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Abstract

Background. Each year, up to 10% of unvaccinated adults contracts seasonal influenza, with half of this proportion developing symptoms. As a result, employers experience significant economic losses in terms of employee absenteeism. Influenza vaccines can be instrumental in reducing this burden. Workplace vaccination is expected to reduce employee absenteeism more than linearly as a result of positive externalities. It remains unclear whether workplace influenza vaccination yields a positive return on investment.

Methods. We simulated the spread of influenza in the seasons 2011-12 up to 2017-18 in Belgium by means of a compartmental transmission model. We accounted for age-specific social contact patterns and included reduced contact behavior when symptomatically infected. We simulated the impact of employer-funded influenza vaccination at the workplace and performed a cost-benefit analysis to assess the employers' return on workplace vaccination. Furthermore, we look into the cost-benefit of rewarding vaccinated employees by offering an additional day off.

Results. Workplace vaccination reduced the burden of influenza both on the workplace and in the population at large. Compared to the current vaccine coverage – 21% in the population at large – an employee vaccine coverage of 90% could avert an additional 355 000 cases, of which about 150 000 in the employed population and 205 000 in the unemployed population. While seasonal influenza vaccination has been cost-saving on average at about €10 per vaccinated employee, the cost-benefit analysis was prone to between-season variability.

Conclusions. Vaccinated employees can serve as a barrier to limit the spread of influenza in the population, reducing the attack rate by 78% at an employee coverage of 90%. While workplace vaccination is relatively inexpensive (due to economies of scale) and convenient, the return on investment is volatile. Government subsidies can be pivotal to encourage employers to provide vaccination at the workplace with positive externalities to society as a whole.

Keywords

Vaccination — Workplace — Influenza — Cost-benefit analysis — Absenteeism — Employee

Highlights

- Workplace vaccination is an efficient and inexpensive intervention
- On average, we found workplace influenza vaccination to be cost-saving
- Employers could have saved €10 per vaccinated employee per year between 2011-2018
- Influenza vaccination reduces the burden of disease and absenteeism among employees
- Vaccinated employees act as a barrier and reduce influenza transmission in society

Introduction

Absenteeism from work causes a large economic burden to society. Seasonal influenza accounts for a significant share of this burden [1]. Indeed, Somes et al. estimated the attack rate for seasonal influenza in unvaccinated adults to be around 10%, with about half of the cases experiencing symptoms [2], while a lower attack rate of 2.3% was found in a 2018 Cochrane review [3]. Furthermore, the timing and intensity of influenza epidemics have been successfully linked to patterns in employee absenteeism [4].

More importantly, seasonal influenza causes considerable mortality and morbidity to society as a whole, in particular to vulnerable subgroups in the population. In the 2018-19 season, an estimated 307,000 Belgians – about 2 to 3 % of the population – contracted seasonal influenza. Of these cases, 2% to 3% required hospitalization, whereas 13% of hospitalized cases developed severe complications and 6% died in the course of hospital stay. Usually, over 80% of deaths occur in people 65 years or older [5]. Inactivated influenza vaccination can directly limit the burden of influenza in healthy children, healthy adults as well as in the elderly [3, 6, 7]. Nevertheless, yearly influenza vaccine effectiveness is uncertain due to, among others, the potential mismatch between vaccine and circulating strains [8].

In most developed countries, influenza vaccination is currently recommended for individuals aged 60-65 and older [9]. However, in the United States of America (US) all individuals older than 6 months are targeted to receive vaccination [10] and in the United Kingdom (UK) children were recently included in routine flu vaccination as well [11]. In Belgium, next to health care workers and risk groups (e.g. chronically ill and people older than 65 years of age), health authorities recommended to vaccinate everyone between 50 and 65 years of age [12]. Despite the economic impact of employee absenteeism, influenza vaccine is usually not reimbursed, nor conveniently available for healthy employees. Indeed, individuals not belonging to a risk group require visits to both GP and pharmacy at a total out-of-pocket cost of about €20 to €30 with mandatory health insurance partly covering the GP visits [13,14].

Alternatively, some employers offer influenza vaccination at the workplace at no cost to the employee. An occupational health service provider in Belgium reported that only 4.3% of employers offered influenza vaccination to their employees in 2019, and that such programs are mainly organized in larger companies [15]. Unsurprisingly, uptake of influenza vaccine in Belgium remains relatively low. Each year, only about 20% of the population at large is vaccinated and about 60% of the elderly [16].

The benefits of employee vaccination translate in a reduction of disease, directly in vaccinated persons, but indirectly also in the work and other social contacts of vaccinated persons. Indeed, successfully vaccinated individuals contribute to herd immunity as they are unable to transmit the pathogen to their social contacts (see Fine et al. [17]). Therefore, absenteeism is expected to reduce more than linearly. Workplace vaccination can be instrumental in reaching a higher influenza vaccination coverage for several reasons, among which: convenience for vaccinnees (e.g. no GP visit and no out-of-pocket cost), economies of scale and a potential return on investment for employers. However, this return on investment is not fully explored yet.

Economic analyses are typically limited to risk groups and focus on societal or health care payer perspectives. Influenza immunization programs in such risk groups are often found to be cost-effective [18]. However, with respect to employer funded vaccination, employees usually do not belong to a risk group. In addition, the majority of the costs related to influenza absenteeism and workplace vaccination are borne by the employer. Research focussing on the perspective of the employer is relatively scarce and is often limited to healthcare settings.

Few analyses have been performed on the economics of workplace influenza vaccination. Lee et al. [19] performed an economic analysis of employer-sponsored workplace vaccination for the prevention of seasonal and pandemic influenza in the US. Others compared the absenteeism of vaccinated and non-vaccinated employees in single companies [20–23]. Bridges et al. [24] describe a double-blind, randomized, placebo-controlled trial on the effectiveness and cost-benefit of influenza vaccination of healthy workers.

Studies that apply a dynamic transmission model are lacking. Nevertheless, because of herd immunity induced at the workplace and in the community, the use of a dynamic transmission model is most appropriate to capture all the benefits of workplace vaccination [25]. Dynamic transmission models account for the positive externalities of herd immunity by accounting for the infectious cases, vaccination and force of infection varying over time. The latter is linked to social contact behavior [26], which depends on age and temporal factors [27]. In addition, health state also plays an important role on social contact behavior [28]. Eames et al. [29] found significant reductions in social contact behavior of symptomatic cases in the UK during the 2009 influenza pandemic. The impact of this adaptive social contact behavior on transmission dynamics was found to be of high importance [30].

In this study, we estimated the cost-benefit of employer-funded influenza vaccination in Belgium with a dynamic transmission model. We accounted for reduced social contact behavior when cases are symptomatically infected. The model is fitted to incidence data from 2011-12 up to 2017-18. The predicted burden of disease under different scenarios (e.g. vaccine coverage) is used to assess the employers' return on investment. Finally, we calculated the cost-benefit of rewarding vaccinated employees by offering an additional day off.

