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Extending influenza vaccination to individuals aged 50–64: A budget impact analysis

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Objectives: Influenza (vernacular name, flu) is a viral infection that causes a high consumption of resources. Several studies have been carried out to provide an economic evaluation of the vaccination programs against influenza. Nevertheless, there is still a lack of evidence about the dynamic effects resulting from the reduction of the transmission power. This study considers the impact on contagiousness of alternative strategies against influenza in people aged 50–64 in Italy, France, Germany, and Spain.
Methods: By using the Influsim 2.0 dynamic model, we have determined the social benefits of different coverage levels in every country compared with the ones currently recommended. We have subsequently performed a Budget Impact Analysis to determine whether the currently recommended coverage results from an optimal budget allocation. A probabilistic sensitivity analysis was also conducted.
Results: We found that in Germany, the optimal coverage level is 38.5 percent, in France 32.4 percent, in Italy 32.75 percent, and 28.3 percent in Spain. By extending the coverage level, social saving tends to increase up to 100 percent for France and Italy and up to 80 percent for Germany and Spain.
Conclusions: Decision makers should allocate the budget for vaccination against influenza consistently with the estimation of the optimal coverage level and with the dynamic effects resulting from the reduction of the transmission power.

Keywords: Influenza vaccine, Basic reproduction number, Economic model

Influenza (vernacular name, flu) is a seasonal viral infection. The infection affects individuals at every age, although for the elderly it is the first cause of hospitalization and the fourth cause of death (25).

In addition, influenza causes a high consumption of resources both from a social and a third-party payer (TPP) perspective. In 1981, the Office for Technology Assessment (United States) estimated a cost for a TPP between 1 and 3 billion dollars and 15 billion dollars for loss of productivity (22). The vaccination against influenza is actually recommended by the World Health Organization (27).

Despite the findings of Jefferson et al. (18), the European Scientific Working Group on Influenza (7) states that the recommendations in favor of a vaccination policy are principally targeted at individuals at high risk of complication. Although there is a general consensus about which categories of individuals should be considered at high risk (3), different guidelines have been published in the European countries. In recent years, several studies have been carried out to provide an economic evaluation of the vaccination strategies against influenza (1;2;24). Aballea et al. (1;2), estimated the productivity gains in terms of number of working weeks in

Italy, Germany, France, and Spain ranging from 77.319 (in Germany) to 151.737 (in France). These results were based on a decision tree focused on the minimization of the cost per quality-adjusted life-years (QALYs). However, the studies did not consider the dynamic effects resulting from the reduction of the transmission power. This should be taken into account to determine the optimal vaccination coverage for the health system. This study considers the impact on contagiousness of alternative strategies against influenza in people aged 50–64. We determine the social savings (in million Euros) of different coverage levels starting from the currently recommended in every country.

METHODS

Study Design

The Influsim 2.0 (6) dynamic model was used to simulate the course of an influenza spread in Italy, France, Germany, and Spain for people aged 50–64 and to estimate the incremental social savings of different vaccination strategies. The incremental social savings were defined as the difference with respect to savings in terms of weeks of absence from work, general practitioner (GP) visits, antiviral drugs, and hospital admissions resulting from the extension of the vaccination of 1 percent.

A social perspective was considered because alternative strategies against influenza largely affect the productive sector in terms of gains/losses of working days.

First, we estimated the resources involved in the implementation of the current recommendations which include vaccination for a high-risk population (20 percent in Spain and 25 percent of the aged 50–64 in the other countries). Second, we considered that the extension of the coverage leads to an increase of costs for vaccine doses which are compensated by a lower consumption of antiviral drugs. Third, we defined the optimal budget allocation as the one that maximized the number of vaccine doses given a stock of antiviral drugs to treat the infected population. Finally, we estimated the additional budget for different coverage levels and the incremental social savings.

Model Specification

Influsim 2.0 has been implemented by the Department of Biometry, University of Tubingen. It is based on a system of 1,081 differential equations to consider every clinical, demographic. and social parameter that is relevant to plan a strategy against influenza (6). We simulated the course for Italy, France, Germany, and Spain using a country-specific population aged 50–64. The effect of contagiousness among age groups was also included in the simulation (25). We considered a population of 10.748.040 individuals for Italy, and respectively 10.630.900, 15.502.340, and 7.064.182 for France, Germany, and Spain (9;10;13;14). To model the contagiousness, we used the basic reproduction number (BRN) defined as the mean number of secondary cases that a typical single infected case will cause in a population with no immunity to the disease in the absence of interventions to control the infection (5). Table 1 shows the input parameters used for the structural hypothesis of the model.

Identification, Measurement, and Evaluation of Costs

The basic measure to model costs was given by the length of the infection. The cost drivers were identified in weeks of absence from work, number of GP visits, number of hospital admissions, doses of antiviral drugs, and doses of vaccine (1;2).

