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
A strategy to vaccinate healthy working adults against influenza was compared to no vaccination.

Type of intervention
Primary prevention.

Economic study type
Cost-benefit analysis.

Study population
The study population was defined as healthy working adults aged between 18 and 64 years. The patient characteristics and inclusion/exclusion criteria were not reported.

Setting
The study was set in the community in the United States. The author stated explicitly that it was assumed that the vaccination would occur in work site-based clinics, community health department clinics, or at other non-traditional sites such as public clinics in drug stores and grocery stores.

Dates to which data relate
Efficacy data and resource use data was taken from literature published between 1953 and 1999, in which the primary data ranged from 1918 to 1998. The price year used was 1998.

Source of effectiveness data
The study was based on a synthesis of completed studies.

Modelling
The study used a basic cost model in which both direct and indirect costs were included. The purpose of this model was to assess the net costs or savings associated with the use of inactivated influenza virus vaccine in healthy working adults compared with no vaccine.

Outcomes assessed in the review
The outcomes used in the model were:

- influenza illness rate;
- work absenteeism;
reduced work effectiveness per illness episode;
reduced work effectiveness level;
number of health care provider visits per illness episode;
hospitalisation rate for influenza complications;
death rate;
work absenteeism for vaccination;
likelihood of work loss for vaccination;
work absenteeism for potential side effects due to vaccination;
number of health care provider visits for potential side effects;
Guillain-Barre syndrome rate;
vaccine effectiveness in year with good match;
vaccine effectiveness in year with poor match; and
likelihood of good vaccine match.

Study designs and other criteria for inclusion in the review
The study designs included in the review were as follows: clinical trials, observational studies, systematic reviews, surveys, controlled trials, and double-blinded placebo-controlled trials. The author did not report any inclusion/exclusion criteria.

Sources searched to identify primary studies
The author did not specify the sources searched or the search strategy used to identify studies for the synthesis of data. It was stated, however, that the study used both published and unpublished data.

Criteria used to ensure the validity of primary studies
The author did not report the criteria used to judge the validity of the studies included in the synthesis of data.

Methods used to judge relevance and validity, and for extracting data
The author did not report the criteria used to judge the relevance or validity of the data or to determine which data were extracted.

Number of primary studies included
The author used 30 published studies and 3 sets of unpublished observations to derive the data for the model.

Methods of combining primary studies
The method of combining data from more than one source was not described within the study.

Investigation of differences between primary studies
The author did not report whether there were differences in efficacy data between the studies used or whether the reasons for these were investigated.

Results of the review
The author reported the base-case variables used in the model as follows:

- influenza illness rate, 5% (range: 5 - 15);
- work absenteeism, 2 days per illness episode (range: 0.75 - 4);
- reduced work effectiveness per illness episode, 0.7 days (range: 0.5 - 0.9);
- reduced work effectiveness level, 50% (range: 30 - 70);
- number of health care provider visits per illness episode, 0.45 (range: 0.25 - 0.65);
- hospitalisation rate for influenza complications, 4/10,000 (range: 1/10,000 - 7/10,000);
- death rate, 1/100,000 (range: 0.5/100,000 - 2/100,000);
- work absenteeism for vaccination 0.5 hours per vaccination (range: 0.25 - 0.75);
- likelihood of work loss for vaccination, 0.5 (range: 0 - 1);
- work absenteeism for potential side effects due to vaccination, 10 days per 1000 (range: 0 - 20);
- number of health care provider visits for potential side effects, 5 per 1000 (range: 0 - 10);
- Guillain-Barre syndrome rate, 1 per 1 million persons (range: 0.5 - 2);
- vaccine effectiveness in year with good match, 75% (range: 60 - 90);
- vaccine effectiveness in year with poor match, 35% (range: 0 - 50); and
- likelihood of good vaccine match, 80% (range: 72 - 85).

Measure of benefits used in the economic analysis
The measure of benefit was the monetary value of lost productivity due to morbidity and mortality. The human capital approach was used to derive monetary values. The monetary values of outcome are therefore indirect costs (see below).

Direct costs
The author included the following direct health care costs in the model: the cost of the vaccination and its administration, $10 (range: $5 - $15).

The cost of a health care providers visit, including procedures and medications and the cost of an initial outpatient visit for influenza illness, including the cost of physicians' fees and medication were both estimated to be $102 (range: $80 - $123).

The cost per hospital admission for influenza-associated complications was estimated at $5,669 (range: $3,669 - $7,669), and medical care costs per episode of vaccine-associated Guillain-Barre syndrome, were estimated at $11,0674. These costs were derived from published data and were used to calculate the following estimates: the cost of vaccination, the cost of potential side effects due to vaccination and the costs averted due to vaccination.