Materials and methods

Transmission model

We built on a compartmental transmission model developed by Santermans et al. [30] to simulate the spread of influenza in the Belgian population for flu seasons 2011-12 up to 2017-18. The model structure is presented in Figure 1 and each compartment is subdivided by age and employment status (employed versus unemployed), which is based on data obtained from Statbel [31]. We used five age groups: [0-4], [5-19], [20-44], [45-64] and 65+ years of age. At the beginning of the simulation, a proportion μ gets vaccinated (V) with an inactivated influenza vaccine, which we assumed to be an all-or-none vaccine with an efficacy of ε, (0 ≤ ε ≤ 1). The force of infection, λ, represents the rate at which individuals are infected at time t, moving a proportion of the susceptible population to the exposed compartment (E). All exposed individuals (E) are initially asymptomatically infected (I_1^a) at a rate γ. In a next step, a proportion ϕ becomes symptomatic (I^s) at a rate θ, while the remaining proportion stays asymptomatic (I_2^a). In line with the work of Santermans et al. [30], we applied a different degree of infectiousness to symptomatic versus asymptomatic infection. Likewise, the recovery rate distinguishes symptomatic (σ^s) from asymptomatic (σ^a) cases, moving people to the recovered (R) compartment. An overview of the model parameters is presented in Table 1 with corresponding references.

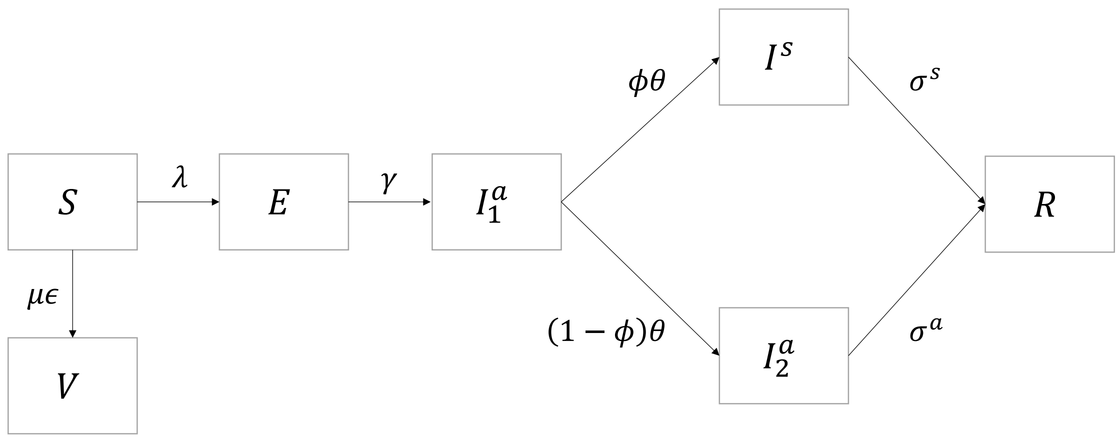

Fig. 1. Model structure to simulate the transmission of influenza. Individuals are either susceptible (S), successfully vaccinated (V), exposed to influenza (E), infectious (I) or recovered (R). Superscripts distinguish between symptomatic (s) or asymptomatic (a) infection. Each compartment is split into age- and work-specific sub-compartments. Parameter values and model features are provided in the main text and Table 1.

We estimated the transmission probability using the social contact hypothesis by Wallinga et al. [26] with proportionality factors q^a and q^s for asymptomatically and symptomatically infected individuals, respectively. In order to include seasonal transmission dynamics, we applied a sinusoidal function to the model's force of infection as described in Goeyvaerts et al. [32]. The force of infection is specified as:

$$\lambda = \beta^s * I^s + \beta^a * (I_1^a + I_2^a) * z(t),$$

$$\beta^s = q^s * \frac{M^s}{N} * z(t),$$

$$\beta^a = q^a * \frac{M^a}{N} * z(t),$$

$$z(t) = 1 + \delta \sin\left(\frac{2\pi(t-t_0)}{365}\right)$$

with the social contact matrix M^s representing the contact behavior of symptomatically infected individuals and M^a the contact behavior for individuals in any other health state. We derived the social contact matrices from Belgian survey data that were collected between May 2005 and September 2006 in the context of the POLYMOD study, the details of which are described by Mossong et al. [33]. We extracted these data using the socialmixr package in R [34] and distinguished between social contact behavior during holidays and regular (i.e. non-holiday) days, as described in Hens et al. [35]. In order to incorporate adaptive social contact behavior when people are symptomatically infected (e.g. staying home from work or school), we applied location-specific reduction rates from a survey in England during the 2009 influenza pandemic, that were reported by Van Kerckhove et al. [28, 29]. Diagnosed patients were recruited at antiviral distribution centres in England and a social contact survey was provided to patients that received an antiviral prescription. Patients were asked to fill out the social contact diary once when showing ILI symptoms and once when symptoms had disappeared. A second part of the study focused on social contacts during the school term versus social contacts during a school holiday [29].

The observed reductions are mostly driven by individuals staying at home, thereby limiting their social contact behavior elsewhere. Based on the social contact matrix for healthy and asymptomatic individuals (M^a), we calculated M^s as follows:

$$M^a = M^{home} + M^{school\,\&\,work} + M^{transport} + M^{leisure} + M^{other},$$

$$M^s = M^{home} + 0.09M^{school\,\&\,work} + 0.13M^{transport} + 0.06M^{leisure} + 0.25M^{other}$$

Social contact matrices for regular and holiday periods and the corresponding age-specific reduction due to illness are presented in Figure 2. For example, individuals between 5 and 19 years of age have more contacts with each other during regular periods compared to holidays (left pane vs. right pane). During regular periods, the number of contacts between an individual of age 5-19 and individuals of the same age is reduced by 82% when this individual experiences symptomatic influenza. The reduction is lower during holiday periods.

Incidence and vaccine effectiveness data

The transmission model was first calibrated to reproduce the observed influenza incidence in Belgium from 2011-2018. We selected these influenza seasons because of (1) data availability on incidence and age-specific vaccine effectiveness, and (2) to prevent interference from the 2009 influenza pandemic on seasonal patterns. Data were obtained from the National Reference Centre for Influenza in terms of reported influenza-like-illness (ILI) cases per 100 000 individuals, the number of cases tested for influenza and number of positive influenza cases per week. We aggregated the ILI data into the selected age groups and calculated a weekly proportion of positive cases for each flu season (from week 40 until week 39 the year after). Due to data-sparseness, we could not directly calculate the proportion of positive cases by age. Therefore, we used the population-based weekly ILI+ proportion to estimate the number of influenza cases by age from the weekly reported age-specific ILI cases. We verified that the proportions of influenza positive cases relative to ILI cases (mean: 0.20; confidence interval: 0–0.71, right-tailed p-value at 5%) were in line with estimates found in literature [36]. Season-specific vaccine effectiveness estimates were based on primary care data from the I-MOVE multi-center case-control study [37]. We refer to Valenciano et al. for further methodological details of the I-MOVE study [38-39]. We used the point estimates for the age-specific vaccine effectiveness against any influenza for our analysis and substituted the negative values by zero (i.e. no effect). All vaccine effectiveness estimates are provided in Table 2. Vaccine coverage for influenza in Belgium was retrieved from [16] to calibrate our transmission model.

