

# The economic evaluation of influenza vaccination in the elderly population: a model based on Bayesian Networks

*La valutazione economica della vaccinazione influenzale nella popolazione anziana: un modello basato sulle Bayesian Networks*

Gianluca Baio, Fabio Corradi<sup>1</sup>

Department of Statistics "G. Parenti"

University of Florence

baio@ds.unifi.it, corradi@ds.unifi.it

**Keywords:** Health Economics, Influenza vaccination, Influence Diagrams.

## 1. Introduction

Influenza infection is a major cause of illness, morbidity and mortality throughout the world, affecting 5-15% of global population each year. The high-risk groups of influenza complication include mainly elderly and patients with cardiovascular or pulmonary disorder, and metabolic disease (diabetes). The influenza vaccination has proved to be effective in reducing acute complications among high-risk patients, particularly in influenza-like illness, hospitalisation and mortality from all causes.

The burden of influenza on health care systems becomes highly relevant, since the increasing proportion of population aged over 65. Therefore, substantial public health implications arise from the decision maker perspective, when programming an annual vaccination strategy. In particular, the public decision maker faces a strategic problem when deciding: *a)* whether to implement a vaccination campaign, and *b)* which vaccine(s) to prescribe. On the one hand, a vaccination program can result in an effective strategy, both from the financial and the clinical point of view, in light of the reduction of hospitalisations and deaths among the elderly. On the other hand, the cost effectiveness of this choice is highly dependent on some exogenous parameters, such as influenza attack rate (which is likely to vary from year to year), and coverage rate (i.e. the proportion of patients that are actually vaccinated). Given the presence on the pharmaceutical market of at least two types of influenza vaccines (the standard and the more recent subunit vaccine adjuvated with MF59), in order to take into account pros and cons, over the entire population, the decision should be taken integrating pre-constituted opinions and empirical data.

The aim of this paper is then to build a decision model which allows the decision makers to evaluate the possible results under different scenarios, and to choose the decision associated to the highest expected utility, expressed in terms of incremental cost effectiveness ratio (*ICER*). The paper is structured as follows: section 2 presents the statistical approach used in the definition of the model and section 3 describes the main results and conclusions obtained.

## 2. Material and Methods

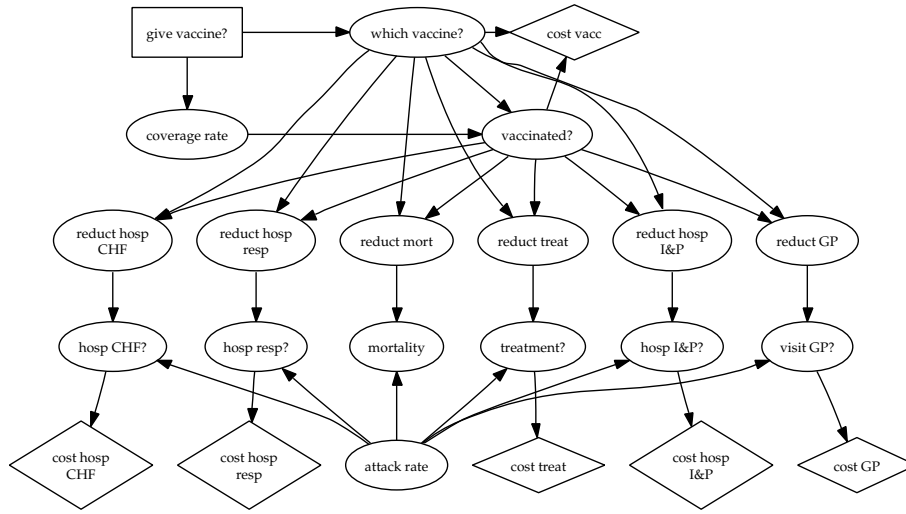
The decision problem under study has been reconstructed and represented in terms of an Influence Diagram (ID), Howard and Matheson (1981); Dawid (2002), using a set

---

<sup>1</sup>59, viale Morgagni, 50124 Florence (Italy)

of *a*) random nodes, each associated to a local probability distribution, *b*) decision node (whether to vaccinate the reference population or not), and *c*) utility nodes, expressed in terms of costs associated to each possible choice. Among the random nodes, we distinguished three different kinds of variables. First, we have the *exogenous* variables (i.e. the coverage rate, which is dependent on the reference population, and the attack rate, which the decision maker cannot directly control, as it is flu-season dependent). Second, we can consider the vaccine-dependent variables (i.e. variables taking into account the reduction in the utilisation of health resources generated by the vaccination). Finally, there are the risk measures (i.e. variables used to estimate the probability of death, hospitalisation, GP visits, and of incurring in influenza related drug prescription). The ID is represented in Figure 1.

