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The economic impact of providing dengue vaccination in the workplace in Brazil

O impacto econômico da vacinação contra dengue no local de trabalho no Brasil

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DOI: 10.21115/JBES.v9.suppl1.58-70

Keywords:
corporate setting, cost-benefit analysis, dengue vaccination, economic impact

ABSTRACT

Objective: To estimate the economic value of implementing a workplace dengue vaccination program from an employer perspective. **Methods:** The cost of a vaccination program was compared with the economic benefits in terms of reduced absenteeism and presenteeism in companies in Brazil. Input data were obtained from published literature and national databases. The time horizon was five years, including a 2-year vaccination program. Sensitivity analyses were performed to evaluate the impact of key parameters' uncertainty. **Results:** 846 cases were simulated among the employees over five years, accountable for 2,112 sick leave days and 7,120 sick days at work. Assuming a coverage rate of 30%, vaccination reduced the number of sick leave days and sick days at work by 17.5% over five years compared to no vaccination. Considering an employee vaccine co-payment of 50%, the levels of remaining investment per dose administered for the employer in the retail sector ranged from US$ 17.99 to US$ 27.99, according to different vaccine price scenarios, and from US$ 6.10 to US$ 16.10 in the service sector. In the energy sector, vaccination was cost-saving in all price scenarios, ranging from a profit for the employer of US$ 21.14 to US$ 31.14. Results were most sensitive to the level of co-payment, overall time horizon of the analysis, dengue incidence, and employee contribution to operating income. **Conclusions:** Dengue contributes a significant proportion of absenteeism and presenteeism in private companies. Our analysis suggests that dengue vaccination in the workplace may be considered as a valuable investment and, in some cases, a cost-saving option for employers.

Palavras-chave:
ambiente corporativo, análise custo-benefício, vacinação contra dengue, impacto econômico

RESUMO

Objetivo: Estimar o valor econômico da implementação de um programa de vacinação contra a dengue no local de trabalho sob a perspectiva do empregador. **Métodos:** O custo de um programa de vacinação foi comparado com os benefícios econômicos em termos de redução do absenteísmo e do presenteísmo em empresas no Brasil. Os dados foram baseados na literatura publicada e em bases de dados nacionais. O horizonte temporal foi de cinco anos, incluindo um programa de vacinação de dois anos. Foram realizadas análises de sensibilidade para avaliar o impacto das incertezas de parâmetros-chave. **Resultados:** Oitocentos e quarenta e seis casos foram simulados entre os empregados em cinco anos, os quais foram responsáveis por 2.112 dias de licença médica e 7.120 dias com a doença no ambiente de trabalho. Assumindo uma taxa de cobertura de 30%, a vacinação reduziu o número de dias de licença médica devido à doença e os dias com a doença no ambiente de trabalho em 17,5% ao longo de cinco anos em comparação com a não realização da vacinação. Considerando um copagamento da vacinação pelos funcionários de 50%, os níveis de investimento remanescente por dose administrada para o empregador no setor varejista variaram

Received on: 07/19/2017 **Approved for publication on**: 09/01/2017
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Study carried out: This study was carried out within Sanofi Pasteur.
Funding information: This study was funded by Sanofi Pasteur.
Conflicts of interest: All authors are employees of Sanofi Pasteur.
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de US$ 17,99 a US$ 27,99 de acordo com diferentes cenários de preços da vacina e de US$ 6,10 a US$ 16,10 no setor de serviços. No setor de energia, a vacinação resultou em economia de custos em todos os cenários de preços, que vão desde uma economia para o empregador de US$ 21,14 até US$ 31,14. Os resultados foram mais sensíveis ao nível de copagamento, horizonte de tempo global da análise, incidência de dengue e contribuição dos funcionários para a receita operacional. **Conclusões:** A dengue contribui com uma parcela significativa do absenteísmo e do presentismo em empresas privadas. Nossa análise sugere que a vacinação contra dengue no local de trabalho pode ser considerada um investimento valioso e, em alguns casos, uma opção que traz economia para os empregadores.

Introduction

Dengue is a mosquito-borne viral disease caused by four immunologically distant serotypes (Andraud *et al.,* 2012). Infection with any of the dengue serotypes may be asymptomatic or manifest as dengue fever, which may deteriorate to dengue hemorrhagic fever and dengue shock syndrome (Bargeron Clark *et al., 2*012; Blacksell, 2012). A recent analysis of the global burden of dengue (Shepard *et al.,* 2016) suggested that in 2013 there were 58.4 million symptomatic infections worldwide, with a global annual cost of $ 8.9 billion (95% uncertainty intervals, $ 3.7-19.7 billion). The cost burden in Latin America and the Caribbean was estimated at $ 1.7 billion (95% uncertainty intervals, $0.71-3.86 billion).

A dengue vaccine, designed to be administered as a three-dose schedule every six months, has been approved in some dengue-endemic countries for use in individuals mainly within the age range of 9–45 years (or 9–60 years in some countries). Modelling analyses suggest that dengue vaccination can significantly reduce the public health burden of dengue in dengue-endemic countries, with higher vaccination coverage systematically leading to a greater reduction in the burden of dengue (Coudeville *et al.*, 2016; Flasche *et al.*, 2016).

Workplace dengue vaccination may help increase coverage, with employers providing vaccination to their employees who may not be covered under publicly funded vaccination schemes. Such vaccination campaigns have potential benefits for the employee, in terms of reducing the risk of acquiring dengue, and for the employer through reductions in absenteeism and presenteeism (reduced functioning at work) and their associated costs. These benefits extend to society in general by reducing the number of potentially infective people in the population and thereby reducing the healthcare costs of treating dengue. The global burden of dengue study conducted by Shephard *et al.* (online appendix) estimated the indirect costs of dengue in Latin America at US $1.1 billion (Shepard *et al.*, 2016), which represents 65% of all costs associated with the burden of dengue in the region.

Previous studies regarding the use of vaccination in private companies have mainly focussed on influenza vaccines and have shown that vaccination can reduce the disease burden for the employer in a variety of countries and industries (Beran & Moravik, 2003; Bridges *et al.*, 2000; Burckel *et al.*, 1999; Campbell & Rumley, 1997; Kawabayashi *et al.*, 2013; Lee *et al.*, 2010; Leighton *et al.*, 1996; Liu *et al.*, 2004; Lugovskaia *et al.*, 2014; Mixeu *et al.*, 2002; Morales *et al.*, 2004; Olsen *et al.*, 1998; Samad *et al.*, 2006).

The potential benefits of workplace dengue vaccination on dengue-related absenteeism and presenteeism as well as other economic benefits to the employer need to be defined. The objective of this study was to develop a cost-benefit model to assess the value of the introduction of dengue vaccination in the workplace from the employer's perspective for three different corporate sectors in Brazil.

