BMJ Open

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027832
Article Type:	Research
Date Submitted by the Author:	09-Nov-2018
Complete List of Authors:	Hansen Edwards, Christina; Nasjonalt folkehelseinstitutt, Tomba, Gianpaolo; Universita degli Studi di Roma La Sapienza, Dept. of Mathematics Sonbo Kristiansen, Ivar; University of Oslo, Health Management and Health Economics White, Richard; Nasjonalt folkehelseinstitutt de Blasio, Birgitte; Nasjonalt folkehelseinstitutt
Keywords:	Human influenza, Infection control < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, HEALTH ECONOMICS

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.Hansen.Edwards@fhi.no

Keywords: Human Influenza; Infection Control; Epidemiology; Public Health; Health Economics

Word count: 4234

Abstract

Objectives: To quantify population level health and economic consequences of sick leave among workers with influenza symptoms.

Interventions: Compared with current sick leave practice (baseline) we evaluated the health and cost consequences of: I) Increasing the proportion of workers on sick leave from 65% (baseline) to 80% or 90%; II) shortening the maximum duration from symptom onset to sick leave from 4 days (baseline) to 2 days, 1.5 days, 1 day, and 0.5 days; and III) combinations of I and II.

Methods: A dynamic compartmental influenza model was developed using Norwegian population data and survey data on employee sick leave practices. The sick leave interventions were simulated under 12 different seasonal epidemic and 36 different pandemic influenza scenarios. These scenarios varied in terms of transmissibility, the proportion of symptomatic cases, and illness severity (risk of primary care consultations, hospitalizations and deaths). Using probabilistic sensitivity analyses, a net health benefit approach was adopted to assess the cost-effectiveness of the interventions from a societal perspective.

Results: Compared with current sick leave practice, sick leave interventions were cost-effective for 31 (65%) of the pandemic scenarios, and 11 (92%) of the seasonal scenarios. Economic benefits from sick leave interventions were greatest for scenarios with low transmissibility, high symptomatic proportions, and high illness severity. Overall, the health and economic benefits were greatest for the intervention involving 90% of sick workers taking sick leave within one-half day of symptoms. Depending on the influenza scenario, this intervention resulted in a 44.4–99.7% reduction in the attack rate. Interventions involving sick

leave onset beginning 2 days or later, after the onset of symptoms, resulted in economic losses.

Conclusions: Prompt sick leave onset and a high proportion of sick leave among workers with influenza symptoms may be cost-effective, particularly during influenza epidemics and pandemics with low transmissibility or high morbidity.

Article Summary

Strengths and limitations of this study

- Although national recommendations for flu management often advise sick leave from work, no systematic studies of health and cost consequences of such recommendations have been published, and no studies have evaluated the effects of sick leave interventions in detail.
- This study uses mathematical modelling to compare current sick leave practice with 14 alternative sick leave interventions, related to the proportion of ill employees taking sick leave and the timeliness of sick leave relative to symptoms, to investigate the epidemiological effects of these interventions and their economic consequences
- Some of the parameters used in the modelling and evaluation are not influenza-specific, such as the above current sick leave practice, but rather based on influenza-like illness (ILI), being derived from interviews unaccompanied by test results.
- All interventions were assessed for a variety of potential epidemic and pandemic influenza scenarios with varying characteristics.
- We have studied the population-wide effects for the Norwegian setting and our findings may not be directly transferrable to other settings or sub-groups.

Introduction

Seasonal influenza affects 5–15% of the world's population annually. Globally, influenza epidemics are responsible for 250,000–500,000 deaths and 3–5 million cases of severe illness per year.[1] During an influenza pandemic the disease burden may increase substantially. The disease also imposes a considerable cost burden on the healthcare system, but the greatest proportion of costs are indirect costs resulting from lost workdays.[2]

When influenza-infected workers report to work, their co-workers are at risk of becoming infected. We recently conducted a literature review on influenza transmission in the workplace and assessed sick leave recommendations during influenza in 18 European countries.[3] We found that while pandemic preparedness plans of many European countries officially advise sick workers to be absent from work, only one study was identified that had assessed the effectiveness of sick leave interventions during influenza.[3] This was a modelling study from the US that indicated that liberal sick leave policies and increased payment compensations during sick leave would reduce workplace transmission up to 39%[3 4]. Norway is a western-European society with generous social welfare programs, so few workers lose income as a result of sick leave due to influenza-like symptoms.[5-7] No studies to date have ascertained whether sick leave during influenza is a cost-effective way of reducing the spread of influenza. In addition, countries that advise workers with influenza to take sick leave recommend diverse sick leave strategies.[3]

Influenza transmission depends on a complex interaction between the host, pathogen and the environment. Characteristics, such as the attack rate and disease severity of a particular influenza season, may affect which sick leave strategies are most cost-effective to implement. The effectiveness of sick leave as a mitigation intervention is limited by

asymptomatic transmission. The proportion of asymptomatic cases reported in the literature varies between 25% and 75%,[8-11] and asymptomatic cases may shed reduced amounts of the virus.[12] Moreover, in symptomatic individuals, virus shedding may begin 1–2 days prior to the onset of symptoms.[9 10] During the symptomatic phase, workers can either choose to be present at work while feeling ill ("presenteeism") or to remain at home ("absenteeism"). Studies have suggested that workplace presenteeism during influenza infection is widespread.[13 14] From a public health and socioeconomic perspective, incentivising sick leave during influenza infection may reduce disease transmission enough to reduce the overall costs to society[15]. From the perspective of an employer, however, the burden of work absenteeism may be considerable, as the value of the work employees would have produced is lost.[16 17]

Using a model framework, we attempted to quantify the costs and health consequences of increasing sick leave among workers with influenza symptoms. In our study we define sick leave as the period of time a worker is absent from paid work due to influenza symptoms. We simulated the effect of implementing different sick leave policies during an influenza outbreak in the Norwegian population. We conducted a survey to inform the model with local data on current influenza-related sick leave behaviour in Norway, and compared different sick leave interventions with current practice.

Material and methods

Modelling assumptions

We developed a model to quantify the number of mild, moderate and severe influenza cases. A scenario-based approach was applied to account for the fact that influenza, particularly pandemic influenza, varies in terms of transmissibility, likelihood of symptomatic infections, and illness severity (i.e. risk of primary care visits, hospitalizations and death). We differentiated between interventions (variation in sick leave behaviour) and scenarios (variations in influenza characteristics), and studied each sick leave intervention given each distinct influenza scenario. In total, we analysed current sick leave practice (baseline), and 14 alternative sick leave interventions combined with 48 influenza scenarios. The health outcomes from the disease model were used in an economic model to estimate costs and quality adjusted life years (QALYs). Because the parameters of the economic model were uncertain, we used Monte Carlo simulations to explore the consequences of the uncertainty. In this paper, we outline the main characteristics of the models and their input parameters. A detailed description of the survey and models is provided in Supplementary file 1.

Influenza-related sick leave

During epidemics, Norwegian health authorities advise that workers with symptoms of influenza remain at home until feeling well enough to work. During pandemics, sick leave is recommended until at least 24 hours following defervescence[3 18]. Lacking data on influenza-related absences, we conducted a web-based survey in a convenience sample of 490 Norwegian employees. In total, 46% (224/490) of the participants reported having experienced influenza-like symptoms during the previous influenza season. Based on expert opinion, influenza-like symptoms, for the purposes of the survey, included: fever, cough, sore

throat, headache, fatigue, muscle pain, and/or stuffy nose. Among participants reporting influenza-like-symptoms, 74% took sick leave. The duration of absence varied from 1–13 workdays (mean of 2.4 days), and individuals waited from 1–8 days (mean of 2.7 days) after the onset of symptoms to take leave. Among those who took sick leave, 24% began on the first day that they experienced symptoms, 43% on the second day, 19% on the third day, while 14% waited at least four days before taking sick leave.

The survey respondents were mostly public sector employees who have high job security. There is evidence that workers with lower job security are more likely to attend work despite feeling ill,[19] therefore we lowered the baseline sick leave rate in our model to 65% to make the results more representative of the general working population in Norway.

In the baseline sick leave setting, we assumed that symptomatic workers would stay at home for an average of 3.5 calendar days for seasonal influenza, adjusting for a working week of five days. For pandemic influenza, we increased this period to 6.5 calendar days, in line with the Norwegian national guidelines during the 2009 H1N1 pandemic that suggested one week of absence from the onset of symptoms. Consistent with the survey, we assumed that among those workers who take sick leave because of influenza, 24%, 43%, 19%, and 14% would initiate sick leave on the first, second, third, and fourth day relative to symptom onset, respectively. We found no data in the literature on the proportion of children absent from school or day-care due to influenza-like illness. Therefore, we assumed that 90% of children with influenza would remain at home, with cumulative withdrawal rates of 33%, 67%, and 100% on the first, second, and third day relative to symptom onset, respectively.

Interventions

We considered all combinations of the following interventions aimed at increasing the proportion of workers taking sick leave and/or reducing the delay from symptom onset to withdrawal from the workplace: I) proportion of symptomatic workers taking sick leave: 65%, 80% and 90%, and II) maximum time from symptom onset to sick leave: 0.5 days, 1 day, 1.5 days, 2 days and 4 days. These interventions were chosen based on the results from our survey on sick-leave behaviour, and on perceived feasibility. Interventions were compared to the baseline sick leave practice, defined as 65% of ill workers taking sick leave after a maximum of four days with symptoms. In children, the baseline pattern of sick leave was kept constant.

We simulated interventions with less than 4 days of maximum delay from symptoms onset to sick leave using a truncated variant of the baseline daily withdrawal proportions. For example, in the case of a maximum of 2 days delay, 24% would initiate sick leave when symptoms first appeared, 43% on the following day, and the remaining 33% on the next day.

Main features of the influenza model and the economic model

We developed an age-structured, deterministic simulation model (Fig 1) for the spread of influenza in Norway (population: 5.05 million in January 2013). The social mixing structure, representing mixing within households, schools, workplaces, and general society, was reconstructed from simulations based on real demographic data. People at home with influenza illness were assumed to not mix with other people at work/school, or in the general population. We calibrated the model to a broad spectrum of seasonal and pandemic influenza scenarios: seasonal epidemics at an effective reproductive number (R_eff) of 1.2, 1.3, and 1.4, assuming 35% of children and 25% of adults would develop symptoms (low symptomatic proportions), or that 65% of children and 55% of adults would develop symptoms (high

symptomatic proportions). For pandemic influenza, we constructed scenarios at a basic reproductive number (R_0) of 1.4, 1.6, and 1.8, also assuming low or high symptomatic proportions as described above. The reproductive number is defined as the number of secondary cases that one influenza case would produce, and can be regarded as a measure of transmissibility.

We assumed that individuals become infectious prior to the onset of symptoms, and that their infectivity would peak approximately on the first day of symptoms and would last for seven days, according to a given infectivity profile (Figure SMM2, Supplementary File 1). Individuals with asymptomatic infection were assumed to be half as infectious as those with symptoms, but with a similar contour of infectivity.

We developed a probabilistic health economic model to translate the output from the infection model into costs of healthcare, costs of sick leave (productivity losses), and the intervention costs for each intervention. Productivity losses are highly relevant in sick leave intervention studies, and therefore we assessed cost-effectiveness from a societal perspective. To ease comparison between the interventions and scenarios, we used a net health benefit (NHB) approach assuming that the value of a QALY (λ) is NOK 570,807 ($98,060 USD[20]) in line with Norwegian guidelines.[21] By definition, NHB=QALY gains - (cost of intervention/ λ). This means that an intervention is cost-effective if NHB expressed as QALYs is greater than zero. All costs were measured in 2012 Norwegian Kroner (NOK) ($1.00 USD= NOK 5.82)[20].

The age-specific incidence of symptomatic influenza from simulations of the dynamic model was used as input data for the economic analyses. We used the estimates adopted in the 2014 Norwegian pandemic preparedness plan for the proportion of clinical cases that would

require healthcare (visit to a GP, hospitalisation, or intensive care treatment), and used estimates of mortality from the same source.[22] The plan includes three distinct morbidity/mortality estimates for moderate, severe, and very severe pandemics. The morbidity during seasonal influenza was assumed to be similar to that observed during a moderate pandemic.

The dynamic influenza model was developed in Matlab version R2013a using the ode45 solver. The economic model was developed in STATA-13 and Excel 2010.

Results

This section is organised as follows: First, we present the baseline disease burden and baseline economic costs for each of the main scenarios. Second, we describe the health impacts of the sick leave interventions. Third, we present the results of the cost-effectiveness analyses. Lastly, we present results from the sensitivity analyses, in which we have assumed extra mixing in the household and general population in individuals who are absent from work. We present the epidemiological results by reporting relative changes in the clinical attack rate (AR), which is defined as the proportion of the population that acquire a clinical infection. The comparative changes in GP visits, hospitalisations, and mortalities closely mimicked changes in the AR. We report the cost-effectiveness results in terms of mean NHB. Complete tables for all results related to the epidemiologic outcomes, direct and indirect costs in the economic model, including probabilistic variation, are presented in Supplementary file 2.

Baseline scenarios

Table 1 shows the key epidemiologic and economic results for each of the baseline scenarios for seasonal and pandemic influenza. In the absence of any intervention, the model produced clinical attack rates (ARs) ranging from 3.2–16.9% for seasonal influenza at an R_eff of 1.2–1.4, and 9.4–34.8% for pandemic influenza at an R_0 of 1.4–1.8. Visits to a GP and hospitalisations ranged from 478–2,521 and 23–122 per 100,000 people for seasonal epidemics, and from 1,398–8,688 and 67–1,207 per 100,000 for pandemics. The corresponding mortality ranged from 5–26 expected deaths per 100,000 people for seasonal influenza, and from 15–243 deaths for pandemic influenza.

Table 1: Key population baseline epidemiological and economic outcomes for seasonal epidemics and severe pandemics in each of the scenarios considered.

	Seasonal influenza R_eff[b]			Pandemic influenza severe (moderate; very severe)[a] R_0[c]		
Baseline outcomes in the total population	**1.2**	**1.3**	**1.4**	**1.4**	**1.6**	**1.8**
Low symptomatic proportions						
Clinical attack rate, AR (%)	3.2	5.3	7.0	9.4	13.0	15.6
Median number of GP visits per 100,000 population	478	789	1,053	1,866 (1,398; 2,334)	2,587 (1,939; 3,236)	3,115 (2,334; 3,896)
Median number of hospitalisations (per 100,000 population)	23	38	51	184 (67; 325)	255 (93; 450)	307 (112; 541)
Median number of deaths (per 100,000 population)	5	8	11	21 (15; 65)	30 (20; 90)	35 (24; 109)
Mean total costs (million USD)	94	155	205	473 (401; 569)	656 (557; 789)	790 (670; 950)
Productivity losses (% of total costs)	83	83	83	75 (88; 62)	75 (88; 62)	75 (88; 62)
High symptomatic proportions						
Clinical attack rate, AR (%)	9.0	13.3	16.9	22.3	29.5	34.8
Median number of GP visits per 100,000 population	1,342	1,983	2,521	3,329 (4,442; 5,557)	5,892 (4,415; 7,370)	6,946 (5,205; 8,688)
Median number of hospitalisations (per 100,000 population)	65	96	122	438 (160; 772)	581 (212; 1,024)	685 (251; 1,207)
Median number of deaths (per 100,000 population)	14	20	26	50 (34; 155)	66 (44; 1,024)	78 (53; 243)
Mean total costs (million USD)	257	378	479	1,134 (963; 1,363)	1,503 (1,276; 1,807)	1,770 (1,503; 2,128)
Productivity losses (% of total costs)	82	82	82	75 (88; 62)	75 (88; 62)	75 (88; 62)

a= moderate (severe; very severe) refers to illness severity in the influenza scenario, b=effective reproductive number, c= basic reproductive number, cd= 35% of children aged < 16 years, and 25% of adults aged 16+ years develop symptoms, e=65% of children aged < 16 years, and 55% of adults aged 16+ years develop symptoms

The mean total costs of influenza in Norway, including productivity losses and healthcare resource use ranged from $94–$479 million USD for seasonal epidemics, $401–1,503 million for moderate pandemics, $473–1,770 million for severe pandemics, and $569–2,128 million for very severe pandemics. Production losses made up the majority of the total costs. The proportion of the total costs owing to productivity losses was 82–83% during seasonal influenza, and 62–82% during pandemic influenza. The proportion was lowest during very severe pandemic influenza, where the healthcare costs increased substantially. (Fig S1).

