirect costs associated with the illness, such as the use of medical services, medications, child-care and the impact on carers and domestic work. Also excluded are the costs of vaccination in terms of lost productivity resulting from employees missing work to be vaccinated and sickness-related absence due to associated adverse events, although these are likely to be minimal since influenza vaccines have a very favourable safety profile.[15] Additionally, the tax relief that an employer would receive on the costs of implementing a vaccination programme has been excluded. Hence, our estimated cost-benefit ratios may be an underestimate. Notwithstanding this, our model assumed that if employers did not implement a vaccination programme then none of the employees would be vaccinated. However, in the UK, influenza immunisation is available for persons with specified chronic conditions considered to be at higher risk.[20] Thus, in reality, some of the employees may receive vaccination for influenza even without an occupational vaccination programme.

Our analyses of other economic studies on vaccinating healthy working adults against influenza found favourable cost-benefit ratios associated with vaccination in relation to avoided sickness-related absences. Thus, in two US-based studies, one a randomised controlled study and the other, a non-randomised prospective study, the relevant cost-benefit ratios were 1 : 2.64 and 1 : 1.37 respectively.[34-37] Additionally, in two modelled studies for France and Brazil, in which influenza rates were assumed to be 10%, the cost-benefit ratios were 1 : 2.65 and 1 : 2.26 respectively.[36,37] The comparable ratio from a retrospective study in Canada was 1 : 8.76.[38] Conversely, some studies showed less favourable results for influenza vaccination. One prospective study with a serologically confirmed influenza rate of

1.6% found vaccination to incur higher costs than the benefits, with the relevant cost-benefit ratio being 1 : 0.11.[23] A more recent US-based randomised controlled trial reported influenza rates of 4.4% and 10% in 1997/98 and 1998/99 respectively among non-vaccinated employees.[21] A higher cost was associated with absenteeism in the vaccinated group in 1997/1998, while the costs of vaccination were higher than the benefits of avoided sickness-related absences in 1998/1999 with a cost benefit ratio of 1 : 0.37.

Conclusions

Based on our model, we conclude that implementation of an occupational influenza vaccination programme with Influvac® would be expected to reduce the incidence of influenza among a workforce, resulting in less absenteeism from work and averted lost productivity. Even if the incidence of influenza is as low as 2%, it may be a worthwhile investment for UK employers to vaccinate their employees.