Methods

Model structure

A decision tree model was created using Microsoft Excel to assess the costs and benefits of implementing a dengue vaccination program from an employer's perspective. A modelling approach was chosen since it allows flexibility to vary a number of factors which might influence the cost–benefit, such as the duration of the vaccination campaign, the levels of coverage provided and the incidence of dengue. This allows for a more realistic calculation of the cost–benefit of workplace dengue vaccination to the employer. A user-friendly interface for the model, called DengueCorp, was developed to simplify its use in real-world settings.

The model commences with the employer introducing a dengue vaccination program, with a vaccination campaign every six months. When the vaccination campaign commences, all employees are offered the option whether or not to get vaccinated. Once they received their first dose, they were assumed to comply with the whole dengue vaccination schedule (i.e. receive two further doses to complete the vaccination) to comply with the approved 3-dose vaccination schedule. Employees who rejected the initial option of vaccination were assumed to decline future participation in the vaccination program. Staff turnover was considered and assumed to be constant over time, with the same numbers leaving as entering the company each year. At the start of each campaign (Figure 1), employees that entered the company during the preceding six months were eligible to start the vaccination program. In other words, the vaccination for new employees could be started at any campaign; for instance, a new employee arriving in September could get his first dose at the third campaign. For employees leaving the company, only the benefits when inside the company were considered.

The probability of contracting dengue was based on the interaction between the employees' vaccination status (vaccinated or unvaccinated), the local incidence of dengue and the likelihood that previously vaccinated employees may no longer be protected since the vaccine has not demonstrated lifetime protection. In a case of dengue infection, the employee either took sick leave or did not. Those who took sick leave either remained at home or were hospitalized. Those who continued working were assumed to be less productive (presenteeism). Absentees were either replaced by a contract worker or by the remaining workforce working overtime or were not replaced (Figure 2).

A reduction in the operating income was assumed when absent employees were not replaced based on the annual employee contribution to the company's operating income. The model included healthcare costs paid by the employer (if any) and also a possible diminution of the cost of work while an employee is on sick leave. The number of working days was set at the level of 365 days per year.

The model time horizon was divided into two components: duration of the vaccination program (possible range 1–5 years) and the time horizon of the analysis corresponding to the time elapsed since the vaccination program ended (possible range 0–10 years). The objective of extending the time horizon beyond the duration of the initial vaccination program was to ensure all the benefits of dengue vaccination were captured. An example of this can be seen in Figure 1, where there is a two-year vaccination program and the three-year horizon after the program.

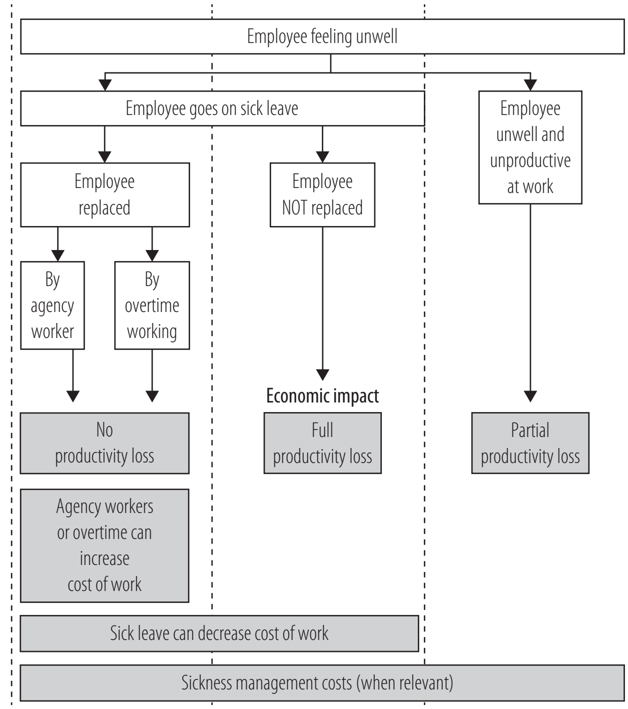


Figure 2. Absenteeism, presenteeism, worker replacement and their associated economic impacts considered in the model.

Model outcomes

The outcomes of the model included the health benefits to employees (in terms of reduced dengue episodes, including dengue hospitalizations, and fewer days with dengue symptoms), the economic benefits to the employers (in terms of reduced employees days of absences and presenteeism and their associated savings) and the overall investment required by the employer (the cost of providing the vaccination program net of savings from reduced dengue-related illness and any co-payments by employees).

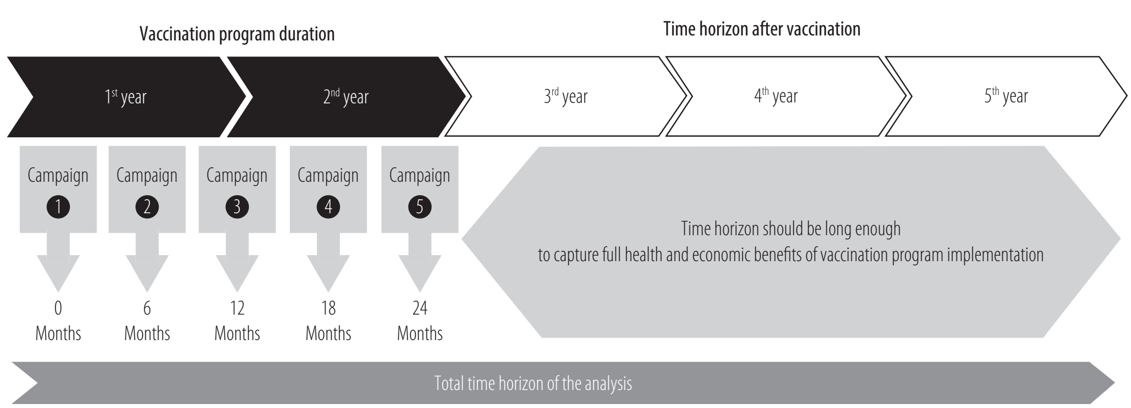


Figure 1. Components of the time horizon of the analysis. In this example there is a 2-year vaccination program and a 3 year time horizon post-vaccination. Figures are in months (i.e. a campaign every 6 months).

Considering the past epidemiology reported in the national surveillance system databases in Brazil, the model first describes what would be the situation without a vaccination program. It simulates the number of employees who would be infected with dengue virus in the following years and the resulting economic impact on the company in terms of increased sick leave days and sick days at work.

Model adaptation

The model included three 'typical' Brazilian companies. Brazil was chosen since it had the most accurate data available to populate the model. We considered a fictive population of 10,000 employees targeted by vaccination (18-45 years old) in each of the three 'typical' companies.

