Evaluation of a mass influenza vaccination campaign

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
The health technology studied was a mass influenza vaccination campaign for people aged 3 years or older. The vaccine used was Influenza HA vaccine (1 mL vial containing A/Beijing/262/95 200CCA/mL, A/Sydney/5/97 350 CCA/mL, and B/Shangdong 300CCA/mL). The vaccine was administered subcutaneously at a dose of 0.5 mL for adults, 0.3 mL for children aged 6 to 12 years, and 0.2 mL for children aged 3 to 5 years.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised Japanese individuals (male and female) aged 3 years or older.

Setting
The setting was the community. The economic analysis was carried out in Kawaura, Kumamoto Prefecture, Japan.

Dates to which data relate
The vaccination date was 17 November 1999. The effectiveness and resource data were collected between 1 December 1999 and 31 March 2000. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
No power calculations were performed to determine the sample size. A total of 5,563 doses of vaccine were administered to 2,952 residents aged 3 years or older, within a population of 6,865 individuals. The overall vaccination rates were 43% for all residents, 40.7% for females, 36.8% for males, 75% for those aged 3 to 14 years, 31% for those aged 15 to 64, and 55% for those aged at least 65 years. Over 90% of the vaccinated individuals received a second dose.

Study design
This was a prospective cohort study using the medical records of a single institution (the only hospital available in the town in which the study was carried out). The duration of follow-up was 4 months, starting 2 weeks after the vaccination campaign. There was no loss to follow-up. Each individual made the decision on whether to be vaccinated or not, but written informed consent was necessary before the vaccine could be administered.

**Analysis of effectiveness**

The analysis of the clinical study (intention to treat or treatment completers only) was not stated. The primary health outcomes used in the analysis were:

- the number of admissions to the hospital with a respiratory disease for both vaccinated and non-vaccinated residents, and the corresponding number of fatal outcomes;
- the number of admissions with a non-respiratory disease for both vaccinated and non-vaccinated residents, and the number of associated fatal outcomes;
- the relative risk between the vaccinated and the non-vaccinated for each one of these outcomes;
- the attack rate for influenza-like illness (ILI) and the relative risk of ILI for the non-vaccinated, for those vaccinated only once, for those vaccinated twice, and for all those vaccinated; and
- the efficacy of the vaccine.

ILI was defined as having fever greater than 38 degrees C with a cough or muscle or joint pain, plus either headache, appetite loss, or general fatigue. In order to estimate the vaccine efficacy between those immunised and those who were not, in terms of attack rate, ILI and relative risk (RR), a vaccination request list was used to categorise the individuals. Two hundred vaccinees and 200 non-vaccinees were randomly selected for this purpose by the local health centre, from the vaccination request list. The median age of the vaccinees was 45 years (range: 4 - 81), and there were 95 males and 105 females. The median age of the non-vaccinees was 42 years (range: 3 - 84), and there were 102 males and 98 females. Only 241 of these individuals responded (median age 39 years; range: 4 - 78), of which 108 were males and 133 were females. Seventy-one of these were non-vaccinated, 161 were vaccinated and 10 gave invalid responses.

Not all of the individuals included in the observational study were accounted for in the analysis. Paediatric patients aged less than 15 years were excluded because the effectiveness data were derived from records obtained from the town hospital, and most of these children were referred out of town. None of those residents aged 15 years or older were admitted anywhere else other than the town hospital. Moreover, 10 individuals were not accounted for in the estimation of the vaccine efficacy since they gave invalid responses.

**Effectiveness results**

A total of 233 town residents were admitted to the hospital. Of these, 3 had been vaccinated twice while 19 had not been vaccinated at all.

The RRs were calculated as the proportion of events among those vaccinated divided by the proportion of events among those non-vaccinated.

The proportion of hospitalisations with respiratory disease was 3 out of 1,203 for the vaccinated versus 19 out of 1,003 for the non-vaccinated. The RR was 0.13 (95% confidence interval, CI: 0.04 - 0.44).

The proportion of deaths from respiratory diseases was 1 out of 1,203 for the vaccinated versus 3 out of 1,003 for the non-vaccinated. The RR was 0.28 (95% CI: 0.03 - 2.67).

The proportion of hospitalisations with non-respiratory disease for those aged at least 15 years was 27 out of 2,242 for the vaccinated versus 91 out of 3,326 for the non-vaccinated. The RR was 0.44 (95% CI: 0.29 - 0.67).

The proportion of hospitalisations with non-respiratory disease for those aged at least 65 years was 26 out of 1,203 for...
the vaccinated versus 68 out of 1,003 for the non-vaccinated. The RR was 0.32 (95% CI: 0.20 - 0.50).

The proportion of deaths from non respiratory diseases was 3 out of 1,203 for the vaccinated versus 8 out of 1,003 for the non-vaccinated.

The attack rate for ILI was 4 out of 10 (5.7%) for the non-vaccinated, 5 out of 46 (10.9%) for those vaccinated only once, 3 out of 115 (2.6%) for those vaccinated twice, and 8 out 161 (5.0%) for all those vaccinated. The RR was 1.90 (95% CI: 0.54 - 6.71) for those vaccinated once in comparison with the non-vaccinated. The RR was 0.46 (95% CI: 0.11 - 1.98) for those vaccinated twice in comparison with the non-vaccinated. The RR was 0.87 (95% CI: 0.27 - 2.79) for all the vaccinated in comparison with those non-vaccinated.