Epidemiological impact of sick leave interventions in workplaces

Figures 2 and 3 display the intervention effects on the AR, the epidemic peak delay, and changes in the epidemic curves when compared to the baseline scenarios.

For the seasonal influenza scenarios, the AR was reduced by 44.4–98.8% (mean value of 85.4%) compared with the baseline values (Fig 2A). The interventions achieved the highest reduction at the lowest transmissibility of R_eff = 1.2 (blue) and at high symptomatic proportions (solid lines); the relative minimum AR was 60.3% assuming low symptomatic proportions (stippled lines). As expected, the interventions with a high proportion of workers on sick leave (90%) and early withdrawal from work/school (0.5 days) had the greatest effect. General trends in the pandemic scenarios were similar to those obtained in the seasonal epidemics. However, as the transmissibility in these scenarios was higher on average, the interventions were less effective. Overall, the interventions reduced the AR by 63.6–99.7% (mean AR of 91.0%) relative to their baseline values (Fig 2B). Pandemic scenarios with low symptomatic proportions had a relative minimum AR of 77.3%.

In the seasonal influenza scenarios, the interventions delayed the epidemic peak by 0 to 58 days. The delay was particularly pronounced at R_eff = 1.2 (Fig 2C and Fig 3, left column top panel). The scenarios assuming low symptomatic proportions had a maximum time delay of 43 days, and most cases, exhibiting a delay of 1–2 weeks. Pandemic scenarios resulted in shorter peak time delays than the seasonal scenarios, ranging from 0–20 days (Fig 2D and Fig 3, right column); the delay of time to peak was at most 10 days in scenarios with low symptomatic proportions.

The median age among avoided clinical cases was similar within each scenario, ranging from 26.7–33.6 years for the seasonal scenarios, and from 33.6–38.1 years for the pandemic scenarios (Fig S2 and Fig S3). More infections were avoided in younger individuals when transmissibility or symptomatic proportions were low.

Cost-effectiveness of sick leave interventions in workplaces

Figure 4 summarises the results of the cost-effectiveness analyses for seasonal influenza (Fig 4A), and for pandemics assuming moderate, severe, and very severe illness (Fig 4B–D, respectively).

In total, for 100% (6/6) of seasonal influenza scenarios, sick leave interventions were cost-effective compared to current sick leave practice; cost-effective interventions were obtained for 50% (3/6) of moderate, 50% (3/6) of severe, and 87% (5/6) of very severe pandemic scenarios. In general, the mean NHB was higher at low transmissibility (blue) compared to high transmissibility (red) assuming that all other factors remained equal (Fig 4). The mean NHB was larger at high symptomatic proportions (squares) compared to low symptomatic proportions (crosses), for similar transmissibility.

In the pandemic scenarios assuming low symptomatic proportions, interventions were cost-effective for R_0 < 1.6, except in the case of a very severe pandemic where interventions were also cost-effective for R_0 = 1.6 (Fig 4B-D). For pandemic influenza with high symptomatic proportions, all scenarios at R_0 < 1.8 produced cost-effective interventions. For very severe pandemic scenarios, cost-effective interventions were also found for R_0 = 1.8.

In 16 of the 17 scenarios for which interventions were cost-effective, the superior intervention was for 90% of ill workers to take sick leave within one-half day of the onset of symptoms. (Fig 4 and Fig S1). While in one scenario, a seasonal epidemic at R_eff = 1.4 with low symptomatic proportions, 90% of symptomatic workers taking sick leave was the most cost-effective intervention. In this particular case, the combination of 90% of symptomatic workers taking sick leave and sick leave onset within 0.5 days ranked third in terms of cost effectiveness. Generally, when symptomatic proportions were low, the only cost-effective interventions were those in which sick leave onset occurred within 0.5 days, or interventions solely increasing the adherence. In contrast, scenarios with high symptomatic proportions produced cost saving results for a variety of different interventions.

Among the cost-effective interventions, the largest mean NHB was in the range 31–535 quality adjusted life years (QALYs) for low symptomatic proportions and 1,506–2,898 QALYs for high symptomatic proportions in the seasonal scenarios. For pandemic scenarios with low symptomatic proportions, interventions were cost-effective for moderate and severe scenarios with low transmissibility (R_0=1.4), and for very severe scenarios with low and moderate transmissibility (R_0=1.4 and R_0=1.6). The largest mean NHBs were 292, 477, and 170–1,185 QALYs for assumptions of moderate, severe, and very severe morbidity/mortality, respectively. For high symptomatic proportions, the QALY value varied

from 345–3,749, 1,966–4,481, and 1,859–7,256 for moderate, severe, and very severe morbidity/mortality, respectively.

Notably, interventions that focused exclusively on increasing the proportion of workers taking sick leave during influenza, had comparatively high probabilities of being cost-effective, as shown by the stochastic simulations and illustrated in acceptability curves (Fig S4). Conversely, interventions with sick leave starting later than one day after the onset of symptoms were generally not cost-effective, except for scenarios with high symptomatic proportions, or when combined with an increased proportion of symptomatic workers taking sick leave.

Sensitivity analyses: assuming extra mixing for individuals absent from work

In the sensitivity analyses where additional mixing in the household and the general population was assumed, the effectiveness of sick leave interventions was somewhat diminished compared with the main scenarios (Fig S5). However, on the whole, the cost-effectiveness and ranking of the different interventions under the various scenarios were retained (Fig S6 and Fig S7). The reduction in the AR relative to the baseline varied from 52.7–99.4% in the seasonal scenarios, and 69.1–99.7% in the pandemic scenarios (Fig S5). In total, 83% (5/6) of seasonal scenarios, and 33% (2/6) of moderate, 50% (3/6) of severe, and 67% (4/6) of very severe pandemic scenarios produced cost-saving interventions. Consistent with the results obtained in the main analyses, the best intervention for the scenarios with cost-effective results was 90% of symptomatic workers taking sick leave with withdrawal at 0.5 days after the onset of symptoms. For this intervention, the mean NHB varied from 101–2,192 QALYs for seasonal epidemics, and from 168–2,414, 131–3,019, and 388–5,314 QALYs for moderate, severe, and very severe pandemics, respectively.

Discussion

We have shown that the effectiveness of sick leave during influenza on reducing the spread of the disease is dependent on: i) timing of absence onset, ii) the proportion of ill workers leaving work and iii) the characteristics of the influenza epidemic (transmissibility, influenza severity, etc.). The results of our study indicate that the earlier the absence and the greater the proportion leaving work, the greater the effectiveness. Leaving work more than two days after onset of symptoms has minimal impact on the spread of the disease. Even when taking costs of lost production into account, early absence among high proportions of workers is cost-effective in most disease scenarios. Exceptions are pandemics with low transmissibility and general epidemics with low symptomatic proportions.

The modelling approach allowed us to simulate population level effects of different sick leave interventions under a range of possible influenza scenarios, providing information that would not readily be observed in real-life studies. The scenarios presented are largely consistent with a recent review on pandemic influenza scenarios in Europe, in which the authors argued for the use of multiple scenarios based on the recent experience from the 2009 H1N1 pandemic[23]. Other studies address the effects of expanding the right to sick leave[4 24], but since access to paid sick leave is more or less universal in Norway, we have focused specifically on different sick leave interventions. Our study is the first to investigate epidemiological and economic outcomes of workplace-based interventions on a population level. We are also the first, to our knowledge, to investigate the effects of the timeliness of sick leave initiation relative to symptom onset during influenza.

Our results indicate that early withdrawal is important for cost-effectiveness, but this result may depend on the ability to differentiate influenza from other illnesses with similar

symptoms. Because influenza symptoms are non-specific, and it is unknown whether sick leave interventions are cost-effective for illnesses with influenza-like symptoms, e.g. respiratory syncytial virus (RSV), early withdrawal may not be as cost-effective in practice. Influenza surveillance data, which is available in many countries, could be used to restrict recommendations to apply only in geographic regions where influenza activity is rising. Another central question is how these sick leave recommendations can be communicated effectively to the working population and the costs of achieving the sick leave behaviours described. In our study, the cost-effective interventions were also assumed to be the most costly to implement, with a mean cost of $5.6 million; but the true cost is uncertain. A pilot study could be initiated to assess costs and feasibility of earlier sick leave and increased proportion of symptomatic workers taking sick leave.

Our study has several limitations. The profile of infectiousness assumed in our model was an influential variable. Although it was based on data from a household study, we acknowledge that there is uncertainty related to how infectiousness changes over time, and to the relative infectivity of an asymptomatic infection. The proportion of GP visits and hospital admissions, and the case-fatality rate assumed under different influenza scenarios were based on estimates proposed by Norwegian experts, and were not age-specific. A recent review reported lower estimates in other European countries,[23] but these values are likely country-specific. Another limitation of this study was that influenza illness has been shown to reduce productivity at work,[25] however, this may vary depending on occupation. We assumed that 8% of workers would continue to work from home during their illness and while taking care of sick children, but information on this topic is scarce. A study from Sweden found that 60% of parents work from home when their children are sick[26] thus our assumption may underestimate the economic benefit of the intervention. The economic benefits from earlier

onset of sick leave may also have been underestimated. It seems plausible that earlier sick leave onset could lead to a quicker recovery, however, we could not find any evidence of this in the literature; therefore, we assumed the recovery period to be constant, and independent of sick leave onset. Finally, influenza cases and workplace absences were modelled to occur randomly on a population level. In reality, absences may cluster in specific workplaces, which may cause understaffing for critical functions and a subsequent increase in cost.

We assumed that the number of days of sick leave was 3.5 calendar days for seasonal influenza and 6.5 calendar days for pandemic influenza. Because we found that the epidemiological benefits of sick leave were limited after 2 days of symptoms, we also explored the effect of assuming the same number of total absence days during pandemics as during epidemics (3.5 calendar days). This resulted in higher economic benefits for interventions involving early onset within one day, but lower benefits for other interventions.

Current recommendations on sick leave during influenza are typically focused on the duration of sick leave, but the present results suggest that recommendations may be improved by encouraging prompt initiation of sick leave. However, although sick leave can reduce the spread of influenza, our findings indicate that this effect is insufficient to offset an ongoing epidemic or pandemic so, ideally, sick leave interventions could be implemented as supplements to other existing strategies. Economic evaluations of mitigation interventions such as vaccines, antivirals, and school closures, are common in the literature.[27-29] In contrast, studies on sick leave interventions are limited [28 29], which is somewhat surprising considering that this is a widespread recommendation in national pandemic preparedness plans.[3] Moreover, pharmaceutical interventions are limited by availability[30]; therefore non-pharmaceutical interventions can be considered as viable backup strategies. As a result, there

is a need for quantitative modelling for policy planning and decision-making purposes. The present economic results are based on Norwegian demographic and economic assumptions, and several factors would need to be recalculated for use in other countries. Nevertheless, our model provides a structure for analysing this problem and provides a method, which could be employed by other researchers.

The findings in this paper indicate that there are epidemiological and economic benefits from sick leaves during influenza, however further studies are needed to assess these effects in more detail and in other settings. Future studies should consider collecting additional data on influenza transmission pathways, sick leave practice and the behaviour of workers during sick leave. Ideally, such studies should also aim to test for influenza to establish aetiology, rather than relying on self-reported influenza status. Moreover, it is of importance to conduct studies to explore the effects of sick leave interventions within specific occupational groups. For example, influenza has been found to be less prevalent in janitors and technicians compared with other occupations.[31] Likewise, some workers may be more likely to spread influenza (e.g. a waiter in a restaurant), or be more likely to spread influenza to high-risk persons (e.g. healthcare workers). Finally, investigations into the cost-effectiveness of sick leave interventions for other communicable diseases, perhaps especially those with high illness severity or low transmissibility, are warranted.

Conclusion

Recommending early absence from work among all workers with influenza symptoms represents an effective intervention during influenza epidemics and pandemics. The intervention is also cost-effective in most influenza scenarios.

List of abbreviations

AR: Attack rate

QALY: Quality adjusted life year

R_0: Basic reproductive number

R_eff: Effective reproductive number

NHB: Net health benefit

GP: General practitioner

EQ-5D: EuroQol 5 D

Author contributions

The study was designed by BFdB, CHE, and ISK. The mathematical model was designed by BFdB and GST, and the economic model was developed by CHE, ISK, and RW. The data analysis was performed by CHE and BFdB. The manuscript was prepared by CHE and BFdB. All authors revised and accepted the final manuscript.

Acknowledgements

The authors wish to thank Siri Helene Hauge and Olav Hungnes of the Norwegian Institute of Public Health for their insightful comments and guidance on influenza and influenza-related policies. We would also like to thank Arna Desser for her assistance with proofreading the article.

Data sharing

The main sources of data have been provided in the text of the main article or in the supplementary files, however, additional information can be provided by the authors on request.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interests

All authors have completed the ICMJE uniform disclosure form and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

Ethical considerations

Informed consent was obtained from all survey participants of the survey. The study was reviewed by the Data Protection Official at the University of Oslo, and it was considered that approval from an ethical committee was not required due to the nature/content of the study.

References

1. World Health Organization. Influenza (seasonal) factsheet No211: World Health Organization; 2009 [08.10.2013]. Available from: http://www.who.int/mediacentre/factsheets/fs211/en/.

2. Xue Y, Kristiansen I, de Blasio B. Modeling the cost of influenza: the impact of missing costs of unreported complications and sick leave. *BMC public health* 2010;**10**(1):724. doi: 10.1186/1471-2458-10-724.

3. Edwards CH, Tomba GS, Blasio BFd. Influenza in workplaces: transmission, workers' adherence to sick leave advice and European sick leave recommendations *European Journal of Public Health* 2016;**1-8**. doi: 10.1093/eurpub/ckw031.

4. Kumar S, Grefenstette JJ, Galloway D, et al. Policies to reduce influenza in the workplace: impact assessments using an agent-based model. *American Journal of Public Health* 2013;**103**(8):1406-11. doi: 10.2105/AJPH.2013.301269.

5. National Insurance Act. Act 1997-02-28-19. Act relating to national insurance Avd I 1997 Nr. 5LOV-1997-02-28-19 [04.07.2014]. Available from: https://lovdata.no/dokument/NL/lov/1997-02-28-19.

6. Intensjonsavtale om et mer inkluderende arbeidsliv 4. mars 2014 - 31. desember 2018 (IA-avtalen) 2014 [04.07.2014]. Available from: https://www.regjeringen.no/globalassets/upload/asd/dokumenter/2014/ia_20142018/signert_ia_avtale.pdf.

7. Ose SO, Dyrstad K, Slettebak R, et al. Evaluering av IA-avtalen (2010-2013) 2013 [03.07.2014]. Available from: http://www.sintef.no/prosjekter/evaluering-av-ia-avtalen-2010-2013/.