Data sources

Company

Data to create the three 'typical' Brazilian companies were taken from a Brazilian database which lists the top 500 companies in Brazil (Exame.com, 2016). The data were aggregated to identify the largest sectors (based on the number of companies in each sector) operating in Brazil (retail, services and energy) and then averaged to create a 'typical' company operating in each of the three sectors. By choosing the largest sectors, we ensured that the companies were largely representative of other companies in the sector and, therefore, made the results more generalizable across the whole sector.

The same sources provided the cost of employing each worker and the annual estimated contribution each worker made to the company's operating income (calculated by dividing the annual operating income of the company by the number of employees).

Epidemiology data

The incidence levels of dengue were taken from the national surveillance system database (Sistema de Informacao de Agravos de Notificacao [SINAN], 2016). Following WHO recommendations of vaccinating in high-burden-of-disease areas, the mean incidence in the highly endemic zone in Brazil was considered. The highly endemic zone, defined with Brazilian epidemiological experts, covered 22 states and 788 municipalities in three other states in Brazil (see detail in Table 1). Also, in order to better fit with our fictive population of employees targeted by vaccination, incidences of age groups from 15 to 19, 20 to 39 and 40 to 59 years old only were used to calculate the mean incidence. These age groups were the only ones available. Finally, in order to take into account the epidemiological variability of dengue, an average incidence from 2010 to 2015 was considered. The uncertainty of these estimations was evaluated in sensibility analyses with an incidence variation of ±20%.

Table 1. Model inputs for the base case. All costs are in US$ 2016

	Base case			Source
Company-specific				
No of employees targeted for vaccination	10,000			Based on largest 500 companies by sector (Exame.com, 2016)
Employee turnover	13.0%			Mercer 2014 Turnover Survey, average employees involuntary turnover in Brazil 2011-2014
Annual employee contribution to company's operating income (company total operating income divided by company total number of employee)	Retail: 25,615	Services: 68,850	Energy: 205,827	Employee contribution and cost of work based on the sector average of the largest 500 companies, employee turnover based on Mercer survey (Exame.com, 2016)
Annual employee cost of work	Retail: 9,012	Services: 23,026	Energy: 37,467	
Vaccination-specific				
Duration of vaccination program (years)	2			Assumptions. The coverage rate was based upon previous experience with influenza vaccination within companies
Vaccination coverage rate for the 1st dose	30%			
Compliance for 2nd dose	100%			
Compliance for 3rd dose	100%			
Cost per dose (1^{st}-3^{rd} dose US$)	50, 60, 70			
Co-payment	50%			
Fixed costs per campaign	200			
Time horizon after dengue vaccination program (years)	3			

	Base case	Source
Vaccine efficacy against ambulatory episodes: 1st, 2nd and 3rd doses	65.6%	(Hadinegoro *et al.,* 2015) For Ambulatory episodes in particular no published data exists, therefore, vaccine efficacy "for any dengue episode" is used as proxy
Vaccine efficacy against hospitalized episodes: 1st, 2nd and 3rd doses	80.8%	
Expected duration of protection (1st dose)	2.5 years	These assumptions are not based on direct clinical trial evidence but are supported by clinical data modeling insights (Coudeville *et al.*, 2015) and other vector-borne vaccine performances (Desai *et al.*, 2012; Gotuzzo *et al.*, 2013)
Expected duration of protection (2nd dose)	5 years	
Expected duration of protection (3rd dose)	10 years	
SICK LEAVE AND WORKER REPLACEMENT		
Any sickness		
Employee's cost of work on sick leave (for employer)	100%	(Deloitte 2016)
Percentage of employees on sick leave replaced	10%	Assumption
Percentage of employees replaced`	Agency worker: 10% Overtime: 10%	
Increased cost of work if overtime used to replace absent employee (factor)	50%	(Deloitte 2016)
Increased cost of work if agency worker used to replace absent employee (factor)	10%	Assumption
Dengue specific		
Productivity loss when sick at work	54%	(Keech *et al.*, 1998b)
Sick leave in an ambulatory episode	30%	(Suaya *et al.,* 2009)
Leave duration in ambulatory episode (days)	7.1	(Suaya *et al.,* 2009)
Leave duration in hospitalized episode (days)	10.7	
Epidemiology specific		
Incidence	0.55%	Average 2010-2015 incidences for age groups from 15 to 19, 20 to 39 and 40 to 59 years old only in 22 States with high endemicity (AC, AM, RR, PA, AP, TO, MA, PI, CE, RN, PB, PE, AL, SE, BA, ES, RJ, MS, MT, GO, RO, DF) and 788 municipalities in total in 3 states (Parana, Mina Gerais and Sao Paulo) (SINAN + local experts for definition of endemic states)
Share of hospitalizations	8.21%	(Teixeira *et al.,* 2013) and SIH database (Probable dengue cases considered, mean 2010-2013)
Underreporting factor for ambulatory cases	3.2	(Martelli *et al.,* 2015)
Underreporting factor for hospitalized cases	1.6	
Symptoms duration for ambulatory cases (days)	10.9	(Martelli *et al.*, 2011)
Symptoms duration for hospitalized cases (days)	11.2	(Martelli *et al.,* 2011)
Duration of hospital stay (days)	3.1	(Martelli *et al.,* 2011; Suaya *et al.,* 2009)

There was also an allowance for underreporting of dengue since not all symptomatic dengue cases are notified to the authorities. The level of underreporting was taken from a previous study in Brazil (Martelli *et al.*, 2015) and differentiates between the level of underreporting of hospitalized and ambulatory cases.

Vaccination

The efficacy of dengue vaccine against hospitalized episodes considered in the model was 80.8%. As there was no specific data published for ambulatory episodes, the vaccine efficacy of 65.5%, which is related to any dengue episodes, was used as a proxy (Hadinegoro *et al.* 2015).

We considered a 10-year protection after the third dose based on the duration of vaccine protection against other vector-borne diseases (Japanese encephalitis vaccine (Desai *et al.,* 2012) and yellow fever vaccine (Gotuzzo *et al.*, 2013)). We can consider this assumption conservative since a duration of protection of above 20 years has been reported for the live-attenuated yellow fever vaccine (Gotuzzo *et al.,* 2013) and considering the waning rate and duration of protection estimated from long-term follow-up of phase III trials for pre-exposed people (Coudeville *et al.*, 2016). For the first and second doses, durations of protection were estimated internally.

The base case considered a 2-year vaccination program consisting of three campaigns in the first year and two in the second year. It was assumed that 30% of employees would be vaccinated in year one (with all three doses). In the second year 30% of new employees, who had joined the company through turnover, would be vaccinated. The overall time horizon was five years (Figure 1).

Since the vaccine price to employers was not known in Brazil at the time of the analysis, three costs per dose were considered ($ 50, $ 60 and $ 70) in the base case. This was based on the vaccine's private price in The Philippines at the time of the analysis. It was assumed in the base case that the level of co-payment from employees was 50%, meaning 50% of the vaccine price was paid by the employer and 50% by the employee.