The vaccine efficacy was estimated as 54% for those receiving two doses and 13% for those receiving either one or two doses (this result was not shown). For the RR of hospitalisation due to respiratory illness, the efficacy of the vaccine was calculated as 87% (all the patients were aged at least 65 years).

Clinical conclusions
The vaccination campaign was shown to be effective in reducing the risk of being hospitalised among those who were vaccinated. However, no statistically significant differences were found between the attack rates and RR of ILI according to whether immunisation had been carried out or not.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported (see the 'Effectiveness Results' section). Hence, a cost-consequences analysis was conducted.

Direct costs
Although in an overall sense a community perspective was adopted, a number of perspectives were reflected in the cost analysis due to the variation in entitlements surrounding the costs (some costs were borne by the state, some by social insurance, and some by the individual).

The resource quantities and the costs were not reported separately. The only resource quantity that was provided separately from the costs was the number of doses of vaccine. The costing was performed prospectively using resource quantities collected from the medical records of the town hospital during the same period. The costs considered for the vaccination campaign were for the vaccine, distribution, administration, syringes, needles and town physicians. The costs considered for the comparator (non-vaccination) were the estimated costs for hospitalisation due to influenza, followed by respiratory illness among the non-vaccinated. It was not stated why the costs of hospitalisation for influenza followed by non-respiratory illness were not considered in the analysis. Residents older than 13 years and younger than 65 were charged the wholesale cost of the vaccine, while medical insurance paid the medical costs arising from hospitalisation. The town faced the rests of the costs. The costs were not discounted due to the short timeframe of the cost analysis (less than 1 year). The study reported the average costs. The price year was not reported.

Statistical analysis of costs
The authors provided mean values and the standard deviation (SD) for the estimation of the medical costs related to treatment of non-vaccinated inpatients with acute respiratory illness.

Indirect Costs
The indirect costs were not reported.

Currency
Japanese yen (Y) and US dollars ($).
Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The town spent a total of ¥5.78 million ($56,700) for the mass vaccination.

The per-shot cost was estimated as ¥1,683 ($16.50).

The authors reported that the costs of two of the non-vaccinated inpatients with ILI followed by respiratory disease were not calculable.

The estimated costs for the other 17 non-vaccinated inpatients with respiratory illness were ¥73,000 - ¥813,080 (mean +/- SD: 260,339 +/- 175,830). The median number of days of hospitalisation was 11 (range: 4 - 30).

Had these patients been vaccinated, 87% may have been able to avoid hospitalisation, and the corresponding savings would have been equivalent to 76% of the total campaign costs.

No severe adverse effects were reported and, therefore, they were not accounted for in the analysis.

Synthesis of costs and benefits
Not applicable due to the cost-consequences approach adopted.

Authors' conclusions
The relative risk (RR) for hospitalisation for respiratory disease (RR 0.13, vaccine efficacy 87%) showed that influenza vaccination is a very effective preventive measure. However, the authors considered that the vaccination campaign was not cost-effective since it did not produce savings of money, because the two-dose vaccination policy nearly doubled the campaign costs.

CRD COMMENTARY - Selection of comparators
The rational for the selection of the comparators, vaccination and non-vaccination, was reasonable and was in accordance with similar studies in the literature.

Validity of estimate of measure of effectiveness
The analysis used a prospective cohort study, which was appropriate for the study question. However, the absence of randomisation introduces the possibility of numerous biases, making the interpretation of results problematic. Self-reporting of illness can be unreliable and, as no blinding could be carried out, the validity of the differential rates of reported ILI is questionable. Moreover, the resulting groups of vaccinated and non-vaccinated that were used to calculate the attack rate, ILI and RR were not shown to be comparable at analysis. They were also not shown to be representative of the whole population. The authors commented on additional limitations related to the reported effectiveness. In particular, that the incomplete response rates and reliance on a simple questionnaire to judge the attack rates did not allow the full evaluation of the vaccine efficacy. However, the use of a single community with good internal controls and cooperation is likely to have had a positive impact on the validity of the results.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The authors stated that the use of two vaccine doses considerably increased the cost of the vaccination campaign, while its additional immunogenicity compared to a single dose has not been proven. Moreover, they reported a number of limitations that compromised the cost-effectiveness results. One of these was related to the exclusion of two individuals in the estimation of the medical expenses. As a consequence of this exclusion, the expenses may have been underestimated against the vaccination campaign. The costs and the quantities were not reported separately, which limits the generalisability of the results to other settings. Moreover, the lack of a price year also hinders reflation exercises to other settings. The indirect costs were not included in the analysis, but are clearly relevant (for example, lost productivity and care by relatives) for this patient domain if a societal perspective were to be adopted (more likely in the UK National Health Service context).

Other issues
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of the generalisability to other settings was not addressed.

Implications of the study
The results of the study should be helpful in modelling mass vaccination campaigns. The results also support the view that vaccination programmes are associated with health benefits, although in this case they involve increased expenditure.

In order to increase vaccine coverage in the Japanese population, the authors suggest that further efforts will have to be made by public health authorities. These will have to provide a better understanding of the differences between a common cold and influenza, and of the efficacy of influenza vaccine, to both the medical community and the public. They also suggest that, in order to determine the optimal vaccination strategy for Japanese citizens, further efforts are necessary.

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