The author presented resource use and prices separately for most items. The price year used was 1998. Prices were
referred to a common price year. The method used was not reported. Discounting of the direct costs was not reported.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
The author included the following indirect costs in the model: the economic cost of morbidity, valued as time from work multiplied by the median hourly wage for full time, year-round working adults, $15 (range: $10 - $30) and premature death. The indirect cost of premature death was estimated as the present net value of future lifetime earnings and housekeeping service foregone for someone dying between the ages of 20 and 64 years weighted, for sex and expected age at death. The base case estimate used a 3% discount rate, while a 5% discount rate was used for the worst-case scenario. The author reported that these rates were selected to be consistent with current guidelines.

**Currency**
US dollars ($). No currency conversions were reported.

**Sensitivity analysis**
Monte Carlo simulation was used to calculate the mean net costs or savings along with the 95% probability interval, and sensitivity analysis. Sensitivity analyses were also used to explore the sensitivity of the cost model to different values of the input variables.

**Estimated benefits used in the economic analysis**
The estimated benefits of the model are described as indirect costs below.

**Cost results**
The total direct costs of vaccination were estimated as $10.64 and the indirect costs were $6.05. The total direct costs averted by vaccination were estimated as $3.99 (i.e. the costs of no vaccination) and the indirect costs were estimated as $26.36.

**Synthesis of costs and benefits**
Vaccination resulted in a net benefit of $13.66 for each person vaccinated. The best-case scenario reported a greater saving of $174.32, while the worst-case scenario generated a net cost of $21.27 per person vaccinated.

The author reported, however, that the best-case and worst-case scenarios were substantially more extreme than the range of plausible values derived from the multivariate Monte Carlo simulation. The 95% probability interval for the average cost savings ranged from net savings of $32.97 to net costs of $2.18 per person vaccinated. According to the probability distribution generated for the net costs, vaccination resulted in net savings 95% of the time.

The cost model was most sensitive to the influenza illness rate, absenteeism due to influenza, and hourly wages. The model was insensitive, however, to rates of health care use or the costs of health care (health care provider visits and hospitalisations) resulting from either influenza or possible side effects due to vaccination.

**Authors' conclusions**
Influenza vaccination of healthy working adults on average is cost saving. The author clearly stated that the findings reported in the study support a strategy for routine, annual vaccination for healthy working adults aged between 18 and 64 years. This is especially the case when the vaccination occurs in efficient and low-cost sites.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used; namely that healthy working adults traditionally have not been included among the priority groups targeted for annual influenza vaccination. You, as a user of this database should decide if this is a relevant comparator in your own setting.

Validity of estimate of measure of effectiveness
The author did not state explicitly that a systematic review of the literature had been undertaken and the methods used to identify relevant research and to minimise bias were unclear. The author did not clearly consider the impact of differences between the primary studies when estimating effectiveness. The author used sensitivity and Monte Carlo simulation analysis to assess the impact of variability in the data on the results. The methods and programme used for the simulation analysis were described, but the author did not describe the underlying model or report whether the validity of the model structure was tested.

Validity of estimate of measure of benefit
The authors used indirect costs to value health benefits in monetary terms. This is appropriate for a study population with full employment, but may undervalue the benefit to people in this age group who are not in paid employment. The valuation method used excludes the impact of morbidity and mortality on other aspects of people's lives.

Validity of estimate of costs
All categories of costs relevant to the perspective adopted were included in the analysis. Some relevant costs were omitted from the analysis, the economic value of leisure time was not included and the economic value of human life was not fully represented. As the analysis did not consider these costs the benefits of the vaccine may have been underestimated.

Resource use quantities were taken from published studies and unpublished data. A sensitivity analysis of quantities was conducted.

Unit costs were taken from published sources and a sensitivity analysis of these prices was conducted. The author discounted indirect costs accordingly and standardised all costs to 1998 dollars using the appropriate component of the consumer price index.

Other issues
The author made appropriate comparisons of the findings with those from other studies. The issue of generalisability was addressed in the context of all recently published trials concerning the influenza vaccine. The author postulated that the generalisability of the findings from recent trials to other influenza seasons, and to the general working adult population, is uncertain given the demographic characteristics of the study populations and the year-to-year variability of illness rates, vaccine effectiveness rates, and other clinical and economic benefits.

The study addressed healthy adults and this was reflected in the author's conclusions.

The author reported a number of limitations to the study namely; the findings are valid only insofar as the underlying assumptions and values used for the individual variables included in the model are valid. The author also stated that every attempt was made to select representative and even conservative estimates for the uncertain parameters included in the model, and the results of the sensitivity analyses suggest that the findings were robust.

Implications of the study
The author states that, although the Advisory Committee on Immunization Practices for the Centres for Disease Control and Prevention and the American Academy for Family Practice recently lowered their age-based recommendations for influenza vaccination from 65 to 50 years of age, the results of this study suggest that substantial health and economic benefits might be realised from vaccinating all working adults against influenza, especially when immunisation occurs
at the work site or in other efficient and low-cost setting.

**Source of funding**
None stated.

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