The costs did not relate to complications. The prices in Euros to value the resources (see Table 2) were extracted from literature and international database (8;11;12;15;16;20;21;23;26). The human capital approach was used to estimate the production losses. Patients' time off work was measured in terms of hourly wages with the assumption that it reflects productivity. The average annual costs of work in different sectors of activity were estimated according to the data previously published (9;10;13;14).

Sensitivity Analysis

We performed a one-way probabilistic sensitivity analysis (PSA) to model the uncertainty of the parameters. Supplementary Table 1 (which can be viewed online at www.journals.cambridge.org/thc2010020) shows the values of the alpha and beta parameters used to fit the random distributions consistently with the international guidelines (17). Second, we conducted a Monte Carlo simulation to assess the uncertainty through the different parameters. The heterogeneity of the epidemic spread, was assessed ranging the BRN from 1.68 to 3.

RESULTS

Base Case

Table 3 shows the incremental social savings after the solution of the optimization problem for different coverage levels in Italy, France, Germany, and Spain.

Italy

In Italy, the budget to cover 25 percent of the aged 50–64 and to purchase the antiviral drugs is 67 million Euros. The optimal budget allocation suggests the extension of the coverage to 32.75 percent with an incremental social saving of 125 million Euros. The extension of the coverage up to 100 percent always increases the social savings. In conclusion, with a total budget spending of 114 million Euros the entire population aged 50–64 is vaccinated and the total social savings are 600 million Euros.

Table 1. Model Specification: Input Parameters

Parameter		Mean (min-max)[a]	Source
Absenteeism (% reduction)	Antiviral drugs	13% (11%-15%)	(1;2)
	Vaccine	29% (19%-35%)	(1;2)
Hospital admissions (% reduction)	Antiviral drugs (Oseltamivir for individuals at high risk of complications)	25% (17%-30%)	(1;2)
	Antiviral drugs (Oseltamivir for individuals at low risk of complications)	84% (78%-100%)	
	Antiviral drugs (Zanamivir for individuals at high risk of complications)	33% (28%-36%)	(1;2)
	Antiviral drugs (Zanamivir for individuals at low risk of complications)	64% (60%-72%)	
	Vaccine	50% (43%-56%)	(1;2)
GP visits (% reduction)	Antiviral drugs	24% (19%-26%)	(1;2)
	Vaccine	29% (19%-35%)	(1;2)
Basic reproduction number		2 (1,68–3)	(5)
Average duration for the latent status		1,9 (1–4)	(6)
Average duration for the asymptomatic stage		4,1 (1–5)	(6)
Average duration for the moderate stage		7 (5–12)	(6)
Average duration for the severe stage		7 (5–11)	(6)
Average duration of the convalescence period		5 (3–9)	(6)
% Asymptomatic		33% (15%-45%)	(6)
% Severe among symptomatic		50% (21%-57%)	(6)
% Hospital admissions among severe HR 20–59		2,76% (0,15%-4%)	(6)
% Hospital admissions among severe HR >59		7,77% (4,6%-9,8%)	(6)
% Hospital admissions among severe LR 20–59		2,34% (1,3%-4,34%)	(6)
% Hospital admissions among severe LR >59		3,56% (2,6%-5%)	(6)
% contagiousness during the first half of the infection		50% (38%-71%)	(25)
Relative contagiousness compared to the moderately severe cases		50% (38%-71%)	(25)

[a]Standard deviation, alpha, and beta parameters as well as the statistic distribution assumed for probabilistic sensitivity analysis are available in Supplementary Table 1 published in the online version of the manuscript.
HR, high risk of complications; LR, low risk of complications; GP, general practitioner.

Table 2. Prices of the Identified Cost Drivers

Cost drivers	Italy	France	Germany	Spain
Absenteeism (per week)	€850,00[9]	€1.000,00[13]	€1.000,00[10]	€653,30[14]
GP visit	€20,00[21]	€25,00[16]	€15,00[26]	€18,80[4]
Hospital admissions	€3.700,00[21]	€3.950,00[16]	€4.750,00[11]	€3.344,00[23]
Oseltamivir	€35,00[12]	€35,00[8]	€35,00[15]	€35,00[20]
Zanamivir	€31,50[12]	€31,50[8]	€31,50[15]	€31,50[240]
Vaccine + administration	€8,76[21;12]	€6,26[8]	€7,00[15;26]	€3,83[4;20]

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Table 3. Results: Incremental Social Savings and Additional Level for Different Coverage Levels

Coverage level	Additional budget (A)	Incremental social savings
Italy		
32,75%	0	€124.864.766,15
50%	€10.454.483,24	€174.684.095,08
80%	€21.245.849,12	€253.804.339,72
100%	€15.545.766,08	€53.216.781,13
France		
32,50%	0	€117.570.682,53
50%	€6.297.165,32	€304.835.154,74
80%	€19.938.005,20	€160.518.740,44
100%	€11.625.336,80	€156.386.116,03
Germany		
38,5%	0	€147.609.690,48
50%	€5.767.383,70	€293.020.682,01
80%	€24.567.914,00	€381.318.659,92
100%	€19.231.981,00	€10.212.279,3
Spain		
28%	0	€129.077.030,80
50%	€4.783.612,30	€310.200.786,23
80%	€2.730.245,12	€288.024.584,30
100%	€1.291.593,41	€86.095.085,33