Costs of absenteeism, presenteeism and worker replacement

Regarding absenteeism and replacement costs, data was obtained from national sources and regulations in Brazil (Deloitte, 2016; Gerencie.com, 2016; Tusalario.org, 2016). Presenteeism was taken from a previous study of workers with influenza (Keech *et al.*, 1998a) where workers were found to work at 46% of their normal capacity when they were sick. Working days lost by ambulatory and hospitalised dengue cases were taken from previously published studies in Brazil (Suaya *et al.*, 2009). Both costs and benefits were calculated in US$ 2016 prices.

Full information on the values included in the base case for each of the three scenarios and the data sources can be found in Table 1.

Sensitivity analyses

Univariate deterministic sensitivity analyses were performed on the key uncertain variables. The key variables varied by ±20% of the base case value or within the 'plausible' ranges allowed by local regulation to allow for uncertainty in the estimates of each parameter value. Full details of the parameter values tested can be found in Table 2. The data sources were the same as those used in the base case. Multivariate deterministic sensitivity analyses were also performed on those parameters which were found to have the largest impact.

Results

Taking into account that the same epidemiological data and cohorts of 10,000 employees were considered for each scenario, the results related to number of dengue cases, number of days with symptoms and number of days of sick leave or sick days at work were identical in the three companies. Moreover, considering that the vaccination program is identical for each company, vaccination health benefits and vaccination investment for the employer are also identical in the three sectors. What varied per sector is the dengue costs avoided and, therefore, the final net investment for the employer, subtracting the vaccination investment from the economic benefits.

Without vaccination

Based on past epidemiology, the model simulated that 846 employees of each company would contract dengue disease in the next five years, accountable for 2,112 sick leave days and 7,120 sick days at work. This loss of productivity would represent an amount of $ 410,856 for the company operating in the retail sector, $ 1,103,313 for the service sector and $ 3,271,848 for the energy sector.

Impact of vaccination on employees' health and on productivity and associated investment

Results from the base case analyses for each company are summarized in Table 3.

The benefit to employee health following the introduction of a dengue vaccination would be 146 dengue episodes avoided, with 1,598 symptom days saved (reduction of 17% compared to no dengue vaccination). This would translate into 377 days of sick leave avoided (an 18% reduction), and a reduction of 1,221 presenteeism days (a 17% reduction). These savings are valued at $ 71,481 for the retail sector, $ 191,949 for the service sector and $ 569,096 for the energy sector.

Depending on the vaccine price scenario, the investment required by the three companies would range from $ 507,450 to $ 710,031 (if the employer pays for the entire vaccination program) and from $ 253,725 to $ 355,015 after the consideration of the employee co-payment (50% in our base case).

After considering the savings generated with the vaccination program, the net investment would range from $ 182,244 to $ 283,534, equivalent to $ 17.99 to $ 27.99 per vaccine dose administered in the retail company. In the service sector, the net investment would range from $ 61,776 to $ 163,066, equivalent to $ 6.10 to $ 16.10 per vaccine dose administered. Finally, in the company operating in the energy sector, the required net investment would range from savings of $ 214,081 ($ 21.14 per dose) at a price of $ 70 per vaccine dose to savings of $ 315,371 ($ 31.14 per dose) at a price of $ 50 per vaccine dose.

Sensitivity analyses

The deterministic sensibility results of the retail sector company were most sensitive to the employee co-payment

Table 2. Variations in sensitivity analyses. All costs are in US$ 2016.

Parameter	Range of variance compared to base case	Retail		Services		Energy	
		Low	High	Low	High	Low	High
Operating Income	Assumption, ±20% relative	20,492	30,738	55,080	82,620	164,662	246,992
Annual employee cost of work	Assumption, ±20% relative	7,210	10,815	18,421	27,631	29,973	44,960
		All sectors					
Employee turnover	Assumption, ±20% relative	10%	16%				
Duration of vaccination program (years)	Max/min allowed by model	1	5				
Vaccination coverage rate for the 1st dose	Assumption, ±10% absolute	20%	40%				
Compliance for 2nd dose	Assumption, ±20% relative	80%	100%				
Compliance for 3rd dose	Assumption, ±20% relative	80%	100%				
Co payment	Assumption, ±20% relative	40%	60%				
Fixed costs per campaign	Assumption, ±20% relative	160	240				
Time horizon after dengue vaccination program (years)	Max/min allowed by model	1	10				
Employee's cost of work on sick leave (for employer)	Assumption regarding local legislation and practices	50%	100%				
Expected vaccine protection duration 1st dose	Assumption	1.25	3.75				
Expected vaccine protection duration 2nd dose	Assumption	2.5	7.5				
Expected vaccine protection duration 3rd dose	Assumption	5	15				
Percentage of employees on sick leave replaced	Assumption, ±20% relative	8%	12%				
Increased cost of work if overtime used to replace absent employee (factor)	Assumption regarding local legislation and practices	1.25	1.8				
Percentage of employees replaced by an agency worker	Assumption, ±20% relative	8%	12%				
Increased cost of work if agency worker used to replace absent employee (factor)	Assumption	1.1	1.3				
Sick at work value loss	Assumption, ±20% relative	43%	65%				
Sick leave in ambulatory episode	Assumption, ±20% relative	24%	36%				
Leave duration in ambulatory episode (days)	Assumption, ±20% relative	5.7	8.5				
Leave duration in hospitalized episode (days)	Assumption, ±20% relative	8.6	12.8				
Incidence	Assumption, ±20% relative	0.44%	0.66%				
Share of hospitalizations	Assumption, ±20% relative	6.57%	9.85%				
Underreporting factor for ambulatory cases	Assumption, ±20% relative	2.6	3.8				
Underreporting factor for hospitalized cases	Assumption, ±20% relative	1.3	1.9				
Symptoms duration for ambulatory cases (days)	Assumption, ±20% relative	8.7	13.1				
Symptoms duration for hospitalized cases (days)	Assumption, ±20% relative	9.0	13.4				
Duration of hospital stay (days)	Assumption, ±20% relative	2.48	3.72				

Table 3. Base case results. All costs in 2016 US$.

