Influenza vaccination among healthy employees: a cost-benefit analysis
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Influenza vaccination of healthy working adults (healthy municipal homemakers). The vaccine offered was the Connaught inactivated trivalent split influenza vaccine (Fluzone) containing two influenza A components and one influenza B component.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study looked at healthy adults working as municipal homemakers caring for elderly people and families with small children at their homes. Municipal homemakers were deemed to be potential transmitters and contractors of influenza, because of their work with older people and other people belonging to high-risk groups. Known allergies to chicken proteins, pregnancy and any acute infection were criteria for exclusion.

Setting
The setting was community. The economic analysis was carried out in Helsinki, Finland.

Dates to which data relate
Effectiveness and resource use data corresponded to the period 1990 - 1991. The price year was 1991.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing appears to have been conducted mainly on the same patient sample as that used in the effectiveness analysis and appears to have been conducted retrospectively.

Study sample
Power calculations were not used to determine the sample size. Vaccination was offered to all municipal homemakers (n=458) in three city districts. Homemakers in the other four districts (n=672) remained as controls. All subjects in both groups received a questionnaire covering background data, and the study sample comprised those subjects who returned this questionnaire. Full follow-up was available for 351 subjects in the intervention group (of whom 165 (47%) received the vaccination) and 492 in the control group. With the exception of one male, the participants were
females aged between 18 and 62 years of age.

**Study design**
This was a non-randomised study with concurrent controls, carried out in seven districts of a capital city. The duration of follow-up was 8 months (acute respiratory infections were followed clinically and with laboratory samples for 8 months). Regarding the number lost to follow-up, it was reported that full follow-up was achieved for 351 patients in the intervention group (exclusion and incomplete participation, 107 subjects), and 492 patients in the control group (incomplete participation, 180 subjects). Pre-vaccination blood samples were taken at the time of vaccination, and post-vaccination samples were taken 22 to 44 days later. Post-epidemic sera from the intervention group were collected in May 1991. During the period between vaccination and collection of post-epidemic samples (September to May), all homemakers were asked to report acute respiratory infections (ARIs) to the occupational health service staff. They were then asked to schedule visits for the collection of acute and convalescent phase blood samples and nasopharyngeal secretion (NPS) samples for the detection of viral antigens. The NPS specimens were aspirated through the nostrils with a disposable mucus extractor. The influenza activity in the season 1990-91 was low in Finland, fitting the observed attack rate of 1.5%.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness was intention to treat (intention to vaccinate). The clinical outcome measures were influenza and other acute respiratory infection (ARI), sick-leave days, and adverse reactions. Vaccinated subjects were asked to report adverse reactions using the questionnaire about local symptoms (pain, redness, swelling) and systemic symptoms (fever, symptoms of ARI, headache, arthralgia, fainting, allergic reaction). The sera were studied for hemaglutination inhibiting and complement fixing antibodies, and the NPS samples for viral antigens of adenovirus group, influenza A and B, parainfluenza 1, 2, and 3, respiratory syncytial virus, and RNA of Mycoplasma pneumoniae. The length of sick leave was registered and followed up. Visits to other healthcare facilities were not traced. The study groups were reported to be comparable in terms of age, sex, and work setting.

**Effectiveness results**
Influenza infection was confirmed in 10 employees (8 of these in the control group) and other viral infections in 6 employees (5 of them in the control group).

All infections occurred in non-vaccinated persons.

The relative risk of infection in the control group was 2.9, (95% CI: 0.6 - 13.4) for influenza and 3.1, (95% CI: 0.9 - 10.8) for all respiratory infections.

The mean sick leave for influenza was 4.9 days.

The side effects of vaccination were negligible and no working days were lost due to vaccination.

**Clinical conclusions**
During the study period, none of the vaccinated persons had influenza, and the whole intervention group had fewer events of any ARIs than the controls.

**Measure of benefits used in the economic analysis**
The measure of benefits adopted was the number of infections averted.