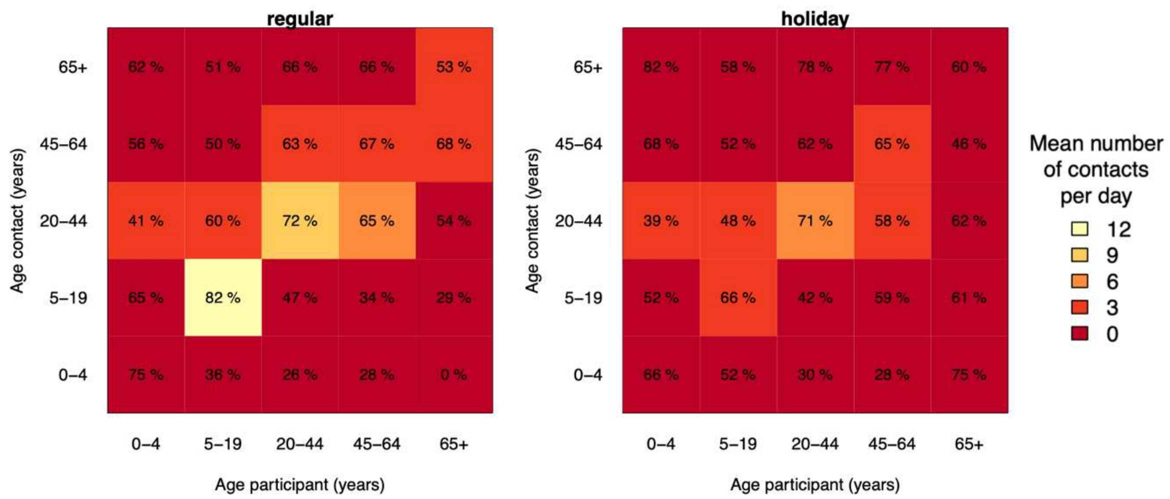

Fig 2. Social contact behavior by age during regular (left) and holiday (right) periods. The colors represent the daily average number of contacts M^{ij} between an individual of age i (horizontal axis) with an individual of age j (vertical axis). The percentages represent the reduction in social contacts when symptomatically infected.

Table 1. Model parameters and notation. Parameter values are based on literature, assumptions or presented by their initial ranges in the parameter estimation (see text).

Notation	Parameter	Value	Source
Transmission model			
	Age groups (years)	[0-4], [5-19], [20-44], [45-64] and 65+	
	Average population size (2011-2018)	637951, 1888883, 3629810, 2994236, 1977824	[40]
$1/\gamma$	Incubation period	2.0 (days)	[30]
$1/\theta$	Latent period	1.5 (days)	[30]
$1/\sigma^s$	Clinical infected period	5.6 (days)	[30]
$1/\sigma^a$	Subclinical infected period	1 (day)	[30]
	Number of infected cases introduced in the population to start the simulation	10	Assumption
ϕ	Proportion symptomatic	Initial range: 0.10 - 0.90	Estimated
q^s	Proportionality factor symptomatic cases	Initial range: 0.05 - 0.095	Estimated
q^r	Relative infectiousness of asymptomatic cases	Initial range: 0 – 1	Estimated
X	Background immunity acquired by previous infection or immunization (population fraction)	Initial range: 0 - 0.50	Estimated
t_i	Introduction of infectious cases into the dynamic model	Initial range: week 30 - 3	Estimated
q^a	Proportionality factor asymptomatic cases	$q^a = q^s * q^r$	
	Reporting rate	70% (in scenario analysis 60% and 80%)	[2]
μ	Vaccine coverage unemployed population by age group	1.90%, 2.73%, 10.90%, 21.25%, 59.63%	[16]
μ	Vaccine coverage employed population	16% (weighted average by age)	[16]
ϵ	Vaccine effectiveness	See Table 2	[37]
Economic analysis			
	Average gross monthly income per season (from 2011-2012 till 2017-2018)	€3192, €3258, €3300, €3414, €3445, €3489, €3558	[41]
	Direct cost absenteeism	0.086 x average income (per day)	[4]
	Indirect cost absenteeism	0 (scenario analysis: 1x direct cost absenteeism) (per day)	Assumption
	Vaccine cost per vaccinated employee including administration	€17.30	[42]

	Productivity loss per vaccine administration	30 min	Assumption
	Indirect cost per vaccinated employee	0.5 x direct cost absenteeism per day / 7.60	Assumption
	Total cost per vaccinated employee	€35.33 – €37.43	Calculated
	Average no. of working days per week	3.9063	Calculated from [43, 44]
	Proportion employed by age group	0%, 1.42%, 71.95%, 59.39%, 0%	[31]

Parameter estimation

We estimated five model parameters (see Table 1) for each season via an active learning approach with 3 iterations [32, 45]. To start, we sampled 50 000 values for each parameter according to a Latin Hypercube design. For each parameter set, we scored the predicted age-specific incidence with the reference data by shape of the curve (using weighted least-squares (WLS)) and the relative difference in total incidence (i.e. the difference in the area under the curve). We selected parameter sets in this two-objective optimization based on the Pareto front according to both scores. We aggregated the parameter ranges from the Pareto front subset per season, extended this range by ±10%, and used this to sample parameter values in the next iteration. We truncated least-square scores at 10^6 to remove simulations with a matching total incidence but totally different timing (shape). After 3 iterations, we selected the parameter set from the Pareto front with the lowest WLS score and a relative difference in incidence of maximum 5%.

Table 2. Vaccine effectiveness against any influenza type by age group and season from a multi-centre case control study in Europe [37]. The pooled vaccine effectiveness is shown with the upper and lower limit of the 95% confidence interval. The estimates for 2011-12 are reported in three age groups due to data sparseness. For the current analysis, we truncated negative values at zero (i.e. no effect).

