MODELLING FOR ENGINEERING & HUMAN BEHAVIOUR 2019

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Instituto Universitario de Matemática Multidisciplinar
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Network computational model to estimate the effectiveness of the influenza vaccine *a posteriori*

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1 Introduction

Influenza or seasonal influenza, known as the flu, is an infectious disease caused by two different virus, which usually belong to the *Orthomyxoviridae* family. It affects mainly the respiratory system, although it can also affect the circulatory and muscular system. The symptoms that produce this virus can be diverse, from high fever, headache and throat irritation to muscle aches and feeling tired [1].

The first records of this disease date from ancient Egypt, and from then until now this disease has been one of the most complex to study and treat due to the high mutations of different nature that the virus suffers every year, making it highly unpredictable. This virus appears every year in the temperate zones of the whole globe, where the difference in the average temperature between the summer and winter is high [1]. These climatic factors, together with the contact between individuals in a population, favor the spread of the disease rapidly. Annually, about three to five million people worldwide are infected by the influenza virus and about 250 to 500 thousand die.

Every year the World Health Organization (WHO) predicts which strains of the influenza virus are most likely to circulate among the population. Because of this, a new vaccine should be developed every season that is capable of immunizing as many individuals as possible. It takes about six months to formulate and produce the required doses, but the vaccine must be ready before the flu outbreak. It is not possible to analyze its effectiveness before its production although it is possible to do it *a posteriori*.

The time between the start of the vaccine development process and its release to the market, as well as the lack of real data (such as vaccine coverage) makes necessary to calculate the effectiveness of the vaccine once the flu season has ended, which usually happens between October and April in the northern hemisphere. In addition, the partial immunization of some people in

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the population who have previously had similar flu periods and the transmission of antibodies generated by the parents to the next generation are added to these problems.

The World Health Organization (WHO) strongly recommends to the population to be vaccinated every year against the flu, in order to prevent the possibility of infection and to reduce the number of infected people [2].

2 Computational network model

Until now, several techniques have been proposed to determine the effectiveness of the influenza vaccine *a posteriori*, although their reliability is currently under discussion. Many of the proposed techniques are based on statistical analysis, however we propose a new and efficient technique based on a computer network model capable of representing the spread of flu in a population.

The network model consists of a graph formed by vertices and edges. Each of the vertices corresponds to an individual of the population and each edge represents the contact (effective or not) of the transmission of the disease between the vertices that join the edge. It is possible to simulate in a network the evolution of the transmission dynamics of an infectious disease such as influenza over time using computer programs.

The generated network has been designed in a flexible way, which allows to introduce specific vaccine strategies and change them if necessary in a quick and simple way. This model builds a population made up of one million individuals, where the total number of relationships changes depending on an average degree. These relationships are generated randomly, in the same way as individuals, through an algorithm for obtaining random numbers. The age of the individuals of the population follows the demographic data of the Community of Valencia.

The data used represent the weekly reported cases over a period of 26 weeks between October 2016 and January 2017. The data includes 95% of the confidence intervals.

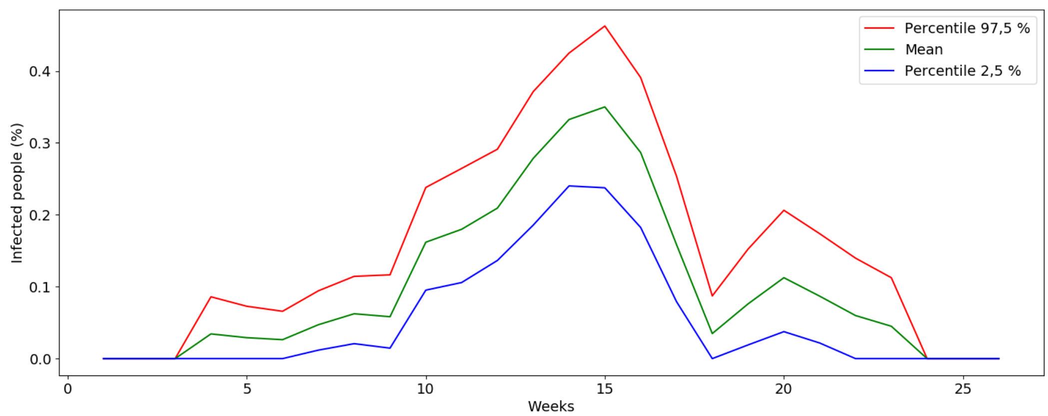

Figure 1: Weekly flu reported cases 2016-2017 [3].