8. Elder AG, O'Donnell B, McCruden EA, et al. Incidence and recall of influenza in a cohort of Glasgow healthcare workers during the 1993–4 epidemic: results of serum testing and questionnaire. *Bmj* 1996;**313**(7067):1241-42.

9. Carrat F, Vergu E, Ferguson NM, et al. Time lines of infection and disease in human influenza: a review of volunteer challenge studies. *American journal of epidemiology* 2008;**167**(7):775-85. doi: 10.1093/aje/kwm375.

10. Lau LLH, Cowling BJ, Fang VJ, et al. Viral shedding and clinical illness in naturally acquired influenza virus infections. *Journal of Infectious Diseases* 2010;**201**(10):1509-16. doi: 10.1086/652241

11. Suess T, Remschmidt C, Schink SB, et al. Comparison of shedding characteristics of seasonal influenza virus (sub) types and influenza A (H1N1) pdm09; Germany, 2007–2011. *PloS one* 2012;**7**(12):e51653. doi: 10.1371/journal.pone.0051653.

12. Patrozou E, Mermel LA. Does influenza transmission occur from asymptomatic infection or prior to symptom onset? *Public health reports* 2009;**124**(2):193.

13. Nichol KL, Heilly SJD, Greenberg ME, et al. Burden of Influenza-Like Illness and Effectiveness of Influenza Vaccination among Working Adults Aged 50–64 Years. *Clinical Infectious Diseases* 2009;**48**(3):292-98. doi: 10.1086/595842

14. Carrat F, Sahler C, Rogez S, et al. Influenza burden of illness: estimates from a national prospective survey of household contacts in France. *Archives of internal medicine* 2002;**162**(16):1842. doi: 10.1001/archinte.162.16.1842.

15. Liao S, Ma Y, Chen J, et al. Paid sick-leave: is it a good way to control epidemics? In: Glass K, Colbaugh R, Ormerod P, et al., eds. Complex Sciences: Second International Conference, COMPLEX 2012, Santa Fe, NM, USA, December 5-7, 2012, Revised Selected Papers. Cham: Springer International Publishing, 2013:213-27.

16. Keech M, Scott A, Ryan P. The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. *Occupational Medicine* 1998;**48**(2):85-90. doi: 10.1093/occmed/48.2.85.

17. Keech M, Beardsworth P. The impact of influenza on working days lost. *Pharmacoeconomics* 2008;**26**(11):911-24. doi: 10.2165/00019053-200826110-00004

18. Norwegian Institute of Public health. Reviderte råd for anbefalinger om sykefravær ved influensaliknende sykdom [Revised advice for recommendations on absenteeism due to influenza-like illness] [13.06.2013]. Available from: https://www.fhi.no/globalassets/migrering/dokumenter/pdf/rapport-om-anbefalinger-om-fravar-ved-sykdom-2009-11-18.pdf.pdf.

19. Johns G. Presenteeism in the workplace: A review and research agenda. *Journal of Organizational Behavior* 2010;**31**(4):519-42. doi: 10.1002/job.630.

20. Central bank of Norway. Exchange rate for USD. 2013. [14.08.2015]. Available from: http://www.norges-bank.no/Statistikk/Valutakurser/.

21. Norwegian Directorate of Health. Helseeffekter i samfunnsøkonomiske analyser. 2007 [20.06.2014]. Available from: https://helsedirektoratet.no/lists/publikasjoner/attachments/643/helseeffekter-i-samfunnsokonomiske-analyser-is-1435.pdf.

22. Ministry of Health and Care Services. Norwegian National Influenza Pandemic Preparedness Plan 2006 [17.07.2014]. Available from: https://www.regjeringen.no/no/dokumenter/nasjonal-beredskapsplan-for-pandemisk-in/id102132/.

23. Napoli C, Fabiani M, Rizzo C, et al. Assessment of human influenza pandemic scenarios in Europe. *Euro Surveill*: 2015;**20**(7).

24. Kumar S, Quinn SC, Kim KH, et al. The impact of workplace policies and other social factors on self-reported influenza-like illness incidence during the 2009 H1N1 pandemic. *American Journal of Public Health* 2012;**102**(1). doi: 10.2105/AJPH.2011.300307.

25. Brouwer WB, Van Exel N, Koopmanschap M, et al. Productivity costs before and after absence from work: as important as common? *Health Policy* 2002;**61**(2):173-87. doi: 10.1016/S0168-8510(01)00233-0.

26. Novus. Unionen – Privata tjänstemän om att vobba 2015: Unionen; 2015 [14.04.2015]. Available from: http://www.unionenopinion.se.

27. Lee VJ, Lye DC, Wilder-Smith A. Combination strategies for pandemic influenza response-a systematic review of mathematical modeling studies. *BMC medicine* 2009;**7**(1):76. doi: 10.1186/1741-7015-7-76.

28. Aledort JE, Lurie N, Wasserman J, et al. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;**7**(1):208. doi: 10.1186/1471-2458-7-208.

29. Crabtree A, Henry B. Non-pharmaceutical measures to prevent influenza transmission: the evidence for individuals protective measures: National Collaborating Center for Infectious Diseases, 2011.

30. Bell D, Nicoll A, Fukuda K, et al. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerging infectious diseases* 2006;**12**(1):81-87. doi: 10.3201/eid1201.051370.

31. Anderson NJ, Bonauto DK, Fan ZJ, et al. Distribution of influenza-like illness (ILI) by occupation in Washington State, September 2009–August 2010. *PloS one* 2012;**7**(11):e48806. doi: 10.1371/journal.pone.0048806.

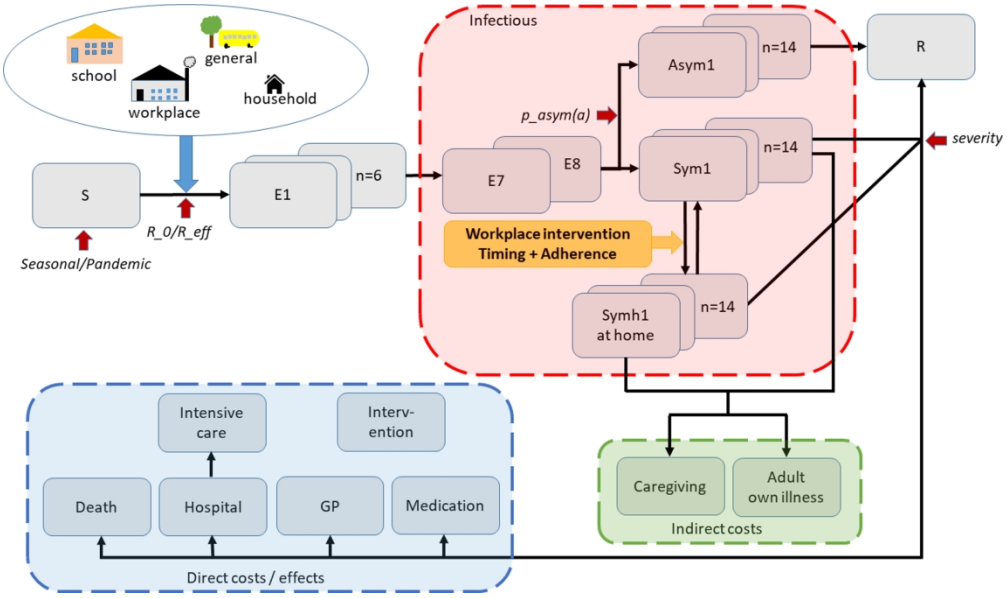


Fig 1

299x176mm (300 x 300 DPI)

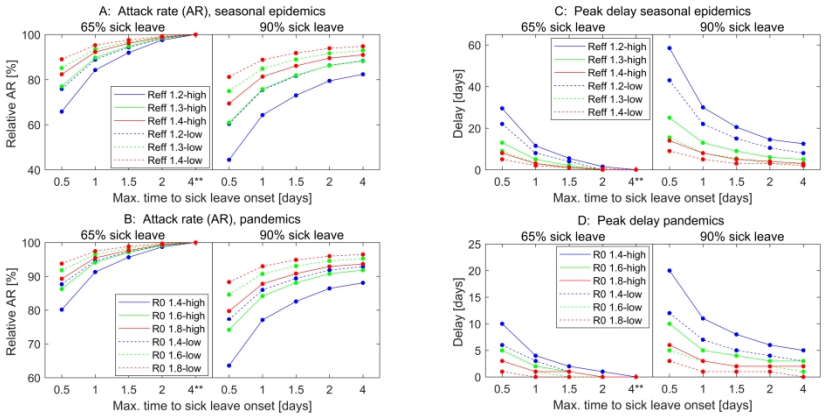


Fig 2

338x148mm (300 x 300 DPI)

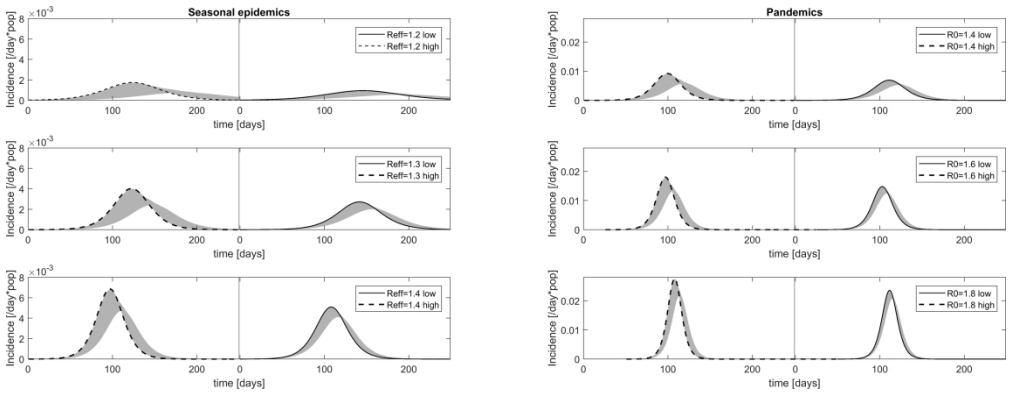


Fig 3

313x120mm (300 x 300 DPI)

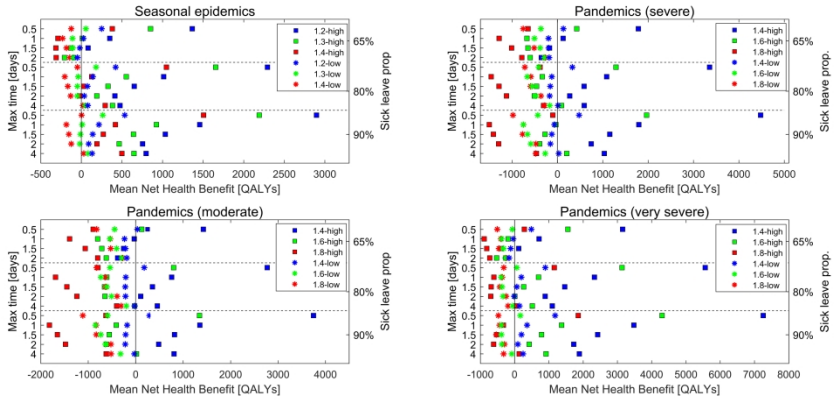


Fig 4

338x143mm (300 x 300 DPI)

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.hansen.edwards@fhi.no

SUPPLEMENTARY FILE 1: MATERIALS AND METHODS

THE INFLUENZA MODEL

An age-stratified compartmental SEIR (*Susceptible-Exposed-Infected-Recovered*) model was developed to simulate the spread of influenza. Due to lack of local data, the social mixing patterns were adapted from published synthetic contact matrices, which were based on the simulation of an agent-based virtual population parameterized with detailed Norwegian census and social demographic data[1]. Mixing between age groups were defined using four setting-specific contact matrices, accounting for contacts within households $\left(\mathbf{M}^{H}\right)$, contacts within schools $\left(\mathbf{M}^{S}\right)$, contacts within workplaces $\left(\mathbf{M}^{W}\right)$ and contacts in the general population $\left(\mathbf{M}^{GP}\right)$. Each matrix provides the relative frequency of contacts between different age classes. The overall contact matrix $\left(\mathbf{M}^{tot}\right)$ was obtained as a linear combination $\mathbf{M}_{ij}^{TOT}=\sum_{K}\alpha_{K}\mathbf{M}_{ij}^{K}$, where α_{K} accounts for the proportion of transmission occurring in the various settings, $K\in\{H,S,W,GP\}$. The weights, α_{K} ,were chosen at 0.3 for households, 0.18 for schools, 0.19 for workplaces and 0.33 for transmission occurring in the general community in accordance with empirical observations and previously published studies on influenza-like diseases[1-5]. Further details on the calculation of the mixing matrices are provided elsewhere [1].

The population was divided into 100 one-year age groups according to the size and age-distribution of the Norwegian population at 1 January 2013[6]. Newly infected individuals pass through an incubation phase which was modelled using 8 compartments ($E_1.E_2...E_8$). The average latency period was assumed at 1.5 days covering the first six compartments. and the mean incubation period was fixed at 1.9 days[7] including the E_1-E_8 compartments. The mean duration of the infectious phase was assumed at 7.5 days, consisting of E_7-E_8 compartments and 14 infectious compartments, all assumed to last for 0.5 days. The infectious

compartments were further split into three groups: people with asymptomatic infection ($Asym_1 ... Asym_{14}$), people with symptomatic infection ($Sym_1 ... Sym_{14}$) and people with symptomatic infection at home ($Symh_1 ... Symh_2$). The timing and the rates of flow between the two latter categories were modelled according to the type of intervention studied, as detailed in the main text. The variation of infectivity as a function of the duration of time since infection (the infectivity profile) was adapted from a study on household transmission[5], which is in alignment with data from the 2009 H1N1 pandemic where most transmission was found to occur early after and to peak around the time of symptom onset[7] (Figure SMM2).