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References

1. Couch RB. Advances in influenza virus vaccine research. Ann N Y Acad Sci 1993; 685: 803-12
2. Fleming DM. The contribution of influenza to combined acute respiratory infections, hospital admissions and deaths in winter. Commun Dis Public Health 2000; 3 (1): 32-8
3. Immunisation against infectious disease (green book). Norwich: The Stationary Office, 1996: 113-20
4. Ashley J, Smith T, Dunnell K. Deaths in Great Britain associated with influenza epidemic of 1989/90: population trends. OPCS. London. HM Stationary Office 1991; 65: 16-20
5. Levy E. French economic evaluations of influenza and influenza vaccination. Pharmacoeconomics 1996; Suppl. 3: 62-6
6. Szucs TD. Influenza: the role of burden-of-illness research. Pharmacoeconomics 1999; 16 Suppl. 1: 27-32
7. Postma MJ, Bos JM, van Gennep M, et al. Economic evaluation of influenza vaccination: assessment for the Netherlands. Pharmacoeconomics 1999; 16 Suppl. 1: 33-40
8. Fedson DS. Evaluating the impact of influenza vaccination: a North American perspective. Pharmacoeconomics 1996; 9 Suppl. 3: 54-61
9. Guest JF, Morris A. Community-acquired lower respiratory tract infections: the annual cost to the National Health Service. Br J Med Econ 1996; 10: 263-73
10. NHS Lung and Asthma Information Agency. Sickness absence from respiratory disease. London: Department of Public Health Sciences, St George's Hospital Medical School, 1992
11. Govaert TME, Thijs CT, Masurel N, et al. The efficacy of influenza vaccination in elderly individuals: a randomised double-blind placebo-controlled trial. JAMA 1994; 272: 1661-5
12. Gross PA, Hermogenes AW, Sacks HS, et al. The efficacy of influenza vaccination in elderly persons: a meta-analysis and review of the literature. Ann Intern Med 1995; 123: 519-27
13. Ahmed H, Nicholson K, Nguyen-Van-Tam J. Reduction in mortality associated with influenza vaccine during 1989-90 epidemic. Lancet 1995; 346: 591-5
14. Ambrosch F, Fedson DS. Influenza vaccination in 29 countries: an update to 1997. Pharmacoeconomics 1999; 16 (1): 47-54
15. Palache AM. Influenza immunisation. J Clin Res 1999; 2: 111-32
16. Fleming DM, Watson JM, Nicholas S, et al. Study of the effectiveness of influenza vaccination in the elderly in the epidemic of 1989/90 using a general practice database. Epidemiol Infect 1995; 115: 581-9
17. Nichol KL, Margolis KL, Wuorenma J, et al. The efficacy and cost effectiveness of vaccination against influenza among elderly people living in the community. N Engl J Med 1994; 22: 778-84
18. Hak E, van Essen GA, Buskens E, et al. Is immunising all patients with chronic lung disease in the community against influenza cost effective?. Evidence from a general practice based clinical prospective cohort study in Utrecht, the Netherlands. J Epidemiol Community Health 1998; 52: 120-5
19. Campbell DS, Rumley MH. Cost-effectiveness of the influenza vaccine in a healthy, working age population. J Occup Environ Med 1997; 39 (5): 408-14
20. Fleming D, Charlton J, McCormick A. The population at risk in relation to influenza immunisation policy in England and Wales. Health Trends 1997; 29 (2): 42-7
21. Buxton Bridges C, Thompson WM, Meltzer MI, et al. Effectiveness and cost-benefit of influenza vaccination of healthy working adults: a randomised controlled trial. JAMA. 2000; 284 (13): 1655-63
22. Office for National Statistics. Quarterly projections of the New Earnings Survey. Labour market trends. Norwich: The Stationary Office, 2000 Jun
23. Kumpulainen V, Makela M. Influenza vaccination among healthy employees: a cost-benefit analysis. Scand J Infect Dis 1997; 29 (2): 181-5
24. Keech M, Scott AJ, Ryan PJ. The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. Occup Med (Lond) 1998; 48 (2): 85-90
25. Demicheli V, Rivetti D, Deeks JJ, et al. Vaccines for preventing influenza in healthy adults (Cochrane Review). Available in The Cochrane Library [database on disk and CD ROM]. Updated quarterly. The Cochrane Collaboration; issue 3, 2000. Oxford: Update Software, 1997
26. Drummond MF, O'Brien BJ, Stoddart GL, et al. Cost benefit analysis. In: Drummond MF, O'Brien B, Torrance GW, et al. Methods for the economic evaluation of health care programmes. Oxford: Oxford University Press, 1998: 205-31
27. Fleming DM, Ayres JG. Diagnosis and patterns of incidence of influenza, influenza-like illness and the common cold in general practice. J R Coll Gen Pract 1988; 38: 159-62

28. Sullivan KM. Health impact of influenza in the United States. Pharmacoeconomics 1996; 9 Suppl. 3: 26-33
29. Glezen WP. Serious morbidity and mortality associated with influenza epidemics. Epidemiol Rev 1982; 4: 25-44
30. Wilde JA, McMillan JA, Serwint J, et al. Effectiveness of influenza vaccine in healthcare professionals. A randomised trial. JAMA 1999; 281 (10): 908-13
31. Koopmanschap MA, Rutten FH. Indirect costs in economic studies: confronting the confusion. Pharmacoeconomics 1993; 4 (6): 446-54
32. de Koning J, Tuyl FA. The relation between labour time, production and employment. Rotterdam: Netherlands Economic Institute, 1984
33. Annual earnings survey 1997. London: The Stationary Office, 1997
34. Nichol KL, Lind A, Margolis KL, et al. The effectiveness of vaccination against influenza in healthy, working adults. N Engl J Med 1995; 33: 889-93
35. Campbell DS, Rumley MH. Cost-effectiveness of the influenza vaccine in a healthy, working-age population. J Occup Environ Med 1997; 39 (5): 408-14
36. Levy E. French economic evaluations of influenza and influenza vaccination. Pharmacoeconomics 1996; 9 (3): 62-6
37. Burckel E, Ashraf T, Galvao de Sousa Filho JP, et al. Economic impact of providing workplace influenza vaccination: a model and case study application at a Brazilian pharma-chemical company. Pharmacoeconomics 1999; 16: 563-76
38. Yassi A, Kettner J, Hammond G, et al. Effectiveness and cost-benefit of an influenza vaccination program for healthcare workers. Can J Infect Dis 1991; 2: 101-8

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