**Figure 1.** The ID representation of the Influenza vaccination problem



In this case, we had not access to a comprehensive database, which could allow us to observe directly all the quantities of interest. For this reason, we followed a two-fold strategy: when possible, we used sample data from an observational study carried out on the elderly population of Pianiga (Venice) during three flu seasons (2000-2001, 2001-2002 and 2002-2003), with the help of four General Practitioners. As for the variables that are not observable in the Pianiga database, we performed a Bayesian meta-analysis of literature data, to obtain the distributions of interest. The estimations of exogenous variables were based on Italian data, while the effectiveness of vaccination (either for the standard vaccine or the MF59) was derived by a set of studies, performed on several countries. For all those variables, defined in the interval  $[0, 1]$ , we performed a standard non informative learning, based on a *Beta* likelihood. To preserve the computational facilities associated to a Bayesian Network, the results were summarised on a grid of 10 values. This strategy also allows a sensitivity analysis, since different scenarios can be considered, for the exogenous and the vaccine-related variables, simply by instantiating them to a given value.

As for the utility measures, while associating a proper numerical utility measure to the risk of death can be cumbersome, it proves to be relatively straightforward to define a (dis)utility measure for all the other risk measures. In fact, the decision maker should weigh the choice of whether to vaccinate the elderly population on the basis of the global reduction of the risks, and on the total costs associated. Hence, we calculated the relevant

direct costs, weighing the unit cost of each health care resource by the occurrence probability that we observed in the Pianiga database, in order to provide an estimation of costs that is strictly related to the clinical practice reality that we are monitoring.

The cost effectiveness analysis was then carried out combining the results obtained from the evidence propagation in the ID. We compared three different health programs: the decision maker chooses *a)* not to vaccinate the population; *b)* to vaccinate the population with a standard vaccine; *c)* to vaccinate the population with the MF59 vaccine. The cost effectiveness analysis is based on the *ICER*. For each pairwise comparison, it is defined as the ratio of the difference in total costs,  $\Delta_c$ , to the difference in any specific effectiveness measure,  $\Delta_e$ . This value represents the difference between the probabilities of occurrence of a given risk under the two alternative programs compared (i.e. "do not vaccinate" vs "give standard vaccine", or "give standard vaccine" vs "give MF59 vaccine", or "do not vaccinate" vs "give MF59 vaccine"). The main effectiveness measure is mortality, although one can evaluate the cost effectiveness of a program with respect to the consumption of any other health care resource considered in the model.

### 3. Results and conclusions

The algorithm of evidence propagation (Jensen and Dittmer (1994)) provides a solution to the ID, i.e. a way to determine the choice associated to the highest expected utility. The total expected utility is calculated and associated to each possible choice. A first result from the ID is that, given the premises described above, the expected (dis)utility, i.e. the total annual cost, equals 53.04 euro per patient, should the decision maker decide not to promote a vaccination campaign, and equals 51.18 euro per patient, in case the decision maker decides to go for a vaccination campaign. This latter result is an average of the two specific situations where the vaccine can be either the standard or the MF59. Consequently, the vaccination proves to be a cost saving program. Nevertheless, it is important to evaluate this result in the light of the benefits that are gained from the population, in terms of risks reduction. Vaccination proves to reduce each risk measure, as depicted in Table 1.