Season	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18
All ages	5.3 [-21.0 – 25.8]	50.0 [37.0 – 60.3]	23.2 [-4.7 – 43.7]	26.6 [13.6 – 37.6]	19.3 [4.0 – 32.2]	28.4 [17.5 – 37.9]	30.0 [19.8 – 39.0]
0-19 years	15.2 [-73.1 – 58.5]	35.6 [-1.8 – 59.2]	8.0 [-84.8 – 54.2]	28.1 [-2.2 – 49.5]	-10.6 [-58.5 – 22.8]	33.1 [1.0 – 54.7]	52.1 [33.1 – 65.7]
20-44 years	19.9 [-12.0 – 42.7]	63.9 [34.2 – 80.2]	20.2 [-62.5 – 60.8]	44.7 [12.4 – 65.2]	36.2 [-1.7 – 60.0]	45.2 [20.6 – 62.1]	50.8 [27.3 – 66.7]
45-64 years		48.5 [23.8 – 65.3]	23.1 [-31.9 – 55.1]	31.3 [8.6 – 48.4]	37.1 [13.9 – 54.0]	29.0 [8.7 – 44.8]	19.4 [-1.7 – 36.1]
65+ years	0.2 [-60.5 – 37.9]	58.5 [29.8 – 75.4]	42.1 [-10.9 – 69.8]	3.9 [-30.8 – 29.4]	8.2 [-33.0 – 36.7]	17.7 [-4.5 – 35.1]	25.4 [4.8 – 41.5]

Cost-benefit analysis

The employers' cost of vaccinating employees consists of both direct and indirect costs related to vaccination: cost of the vaccine, cost of administration and a productivity cost for employees spending time to receive the vaccine, which we assumed to be 30 minutes (Table 1). In total, the cost per vaccinated employee was less than €40. We extracted Belgian employment statistics such as the year-specific mean gross wage and the employed population by age from Statbel [41]. We corrected for part-time employees, public holidays, weekends and 27 additional holidays (average obtained from [44]) to obtain a working day probability of 55.8%. The direct cost of absenteeism per day per employee was estimated to be 8.6% of the gross monthly income as reported by Securex, a Belgian HR services agency [4]. As such, the cost per day of absenteeism depends on the year-specific wage and ranged between €274 and €306. We opted for a conservative approach in which the total cost of absenteeism only accounted for direct costs. This is in line with the marginal productivity theory of wage determination in which the market for labor is in equilibrium when the marginal cost of labor (i.e. wage cost) equals the marginal product of labor. The impact of adding an indirect cost of absenteeism was analyzed in a scenario analysis. The absenteeism per employee is based on the relative incidence of symptomatic cases in the employed compartment. The total cost is based on the costs of the vaccination program and the costs of employee absenteeism. The cost-benefit is then calculated as the difference between the total cost with intervention and the total costs without any vaccination of the employed population.

Employee vaccination

The estimated season-specific transmission parameters were kept constant when modeling the impact of different levels of employee influenza vaccination funded by the employer. We fixed the age specific coverage in the unemployed population to the observed coverage in 2013 throughout all simulations [16]. We varied the vaccination coverage in the employed population between 10% and 90% for each season, assuming that all vaccination of the employed population is administered at the workplace and funded by their employer. We assessed the number of averted cases in the employed and unemployed population compared to the reference without vaccination of the employed population. We evaluated the costs and benefits of the vaccination program per employee and for all Belgian employers combined. Note that we use the term "unemployed" to refer to all people who officially are not receiving any payment for any type of labour.

Scenario analyses

We ran univariate scenario analyses to elaborate on parameter uncertainty and provide an overview in Table 3. First of all, we wanted to investigate the impact of increasing and decreasing the reporting rate by 10% in scenario 1 and 2, since information about this parameter is lacking. In addition, the vaccine effectiveness estimates we used from the I-MOVE study are low compared to other estimates in the literature [46]. Therefore, we applied more optimistic vaccine effectiveness estimates in scenario 3, equal to the highest observed effectiveness by age for each simulated season. Furthermore, we investigated the impact of adding indirect costs of absenteeism to the economic analysis (e.g. the cost of interim replacement, overtime being more expensive and other organizational costs). We assumed this indirect cost to be equal to the direct cost of absenteeism in scenario 4. A recent report estimated this indirect cost to amount between 2.5 and 3 times the direct cost of absenteeism [4]. As such, scenario 4 is still relatively conservative. Finally, in scenario 5, we looked at the impact of removing the sinusoidal function from the force of infection – thereby neglecting the seasonal character of influenza transmission – by setting $z(t) = 1$ during the parameter estimation and health economic evaluation.

Table 3. Scenario analysis

Parameter	Conservative scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Reporting rate	70%	**60%**	**80%**	70%	70%	70%
Vaccine effectiveness (ϵ)	Seasonal	Seasonal	Seasonal	**Max**	Seasonal	Seasonal
Indirect cost of absenteeism	None	None	None	None	**Labor cost**	None
Force of infection (z(t))	Seasonality	Seasonality	Seasonality	Seasonality	Seasonality	**Constant**

Employee incentives

We investigated whether there is scope for incentives in order to persuade employees to get vaccinated, for example by giving vaccinated employees an additional day off or other rewards paid for by the employer. We look into the maximum amount of employee incentives by calculating the benefit-cost ratio per vaccinated employee as a function of the influenza vaccine coverage among all employed individuals.

Results

We used a dynamic transmission model to inform cost-benefit analyses of employer-funded influenza vaccination. We first present our model dynamics and results for the conservative scenario. Afterwards, we report our scenario analyses that are more/less in favor of influenza vaccination and demonstrate the impact of model assumptions and parameter uncertainty.

We estimated the impact of different vaccination strategies on the burden of seasonal influenza. Figure 3 shows the predicted incidence of symptomatic cases (green line) for 2015-16 using the observed vaccine coverage and the reference data on influenza incidence (green dots). The grey lines present the predicted incidence if 0% up to 90% of all employees were vaccinated. As coverage among employees increases, the peak and total number of symptomatic flu cases decreased. Moreover, the peak was delayed when coverage increased. The holiday periods slowed down the transmission at the beginning of the epidemic, whereas the Easter break in April caused a steeper decline at the end of the epidemic.