France

In France, the optimization of the budget available for vaccine doses and antiviral drugs (91 million Euros) suggests the extension of the coverage up to 32.4 percent and an incremental social saving of 117 million Euros. The extension of the coverage up to 100 percent increases the social savings. In conclusion, with a total budget spending of 131 millions of Euro the entire population aged 50–64 is vaccinated and the total social savings are 740 million Euros.

Germany

In Germany, the budget is 71 million Euros and the optimal allocation suggests the extension of the coverage to 38,5 percent and 148 million Euros social savings. However, due to the population composition, the additional spending is higher than the incremental benefit starting from the 80 percent coverage. In conclusion, with a total budget spending of 122 million Euros, the entire population aged 50–64 is immune and the total social savings compared with the starting coverage (25 percent) are 811 million Euros.

Spain

In Spain, the estimated budget is 45 million Euros and its optimal allocation suggests the coverage of 28.3 percent of the population aged 50–64 with an incremental social saving of 129 million Euros. However, the additional spending is higher than the incremental benefit starting from the 80 percent coverage because the whole population is assumed to be immune at this level and social savings are 720 million Euros with a total budget spending of 54 million Euros.

Sensitivity Analysis

One-way PSA shows that the parameters with an higher impact on the increase/decrease of the social savings, are reduction of the absenteeism, percent of severe cases among symptomatic, percent of asymptomatic, and average duration of the convalescence period.

Supplementary Table 2 shows some statistics to resume the results of the Monte Carlo simulations conducted for each country included in the study. The results show the variation in total social savings, for the optimal coverage level and for 50 percent, 80 percent, and 100 percent coverage. The table shows a huge variability of the results. Nevertheless, the confidence interval (95 percent) shows that the results can be considered consistent.

DISCUSSION

In this study, we used a dynamic model to simulate the course of a hypothetic infection caused by influenza. We compared, in terms of incremental social savings, alternative strategies corresponding to different levels of coverage starting from the level currently recommended in Italy, France, Germany, and Spain. In Italy and France, we showed how an optimal budget allocation entails an extension of the coverage level from 25 percent to 32.75 percent and 32.4 percent, respectively. In the analysis, we also considered that the marginal benefits (in terms of social savings) of a coverage expansion tend to decrease because of the progressive reduction in contagiousness.

In Germany and Spain, the optimal coverage would be 38.5 percent and 28.3 percent, respectively. Nevertheless, in these two countries, the total savings decrease starting from an 80 percent coverage level. The population in both cases plays a crucial role. In Germany, the total savings tend to decrease beyond 80 percent coverage level, because 100 percent coverage of a huge population suggests a higher cost for vaccine doses than the incremental social savings.

In Spain, the transmission power would be halted at 80 percent coverage and further extensions would suggest additional costs for vaccination without additional gains.

To test the consistency of our results, we applied the dynamic model with the same assumptions used in Aballéa et al. (1) and (2). For example, in Aballéa et al. (1) it is shown that, in Italy, a vaccination strategy involving 67 percent of the high-risk population and 52 percent of low-risk individuals would save 111.981 weeks of work with respect to a strategy involving the coverage for 42 percent of the high-risk population and 17 percent of the low-risk individuals. We replicated the two strategies with our model and the results showed a saving that ranged from 104.000 (BRN = 1,68) to 143.294 (BRN = 3) weeks of work. However, our study shows that the strategies considered in Aballéa et al. (1) and (2) are sub-optimal. Some limitations have to be underlined in our analysis as follows: (i) Results are based on a simulation with a hypothetical population and the real evolution of a FLU infection should be observed; (ii) Results are not considered in terms of incremental cost-effectiveness ratio (ICER). The reason is that we aimed to add some evidence to the already known results of (1) and (2); (iii) We considered oseltamivir and zanamivir as the antiviral drugs administered to the infected and alternative treatments (both antipyretics and antiviral drugs) should be included; (iv) We did not consider the different types (A-B) of the infection, but we modeled this difference by using the BRN measure.

POLICY IMPLICATIONS

In conclusion, our study was aimed at underlining the need for decision makers to determine optimal vaccination policies with the budget available. This should be made by using analytical supports to model the epidemiological characteristics of the infection, the effects of the extension of the vaccination on the contagiousness and the population composition.

SUPPLEMENTARY MATERIAL

Supplementary Table 1
Supplementary Table 2
www.journals.cambridge.org/thc2010020

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CONFLICT OF INTEREST

All authors report having no potential conflicts of interest.

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