					All sectors				
Employee benefits									
Dengue episodes avoided (days)					146				
Dengue episodes avoided (% versus no vaccination)					17%				
Days with symptoms avoided (days)					1,598				
Days with symptoms avoided (% versus no vaccination)					17%				
Company health benefits									
Days of sick leave avoided (days)					377				
Days of sick leave avoided (% versus no vaccination)					18%				
Days of sick at work avoided (days)					1,221				
Days of sick at work avoided (% versus no vaccination)					17%				
Number of doses									
# doses the 1st year					9,000				
# doses over 2 years (total duration of the vaccination program)					10,129				
		Retail			Services			Energy	
Company economic benefits									
dengue costs avoided (US$)		71,481			191,949			569,096	
Dengue costs avoided (% versus no vaccination)		17%			17%			17%	
Price Assumptions	50 US$	60 US$	70 US$	50 US$	60 US$	70 US$	50 US$	60 US$	70 US$
Company investment									
investment net of co-payment 1st year	$225,300	$270,300	$315,300	$225,300	$270,300	$315,300	$225,300	$270,300	$315,300
Investment net of co-payment 2 years	$253,725	$304,370	$355,015	$253,725	$304,370	$355,015	$253,725	$304,370	$355,015
Net investment (investment less than savings)	**$182,244**	**$232,889**	**$283,534**	**$61,776**	**$112,421**	**$163,066**	**-$315,371**	**-$264,726**	**-$214,081**
Net investment (per dose)	**$17.99**	**$22.99**	**$27.99**	**$6.10**	**$11.10**	**$16.10**	**-$31.14**	**-$26.14**	**-$21.14**

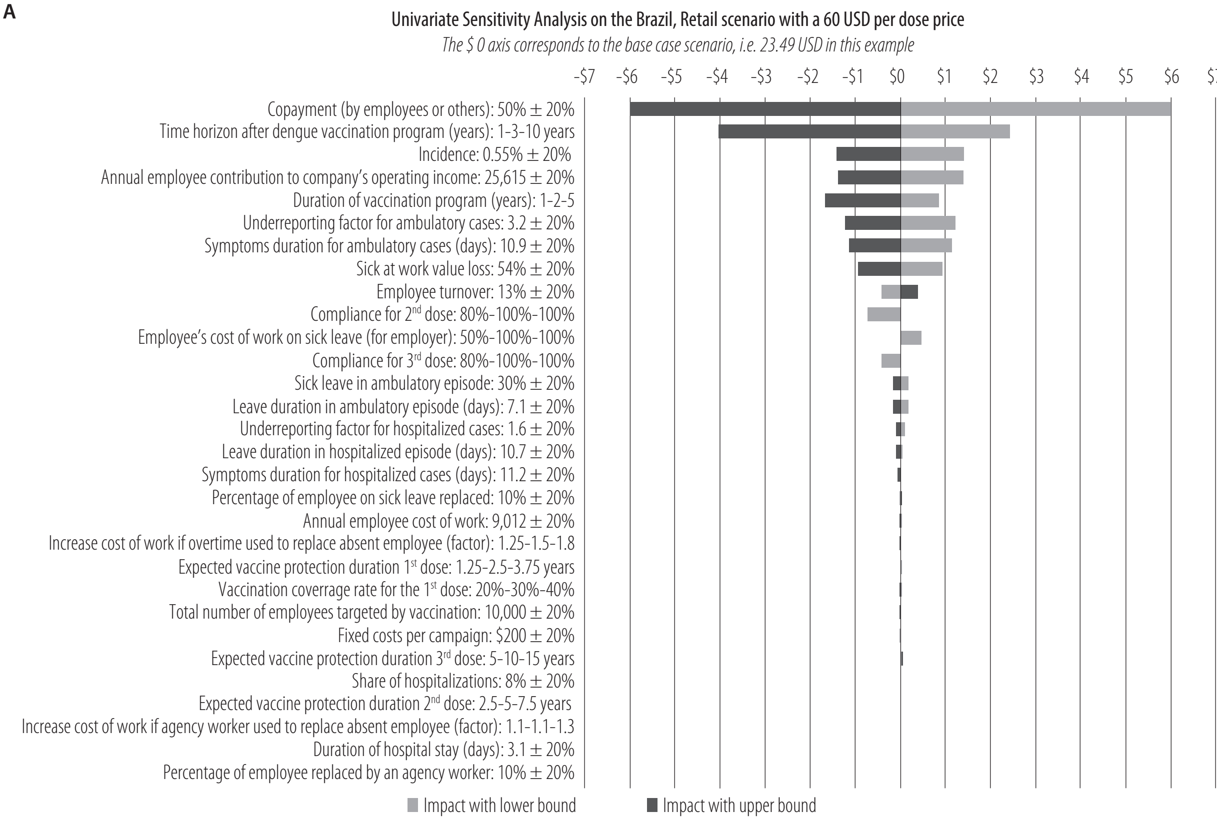
(Figure 3A). The overall investment per dose ranged from a net investment of $16.98 to the employer if the employees paid 60% of the vaccine cost to $ 29.00 if the employer paid 40% of the full vaccine cost. Other important factors influencing the results in the retail sector were the time horizon adopted to assess the benefits, the incidence of dengue, the annual employee contribution to company's operating income and the duration of the vaccination program.

The same factors as those in the retail sector were also influential in the services and energy sectors. The overall time horizon and levels of co-payment had the greatest influence in the service sector, whereas the time horizon and dengue incidence had the largest impact in the energy sector (Figures 3B and 3C). In the services sector, the net investment per dose ranged from $ 0.30 (10 year time horizon) to an investment of $ 17.65 (1 year time horizon) and, in the energy sector, from a saving of $ 58.17 per dose for a 10-year time horizon to a net saving of $ 6.71 for a 1-year time horizon.

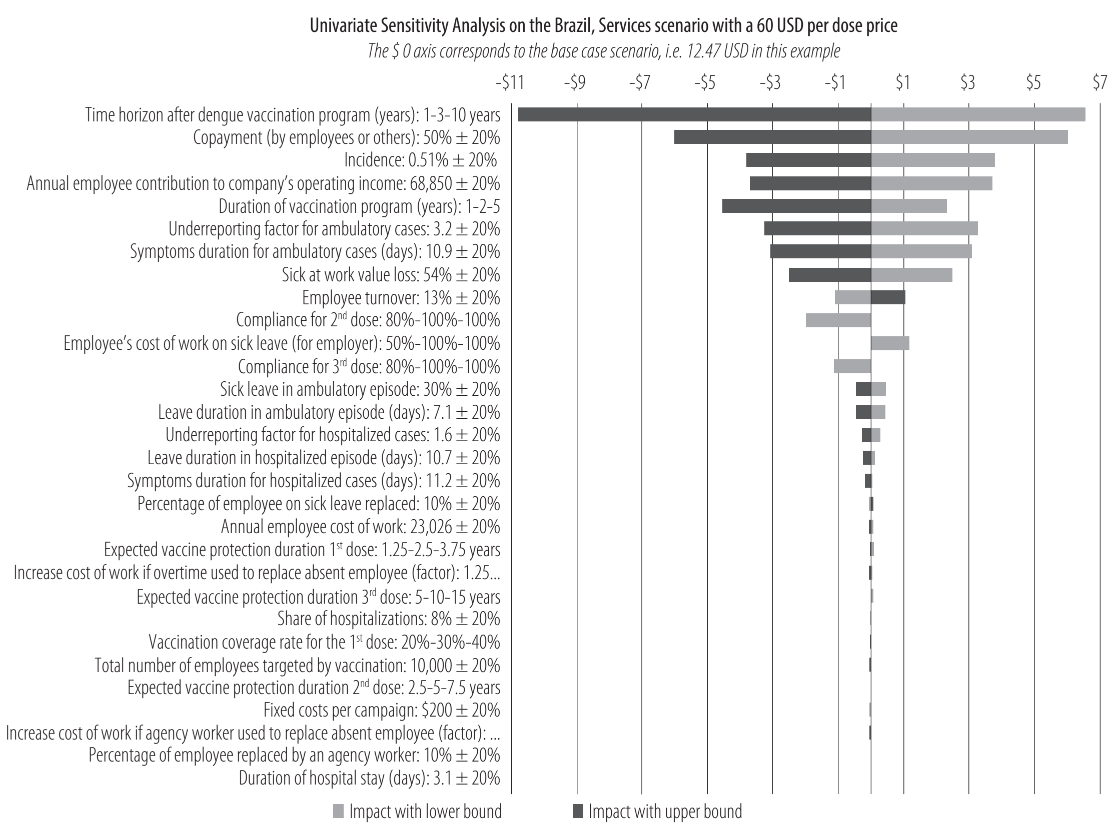
Further analysis was conducted on the most impacting parameters (Figures 4, 5 and 6).