**Table 1.** *Posterior probabilities for risk measures*

| Posterior probabilities for risk measures | MF59 vaccine | Standard vaccine | Do not vaccinate |
|-------------------------------------------|--------------|------------------|------------------|
| GP visit                                  | 0.0604       | 0.0629           | 0.0828           |
| Influenza related treatments              | 0.1102       | 0.1188           | 0.1658           |
| Hospitalisation for I&P                   | 0.0150       | 0.0160           | 0.0200           |
| Hospitalisation for CHF                   | 0.0550       | 0.0580           | 0.0660           |
| Hospitalisation for RD                    | 0.0006       | 0.0006           | 0.0008           |
| Mortality                                 | 0.0023       | 0.0024           | 0.0033           |

I&P = Influenza and Pneumonia  
CHF=Chronic Heart Failure  
RD=Respiratory Diseases

In particular, the alternative based on MF59 vaccine always produces the highest risk reduction. The standard vaccination also proves to be effective in reducing the risk of experimenting the events, as compared to the null option (do not vaccinate the population). The total direct costs per year and per patient are of 50.44 euro in case the decision maker chooses to vaccinate population with the MF59 vaccine, and of 51.92 euro in case the pro-

gram chosen is the vaccination with the standard vaccine. Table 2 presents the *ICER* (that could be interpreted as savings per event averted) for each risk measure and for the three pairwise comparisons.

**Table 2.** *Cost effectiveness analysis for the three pairwise comparisons*

| <i>ICER</i> (savings per event averted) | "MF59" vs<br>"Standard" | "MF59" vs<br>"Do not vaccine" | "Standard" vs<br>"Do not vaccine" |
|-----------------------------------------|-------------------------|-------------------------------|-----------------------------------|
| GP visit                                | 592.00                  | 116.52                        | 56.78                             |
| Influenza related treatments            | 172.09                  | 46.94                         | 24.04                             |
| Hospitalisation for I&P                 | Not comparable          | 13,050.00                     | 5,650.00                          |
| Hospitalisation for CHF                 | 1,480.00                | 522.00                        | 282.50                            |
| Hospitalisation for RD                  | 493.33                  | 237.27                        | 141.25                            |
| Mortality                               | 16,444.44               | 2,718.75                      | 1,298.85                          |

I&P = Influenza and Pneumonia  
CHF=Chronic Heart Failure  
RD=Respiratory Diseases

As appears clear, the vaccination proves to be a highly cost effective strategy, as compared to the null option. Both MF59 and standard vaccine produce a better health status for the population and savings for the health provider. This is mainly due to the fact that the high-cost events (hospitalisations) are reduced (see Table 1), leading to relevant savings for the public payer. The extra cost generated by the vaccine acquisition and dispensation is more than balanced from this advantages.

Probabilistic expert systems have been well discussed so far, also for medical purposes, (see Cowell *et al.* (1999)); nevertheless, the pharmacoeconomics literature has not explored them thoroughly. Moreover, the perspective we took in this work is somehow innovative, in that we approach the problem accounting jointly for the clinical and the economic matter, from the whole reference population point of view. Hence, if on the one hand this model is an application of some well-established theory, on the other hand, as far as we are concerned, it is one of the few examples of economic evaluation of a health decision-making problem, based on this methodology. From our analysis, we provide evidence that the influenza vaccination is a cost effective strategy, as compared to the null option. Moreover, the MF59 vaccine proves to be both more effective and cheaper in the long run, as compared to both the standard vaccination and the null program. The pharmacoeconomics evaluation based on IDs has a huge potentiality, in our opinion, for the reasons we described above. We reckon that statistical, economic and clinical research is to be focused on that topic in the next future.

## References

- Cowell R., Dawid P., Lauritzen S. and Spiegelhalter D. (1999) *Probabilistic Networks and Expert Systems*, Springer-Verlag, New York, NY.
- Dawid A. (2002) Influence diagrams for causal modelling and inference, *Statistical Review*, 70, 161–189.
- Howard R. and Matheson J. (1981) *Readings in Decision Analysis*, Strategic Decision Group, Menlo Park, CA.
- Jensen F. and Dittmer S. (1994) From influence diagrams to junction tree, in: *Proceedings of the tenth Conference on Uncertainty in Artificial Intelligence*, de Mantras L. and Poole D., eds., Morgan Kaufmann Publishers, San Francisco, CA, Edmonton, Canada.