**Direct costs**
Costs were not discounted due to the short time frame of the cost analysis. A few quantities were reported separately from the costs and the cost breakdown was reported separately. The direct cost analysis covered the costs of vaccination
and influenza infections (including occupational health nurse time, physician time, laboratory tests, imaging (ultrasound, X-ray), travel expenses, and prescriptions). The perspective adopted in the cost analysis was not explicitly specified (but is likely to have been that of society). Market prices and average incomes were used for costing. Persons with true influenza infections calculated the costs of infection from consultation at the Occupational Health Centre. The price year was 1991.

**Indirect Costs**
Indirect costs were not discounted due to the short time frame of the cost analysis. The quantity of sick leave days was reported separately from the costs. The indirect cost analysis covered the costs of time lost from work (absence from work). The perspective adopted in the cost analysis was not explicitly specified (but is likely to have been that of society). Average incomes were used for costing. The price year was 1991.

**Currency**
Finish marks (FIM). No conversion was made to any other widely used currencies.

**Sensitivity analysis**
A threshold analysis was performed on attack rate to identify a break-even point between the cost of vaccination and the benefit from averted cases of influenza (costs saved due to cases of infections averted).

**Estimated benefits used in the economic analysis**
The number of expected infections was 5.7 versus 2 observed infections.

**Cost results**
The cost per immunisation was FIM 141, and the average cost per influenza infection was FIM 1,183 (variation, 638.17 - 2,362.81).

**Synthesis of costs and benefits**
The cost per infection averted was FIM 6,270, and the equivalent cost for immunisation FIM 26.52. The break-even point for the attack rate was 8.5%.

**Authors' conclusions**
Influenza vaccination had a slight protective effect against both influenza and other respiratory infections. The cost of vaccination programmes exceeded the benefit from averted infections.

**CRD COMMENTARY - Selection of comparators**
The strategy of no vaccination was explicitly regarded as the comparator. It allowed the active value of the vaccination strategy to be evaluated.

**Validity of estimate of measure of effectiveness**
The internal validity of the effectiveness results cannot be reasonably assured owing to the non-randomised nature of the study design, and the lack of power calculations to justify the sample size. However, the study groups were comparable in terms of age, sex, and work setting and the study sample appears to have been representative of the study population.

**Validity of estimate of measure of benefit**
Estimation of benefits was obtained directly from the effectiveness analysis. The choice of the estimate appears to be justified.

**Validity of estimate of costs**

Positive aspects of the cost analysis were as follows: some resource use quantities were reported separately from the costs; cost breakdown was reported; and the price year was given. However, the following limitations may have adversely affected the validity of the cost analysis: the perspective adopted in the cost analysis was not specified; the details of the resource use profile were not reported; no conversion was made from Finish marks to any other widely used currencies; the details of the methods used to calculate the indirect costs (productivity loss) were not given; no statistical or sensitivity analyses were performed on resource use data or cost data. The generalisability of the cost results outside the study setting may, therefore, be problematic.

**Other issues**

Given the above limitations some caution may need to be exercised in interpreting the study results. The issue of generalisability to other settings or countries was not addressed, although appropriate comparisons were made with other studies. The sample appears to have been representative of the study population. Contrary to the title chosen by the authors for the paper, the study was principally a cost-effectiveness analysis with cost-benefit aspects being addressed in the sensitivity analyses.

**Implications of the study**

A trend toward protection against other ARIs in the vaccinated population was observed and is supported by previous findings. Further studies clarifying the extent and mechanism of this phenomenon are warranted.

Because time lost from work as a result of vaccination strongly influences cost-effectiveness, vaccination programmes should be organised with minimal loss of working time; for example, walk-in vaccination clinics in or near the workplace. Optimal vaccination strategies for working-age populations need to be planned individually. Evidence for the cost-effectiveness of vaccinating healthy adults during periods of low or medium influenza activity appears to be inconclusive.

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