The analysis of the effect of varying the level of co-payment (Figure 4) showed, as might be expected, an inverse relationship between co-payment and net investment. At a vaccine price of $ 60, the energy sector company would start

A


Univariate Sensitivity Analysis on the Brazil, Retail scenario with a 60 USD per dose price
The $ 0 axis corresponds to the base case scenario, i.e. 23.49 USD in this example
-$7 -$6 -$5 -$4 -$3 -$2 -$1 $0 $1 $2 $3 $4 $5 $6 $7
Copayment (by employees or others): 50% ± 20%
Time horizon after dengue vaccination program (years): 1-3-10 years
Incidence: 0.55% ± 20%
Annual employee contribution to company's operating income: 25,615 ± 20%
Duration of vaccination program (years): 1-2-5
Underreporting factor for ambulatory cases: 3.2 ± 20%
Symptoms duration for ambulatory cases (days): 10.9 ± 20%
Sick at work value loss: 54% ± 20%
Employee turnover: 13% ± 20%
Compliance for 2nd dose: 80%-100%-100%
Employee's cost of work on sick leave (for employer): 50%-100%-100%
Compliance for 3rd dose: 80%-100%-100%
Sick leave in ambulatory episode: 30% ± 20%
Leave duration in ambulatory episode (days): 7.1 ± 20%
Underreporting factor for hospitalized cases: 1.6 ± 20%
Leave duration in hospitalized episode (days): 10.7 ± 20%
Symptoms duration for hospitalized cases (days): 11.2 ± 20%
Percentage of employee on sick leave replaced: 10% ± 20%
Annual employee cost of work: 9,012 ± 20%
Increase cost of work if overtime used to replace absent employee (factor): 1.25-1.5-1.8
Expected vaccine protection duration 1st dose: 1.25-2.5-3.75 years
Vaccination coverrage rate for the 1st dose: 20%-30%-40%
Total number of employees targeted by vaccination: 10,000 ± 20%
Fixed costs per campaign: $200 ± 20%
Expected vaccine protection duration 3rd dose: 5-10-15 years
Share of hospitalizations: 8% ± 20%
Expected vaccine protection duration 2nd dose: 2.5-5-7.5 years
Increase cost of work if agency worker used to replace absent employee (factor): 1.1-1.1-1.3
Duration of hospital stay (days): 3.1 ± 20%
Percentage of employee replaced by an agency worker: 10% ± 20%
Impact with lower bound
Impact with upper bound

B


Univariate Sensitivity Analysis on the Brazil, Services scenario with a 60 USD per dose price
The $ 0 axis corresponds to the base case scenario, i.e. 12.47 USD in this example
-$11 -$9 -$7 -$5 -$3 -$1 $1 $3 $5 $7
Time horizon after dengue vaccination program (years): 1-3-10 years
Copayment (by employees or others): 50% ± 20%
Incidence: 0.51% ± 20%
Annual employee contribution to company's operating income: 68,850 ± 20%
Duration of vaccination program (years): 1-2-5
Underreporting factor for ambulatory cases: 3.2 ± 20%
Symptoms duration for ambulatory cases (days): 10.9 ± 20%
Sick at work value loss: 54% ± 20%
Employee turnover: 13% ± 20%
Compliance for 2nd dose: 80%-100%-100%
Employee's cost of work on sick leave (for employer): 50%-100%-100%
Compliance for 3rd dose: 80%-100%-100%
Sick leave in ambulatory episode: 30% ± 20%
Leave duration in ambulatory episode (days): 7.1 ± 20%
Underreporting factor for hospitalized cases: 1.6 ± 20%
Leave duration in hospitalized episode (days): 10.7 ± 20%
Symptoms duration for hospitalized cases (days): 11.2 ± 20%
Percentage of employee on sick leave replaced: 10% ± 20%
Annual employee cost of work: 23,026 ± 20%
Expected vaccine protection duration 1st dose: 1.25-2.5-3.75 years
Increase cost of work if overtime used to replace absent employee (factor): 1.25...
Expected vaccine protection duration 3rd dose: 5-10-15 years
Share of hospitalizations: 8% ± 20%
Vaccination coverage rate for the 1st dose: 20%-30%-40%
Total number of employees targeted by vaccination: 10,000 ± 20%
Expected vaccine protection duration 2nd dose: 2.5-5-7.5 years
Fixed costs per campaign: $200 ± 20%
Increase cost of work if agency worker used to replace absent employee (factor): ...
Percentage of employee replaced by an agency worker: 10% ± 20%
Duration of hospital stay (days): 3.1 ± 20%
Impact with lower bound
Impact with upper bound