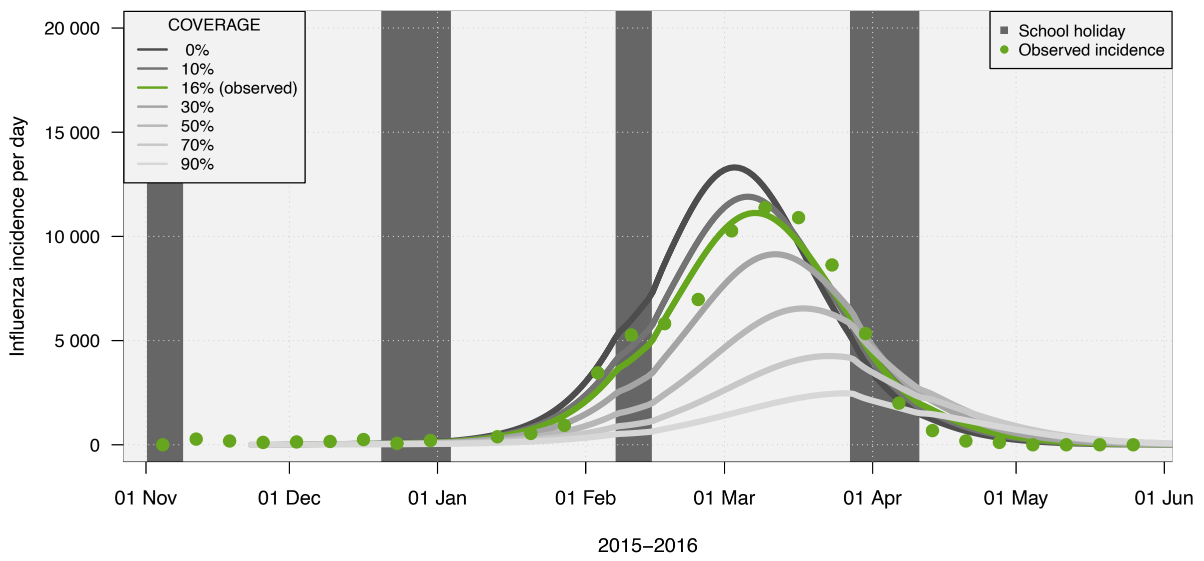

Fig. 3. Predicted seasonal influenza incidence for 2015–16 by employee vaccine coverage (lines) and reference data (dots). Parameter estimates from the conservative scenario (1) were used for these results.

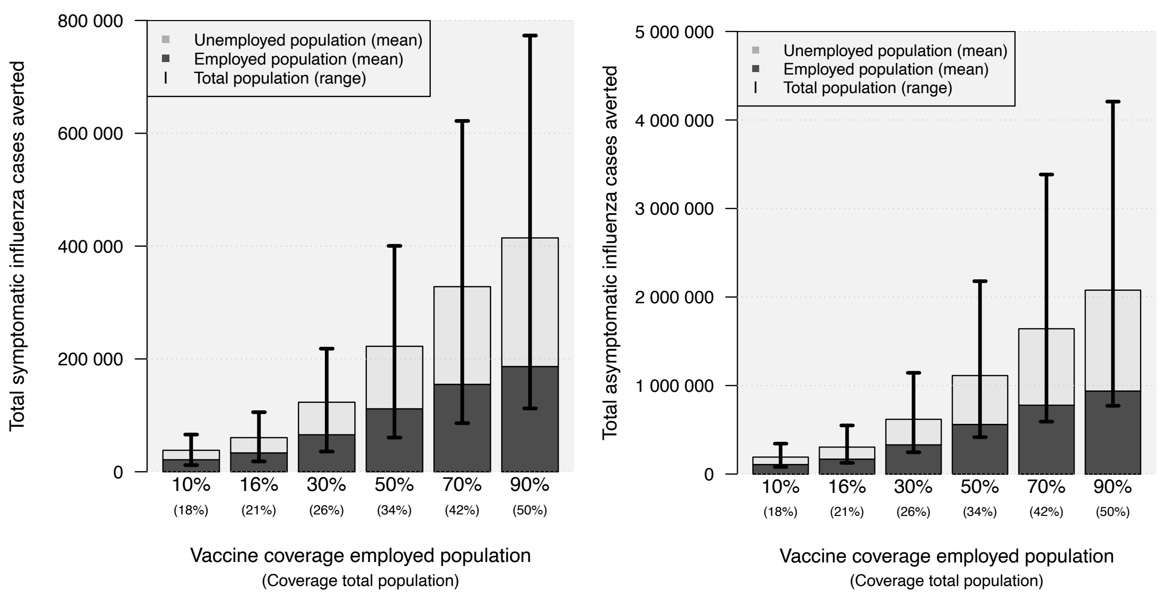

Fig. 4. Symptomatic (left) and asymptomatic (right) seasonal influenza cases averted for different workplace vaccine coverages (each season, average over all seasons). The coverage in the employed population and total population is shown on the x-axis. We applied parameter estimates from the conservative scenario and no vaccination of the employed population as a reference.

Workplace vaccination decreased the number of cases both in the employed and the unemployed population. Herd protection plays an important role such that vaccinated employees can serve as a barrier to limit the spread of influenza in the entire population, beyond the employed population. The number of averted cases – each season, average over all seasons – in the employed and unemployed population is given in Figure 4. Note that we used no vaccination of the employed population as a reference. The second bar in both figures represents the impact of the observed vaccine coverage in the total (21%), employed (16%) and unemployed population. As such, we predicted that on average over 60 000 symptomatic cases have been averted each season, of which 55% in the employed population and 45% in the unemployed population. This intervention translated, on average, into a reduction of 15% in the symptomatic cases on the workplace. The relative fraction of cases averted in the unemployed population increased with vaccine coverage among employees. If employers could increase the coverage among employees to 90%, they could avert up to 415 000 symptomatic cases of seasonal influenza in the population, of which about 185 000 in the employed population.

The cost-benefit analysis from the employers' perspective showed a lot of between-season variability. Figure 5 presents that in some seasons (e.g. 2012-13 and 2017-18) vaccination is an investment with a high return, whereas for other seasons (e.g. 2011-12 and 2013-14) there is a net loss when vaccinating the workforce. Due to the effect of herd immunity, we observed a small decrease in the return on investment when the coverage in the employed population increased, though the overall results and conclusions are stable within seasons. Considering all seven seasons, we calculated that seasonal influenza vaccination has been cost-saving with an average net savings of around €10 per vaccinated employee. For the Belgian economy as a whole, this translated into an average cost-saving of about €6.2 million when applying the observed coverage. If 90% of the employed population would have been vaccinated against seasonal influenza, on average €30 million would have been saved from the employers' perspective, each season.

As coverage increases in Figure 5b, the marginal benefit of employee vaccination decreases, especially so for coverages from 70% and higher. In essence, when a high fraction of employees is successfully vaccinated against influenza, they can no longer transmit the disease to colleagues, and the marginal benefit of vaccination decreases. As such, the optimal investment in employee vaccination between 2011-18 would have been reached at a coverage of 70%. Nevertheless, additional vaccination in employees can still have a pivotal role in protecting their children, parents, partner and other social contacts, as touched upon in previous paragraphs. Hence, herd immunity manifests in the protection of both unemployed individuals and unvaccinated co-workers.

We observed that the level of cost savings could be attributed to seasonal vaccine effectiveness as well as employees' seasonal susceptibility (Table 4). Indeed, seasons with both a high vaccine effectiveness and a high attack rate (e.g. 2012-13 and 2017-18) resulted in a high net-benefit, whereas seasons with a low vaccine effectiveness and/or a low attack rate brought about losses (e.g. 2011-12, 2013-14 and 2016-17).

Table 4. Net-benefit per vaccinated employee by season in the baseline scenario, including season characteristics: vaccine effectiveness, and the attack rate of seasonal influenza at the workplace in the absence of any employee vaccination.