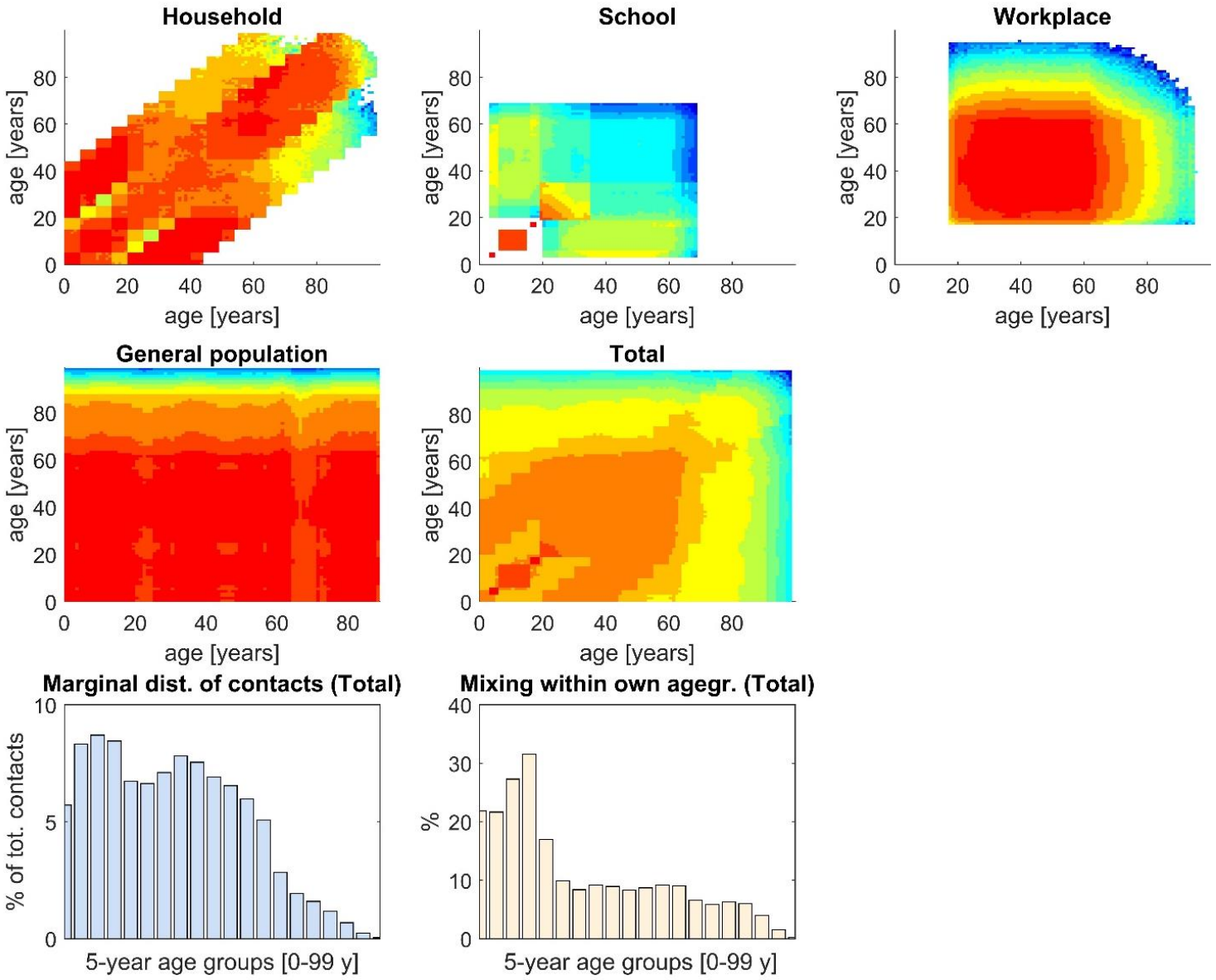


Figure SMM1: ***Mixing patterns by age assumed in the model:*** *Mixing matrices of the relative frequency of contacts among age classes in households, schools, workplace and the general population (top rows). The total mixing matrix was obtained as a weighted sum of the setting-specific matrices. The matrices are represented using a logarithmic scale (blue: low intensity; red: high intensity). The bottom row shows the marginal distribution of contacts (left) and the proportion of contacts with people of the same age (right) in the total matrix, aggregated into five-yearly age groups.*

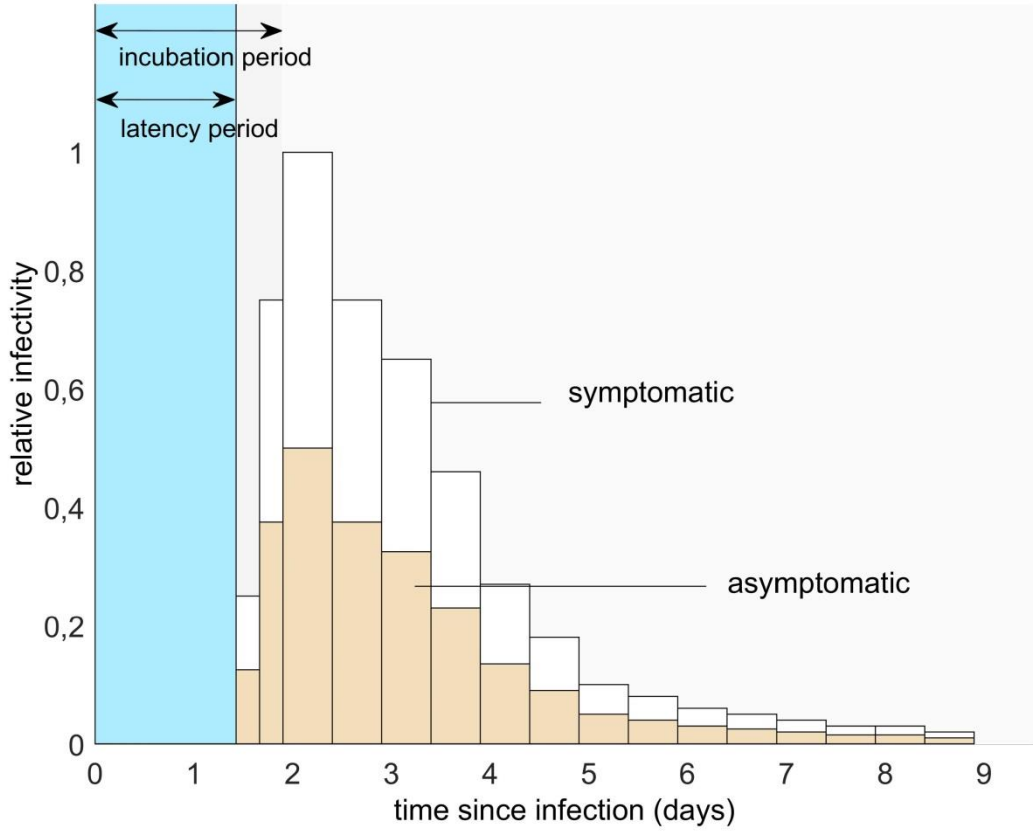


Figure SMM2: Schematic representation of the infectivity profile assumed in the model for individuals with symptomatic and asymptomatic influenza infection. The latency period is 1.5 days, the incubation period is 1.9 days, and infectivity peaks around 2 days after infection.

Recent analyses suggest that approximately 3 in 4 cases of seasonal and pandemic influenza are asymptomatic[8] and we assumed the baseline probability for symptomatic infection to be 0.35 for children <16 years and 0.25 for adults. However, in other scenarios we assumed that 50% of adults and 65% of children < 16 years develop symptoms in accordance with Longini et al.[9]. We assumed higher susceptibility and infectivity in children < 16 years of 1.05 and 1.30, respectively, compared to that of adults based on results from a Norwegian study using data from the 2009-H1N1 pandemic[10].

We modelled pandemic influenza by assuming a fully susceptible population at the simulation outset and using basic reproductive numbers: R_0=1.4, 1.6, or 1.8. For seasonal influenza we assumed that 0. 075, 0.20, and 0.40 of children < 16 years, adults 16-69 years,

and elderly 70+ years were fully immune at the simulation outset based on personal communication with experts at the Norwegian Institute of Public Health. In these simulations we considered effective reproductive numbers: R_eff=1.2, 1.3, and 1.4.

Sensitivity analyses

In the main scenarios we modelled sick leave by eliminating mixing at the workplace (0%) and in the general population (0%). There is lack of knowledge about how people behave during influenza sickness absence[11] , which impacts both their transmission potential and whom they will infect. We therefore performed sensitivity analyses by assuming that people during influenza sick leave would increase their likelihood of transmission in the household and in the general population. This was implemented in the model by adjusting the household mixing matrix (+10%) and the general population mixing matrix (-90%) compared to the mixing assumed in non-infected people at the same age.

COST-EFFECTIVENESS

We developed a probabilistic health economic model to capture the health consequences, healthcare costs, productivity losses from work absences, and campaign cost for each intervention. The age-specific incidence of clinical events was based on results from the dynamic model. The probabilities of clinical events leading to a healthcare encounter (general practitioner (GP) visit or hospitalization) or death were taken from the Norwegian Pandemic Preparedness Plan[12]. The plan includes distinct morbidity estimates for moderate, severe, and very severe pandemics. The morbidity during seasonal influenza was assumed similar to a moderate pandemic (Table SMM1).

Table SMM1: Parameters of the economic model. Mean values and distributions used for the cost-effectiveness analysis.

Parameter	Mean value	Distribution	Source
Probability of dying			
Seasonal /moderate pandemic	0.15%	$Tri(0.0015 \pm 0.0009)$	*
Severe pandemic	0.22%	$Tri(0.0022 \pm 0.00132)$	
Very severe pandemic	0.70%	$Tri(0.0070 \pm 0.0042)$	
Probability of hospitalization			
Seasonal / moderate	0.75%	$Beta(7.49,992)$	**
Severe pandemic	2.0%	$Beta(19.98,979)$	
Very severe pandemic	3.5%	$Beta(34.97,964)$	
Probability of intensive care in hospital			
Seasonal / Moderate Pandemic	10%	$Beta(99,899)$	**
Severe pandemic	17%	$Beta(169,829)$	
Very severe pandemic	25%	$Beta(250,749)$	
Probability of visiting a GP			
Seasonal / moderate Pandemic	15%	$Beta(150,849)$	**
Severe pandemic	20%	$Beta(200,799)$	
Very severe pandemic	25%	$Beta(250,749)$	
Probability of working from home when ill	8%	$Beta(929,10825)$	**[12]
Daily productivity loss adults	Age-specific (5-year)	Log Normal, mean, 20% variation about mean	***[6]
Daily productivity loss caretakers	$337	$lnN(337; 4543)$	***[6]
Productivity lost before and after (per absence)	5%	$lnN(0.95,0.0361)$	***[13]
Productivity when working from home/work	65%	$lnN(0.65,0.017)$	***[14-16]
Cost of a GP consultation	$ 68	$N(68; 185)$	#[17 18]
Cost of medications			
0-14 years (+5% severe+10% very severe)	$10.6	N(10.6,4.48)	#[19 20]
15-64 years (+5% severe+10% very severe)	$10.4	$N(10.4,4.32)$	#[19 20]
65+ years (+5% severe+10% very severe)	$14	$N(14,7.9)$	#[19 20]
Cost of hospitalization			
Non-intensive care	$9503	$Gamma(0.126; 75401)$	##[21]
Intensive care	$20435	$Gamma(4.3; 4768)$	##[21]
National cost of increasing adherence			
to 80%	$2 147 397	$N(2040378, 408076^2)$	
to 90%	$3 006 356	$N(3490120, 698024^2)$	
Cost of earlier onset of sick leave			#[22]
2 days of delay	$1 717 918	$N(1238321, 247664^2)$	
1.5 days of delay	$1 932 658	$N(1762679, 352535^2)$	
1 day of delay	$2 147 397	$N(2418124, 483625^2)$	
0.5 days of delay	$2 576 877	$N(3237432, 647486^2)$	
QALY losses (per case)			
QALY loss un-hospitalized cases	0.0078	$lnN(0.0078.0.000024)$	***[23 24]
QALY loss hospitalized cases	0.017	$lnN(0.017.0.000012)$	
QALY loss influenza mortality	age-specific (1-year)	Normal, 20% variation about the mean	PC

* Triangular distribution; Tri(a ± b) has mean a and standard deviation $b/\sqrt{6}$

** Beta distribution; Beta(a,b) has mean a/(a+b) and standard deviation $\sqrt{\frac{ab}{(a+b)^2(a+b+1)}}$

*** Log-normal distribution, parameters are mean and variance of this distribution, standard deviation is 20% of mean

Normal distribution, parameters are mean and variance of this distribution, standard deviation is 20% of mean

Gamma distribution; Gamma(a,b) has mean ab and standard deviation $b\sqrt{a}$

$PC\ mean = 0.94 - 0.002 \times age$. Personal communication with Kim Rand-Hendriksen(2014).

HEALTHCARE COSTS

We compared the number of GP visits, hospitalizations, and deaths as well as the health-related quality of life, under each sick leave intervention, with the baseline intervention (Table SMM1). The cost of an influenza-related hospitalization was estimated using data from the Norwegian Patient Registry, on patients admitted with ICD-10 diagnoses J10-J11 (influenza) and J12-J18 (pneumonia) and discharged with influenza-associated diagnoses. We estimated the average hospitalization cost per patient by identifying the DRG codes most commonly related to influenza and pneumonia. For intensive care patients we used the DRG for diseases in respiratory organs requiring ventilation support as an estimate for the cost per hospitalized case. Costs were computed using the DRG unit price, trim points and cost weights (for 2013).[21] The cost of a GP consultation was assumed at $68.[17 18]

MEDICATION COSTS

The types of medication and proportion of users was based on findings in Meier et al.[20], while use of throat drops and tissues was assumed. The cost of antibiotics was assumed equal to the cost of Fenoksymetylpenicillin[19] deducted VAT. Costs of over-the-counter drugs were based on the average cost at three pharmacies and four grocery stores in Oslo.

CAMPAIGN COSTS

Each intervention was assumed to involve a campaign to communicate recommendations. We assumed the cost of the baseline intervention (65% compliance,

maximum of 4 days from symptom onset to sick leave) to be similar to the campaign cost associated with the 2009 H1N1 Pandemic in Norway ($USD 1.7 million), equally divided into costs associated with adherence and sick leave onset delay. The campaign costs were assumed to increase by a factor of 1.5 per 10% increase in the adherence, and by a factor of 1.25 per half day reduction in the maximum delay time to work absence. The costs were converted to 2012 monetary equivalents by adjusting for inflation.

HEALTH EFFECTS

Health related quality measures based on the EuroQol-5D[25] were used to compute QALYs (Quality Adjusted Life Years) associated with mortality and morbidity. QALYs associated with mortality were based on the expected value of remaining life years using age-dependent life-expectancies[26] with a yearly discount rate of 4%. The age distribution of deaths was based on those specified in a Norwegian study of seasonal influenza mortality[27].

INDIRECT COSTS

In the baseline intervention (65% compliance, 4 days of maximum delay from symptoms onset to sick leave) we assumed that symptomatic workers would stay at home for an average of 3 workdays for seasonal influenza and 5.21 workdays for pandemic influenza, corresponding to 3.5 and 6.5 calendar days respectively. The average number of workdays lost was higher for interventions that reduced the delay from symptom onset to sick leave, following the implementation of interventions in the dynamic model.

Productivity losses were valued using a human capital approach. Labor costs were based on full-time equivalent wages and the value of labor not returned to the worker. For sick adults, 5-year age-specific wage rates for ages 16-74[6] were used, and for caretakers the average population wage was used. In Norway, all employees have a right to at least 3 days of self-certified leave with full salary, while self-employed workers (8%) may take out insurance

and their income loss during work absenteeism will depend on their insurance policy.[28] About 60% of employees have an inclusive-work life (IW) employer with more flexible sick leave arrangements and a right to 8 days of self-certified leave. Once the self-certified sick leave period ends, additional sick leave days require a GP certificate. The first 16 days are covered by the employer, and additional days by the state. [29-31] For each sick leave event, we included a productivity loss equal to 5% of the labor cost to account for productivity losses before and after the sick leave period[13]. We assumed that 8% of adults on sick leave worked from home, guided by the proportion working from home from a 2009 survey.[12] Sick persons working from home, and workers going to work despite feeling ill were assumed to work at 65% of full capacity[14-16] In Norway, parental leave is 1 year and parents have the right to care benefits during child sickness when the child <12 years.[32] Therefore all ill children between 1 and 12 years of age were assumed to require parental care. We assumed that 15% of parents were homemakers[33] with no associated productivity loss. Overlap between parental and child sickness absences, which was found to be 37.5% in our sick leave survey, was also adjusted for.

SENSITIVITY ANALYSES

For each epidemiological scenario (seasonal influenza R_eff = 1.2-1.4 with moderate morbidity; pandemic influenza R_0= 1.4-1.8 with moderate, severe, or very severe morbidity) we performed a probabilistic sensitivity analysis using Monte Carlo sampling (10 000 draws) of the parameters listed in Table SMM1.