C

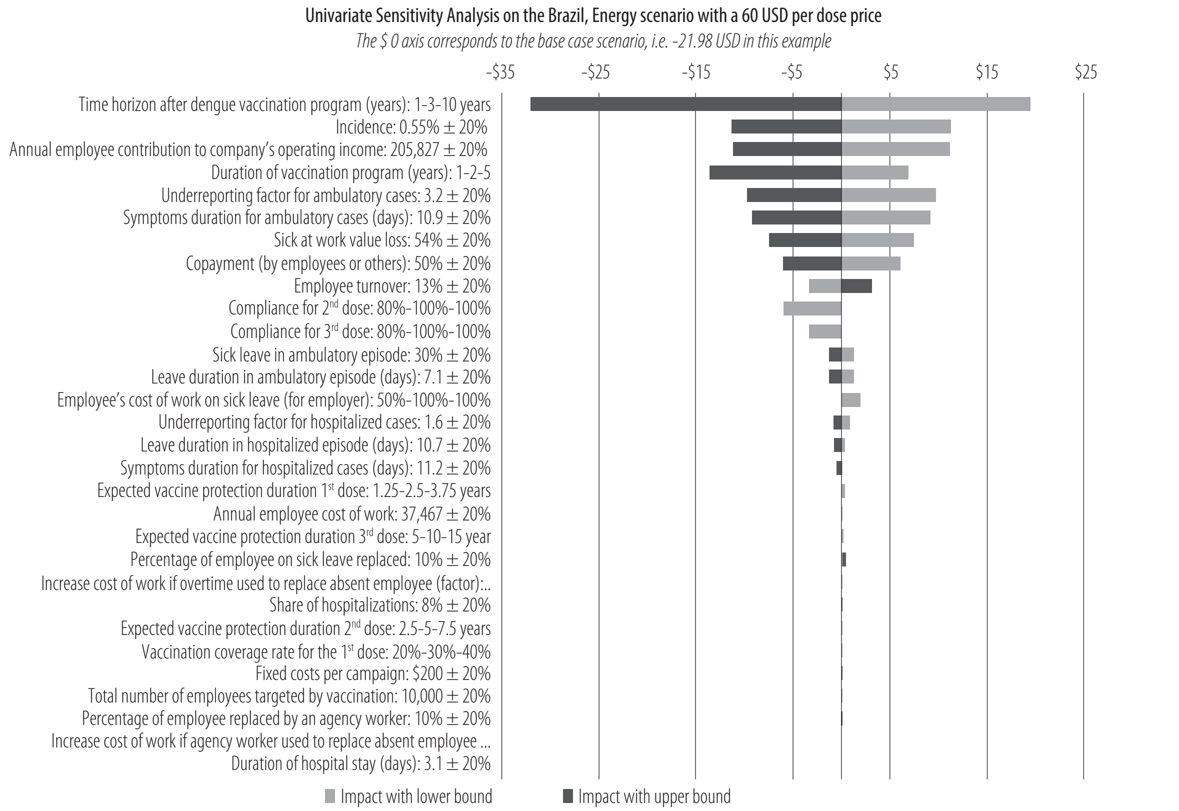


Figure 3. Tornado Diagrams – relative effect in US$. (A) Univariate Sensitivity Analysis on the Brazil, Retail scenario with a 60 US$ per dose price. The $0 axis corresponds to the base case scenario, i.e. 23.49 US$ in this example. (B) Univariate Sensitivity Analysis on the Brazil, Services scenario with a 60 US$ per dose price. The $ 0 axis corresponds to the base case scenario, i.e. 12.47 US$ in this example. (C) Univariate Sensitivity Analysis on the Brazil, Energy scenario with a 60US$ per dose price. The $0 axis corresponds to the base case scenario, i.e. -21.98 US$ in this example.

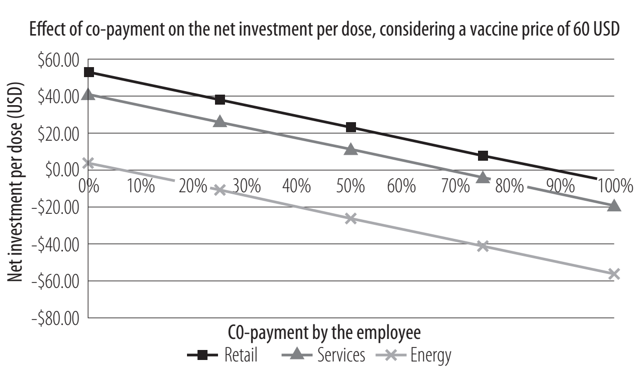


Figure 4. Effect of co-payment on the net investment per dose, considering a vaccine price of 60 US$.

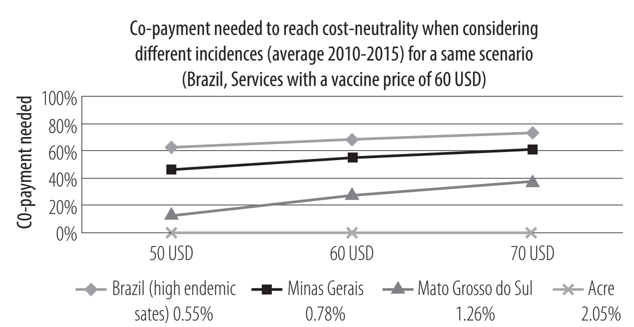


Figure 5. Levels of co-payment needed to reach cost-neutrality when considering different state's incidences (average 2010-2015) for a same scenario (Services sector with a vaccine price of 60 US$).

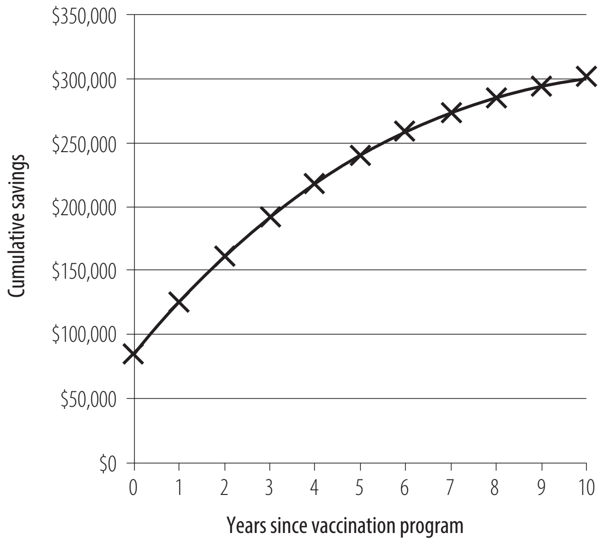


Figure 6. Cumulative savings thanks to the vaccination program considering 0 to 10 year time horizon after the vaccination program, and percentage of total savings captured at each time horizon.

to save costs from introducing the dengue vaccine at an employee co-payment level of 7% or higher, and the services company would start to save money at a co-payment of 69% or higher. The retail sector company would save money at a co-payment of 89% or higher. All three companies would save costs at 100% co-payment (since the vaccination program generates savings for the employer with the only cost being the organisation of the vaccination campaign itself), meaning that the introduction of a vaccination program inside the company, by the employer, is always cost-beneficial for the employer if the employee pays the vaccine.

We also examine the level of co-payment needed in order for the investment in vaccination to be cost-neutral (i.e. break even analysis) according to the level of incidence and the vaccine price, two important parameters influencing the analyses. An example using the Brazilian service sector employer is presented in Figure 5. As might be expected, there is a linear relationship between levels of co-payment and vaccine cost, with higher levels of co-payment required to reach the break-even point as the cost of the vaccine increases. An examination of the interaction between dengue incidence, co-payment and vaccine price showed that, in Brazilian states where the dengue incidence is higher than the considered base case average, lower levels of co-payment were needed to produce a 'break even' investment for the employer. In the Brazilian region of Acre, where the incidence of dengue was four times higher than the base case average over the period 2010–2015 (2.05% compared to 0.55%), the level of co-payment needed to get cost-neutral results was immaterial and the introduction of a dengue vaccine would always be cost-saving for the employer.