Season	**Net-benefit per vaccinated employee at employee vaccination: coverage:**			**Pooled vaccine effectiveness, all ages**	**Influenza symptomatic attack rate at the workplace at 0% coverage (%)**
	10%	**50%**	**90%**		
2011-12	€ –23.66	€ –23.78	€ –24.02	5.3%	2.66%
2012-13	€ 47.56	€ 54.64	€ 46.65	50.0%	8.26%
2013-14	€ –18.65	€ –20.02	€ –22.42	23.2%	1.81%
2014-15	€ 6.75	€ 9.13	€ 10.76	26.6%	5.91%
2015-16	€ 15.11	€ 15.41	€ 10.90	19.3%	5.57%
2016-17	€ –4.40	€ –2.11	€ –2.36	28.4%	3.92%
2017-18	€ 37.78	€ 42.92	€ 32.81	30.0%	7.16%

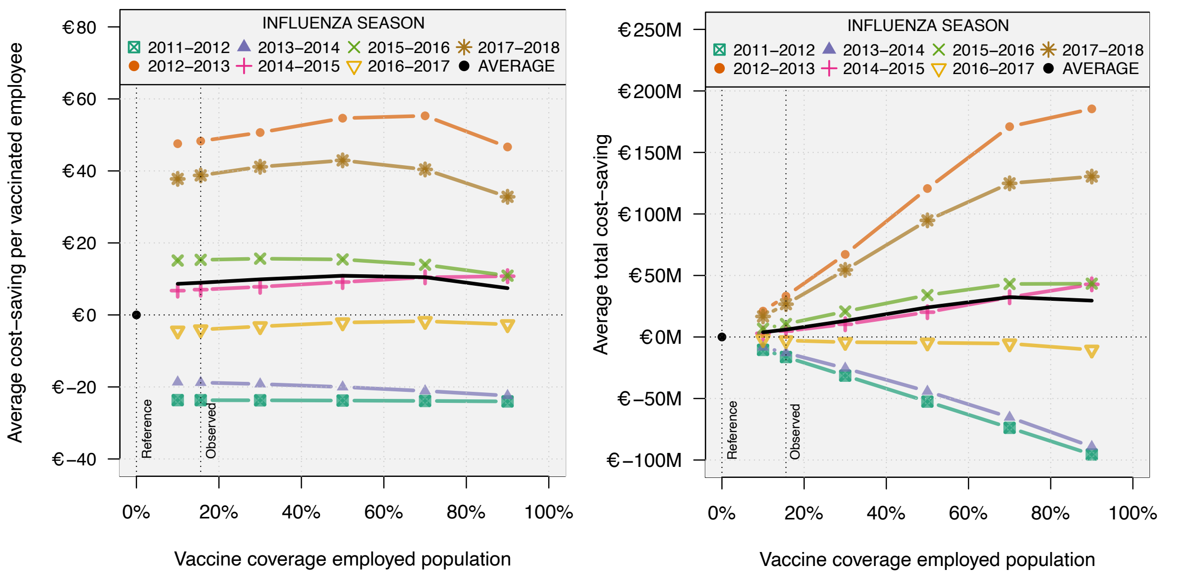

Fig. 5. Cost-savings per vaccinated employee (a) and total savings (b) for different levels of employee vaccination in different influenza seasons. Conservative scenario.

Scenario analyses

We analyzed parameter uncertainty in scenario analyses and present the cost-benefit per employee in Figure 6.

Reporting rate of 60%. If we assumed that the reported incidence accounted for only 60% of the total symptomatic incidence, more cases could potentially be saved and the average cost-savings increased up to €20 per vaccinated employee. For the seasons 2011-12, 2013-14 and 2016-17 a lower reporting rate did not significantly influence cost-savings since these seasons were either low in cases or the vaccine had only a very limited effectiveness, or both.

Reporting rate of 80%. When we assumed that the reported incidence accounted for 80% of the total symptomatic incidence, the average net-benefit decreased. Indeed, employee vaccination in 2016-17 would have caused a net-loss, whereas it was found to be cost-neutral in the conservative scenario. On average, the net-benefit was lower but remained positive at all coverages.

Increased vaccine effectiveness. If we fixed vaccine effectiveness to the reported, age-specific maxima between 2011 and 2018, we observed large increases in the net-savings. As such, employee vaccination would have been cost saving for all seasons up to a coverage of 50%. For two seasons, we predicted a net-cost for an employee coverage of 70% and above. Up to a coverage of 50% employers saved on average more than €40 per vaccinated employee. In total, the net-benefit could have been up to €100 million at a coverage of 70%. Additional vaccination would imply a lower return since the marginal costs exceed the marginal benefits in a population that is already highly immunized. That is, given that vaccines were assumed more effective in this scenario, herd protection effects kicked in sooner. As such, the average net-benefit per employee started decreasing at lower vaccine coverages compared to the reference scenario.

Indirect cost of absenteeism. The scenario in which we included an indirect cost of absenteeism equal to the direct cost of absenteeism resulted in higher cost savings. On average, the cost-benefit would have been up to €50 per vaccinated employee, with a maximum of €150 in the season 2012-13.

Seasonal force of infection. When the seasonal nature of influenza transmission was not taken into account, we estimated an average net loss. While vaccination still delayed the peak of the infection, it had a lower impact on the number of cases. As a result, the model predicted many cases in summer. This is in contrast with the literature on seasonal influenza dynamics in temperate climate countries such as Belgium [47].