To simulate the flu transmission dynamics over time, the model behaves in the same way as in reality. Each individual can go through four different states:

- Susceptible: The individual is healthy and can be infected by infected neighbors.
- Vaccinated: The individual has been effectively vaccinated, that is, the individual is protected against infection.
- Infected: The individual is infected. After a week the individual recovers.
- Recovered: The individual has passed the flu and is no longer infected.

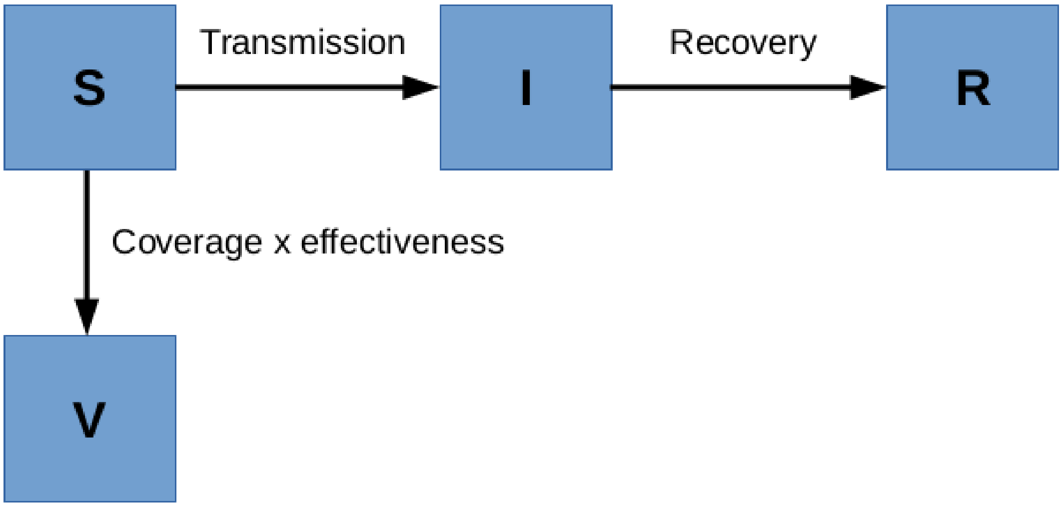

Figure 2: Flow diagram of the influenza transmission dynamics.

A part of the population that is vaccinated is not protected from the flu. This is because the vaccine is not 100% effective and there are cases where it can take effect and others where it has no effect. In cases where it does have effect, people are protected against the flu of the current season. Otherwise, they remain susceptible.

In the network model there are two types of parameters to work with. The unknown parameters, which are the average degree of the computer network, the weekly transmission rate (different for each week) and the effectiveness of the vaccine. The known parameters are the coverage of the vaccine, that is, how many people in the total population should be vaccinated and the recovery time.

3 Model calibration

To calibrate the unknown parameters of the model, we repeatedly applied an optimization algorithm (PSO) with an error function that measures the difference of the model and the confidence intervals of the data. This task is evaluated 50 thousand times.

Following, we select one hundred sets of input parameters of the model in such a way that the 95% confidence interval of the outputs should be as close as possible to the 95% confidence interval of the real data.

4 Results

After selecting the one hundred outputs that best capture the uncertainty of the data, the obtained results can be seen in Fig. 3 and 4:

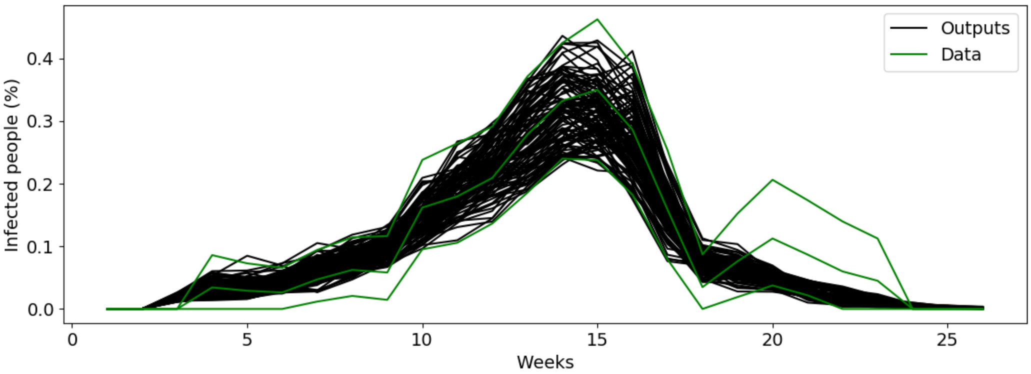

Figure 3: Hundred best model outputs (in black). In green, the data and the 95% CI.