SURVEY ON INFLUENZA-RELATED SICK LEAVE AMONG NORWEGIAN EMPLOYEES

A questionnaire consisting of 14 questions was issued either electronically via Questback©, or on paper via personal distribution to a convenience sample of Norwegian employees in the Oslo area between November 2013 and January 2014. The convenience

sample was selected based on network recruitment, and consisted mainly of public sector employees. All data gathered on paper were folded and placed in an envelope, and were later entered into Questback©, and the original responses were destroyed. The data were stored in Questback© and analyzed in Excel 2013. Once analyses were completed the original data and any imported copies were deleted. The first 6 questions were concerning age, gender, inclusive work life status of employer, household size, the number of children below 12 years living in the household, and presence of influenza-like symptoms in the previous season (defined as August 2012 to April 2013). Questions 7-9 were only asked to the respondents who indicated having children below the age of 12 living in the household. The questions addressed: whether these children had experienced influenza-like symptoms in the previous winter, whether the children were sick simultaneously with the respondent, and if yes, the number of days of sickness overlap. The last 4 questions were asked to respondents who indicated having experienced influenza-like symptoms in the previous season. The respondents were asked to indicate the number of days of symptoms, the number of days spent at home from work during the symptomatic period (and which symptomatic days were spent at home), whether the days spent at home were GP-certified or self-certified, at what day of symptoms a physician was contacted, and on which days (if any) children below the age of 12 were sick simultaneously with the respondent.

A total of 490 employees completed the questionnaire. 72% of the respondents were females, and the remaining 28% were males. The age of the respondents ranged from 20 -70 years, with a mean age of 46. Most (96%) of the employees had employers with an inclusive work life agreement (IW-agreement). There were no apparent differences between employees with and without IW–employers but the proportion of non-IW respondents was too small to meaningfully compare the two.

Among the 490 respondents, 224 reported having experienced symptoms of influenza last season. The number of days of symptoms varied from 1-20 days with a mean and median of approximately 6.5 and 5, respectively. Among the respondents that reported ILI symptoms, 161 respondents were absent from work, 58 respondents did not take time off work, the remaining 5 were missing. The duration of sick leave varied from 1-13 days, with a mean and median of 2.4 and 2 days, respectively.

Sick leave was initiated within 1-8 days after symptom onset. The shortest duration between sickness onset and sick leave was less than 1 day, and the longest duration was 7-8 days. (Figure SMM3). We did not collect any information about which factors affected the likelihood of staying at home. We suspect that in addition to having mild symptoms at onset, possible explanatory factors for delayed onset of sick leave may be social pressure or deadlines at work. In our paper we truncated the final category into 4 days or later (simulated as 4 days maximum) such that 24% took sick leave on the first day following symptom onset, 43% on the second day, 19% on the third day, and the remaining 14% on the 4th day or later.

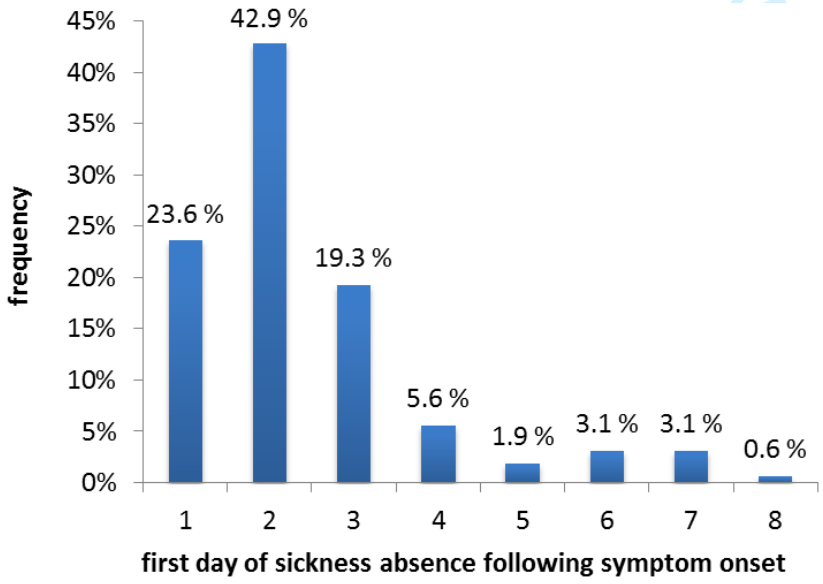


Figure SMM3: Frequency distribution showing the timing of sick leave onset counted in days from the time when symptom appeared (N=161)

The sick leave periods mainly occurred over consecutive days, with the exception of 5 respondents who reported intermittent sick leave histories. For the latter only the first sick leave period was counted. A total of 15 respondents reported being absent on one or more days without experiencing symptoms on these days; these sick leaves did not seem to be linked with sick children in the household.

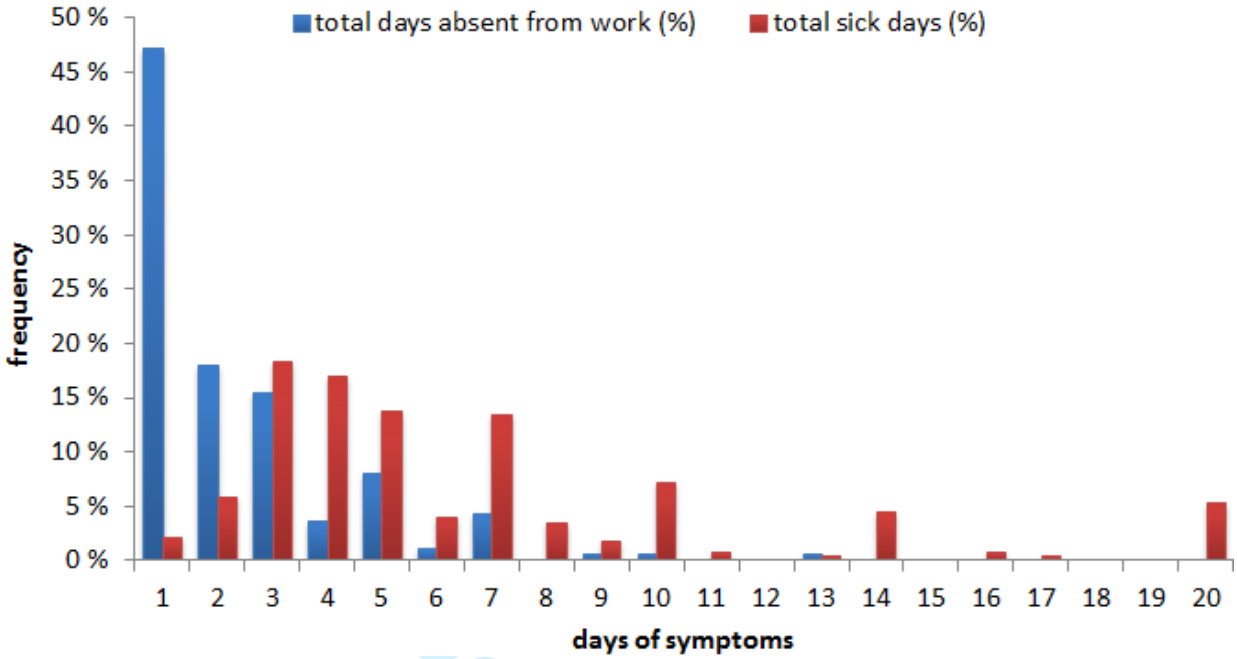


Figure SMM4: Frequency distributions showing the duration of symptoms (N=224) and the distribution of days absent from work (N=161) among respondents with ILI-symptoms.

Of the respondents that had influenza-like illness 20% reported visiting a GP for their symptoms, and 58% of these went on to take sick leave, while 42% continued to work. In total 14% of sick leaves were GP-certified, the remaining were self-certified.

Among the respondents, 155 said they had children <12 years in the household, 101/155 of the children had been ill in the past winter. The number of children was significantly correlated ($p>0.01$) with ILI symptoms in parents. The frequency of ILI symptoms in respondents was 16% higher when the household had one or more children <12 years. There was also a strong correlation ($p>0.01$) between experiencing ILI symptoms and having sick children. Although the correlation works from parent to child, and from child to parent, the latter is perhaps more correct as the sample of parents is non-random. If a child<12 in the household was ill, 74% of parents experienced ILI symptoms, otherwise 23% of parents experienced symptoms.

The survey was an attempt at providing a rough estimate of sick leave practice during influenza among the working population in Norway. Our sample is not representative of the Norwegian working population, and was largely made up of people working within health professions. Some respondents indicated that they had been on sick leave on days without symptoms (N = 6), this may be a result of measurement error or could reflect that the sick leave period was used in its full length as these sick leave periods were 7 days or longer. Since we were asking about past health states and sick leave behavior, recall bias may have been a problem. In the responses replies involving round numbers (10 days, 20 days) were relatively more common. This may have been a result of recall bias.

Survey on influenza-related sickness absence among Norwegian employees [August 2012 - April 2013]

Please enter or circle your response

1. Age:	
2. Gender:	F M

3. Do you have an employer with an agreement about inclusive worklife (IW-agreement)?	Yes No
4. How many people were living in your household last winter? (including yourself)	Yes No
5. How many children under the age of 12 years were living in your household last winter?	Yes No
6. Did you have flu-like symptoms last winter? Typical symptoms of flu are: fever / cough / sore throat / headache / fatigue / muscle pain / stuffy nose)	Yes No

(Questions 7-8 are only relevant if you had children under 12 years living in your household last winter)

7. Were any of the children (under 12 years living in the household) ill with flu-like symptoms in the previous winter?	Yes No
8. Were any children ill at the same time as you?	Yes No

(Questions 9 to 15 are only relevant if you experienced influenza-like symptoms last winter)

Please indicate the following by ticking the relevant day(s)	Symptom start Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	
1. On which days did you experience influenza-like symptoms? (for how long were you ill?)																					More than 14 days
2. On which days did you stay home from work?																					No days
3. Which absence days were GP-certified?																					No days
4. On which day did you visit a GP?																					I did not visit a GP
5. On which days were children less than 12 years living in your household experiencing symptoms as well?																					Not relevant

REFERENCES

1. Fumanelli L, Ajelli M, Manfredi P, Vespignani A, Merler S. Inferring the Structure of Social Contacts from Demographic Data in the Analysis of Infectious Diseases Spread. PLOS Computational Biologya. 2012;8(9):e1002673.

2. Merler S, Ajelli M, Pugliese A, et al. Determinants of the Spatiotemporal Dynamics of the 2009 H1N1 Pandemic in Europe: Implications for Real-Time Modelling. PLoS Comput Biol 2011;7(9):e1002205. doi: 10.1371/journal.pcbi.1002205.

3. Ferguson NM, Cummings DA, Fraser C, et al. Strategies for mitigating an influenza pandemic. Nature 2006;442(7101):448-52. doi:10.1038/nature04795.

4. Cauchemez S, Valleron A-J, Boelle P-Y, et al. Estimating the impact of school closure on influenza transmission from Sentinel data. Nature 2008;452(7188):750-54. doi: 10.1038/nature06732.

5. Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature. 2005;437(7056):209-14. doi:10.1038/nature04017.

6. Statistics Norway. 2014. Available from: http://www.ssb.no/.

7. Ghani A, Baguelin M, Griffin J, Flasche S, van Hoek AJ, Cauchemez S, et al. The early transmission dynamics of H1N1pdm influenza in the United Kingdom. PLoS currents. 2009;1.

8. Hayward AC, Fragaszy EB, Bermingham A, Wang L, Copas A, Edmunds WJ, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. The Lancet Respiratory Medicine. 2014.

9. Longini IM, Nizam A, Xu S, Ungchusak K, Hanshaoworakul W, Cummings DA, et al. Containing pandemic influenza at the source. Science. 2005;309(5737):1083-7.

10. de Blasio BF, Iversen BG, Tomba GS. Effect of Vaccines and Antivirals during the Major 2009 A (H1N1) Pandemic Wave in Norway–And the Influence of Vaccination Timing. PloS one. 2012;7(1):e30018.

11. Edwards CH, Tomba GS, de Blasio BF. Influenza in workplaces: transmission, workers' adherence to sick leave advice and European sick leave recommendations. The European Journal of Public Health 2016;26(3):478-85.

12. Ministry of Health and Care Services. Norwegian National Influenza Pandemic Preparedness Plan 2014.

13. Statistics Norway. Level of living 2009 - Cross sectional study - Working conditions 2012-10-09 ed: Norwegian Social Science Data Services (NSD); 2009.

14. Brouwer WB, Van Exel N, Koopmanschap M, Rutten F. Productivity costs before and after absence from work: as important as common? Health Policy. 2002;61(2):173-87.

15. Keech M, Scott A, Ryan P. The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. Occupational Medicine. 1998;48(2):85-90.

16. Palmer LA, Rousculp MD, Johnston SS, Mahadevia PJ, Nichol KL. Effect of influenza-like illness and other wintertime respiratory illnesses on worker productivity: The child and household influenza-illness and employee function (CHIEF) study. Vaccine. 2010;28(31):5049-56.

17. Smith A. A review of the effects of colds and influenza on human performance. Occupational Medicine. 1989;39(2):65-8.

18. Den norske legeforening. Normaltariff for fastleger og legevakt 2013-2014 [07.07.2014]. Available from: http://normaltariffen.legeforeningen.no/pdf/Fastlegetariff_2013.pdf.

19. Romøren TI, Torjesen DO, Landmark B. Promoting coordination in Norwegian health care. International Journal of Integrated Care. 2011;11(Special 10th Anniversary Edition).

20. Foreningen for utgivelse av norsk legemiddelhåndbok. Norsk legemiddel håndbok for helsepersonell 2013. Oslo: Fagbokforlaget; 2013.

21. Meier CR, Napalkov PN, Wegmüller Y, Jefferson T, Jick H. Population-Based Study on Incidence, Risk Factors, Clinical Complications and Drug Utilisation Associated with Influenza in the United Kingdom. European Journal of Clinical Microbiology and Infectious Diseases. 2000;19(11):834-42. doi: 10.1007/s100960000376.

22. Norwegian Directorate of Health. Innsatsstyrt finansiering 2013. 2012.

23. Norwegian Directorate for Civil Protection Rapport Ny influensa A (H1N1) 2009 Gjennomgang av erfaringene i Norge. 2nd ed, 2010.

24. Baguelin M, Jit M, Miller E, Edmunds WJ. Health and economic impact of the seasonal influenza vaccination programme in England. Vaccine. 2012;30(23):3459-62.

25. Van Hoek AJ, Underwood A, Jit M, Miller E, Edmunds WJ. The impact of pandemic influenza H1N1 on health-related quality of life: a prospective population-based study. PLoS One. 2011;6(3):e17030.

26. EuroQol Research Foundation. EQ-5D 2015. Available from: http://www.euroqol.org/.

27. Statistics Norway. 2013 [updated 30.08.2013]. Available from: http://www.ssb.no.

28. Gran JM, Kacelnik O, Grjibovski AM, Aavitsland P, Iversen BG. Counting pandemic deaths: comparing reported numbers of deaths from influenza A (H1N1) pdm09 with estimated excess mortality. Influenza and other respiratory viruses. 2013;7(6):1370-9.

29. Norwegian Labour and Welfare Administration. Sickness benefits for self-employed and freelancers. 2015

30. National Insurance Act. Act 1997-02-28-19. Act relating to national insurance Avd I 1997 Nr. 5LOV-1997-02-28-19 [04.07.2014]. Available from: https://lovdata.no/dokument/NL/lov/1997-02-28-19.

31. Intensjonsavtale om et mer inkluderende arbeidsliv 4. mars 2014 - 31. desember 2018 (IA-avtalen) 2014 [04.07.2014]. Available from: https://www.regjeringen.no/globalassets/upload/asd/dokumenter/2014/ia_20142018/signert_ia_avtale.pdf.