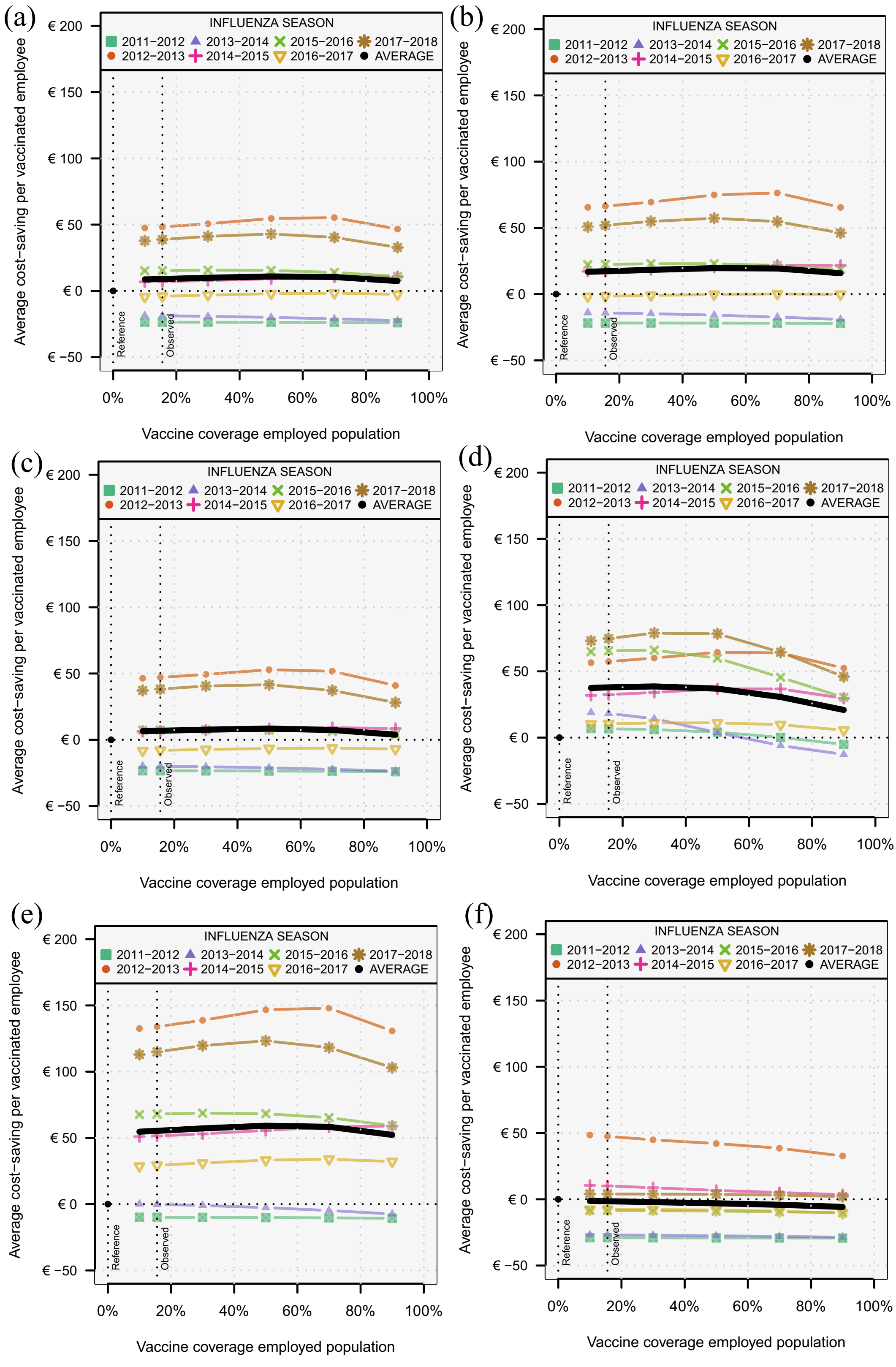

Fig. 6. Scenario analyses of the predicted cost-savings per vaccinated employee per season. (a) Conservative scenario; (b) Reporting rate 60%; (c) Reporting rate 80%; (d) Maximum vaccine effectiveness; (e) Indirect cost of absenteeism; (f) Constant force of infection.

Vaccine incentives

The average daily wage in Belgium was about €300 between 2011 and 2018. Given that the average net-benefit per vaccinated employee in the conservative scenario did not exceed €60 for any season-coverage combination, it was never found beneficial to reward vaccinated employees with an extra day off. At an average net-benefit of €10 per vaccinated employee, there is only a limited financial margin to create incentives for employees to accept vaccination. Furthermore, none of the univariate scenario analyses predicted cost-savings in the range of the estimated cost for a day off. Only a combination of lower reporting rates with increased vaccine efficacy and/or considering indirect costs increases the average cost-saving per employee and, as such, the financial margin to create incentives for employees.

Discussion

We simulated influenza vaccination as an employer-funded intervention and calculated the averted costs of symptomatic employees interrupting their professional activities. We started from the observed coverage in Belgium and predicted what the impact would have been of increased coverage levels. We found that workplace influenza vaccination was on average cost saving using conservative model assumptions. Substantial differences between seasons were found, implying that the decision for employers to vaccinate their workforce is an annually recurring gamble, which could result in significant losses or gains. This is because some seasons tend to be mild with very few cases (e.g. in 2013-14) or, in some seasons, the vaccine strains were not well matched to the circulating strains (e.g. in 2011-12). Note that the season-specific characteristics determined to the largest extent the average cost savings per vaccinated employee, as opposed to the vaccination coverage itself. As such, an employer's decision making process is to a large extent independent of what all other employers decide. The maximum potential savings were estimated to be in the order of €32 million for all employers combined, assuming 70% vaccine coverage in employees. When comparing this to the current vaccine coverage of 16%, there is still a lot of money left on the table, especially in seasons with a high burden and a sufficiently high vaccine effectiveness.

Even though vaccine coverage in people of working age has been suboptimal – at about 16% – in 2013 [16], a 2018 study found that 61.7% of Belgians agrees that seasonal influenza vaccine is important, which is equal to the EU average [48]. Furthermore, a multi-country discrete-choice experiment found vaccine accessibility to be a crucial element for adults when deciding about vaccination [49]. Hence, workplace vaccination can be helpful in reaching higher vaccination rates just by providing an accessible framework for adult vaccination (i.e. at no cost to the vaccine recipient, nor requiring a trip to the GP's office, and without any impact on employees' leisure time). Nevertheless, additional interventions might be needed in order to reach higher vaccine coverages in the face of growing vaccine skepticism in Europe [48]. When Belgian employers decide to give incentives to their employees they should limit the incentives to an amount between €7 and €11 per vaccinated employee, in order for the intervention to be cost-neutral based on our conservative approach. Alternatively, they can give larger incentives to only a few vaccinated employees by using a lottery system. In addition, employers could use an opt-out registration system for flu shot appointments instead of an opt-in, in order to increase vaccine coverage among the workforce. Indeed, opt-out systems have been found successful to increase deceased organ donation and transplantation [50].

Employers need the full picture when deciding about offering workplace influenza vaccination. Namely that: (1) an employer's return on workplace vaccination is largely independent of vaccination coverage in the working population at large (i.e. only a limited scope for free-riders), (2) such a program is on average cost-saving and prevents significant disease at the workplace as well as in society, and (3) there is room for financial employee incentives in addition to relatively cheap interventions such as opt-out registration systems. These insights may help stimulate employers' participation in workplace vaccination programs, and set up employee incentive structures to improve vaccination rates. Workplace influenza vaccination in Belgium is typically organized by occupational health services providers that have ample experience in setting up such programs.

Though currently not considered as a target group for influenza vaccination, employees can play a vital role in reducing the disease and economic burden of influenza. Vaccinating employees substantially reduces the number of cases at the workplace: directly, in vaccinated employees and indirectly in co-workers through herd immunity, thereby reducing absenteeism. Moreover, we observed positive externalities – of which the costs are borne by the employers – to the unemployed population as well. Indeed, vaccinated employees have a lot of contacts with individuals of all ages as observed in Figure 2, such as their children, partner, parents and members of their community. As such they can efficiently fulfill their role as barriers to pathogen transmission in society (i.e. herd protection). There are about 4.7 million working individuals in Belgium, which is only 41% of the total population. Even at an employee coverage of 50%, more than 100 000 symptomatic cases could be prevented on average per season in the unemployed population through indirect protection, which represents 1/3rd of all symptomatic infections in the unemployed population. If all employers would have motivated their employees to get vaccinated and reached 90% coverage, on average 78% of all symptomatic cases would have been prevented, of which almost 230 000 (-74%) cases in the unemployed population and 185 000 (-84%) cases among their employees. Employee vaccination is an interesting intervention from which society, employers and employees all reap the benefits.