At last, extending the time horizon of the analysis in the period following the vaccination campaigns has the effect of capturing, more completely, the benefits of vaccination. In the case of the service sector company, for example, the cumulative benefits of dengue vaccination are valued at $ 84,666 immediately following the end of the vaccination campaign but would increase to $ 301,376 after 10 years (Figure 6).

Discussion

The results of our model suggest that, in Brazil, investment in dengue vaccination campaigns by employers can benefit their company through a reduction in the number of employees affected by dengue, leading to improved productivity and reduced costs. The number of sick leave days was reduced by 377 in the three companies, and the reduction in presenteeism amounted to 1,221 days over a five-year period. Depending on the price of the vaccine, the net investment per dose (after taking into account co-payments and savings) across the three companies ranged from a saving of $ 31.14 in the energy sector to an investment of $ 27.99 in the retail sector.

Sensitivity analyses suggested that the cost-benefit improved as the time horizon after the dengue vaccination program was extended. Indeed, the longer time horizon allows for the benefits of the dengue vaccine to be more fully captured. We took the pragmatic decision to use a five-year horizon in the base case since the need to capture all the benefits must also be balanced against a need to provide results to employers within a realistic timeframe for investment decision making.

The variation in results across sectors was not unexpected since the parameters specific to the company were widely different. As seen in Table 1, the parameters related to the vaccination program, to sick leave and worker replacement and to the disease epidemiology are identical for the three companies. However, significant differences are observed in the annual employee contribution to company operating income and the annual employee cost of work. Indeed, the annual employee contribution to company operating income is identified in the sensitivity analysis as a key parameter in the calculation of the net investment. As observed in the results, the more important the annual employee contribution to operating income, the better the cost-benefit results will be or, in other words, the lower the net investment for the company will be.

Consistent with the current modelling exercise, previous studies have shown the benefits of vaccination against other infectious diseases to companies in Latin America, in terms of cost-savings and reduced work absence or presenteeism. A model-based study in Brazil among workers in a pharma-chemical company estimated a net benefit of influenza vaccination of $ 121,441 per vaccinated employee and a cost-benefit ratio of 1:2.5 (Burckel *et al.*, 1999). Another Brazilian study of the benefits of influenza vaccination, involving a study of commercial aircrew, found a reduction of 39.5% in episodes of influenza-like illness and a 26% reduction in working days lost (Mixeu *et al.*, 2002). Another evaluation of influenza vaccination in Colombia suggested savings of $6.4–25.8 on labour costs and these saving increased to $ 89.3–237.8 when operating income was factored in (Morales *et al.*, 2004).

The data from the current and previous studies are also consistent with employer-funded vaccination schemes from other regions. As well as showing the benefit to the employer in terms of reduced absenteeism, these employer-funded schemes suggested savings to the wider community and society through reduced use of healthcare resources. These included studies of influenza vaccination in Europe, the United Kingdom, Taiwan, Malaysia and the United States (At'kov O. Y. *et al.*, 2011; Beran & Moravik, 2003; Bridges *et al.*, 2000; Campbell & Rumley, 1997; Leighton *et al.*, 1996; Liu *et al.*, 2004; Samad *et al.*, 2006), cervical cancer vaccination in Japan (Kawabayashi *et al.*, 2013) and a combined influenza-pneumococcal vaccination scheme in Russia (Lugovskaia *et al.*, 2014). While these studies covered viruses and conditions other than dengue, they all consistently showed the benefits of vaccination from the perspective of the employer.

There would be particular benefits in Brazil encouraging workplace vaccination since there are no universal publicly-funded vaccination schemes yet. Therefore, this would allow employees greater access to vaccination by supplementing the options offered by private healthcare providers and ensure a larger proportion of the total population was vaccinated against dengue. The level of co-payment was shown to be one of the key factors in the overall cost–benefit of the dengue vaccine in each of the three "typical" companies. The employer funding the majority of vaccination costs would obviously lead to the highest vaccine uptake (and demonstrate the company's commitment to its employees' health). For employees, even with a requirement for some contribution, they would be able to access the vaccine more easily and at a lower cost than what is available to them in the private healthcare sector, which would benefit them as well as the wider society.

One of the limitations of our model, and indeed models in general, is that to some degree they are reliant on assumptions. We have tried to minimize the number of variables which rest on assumptions, by taking the majority of the data inputs from national databases, governmental reports or peer-reviewed publications. We have attempted to minimize the uncertainty inherent in the assumptions with a comprehensive sensitivity analysis. The model results should also be interpreted with some caution since the results will vary by company and industry (for example, depending on operating cost and sick leave policy) and are, therefore, not easily generalizable. These results should not be used as a substitute for company-specific analysis to inform local decision making. However, the basic model approach is customizable to any country or business sector. It is also worth noting that the cost-saving results obtained with 100% level of co-payment can be applied in all other countries and companies. Indeed, in this case, where the vaccine is totally paid for by the employees, the companies generate savings through costs of absenteeism and presenteeism avoided. Therefore, even in cases where an employer does not have the budget to afford to subsidise the actual vaccine cost, it would still be worthwhile organizing and providing the facilities to allow employees to become vaccinated at a lower price than in the private healthcare sector. Since this analysis was conducted from the employers' perspective, it does not take account of the wider societal benefit in terms of potential reductions in the number of dengue-infected people in the community and the subsequent savings in healthcare costs. There are likely to be additional unquantifiable benefits to the introduction of a workplace vaccination for dengue. This includes the demonstration of commitment to employee wellbeing and more generally to corporate social responsibility. These wider, as yet unmeasured benefits are likely to make the use of workplace vaccination programs more attractive to employers in areas where dengue is endemic.

Conclusions

The provision of dengue vaccination in the workplace, based on our model and parameters, would provide health benefits for the employees and would reduce the impact of absenteeism and presenteeism to the employer. These results can be achieved for relatively small investments by the employers and, in some cases, be cost-saving overall. Employers should give consideration to providing dengue vaccine to their employees.

Acknowledgements

This study was designed and funded by Sanofi Pasteur. The authrs would wish to acknowledge the contributions of the following people to the collection of data inputs, modelling development and interpretation of results: Nicolas Baurin, Andres Caicedo, Charlotte Vandeputte, Vanessa Kolbe, Hanna El Fezzazi, Axelle Beriot-Mathiot, Anne-Caroline Weber.

Editorial support was provided by Keith Evans of inScience Communications, Springer Healthcare, funded by Sanofi Pasteur. The authors also thank Jo-Ann West for editorial assistance and manuscript coordination on behalf of Sanofi Pasteur.

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