32. Ose SO, Dyrstad K, Slettebak R, et al. Evaluering av IA-avtalen (2010-2013) 2013 [03.07.2014]. Available from: http://www.sintef.no/prosjekter/evaluering-av-ia-avtalen-2010-2013/.

33. Arbeids- og sosialdepartementet. Working Environment act. Act 2005-06-17-62. Act relating to working environment, working hours an employment protection, etc. as subsequently amended, last by act 23 February 2007-10. 2005

34. Ministry of Children Equality and Social Inclusion. Meld.St.6 En helhetlig integreringspolitikk Mangfold og fellesskap, 2013.

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.Hansen.Edwards@fhi.no

SUPPLEMENTARY FILE 2: TABLES

Overview of tables

Section I: Scenarios with high symptomatic proportion (65% children, and 55% adults assumed to be symptomatic), without assuming extra mixing

A. Seasonal influenza

i. Epidemiology (R_eff = 1.2, 1.3, 1.4)

Table S1 Seasonal influenza with R_eff=1.2: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to Baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	85186	19 %	12733 (10835; 14834)	614 (258; 1208)	61 (25; 122)	129 (68; 193)	611325 (0.35)
	1	37294	8 %	5575 (4744; 6494)	269 (113; 529)	27 (11; 53)	57 (30; 84)	635984 (0.37)
	1.5	18816	4 %	2813 (2393; 3277)	136 (57; 267)	13 (6; 27)	29 (15; 43)	613489 (0.4)
	2	5791	1 %	866 (737; 1008)	42 (18; 82)	4 (2; 8)	9 (5; 13)	593800 (0.42)
80%	0.5	127113	28 %	19000 (16168; 22136)	916 (385; 1803)	91 (37; 182)	193 (101; 287)	621708 (0.31)
	1	70682	16 %	10565 (8990; 12309)	509 (214; 1003)	50 (21; 101)	107 (56; 160)	669174 (0.33)
	1.5	48793	11 %	7293 (6206; 8497)	351 (148; 692)	35 (14; 70)	74 (39; 110)	650302 (0.36)
	2	33292	7 %	4976 (4235; 5797)	240 (101; 472)	24 (10; 48)	50 (26; 75)	631865 (0.38)
	4	26413	6 %	3948 (3360; 4600)	190 (80; 375)	19 (8; 38)	40 (21; 60)	576120 (0.42)
90%	0.5	154284	34 %	23062 (19624; 26867)	1111 (468; 2188)	110 (45; 221)	234 (123; 349)	617623 (0.29)
	1	92579	20 %	13838 (11775; 16122)	667 (281; 1313)	66 (27; 133)	140 (74; 209)	682881 (0.31)
	1.5	68498	15 %	10239 (8712; 11928)	493 (208; 972)	49 (20; 98)	104 (54; 155)	668042 (0.33)
	2	51434	11 %	7688 (6542; 8957)	370 (156; 730)	37 (15; 74)	78 (41; 116)	651487 (0.35)
	4	43842	10 %	6553 (5576; 7635)	316 (133; 622)	31 (13; 63)	66 (35; 99)	592942 (0.39)
*65 %	4	453772		67828 (57717; 79020)	3268 (1376; 6436)	324 (133; 651)	688 (361; 1026)	543911 (0.47)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S2: Seasonal influenza with R_eff=1.3: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	80329	12 %	12007 (10217; 13989)	579 (244; 1139)	57 (24; 115)	122 (64; 182)	979137 (0.34)
	1	35014	5 %	5234 (4454; 6097)	252 (106; 497)	25 (10; 50)	53 (28; 79)	969403 (0.36)
	1.5	17639	3 %	2637 (2244; 3072)	127 (53; 250)	13 (5; 25)	27 (14; 40)	918680 (0.39)
	2	5424	1 %	811 (690; 945)	39 (16; 77)	4 (2; 8)	8 (4; 12)	878566 (0.41)
80%	0.5	121972	18 %	18232 (15514; 21240)	879 (370; 1730)	87 (36; 175)	185 (97; 276)	1046862 (0.3)
	1	67693	10 %	10119 (8610; 11788)	488 (205; 960)	48 (20; 97)	103 (54; 153)	1054240 (0.32)
	1.5	46816	7 %	6998 (5955; 8153)	337 (142; 664)	33 (14; 67)	71 (37; 106)	1001315 (0.34)
	2	32090	5 %	4797 (4082; 5588)	231 (97; 455)	23 (9; 46)	49 (26; 73)	958133 (0.37)
	4	25562	4 %	3821 (3251; 4451)	184 (78; 363)	18 (8; 37)	39 (20; 58)	866658 (0.41)
90%	0.5	149387	22 %	22330 (19001; 26014)	1076 (453; 2119)	107 (44; 214)	227 (119; 338)	1079306 (0.28)
	1	89371	13 %	13359 (11367; 15563)	644 (271; 1268)	64 (26; 128)	136 (71; 202)	1101523 (0.3)
	1.5	66182	10 %	9893 (8418; 11525)	477 (201; 939)	47 (19; 95)	100 (53; 150)	1049057 (0.32)
	2	49821	7 %	7447 (6337; 8676)	359 (151; 707)	36 (15; 71)	76 (40; 113)	1005026 (0.34)
	4	42574	6 %	6364 (5415; 7414)	307 (129; 604)	30 (13; 61)	65 (34; 96)	906483 (0.38)
*65%	4	670396		100208 (85270; 116743)	4829 (2033; 9508)	479 (197; 961)	1017 (533; 1516)	799480 (0.45)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S3: Seasonal influenza with R_eff=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	75094	9 %	11225 (9551; 13077)	541 (228; 1065)	54 (22; 108)	114 (60; 170)	1289546 (0.33)
	1	32607	4 %	4874 (4147; 5678)	235 (99; 462)	23 (10; 47)	49 (26; 74)	1249090 (0.35)
	1.5	16411	2 %	2453 (2087; 2858)	118 (50; 233)	12 (5; 24)	25 (13; 37)	1173732 (0.38)
	2	5042	1 %	754 (641; 878)	36 (15; 72)	4 (1; 7)	8 (4; 11)	1115893 (0.4)
80%	0.5	115520	14 %	17268 (14693; 20117)	832 (350; 1638)	82 (34; 166)	175 (92; 261)	1409130 (0.29)
	1	63970	8 %	9562 (8137; 11140)	461 (194; 907)	46 (19; 92)	97 (51; 145)	1379795 (0.31)
	1.5	44285	5 %	6620 (5633; 7712)	319 (134; 628)	32 (13; 63)	67 (35; 100)	1296818 (0.34)
	2	30449	4 %	4551 (3873; 5302)	219 (92; 432)	22 (9; 44)	46 (24; 69)	1231906 (0.36)
	4	24317	3 %	3635 (3093; 4235)	175 (74; 345)	17 (7; 35)	37 (19; 55)	1109496 (0.4)
90%	0.5	142437	17 %	21291 (18117; 24804)	1026 (432; 2020)	102 (42; 204)	216 (113; 322)	1475222 (0.27)
	1	84951	10 %	12698 (10805; 14793)	612 (258; 1205)	61 (25; 122)	129 (68; 192)	1457307 (0.29)
	1.5	62932	7 %	9407 (8005; 10959)	453 (191; 893)	45 (19; 90)	95 (50; 142)	1371294 (0.31)
	2	47462	6 %	7094 (6037; 8265)	342 (144; 673)	34 (14; 68)	72 (38; 107)	1302964 (0.33)
	4	40612	5 %	6071 (5166; 7072)	293 (123; 576)	29 (12; 58)	62 (32; 92)	1169655 (0.37)
*65%	4	852243		127390 (108399; 148410)	6138 (2584; 12088)	608 (251; 1222)	1292 (678; 1927)	1011674 (0.45)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_eff = 1.2, 1.3, 1.4)

Table S4: Seasonal influenza with R_eff=1.2: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	1490	3227	872	6807	905	-3867	1326	330	1366	989 (657; 1594)	4
	1	23954	2411	382	2980	396	22607	581	145	350	185 (41; 450)	12
	1.5	20708	1757	193	1504	200	20569	293	73	83	-1 (-73; 133)	13
	2	17008	1234	59	463	62	17659	90	22	-90	-115 (-138; -74)	14
80 %	0.5	-19631	5276	1301	10232	1351	-27238	2015	493	2293	1697 (1214; 2617)	2
	1	13041	4456	723	5689	751	10332	1120	274	1015	683 (416; 1197)	6
	1.5	13018	3799	499	3928	519	11872	773	189	652	422 (238; 777)	9
	2	11291	3274	341	2680	354	11191	528	129	413	257 (131; 498)	11
	4	-5723	2034	270	2111	281	-6351	411	102	476	359 (256; 547)	10
90 %	**0.5	-35480	6721	1579	12419	1640	-44397	2445	598	2898	2172 (1589; 3294)	1
	1	4247	5901	948	7452	984	764	1467	359	1459	1023 (674; 1697)	3
	1.5	6641	5244	701	5514	728	4943	1086	265	1035	714 (454; 1210)	5
	2	6393	4719	526	4140	547	5900	815	199	755	515 (319; 885)	8
	4	-10414	3479	449	3503	466	-11353	682	170	798	604 (433; 915)	7
*65 %	4	211806	0	4645	36094	4825	257369	7080	1764	10833	8823 (7078; 12075)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S5: Seasonal influenza with R_eff=1.3: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	43872	3227	822	6419	854	39004	1250	310	852	496 (186; 1067)	4
	1	53290	2411	358	2798	372	52172	545	135	13	-144 (-278; 106)	12
	1.5	39382	1757	181	1410	188	39362	274	68	-127	-206 (-273; -80)	13
	2	27958	1234	56	433	58	28646	84	21	-208	-231 (-253; -193)	14
80 %	0.5	34259	5276	1248	9818	1297	27171	1932	471	1655	1082 (620; 1967)	2
	1	53156	4456	693	5449	720	50750	1072	261	554	237 (-21; 728)	8
	1.5	41397	3799	479	3768	498	40451	741	181	329	109 (-68; 449)	10
	2	31125	3274	328	2583	341	31147	508	124	190	40 (-81; 273)	11
	4	1855	2034	262	2043	272	1313	398	99	384	272 (170; 453)	7
90 %	**0.5	25474	6721	1529	12025	1589	17052	2366	577	2192	1489 (923; 2576)	1
	1	51220	5901	915	7194	950	48062	1415	345	925	507 (167; 1153)	3
	1.5	41271	5244	677	5327	704	39807	1048	255	642	333 (81; 812)	6
	2	31984	4719	510	4010	530	31653	789	192	466	234 (43; 595)	9
	4	2077	3479	436	3402	453	1266	662	164	649	463 (293; 764)	5
*65 %	4	311171	0	6862	53324	7134	378491	10455	2600	16007	13038 (10459; 17843)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S6: Seasonal influenza with R_eff=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)					Mean benefits			Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	81422	3227	769	6001	799	77081	1168	289	382	47 (-242; 582)	5
	1	78925	2411	334	2606	347	78049	507	126	-289	-434 (-559; -201)	12
	1.5	55612	1757	168	1311	175	55716	255	63	-313	-386 (-449; -269)	14
	2	37416	1234	52	403	54	38143	78	19	-311	-332 (-352; -296)	13
80 %	0.5	82904	5276	1182	9299	1229	76469	1828	445	1049	505 (67; 1345)	2
	1	88826	4456	655	5149	681	86797	1012	246	127	-173 (-416; 291)	9
	1.5	66580	3799	453	3565	471	65890	701	170	29	-179 (-347; 142)	10
	2	48709	3274	312	2451	324	48897	482	117	-17	-159 (-275; 63)	11
	4	8790	2034	249	1943	259	8374	378	94	293	187 (88; 360)	6
90 %	**0.5	81119	6721	1458	11465	1516	73402	2255	549	1506	838 (298; 1873)	1
	1	93400	5901	870	6838	904	90690	1344	327	420	22 (-301; 636)	4
	1.5	72285	5244	644	5066	670	71150	996	242	270	-23 (-263; 434)	7
	2	54891	4719	486	3820	505	54799	751	183	192	-28 (-211; 316)	8
	4	13555	3479	416	3245	432	12941	631	156	499	322 (158; 611)	3
*65 %	4	393610	0	8723	67789	9077	479198	13285	3299	20348	16573 (13298; 22686)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