Previous research from the health care payer perspective found children, health care workers, pregnant women and the elderly to be important target groups for influenza vaccination in Belgium, rather than the general working adult population [51,52]. However, from the employers' perspective, including the cost of absenteeism, the cost-benefit results change. Government subsidies can be pivotal to encourage employers to provide and stimulate influenza vaccination at the workplace. Especially so to decrease the losses in seasons with a net-loss, such as the seasons 2011-12 and 2012-13. Beware that employer sponsored vaccination reduces the costs of influenza vaccination covered by the (centralized) health insurance, which in turn increases the scope for government subsidies. Indeed, when individuals switch over from GP & pharmacy based vaccination, the health insurance would no longer have to reimburse between €10.48 and €46.12 for one or two GP consults and about €12.47 for the vaccine when it was administered to a patient belonging to a risk group [13,14]. Note that such a transfer in costs was not included in the current study since we focused on the employers' perspective. Given the low cost of vaccination at the workplace (around €36 per vaccinated employee) and the spill-overs to society, employees could serve as an important target group and provide a safety net for vulnerable subgroups of the population and those that cannot receive the vaccine for medical reasons.

We stress the importance of adaptive social contact patterns for healthy and symptomatic individuals. Reduced social contact behavior for symptomatically infected employees has a significant, dampening, influence on the spread of seasonal influenza [30]. Modelling studies that do not take such effects into account therefore overestimate the effect of interventions. The reduction in transmission could be even larger if susceptible employees also limit their social contacts when seasonal influenza peaks. Teleworking, for example, could be interesting for employers to reduce the prevalence of seasonal influenza at the workplace and reduce absenteeism. Teleworking is unfeasible in a number of sectors and industries, but it was estimated to be, at least partially, possible for 50% of the employees in the US [53]. Interestingly, people that do come to work when they are symptomatically infected, are also less productive [54], reinforcing the importance of staying home when showing influenza symptoms.

This paper documents to our knowledge the first economic evaluation of employee vaccination using a dynamic transmission model and adaptive contact behavior. Lee et al. [19] split their analysis into cost-benefit analyses for the 22 major occupational groups in the US and found influenza vaccination to be cost-saving for the employer for serologic attack rate scenarios of 20% or higher (i.e. pandemics). However, they did not take into account asymptomatic cases and a reduced transmission of influenza when symptomatically infected employees stay home. The majority of non-placebo-controlled, non-randomized studies that were performed in single companies also found cost-saving results for the employer. A study at a Malaysian petrochemical company concluded that workplace vaccination accrues both financial and health benefits, and that financial benefits increased proportionally to vaccination coverage [20]. Similar studies were performed at a financial services company in Essex, UK [21] and a manufacturing company in Minnesota, US [22]. All of these studies found vaccination to significantly reduce absenteeism. However, employees were vaccinated on a voluntary basis in these studies, requiring caution when interpreting the results, as they are prone to selection bias. Burckel et al. performed an economic modeling study using employment data from a pharmaceutical-chemical company in Brazil. They estimated vaccination to be cost saving at $35.45 in 1997, assuming a rather high vaccine efficacy (between 70% and 89%). In sensitivity analyses, the break-even vaccine-efficacy was found to be 32.5% [23].

The study of Bridges et al. [24] found that if the vaccine strains matched with the circulating strains and the vaccine effectiveness was 86%, workplace vaccination would reduce the lost workdays by 32% per vaccinated employee. However, the economic analysis of such a vaccination program resulted in a net cost of $11.17 per person, compared to no vaccination. When the strains differed, the societal cost increased to $65.59 per person and no decrease in absenteeism was observed. As such, the authors conclude that “vaccination of healthy adults younger than 65 years is unlikely to provide societal benefits in most years” [24]. Another clinical trial with trivalent nasal live attenuated influenza vaccine (LAIV) [55] reported a decrease of 18% in work loss and a break-even cost of $43.07 per person vaccinated. None of these studies took reduced social contact behavior into account.

In the scenario analysis, we noticed the relatively high importance of vaccine effectiveness. The vaccine effectiveness that was used in the conservative scenario, derived from the I-MOVE study [37], is rather low compared to vaccine efficacy reported in the literature [46]. The economic value of innovative vaccines against seasonal influenza, such as a universal flu vaccine, highly depends on their effectiveness. Moreover, there are no guarantees that the industry would be able to supply an additional 4 million vaccines at current production capacities.

This study is limited by the uncertainty on influenza incidence and vaccine effectiveness. Given the large confidence intervals for the vaccine effectiveness estimates, these should be interpreted with caution. Even though the I-MOVE study has collected data in a number of European countries, it did not do so in Belgium. Therefore, the vaccine effectiveness estimates might be less representative in case the circulating strains in Belgium differed substantially from the strains observed in the study population, given that vaccine effectiveness against subtypes can vary. We performed scenario analyses to handle parameter uncertainty and present a range of possible outcomes, though a single estimation whether employer funded vaccination is cost-saving is lacking. Other parameters, such as the relative infectiousness of asymptomatic cases, background immunity and the proportion of symptomatic cases have been estimated based on age-specific incidence. We performed a extensive parameter estimation to prevent local optima, but more data on one of these parameters would improve the estimation of others due to correlations. The age categories in our transmission model were restricted to the data on social distancing due to symptomatic illness from the UK. The symptomatic contact data from Eames et al. are likely subject to selection and non-response bias given that the study was confronted with a low participation rate (around 5% in the distribution center setting and around 10% in the school setting) [29]. In addition, the survey was performed in the context of pandemic influenza in England, whereas our study focusses on seasonal influenza in Belgium. Additional data on symptomatic contact behavior in different countries would improve the accuracy of transmission models in general. Workplace contact patterns have likely changed due to the COVID-19 pandemic, making telework the norm for many people with an effect that might last well into the future. Even though the cost-benefit per vaccinated employees stayed relatively constant within scenarios, research on vaccine resistance and incentivizing employees could be beneficial to increase vaccination coverage on the workplace and to more accurately predict the impact of employer sponsored vaccination, of influenza, and perhaps other seasonal infectious diseases requiring re-vaccination. Finally, additional epidemiological information on influenza incidence and associated absence at work with and without vaccination or teleworking, would improve our estimates.

In conclusion, we performed a cost-benefit analysis of employer funded influenza vaccination using a dynamic transmission model. We used Belgian data and observed large between-season differences in terms of incidence, vaccine efficacy and return on investment. We compared the cost of prevention with the cost of employee absenteeism and found that employer funded influenza vaccination was on average cost-saving between 2011 and 2018. The impact on society as a whole is substantial through herd immunity effects and even more promising with next-generation influenza vaccines [56].

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Additional information

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