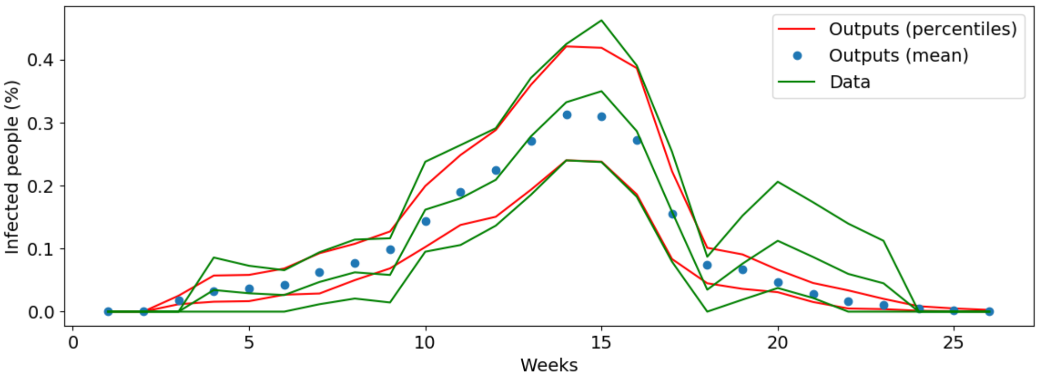

Figure 4: The same figure as Fig. 3, but instead of the 100 model outputs, its 95% CI of the hundred best model outputs.

As we can see in Fig. 3 the one hundred outputs are the black lines and the real data are the green lines. The outputs capture the uncertainty of the data in most of the band. In Fig. 4 the difference with the Fig. 3 is the black lines. We represent the percentiles and the mean of the outputs and the real data (the mean and the percentiles).

The calibration gives us values for the unknown parameters:

	Percentile 2,5%	**Mean**	**Percentile 97,5%**
Average degree	43,47	59,18	67,52
Vaccine effectiveness	14%	29%	57%

Table 1

In Table 1 we can see the values calibrated for the average degree and the vaccine effectiveness. Also, in Fig. 5 we can see how the transmission rate of influenza evolves over the disease season.

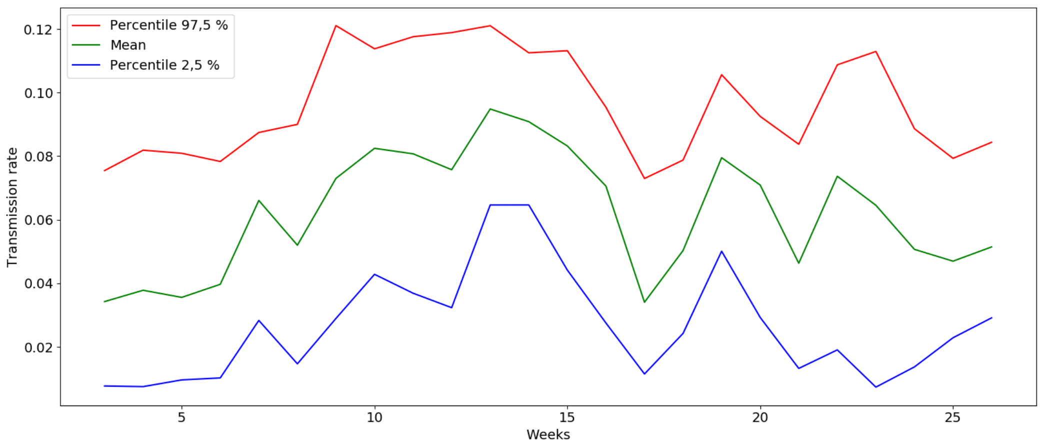

Figure 5: 95% CI of weekly transmission rate over the disease season.

5 Conclusions

We have used a novel technique based on a computational network model to determine the effectiveness of the flu vaccine in a population of individuals.

The techniques used to perform the calibration have taken into account the data and the model building uncertainty.

The estimated effectiveness of the influenza vaccine is low, about 30%.

We will consider to divide the population in to age groups because the coverage and the effectiveness of the vaccine change with the age of the individual.

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References

[1] Moghadami, M., A Narrative Review of Influenza: A Seasonal and Pandemic Disease, Iranian Journal of Medical Sciences, 42 (1): 2–13, 2017.

[2] Recommended composition of influenza virus vaccines for use in the 2006-2007 influenza season, World Health Organization, 2006. https://web.archive.org/web/20060528111237/http://www.who.int/csr/disease/influenza/2007northreport.pdf.

[3] Portero, A., Alguacil A., Sanchis, A., Pastor, E., López, A., Miralles, M., Martin, M., Alberich, C., Roig, F., Lluch, J., Paredes, J. and Vanaclocha, H., Prevención y vigilancia de la gripe en la Comunitat Valenciana. Temporada 2016-2017, 150: 28, Valencia, 2017.