B. Moderate pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S7 Moderate pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	109164	10 %	16317 (13885; 19010)	786 (331; 1548)	78 (32; 157)	166 (87; 247)	2513158 (0.19)
	1	47149	4 %	7048 (5997; 8211)	340 (143; 669)	34 (14; 68)	72 (37; 107)	2516138 (0.19)
	1.5	23671	2 %	3538 (3011; 4122)	170 (72; 336)	17 (7; 34)	36 (19; 54)	2431854 (0.2)
	2	7250	1 %	1084 (922; 1263)	52 (22; 103)	5 (2; 10)	11 (6; 16)	2365359 (0.21)
80%	0.5	176143	16 %	26329 (22404; 30674)	1269 (534; 2498)	126 (52; 253)	267 (140; 398)	2774765 (0.16)
	1	99304	9 %	14844 (12631; 17293)	715 (301; 1408)	71 (29; 142)	151 (79; 224)	2830269 (0.17)
	1.5	70242	6 %	10500 (8934; 12232)	506 (213; 996)	50 (21; 101)	107 (56; 159)	2749509 (0.18)
	2	49898	4 %	7459 (6347; 8689)	359 (151; 708)	36 (15; 72)	76 (40; 113)	2682841 (0.18)
	4	40919	4 %	6116 (5205; 7126)	295 (124; 580)	29 (12; 59)	62 (33; 93)	2521479 (0.19)
90%	0.5	221326	20 %	33083 (28151; 38542)	1594 (671; 3139)	158 (65; 317)	336 (176; 500)	2908475 (0.15)
	1	134589	12 %	20118 (17119; 23437)	969 (408; 1909)	96 (40; 193)	204 (107; 304)	3009496 (0.15)
	1.5	101715	9 %	15204 (12937; 17713)	733 (308; 1443)	73 (30; 146)	154 (81; 230)	2936109 (0.16)
	2	78731	7 %	11768 (10014; 13710)	567 (239; 1117)	56 (23; 113)	119 (63; 178)	2872537 (0.17)
	4	68589	6 %	10252 (8724; 11944)	494 (208; 973)	49 (20; 98)	104 (55; 155)	2700139 (0.18)
*65%	4	1125097		168175 (143104; 195925)	8104 (3412; 15958)	803 (331; 1613)	1706 (895; 2543)	2224435 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S8: Moderate pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	91511	6 %	13679 (11640; 15936)	659 (277; 1298)	65 (27; 131)	139 (73; 207)	3473688 (0.18)
	1	39318	3 %	5877 (5001; 6847)	283 (119; 558)	28 (12; 56)	60 (31; 89)	3396347 (0.19)
	1.5	19698	1 %	2944 (2505; 3430)	142 (60; 279)	14 (6; 28)	30 (16; 45)	3253841 (0.2)
	2	6028	0 %	901 (767; 1050)	43 (18; 85)	4 (2; 9)	9 (5; 14)	3145771 (0.2)
80%	0.5	149846	10 %	22398 (19059; 26094)	1079 (454; 2125)	107 (44; 215)	227 (119; 339)	3944812 (0.15)
	1	84044	6 %	12563 (10690; 14635)	605 (255; 1192)	60 (25; 120)	127 (67; 190)	3899235 (0.16)
	1.5	59422	4 %	8882 (7558; 10348)	428 (180; 843)	42 (17; 85)	90 (47; 134)	3745061 (0.17)
	2	42244	3 %	6314 (5373; 7356)	304 (128; 599)	30 (12; 61)	64 (34; 95)	3626021 (0.18)
	4	34695	2 %	5186 (4413; 6042)	250 (105; 492)	25 (10; 50)	53 (28; 78)	3394931 (0.19)
90%	0.5	189865	13 %	28380 (24149; 33063)	1368 (576; 2693)	136 (56; 272)	288 (151; 429)	4219177 (0.14)
	1	114653	8 %	17138 (14583; 19966)	826 (348; 1626)	82 (34; 164)	174 (91; 259)	4206207 (0.15)
	1.5	86523	6 %	12933 (11005; 15067)	623 (262; 1227)	62 (25; 124)	131 (69; 196)	4049294 (0.15)
	2	66968	4 %	10010 (8518; 11662)	482 (203; 950)	48 (20; 96)	102 (53; 151)	3926011 (0.16)
	4	58372	4 %	8725 (7425; 10165)	420 (177; 828)	42 (17; 84)	89 (46; 132)	3674339 (0.17)
*65%	4	1492094		223033 (189784; 259834)	10747 (4525; 21163)	1065 (439; 2139)	2263 (1187; 3373)	2949234 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S9: Moderate pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	76740	4 %	11471 (9761; 13364)	553 (233; 1088)	55 (23; 110)	116 (61; 173)	4175375 (0.17)
	1	32850	2 %	4910 (4178; 5721)	237 (100; 466)	23 (10; 47)	50 (26; 74)	4035387 (0.18)
	1.5	16437	1 %	2457 (2091; 2862)	118 (50; 233)	12 (5; 24)	25 (13; 37)	3848981 (0.19)
	2	5025	0 %	751 (639; 875)	36 (15; 71)	4 (1; 7)	8 (4; 11)	3709748 (0.2)
80%	0.5	126899	7 %	18968 (16141; 22098)	914 (385; 1800)	91 (37; 182)	192 (101; 287)	4808812 (0.15)
	1	70896	4 %	10597 (9017; 12346)	511 (215; 1006)	51 (21; 102)	108 (56; 160)	4681758 (0.16)
	1.5	50097	3 %	7488 (6372; 8724)	361 (152; 711)	36 (15; 72)	76 (40; 113)	4471246 (0.16)
	2	35652	2 %	5329 (4535; 6208)	257 (108; 506)	25 (10; 51)	54 (28; 81)	4312214 (0.17)
	4	29300	2 %	4380 (3727; 5102)	211 (89; 416)	21 (9; 42)	44 (23; 66)	4029281 (0.18)
90%	0.5	161725	9 %	24174 (20570; 28163)	1165 (490; 2294)	115 (48; 232)	245 (129; 366)	5194371 (0.14)
	1	97147	6 %	14521 (12356; 16917)	700 (295; 1378)	69 (29; 139)	147 (77; 220)	5087180 (0.14)
	1.5	73232	4 %	10946 (9315; 12753)	527 (222; 1039)	52 (22; 105)	111 (58; 166)	4865331 (0.15)
	2	56670	3 %	8471 (7208; 9869)	408 (172; 804)	40 (17; 81)	86 (45; 128)	4696014 (0.16)
	4	49402	3 %	7384 (6284; 8603)	356 (150; 701)	35 (15; 71)	75 (39; 112)	4385040 (0.17)
*65%	4	1758906		262915 (223721; 306297)	12669 (5334; 24947)	1256 (517; 2522)	2667 (1399; 3976)	3472158 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S10: Moderate pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	36981	3227	1117	8723	1164	29204	1724	441	1426	941 (517; 1721)	3
	1	78227	2411	483	3768	503	75885	744	190	-30	-241 (-422; 96)	12
	1.5	62018	1757	242	1892	252	61389	374	96	-252	-358 (-449; -189)	13
	2	47900	1234	74	579	77	48404	114	29	-379	-410 (-439; -358)	14
80 %	0.5	18067	5276	1803	14178	1878	5484	2829	711	2774	1952 (1278; 3216)	2
	1	87467	4456	1016	7993	1059	81854	1594	400	759	298 (-83; 1019)	7
	1.5	79037	3799	719	5654	749	75715	1127	282	355	29 (-241; 541)	10
	2	69723	3274	511	4016	532	67938	800	200	108	-117 (-317; 242)	11
	4	20577	2034	419	3270	436	18487	645	164	456	282 (114; 576)	9
90 %	**0.5	-3233	6721	2265	17815	2360	-18952	3555	894	3749	2718 (1870; 4325)	1
	1	86996	5901	1378	10834	1435	79251	2161	542	1352	729 (209; 1706)	4
	1.5	84859	5244	1041	8187	1084	79791	1632	409	819	353 (-43; 1091)	5
	2	79416	4719	806	6337	839	76152	1263	316	486	135 (-183; 701)	8
	4	29984	3479	702	5481	731	26549	1081	275	810	517 (236; 1008)	6
*65 %	4	849556	0	11516	89492	12003	962567	17912	4690	34343	29395 (25035; 37393)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S11: Moderate pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	134416	3227	937	7313	977	128417	1438	362	129	-281 (-633; 375)	3
	1	140544	2411	402	3142	420	138991	618	156	-800	-974 (-1126; -694)	14
	1.5	100513	1757	202	1574	210	100285	309	78	-713	-799 (-876; -659)	13
	2	69362	1234	62	482	64	69989	95	24	-619	-643 (-670; -599)	10
80 %	0.5	166338	5276	1534	12062	1600	156418	2396	592	801	100 (-471; 1191)	2
	1	195492	4456	860	6765	898	191425	1343	331	-609	-999 (-1323; -387)	8
	1.5	159571	3799	608	4783	635	157344	949	234	-655	-923 (-1161; -494)	12
	2	130620	3274	432	3400	451	129610	675	166	-647	-830 (-1007; -524)	11
	4	56838	2034	355	2772	371	55374	544	136	-21	-160 (-312; 91)	5
90 %	**0.5	178317	6721	1943	15283	2028	165785	3036	750	1345	467 (-266; 1845)	1
	1	225494	5901	1174	9229	1224	219768	1832	452	-409	-927 (-1384; -99)	6
	1.5	193538	5244	886	6965	924	190008	1382	340	-556	-938 (-1291; -310)	7
	2	166726	4719	685	5391	715	164655	1069	263	-610	-896 (-1180; -412)	9
	4	90551	3479	597	4665	623	88145	916	229	17	-219 (-473; 202)	4
*65 %	4	1126217	0	15272	118683	15947	1276119	23709	6165	45580	39025 (33234; 49618)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S12: Moderate pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	210005	3227	785	6132	821	205494	1202	299	-894	-1236 (-1530; -689)	6
	1	187855	2411	336	2625	352	186953	514	128	-1392	-1535 (-1665; -1302)	9
	1.5	129498	1757	168	1313	176	129597	257	64	-1064	-1134 (-1200; -1016)	7
	2	85337	1234	51	402	54	86065	79	20	-799	-817 (-843; -779)	5
80 %	0.5	283680	5276	1299	10215	1358	276085	2022	493	-794	-1385 (-1871; -462)	4
	1	279186	4456	726	5707	759	276450	1129	275	-1690	-2014 (-2292; -1500)	13
	1.5	221679	3799	513	4032	536	220397	797	194	-1450	-1670 (-1876; -1306)	10
	2	177379	3274	365	2870	382	177037	567	138	-1238	-1387 (-1544; -1126)	8
	**4	85121	2034	300	2341	314	84200	458	113	-401	-510 (-652; -294)	1
90 %	0.5	323719	6721	1655	13018	1730	314036	2576	628	-626	-1371 (-1998; -193)	3
	1	333850	5901	994	7820	1039	329897	1547	376	-1818	-2245 (-2643; -1538)	14
	1.5	278121	5244	750	5895	784	275937	1165	283	-1649	-1961 (-2274; -1430)	12
	2	234430	4719	580	4562	606	233401	902	219	-1479	-1709 (-1969; -1291)	11
	4	138062	3479	506	3948	529	136560	772	190	-621	-806 (-1043; -443)	2
*65 %	4	1325878	0	18003	139906	18830	1502617	27902	7212	53730	46006 (39177; 58470)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

C. Severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S13: Severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	109164	10 %	21775 (19022; 24763)	2148 (1312; 3292)	364 (219; 565)	244 (128; 364)	2513155 (0.19)
	1	47149	4 %	9405 (8216; 10695)	928 (567; 1422)	157 (95; 244)	105 (55; 157)	2516134 (0.19)
	1.5	23671	2 %	4722 (4125; 5370)	466 (285; 714)	79 (47; 123)	53 (28; 79)	2431850 (0.2)
	2	7250	1 %	1446 (1263; 1645)	143 (87; 219)	24 (15; 38)	16 (9; 24)	2365355 (0.21)
80%	0.5	176143	16 %	35135 (30693; 39957)	3466 (2118; 5312)	588 (353; 912)	394 (207; 587)	2774762 (0.16)
	1	99304	9 %	19808 (17304; 22526)	1954 (1194; 2995)	331 (199; 514)	222 (117; 331)	2830265 (0.17)
	1.5	70242	6 %	14011 (12240; 15934)	1382 (844; 2118)	234 (141; 364)	157 (82; 234)	2749505 (0.18)
	2	49898	4 %	9953 (8695; 11319)	982 (600; 1505)	166 (100; 258)	112 (59; 166)	2682837 (0.18)
	4	40919	4 %	8162 (7130; 9282)	805 (492; 1234)	137 (82; 212)	92 (48; 136)	2521475 (0.19)
90%	0.5	221326	20 %	44148 (38567; 50206)	4356 (2661; 6675)	738 (444; 1146)	495 (260; 738)	2908472 (0.15)
	1	134589	12 %	26847 (23452; 30531)	2649 (1618; 4059)	449 (270; 697)	301 (158; 449)	3009492 (0.15)
	1.5	101715	9 %	20289 (17724; 23073)	2002 (1223; 3068)	339 (204; 527)	228 (119; 339)	2936105 (0.16)
	2	78731	7 %	15705 (13719; 17860)	1549 (946; 2375)	263 (158; 408)	176 (92; 262)	2872533 (0.17)
	4	68589	6 %	13682 (11952; 15559)	1350 (825; 2069)	229 (138; 355)	153 (80; 229)	2700135 (0.18)
*65%	4	1125097		224424 (196051; 255221)	22142 (13526; 33933)	3754 (2257; 5828)	2517 (1320; 3751)	2224431 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S14: Severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	91511	6 %	18254 (15946; 20759)	1801 (1100; 2760)	305 (184; 474)	205 (107; 305)	3473683 (0.18)
	1	39318	3 %	7843 (6851; 8919)	774 (473; 1186)	131 (79; 204)	88 (46; 131)	3396342 (0.19)
	1.5	19698	1 %	3929 (3432; 4468)	388 (237; 594)	66 (40; 102)	44 (23; 66)	3253836 (0.2)
	2	6028	0 %	1202 (1050; 1367)	119 (72; 182)	20 (12; 31)	13 (7; 20)	3145766 (0.2)
80%	0.5	149846	10 %	29890 (26111; 33992)	2949 (1801; 4519)	500 (301; 776)	335 (176; 500)	3944807 (0.15)
	1	84044	6 %	16764 (14645; 19065)	1654 (1010; 2535)	280 (169; 435)	188 (99; 280)	3899230 (0.16)
	1.5	59422	4 %	11853 (10354; 13479)	1169 (714; 1792)	198 (119; 308)	133 (70; 198)	3745056 (0.17)
	2	42244	3 %	8426 (7361; 9583)	831 (508; 1274)	141 (85; 219)	94 (50; 141)	3626016 (0.18)
	4	34695	2 %	6921 (6046; 7870)	683 (417; 1046)	116 (70; 180)	78 (41; 116)	3394926 (0.19)
90%	0.5	189865	13 %	37873 (33084; 43070)	3737 (2283; 5726)	633 (381; 983)	425 (223; 633)	4219173 (0.14)
	1	114653	8 %	22870 (19979; 26008)	2256 (1378; 3458)	383 (230; 594)	256 (135; 382)	4206202 (0.15)
	1.5	86523	6 %	17259 (15077; 19627)	1703 (1040; 2610)	289 (174; 448)	194 (102; 288)	4049289 (0.15)
	2	66968	4 %	13358 (11669; 15191)	1318 (805; 2020)	223 (134; 347)	150 (79; 223)	3926006 (0.16)
	4	58372	4 %	11644 (10171; 13241)	1149 (702; 1760)	195 (117; 302)	131 (68; 195)	3674334 (0.17)
*65%	4	1492094		297630 (260001; 338472)	29364 (17938; 45001)	4978 (2994; 7729)	3338 (1751; 4975)	2949228 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S15: Severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	76740	4 %	15307 (13372; 17408)	1510 (923; 2314)	256 (154; 397)	172 (90; 256)	4175369 (0.17)
	1	32850	2 %	6553 (5724; 7452)	646 (395; 991)	110 (66; 170)	73 (39; 110)	4035381 (0.18)
	1.5	16437	1 %	3279 (2864; 3729)	323 (198; 496)	55 (33; 85)	37 (19; 55)	3848975 (0.19)
	2	5025	0 %	1002 (876; 1140)	99 (60; 152)	17 (10; 26)	11 (6; 17)	3709742 (0.2)
80%	0.5	126899	7 %	25313 (22112; 28786)	2497 (1526; 3827)	423 (255; 657)	284 (149; 423)	4808806 (0.15)
	1	70896	4 %	14142 (12354; 16082)	1395 (852; 2138)	237 (142; 367)	159 (83; 236)	4681752 (0.16)
	1.5	50097	3 %	9993 (8730; 11364)	986 (602; 1511)	167 (101; 259)	112 (59; 167)	4471240 (0.16)
	2	35652	2 %	7112 (6212; 8087)	702 (429; 1075)	119 (72; 185)	80 (42; 119)	4312208 (0.17)
	4	29300	2 %	5845 (5106; 6647)	577 (352; 884)	98 (59; 152)	66 (34; 98)	4029275 (0.18)
90%	0.5	161725	9 %	32259 (28181; 36686)	3183 (1944; 4878)	540 (324; 838)	362 (190; 539)	5194365 (0.14)
	1	97147	6 %	19378 (16928; 22037)	1912 (1168; 2930)	324 (195; 503)	217 (114; 324)	5087174 (0.14)
	1.5	73232	4 %	14608 (12761; 16612)	1441 (880; 2209)	244 (147; 379)	164 (86; 244)	4865326 (0.15)
	2	56670	3 %	11304 (9875; 12855)	1115 (681; 1709)	189 (114; 294)	127 (67; 189)	4696009 (0.16)
	4	49402	3 %	9854 (8608; 11207)	972 (594; 1490)	165 (99; 256)	111 (58; 165)	4385034 (0.17)
*65%	4	1758906		350851 (306493; 398996)	34615 (21145; 53048)	5868 (3529; 9111)	3934 (2064; 5864)	3472152 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S16: Severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	36979	3228	1490	24870	1222	12624	1913	651	1784	1312 (866; 2106)	4
	1	78221	2411	644	10742	528	68719	826	281	125	-79 (-272; 264)	12
	1.5	62013	1757	323	5393	265	57789	414	141	-175	-277 (-374; -105)	13
	2	47896	1235	99	1652	81	47299	127	43	-355	-386 (-417; -333)	14
80 %	0.5	18051	5275	2405	40253	1971	-21303	3139	1049	3356	2554 (1838; 3839)	2
	1	87452	4455	1356	22693	1111	66746	1768	590	1087	639 (230; 1359)	6
	1.5	79022	3799	959	16052	786	65024	1250	416	587	273 (-20; 782)	10
	2	69708	3274	681	11403	558	60339	887	295	272	54 (-159; 415)	11
	4	20605	2034	559	9322	458	12301	715	242	590	422 (243; 722)	9
90 %	**0.5	-3261	6720	3022	50578	2477	-52618	3944	1318	4481	3479 (2570; 5087)	1
	1	86969	5900	1838	30757	1506	58769	2396	799	1797	1194 (635; 2168)	3
	1.5	84832	5244	1389	23244	1138	64304	1810	603	1154	705 (275; 1438)	5
	2	79388	4719	1075	17992	881	64160	1400	466	746	403 (64; 974)	8
	4	30029	3480	936	15626	768	16179	1199	406	1034	753 (453; 1254)	7
*65 %	4	849564	0	15361	256371	12601	1133896	19916	6917	38094	33367 (28728; 41449)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S17: Severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	134406	3228	1249	20848	1026	114510	1594	534	426	30 (-345; 693)	3
	1	140533	2411	537	8957	441	133008	684	229	-672	-840 (-1002; -555)	14
	1.5	100505	1757	269	4488	221	97285	343	115	-649	-733 (-815; -590)	13
	2	69357	1235	82	1373	68	69068	105	35	-599	-622 (-651; -578)	12
80 %	0.5	166319	5275	2046	34243	1680	133624	2654	873	1291	612 (-4; 1702)	2
	1	195473	4455	1147	19206	942	178632	1487	489	-334	-710 (-1060; -101)	8
	1.5	159551	3799	811	13579	666	148293	1051	345	-461	-721 (-975; -291)	10
	2	130599	3274	577	9654	474	123169	747	245	-509	-688 (-875; -381)	11
	4	56873	2034	474	7904	389	50140	602	201	91	-42 (-206; 209)	5
90 %	**0.5	178280	6720	2592	43389	2129	136891	3362	1107	1966	1114 (329; 2486)	1
	1	225459	5900	1565	26201	1286	202307	2029	666	-34	-536 (-1026; 292)	6
	1.5	193502	5244	1181	19773	970	176822	1530	502	-273	-647 (-1022; -18)	7
	2	166691	4719	914	15304	751	154441	1184	388	-391	-670 (-974; -183)	9
	4	90609	3480	797	13298	654	79339	1014	338	205	-21 (-295; 403)	4
*65 %	4	1126228	0	20371	339996	16741	1503337	26343	9092	50532	44255 (38108; 54983)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S18: Severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	209988	3228	1048	17483	862	193823	1330	441	-647	-979 (-1292; -418)	5
	1	187840	2411	448	7484	369	181949	569	188	-1286	-1426 (-1563; -1186)	9
	1.5	129487	1757	224	3745	185	127091	285	94	-1011	-1079 (-1150; -959)	7
	2	85330	1235	69	1145	56	85294	87	29	-783	-801 (-827; -762)	6
80 %	0.5	283659	5275	1733	28999	1425	256776	2236	727	-382	-957 (-1478; -36)	3
	1	279165	4455	968	16201	796	265654	1248	405	-1461	-1772 (-2075; -1261)	13
	1.5	221657	3799	684	11448	563	212760	882	286	-1288	-1502 (-1722; -1139)	10
	2	177355	3274	487	8147	401	171594	627	203	-1123	-1266 (-1435; -1007)	8
	**4	85161	2034	400	6675	329	79791	506	166	-307	-414 (-563; -194)	2
90 %	0.5	323676	6720	2208	36958	1816	289414	2850	926	-101	-816 (-1500; 348)	1
	1	333809	5900	1326	22200	1091	315091	1711	555	-1503	-1921 (-2344; -1217)	14
	1.5	278079	5244	1000	16735	823	264765	1289	417	-1411	-1715 (-2049; -1184)	12
	2	234388	4719	774	12950	637	224746	997	322	-1295	-1518 (-1796; -1102)	11
	4	138129	3480	674	11255	555	129124	854	281	-463	-643 (-892; -275)	4
*65 %	4	1325894	0	24014	400794	19768	1770469	30986	10636	59545	52139 (44898; 64795)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

D. Very severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S19: Very severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	109164	10 %	27237 (24244; 30447)	3785 (2640; 5241)	944 (648; 1325)	761 (399; 1133)	2513148 (0.19)
	1	47149	4 %	11764 (10471; 13150)	1635 (1140; 2264)	408 (280; 572)	329 (172; 489)	2516126 (0.19)
	1.5	23671	2 %	5906 (5257; 6602)	821 (572; 1136)	205 (141; 287)	165 (86; 246)	2431842 (0.2)
	2	7250	1 %	1809 (1610; 2022)	251 (175; 348)	63 (43; 88)	51 (26; 75)	2365347 (0.21)
80%	0.5	176143	16 %	43949 (39119; 49129)	6107 (4259; 8457)	1522 (1046; 2138)	1228 (643; 1828)	2774755 (0.16)
	1	99304	9 %	24777 (22054; 27697)	3443 (2401; 4768)	858 (590; 1205)	692 (363; 1030)	2830258 (0.17)
	1.5	70242	6 %	17526 (15600; 19591)	2435 (1699; 3372)	607 (417; 852)	490 (256; 729)	2749498 (0.18)
	2	49898	4 %	12450 (11082; 13917)	1730 (1207; 2396)	431 (296; 606)	348 (182; 518)	2682830 (0.18)
	4	40919	4 %	10210 (9087; 11413)	1419 (989; 1965)	354 (243; 497)	285 (149; 425)	2521468 (0.19)
90%	0.5	221326	20 %	55222 (49153; 61731)	7673 (5352; 10626)	1913 (1314; 2686)	1543 (808; 2297)	2908465 (0.15)
	1	134589	12 %	33581 (29890; 37539)	4666 (3255; 6462)	1163 (799; 1633)	938 (491; 1397)	3009486 (0.15)
	1.5	101715	9 %	25378 (22589; 28370)	3526 (2460; 4883)	879 (604; 1234)	709 (371; 1055)	2936098 (0.16)
	2	78731	7 %	19644 (17485; 21959)	2730 (1904; 3780)	681 (467; 955)	549 (287; 817)	2872526 (0.17)
	4	68589	6 %	17113 (15233; 19130)	2378 (1659; 3293)	593 (407; 832)	478 (250; 712)	2700128 (0.18)
*65%	4	1125097		280718 (249867; 313805)	39006 (27206; 54017)	9725 (6680; 13653)	7844 (4108; 11675)	2224423 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S20: Very severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	91511	6 %	22832 (20323; 25524)	3173 (2213; 4393)	791 (543; 1111)	638 (334; 950)	3473673 (0.18)
	1	39318	3 %	9810 (8732; 10966)	1363 (951; 1888)	340 (233; 477)	274 (144; 408)	3396333 (0.19)
	1.5	19698	1 %	4915 (4375; 5494)	683 (476; 946)	170 (117; 239)	137 (72; 204)	3253826 (0.2)
	2	6028	0 %	1504 (1339; 1681)	209 (146; 289)	52 (36; 73)	42 (22; 63)	3145756 (0.2)
80%	0.5	149846	10 %	37387 (33279; 41794)	5195 (3623; 7194)	1295 (890; 1818)	1045 (547; 1555)	3944798 (0.15)
	1	84044	6 %	20969 (18665; 23441)	2914 (2032; 4035)	726 (499; 1020)	586 (307; 872)	3899221 (0.16)
	1.5	59422	4 %	14826 (13197; 16574)	2060 (1437; 2853)	514 (353; 721)	414 (217; 617)	3745047 (0.17)
	2	42244	3 %	10540 (9382; 11782)	1465 (1022; 2028)	365 (251; 513)	295 (154; 438)	3626007 (0.18)
	4	34695	2 %	8657 (7705; 9677)	1203 (839; 1666)	300 (206; 421)	242 (127; 360)	3394917 (0.19)
90%	0.5	189865	13 %	47372 (42166; 52956)	6582 (4591; 9116)	1641 (1127; 2304)	1324 (693; 1970)	4219164 (0.14)
	1	114653	8 %	28607 (25463; 31978)	3975 (2772; 5505)	991 (681; 1391)	799 (419; 1190)	4206193 (0.15)
	1.5	86523	6 %	21588 (19215; 24132)	3000 (2092; 4154)	748 (514; 1050)	603 (316; 898)	4049280 (0.15)
	2	66968	4 %	16709 (14873; 18678)	2322 (1619; 3215)	579 (398; 813)	467 (245; 695)	3925997 (0.16)
	4	58372	4 %	14564 (12964; 16281)	2024 (1412; 2802)	505 (347; 708)	407 (213; 606)	3674324 (0.17)
*65%	4	1492094		372285 (331371; 416165)	51730 (36081; 71636)	12897 (8859; 18107)	10402 (5448; 15483)	2949219 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S21: Very severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	76740	4 %	19147 (17043; 21404)	2661 (1856; 3684)	663 (456; 931)	535 (280; 796)	4175358 (0.17)
	1	32850	2 %	8196 (7295; 9162)	1139 (794; 1577)	284 (195; 399)	229 (120; 341)	4035370 (0.18)
	1.5	16437	1 %	4101 (3650; 4585)	570 (397; 789)	142 (98; 199)	115 (60; 171)	3848964 (0.19)
	2	5025	0 %	1254 (1116; 1402)	174 (122; 241)	43 (30; 61)	35 (18; 52)	3709731 (0.2)
80%	0.5	126899	7 %	31662 (28182; 35394)	4400 (3069; 6092)	1097 (753; 1540)	885 (463; 1317)	4808796 (0.15)
	1	70896	4 %	17689 (15745; 19774)	2458 (1714; 3404)	613 (421; 860)	494 (259; 736)	4681741 (0.16)
	1.5	50097	3 %	12499 (11126; 13973)	1737 (1211; 2405)	433 (297; 608)	349 (183; 520)	4471229 (0.16)
	2	35652	2 %	8895 (7918; 9944)	1236 (862; 1712)	308 (212; 433)	249 (130; 370)	4312197 (0.17)
	4	29300	2 %	7311 (6507; 8172)	1016 (709; 1407)	253 (174; 356)	204 (107; 304)	4029264 (0.18)
90%	0.5	161725	9 %	40351 (35917; 45107)	5607 (3911; 7765)	1398 (960; 1963)	1127 (591; 1678)	5194354 (0.14)
	1	97147	6 %	24239 (21575; 27096)	3368 (2349; 4664)	840 (577; 1179)	677 (355; 1008)	5087163 (0.14)
	1.5	73232	4 %	18272 (16264; 20425)	2539 (1771; 3516)	633 (435; 889)	511 (267; 760)	4865315 (0.15)
	2	56670	3 %	14139 (12586; 15806)	1965 (1370; 2721)	490 (336; 688)	395 (207; 588)	4695998 (0.16)
	4	49402	3 %	12326 (10971; 13779)	1713 (1195; 2372)	427 (293; 600)	344 (180; 513)	4385023 (0.17)
*65%	4	1758906		438856 (390626; 490583)	60980 (42533; 84446)	15203 (10443; 21345)	12262 (6423; 18252)	3472141 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S22: Very severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	36980	3226	1863	46903	1280	-9840	3055	2028	3155	2757 (2186; 3598)	4
	1	78230	2409	805	20258	553	59024	1318	875	716	546 (296; 909)	12
	1.5	62021	1756	404	10170	277	52925	662	439	122	37 (-89; 218)	13
	2	47903	1234	124	3115	85	45813	202	134	-265	-290 (-330; -234)	14
80 %	0.5	18054	5277	3007	75685	2065	-57425	4979	3268	5565	4889 (3986; 6256)	2
	1	87457	4456	1695	42669	1164	46386	2803	1837	2329	1953 (1435; 2724)	6
	1.5	79029	3799	1199	30181	823	50625	1980	1297	1464	1200 (830; 1743)	9
	2	69716	3274	852	21440	585	50113	1405	920	894	707 (439; 1096)	11
	4	20557	2033	698	17581	480	3831	1139	753	1100	956 (733; 1280)	10
90 %	**0.5	-3252	6722	3778	95099	2594	-98001	6257	4107	7256	6411 (5269; 8130)	1
	1	86982	5901	2297	57830	1577	31178	3798	2490	3480	2972 (2266; 4015)	3
	1.5	84845	5244	1736	43705	1192	43456	2868	1878	2424	2040 (1500; 2831)	5
	2	79403	4718	1344	33829	923	48026	2217	1451	1728	1432 (1011; 2045)	8
	4	29951	3477	1171	29470	804	1984	1910	1263	1890	1648 (1275; 2188)	7
*65 %	4	849562	0	19205	480727	13196	1362690	32010	21549	52521	48597 (42719; 57176)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S23: Very severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	134422	3226	1562	39318	1075	95693	2531	1665	1555	1220 (741; 1924)	3
	1	140551	2409	671	16893	462	124935	1087	715	-187	-328 (-537; -27)	12
	1.5	100519	1756	336	8463	231	93244	544	358	-407	-476 (-582; -325)	13
	2	69366	1234	103	2590	71	67837	167	110	-525	-545 (-580; -498)	14
80 %	0.5	166326	5277	2558	64385	1759	102901	4185	2721	3136	2561 (1793; 3718)	2
	1	195483	4456	1435	36112	987	161406	2344	1522	698	380 (-59; 1029)	7
	1.5	159562	3799	1014	25532	698	136117	1655	1074	267	43 (-273; 504)	10
	2	130611	3274	721	18151	496	114517	1175	762	8	-150 (-379; 181)	11
	4	56813	2033	592	14907	407	42939	954	625	516	400 (201; 676)	8
90 %	**0.5	178298	6722	3241	81581	2229	97969	5302	3447	4303	3582 (2595; 5050)	1
	1	225478	5901	1957	49264	1346	178812	3196	2076	1373	941 (329; 1830)	4
	1.5	193523	5244	1477	37177	1016	159097	2410	1564	787	464 (-1; 1139)	6
	2	166712	4718	1143	28775	786	140726	1863	1208	428	184 (-189; 704)	9
	4	90510	3477	996	25080	685	67226	1606	1052	920	724 (389; 1188)	5
*65 %	4	1126220	0	25469	637537	17532	1806758	42237	28324	69519	64295 (56519; 75690)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S24: Very severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	210016	3226	1310	32972	903	178057	2102	1373	286	8 (-395; 595)	3
	1	187865	2409	561	14114	386	175213	899	587	-888	-1004 (-1180; -751)	14
	1.5	129505	1756	281	7062	193	123725	450	294	-812	-869 (-959; -742)	13
	2	85342	1234	86	2159	59	84272	138	90	-722	-737 (-768; -697)	12
80 %	0.5	283669	5277	2166	54526	1493	230762	3510	2265	1157	669 (17; 1649)	2
	1	279177	4456	1210	30462	834	251126	1958	1262	-603	-872 (-1247; -322)	8
	1.5	221670	3799	855	21526	589	202500	1382	890	-683	-870 (-1140; -479)	10
	2	177370	3274	609	15319	419	164297	982	632	-693	-821 (-1024; -539)	11
	4	85093	2033	500	12589	345	73692	798	519	46	-47 (-226; 190)	5
90 %	**0.5	323700	6722	2761	69490	1902	256269	4472	2885	1859	1246 (396; 2499)	1
	1	333833	5901	1658	41742	1143	295191	2682	1728	-328	-694 (-1213; 65)	6
	1.5	278105	5244	1250	31466	862	249771	2020	1300	-527	-793 (-1203; -223)	7
	2	234414	4718	967	24350	667	213148	1562	1005	-612	-812 (-1142; -363)	9
	4	138015	3477	843	21226	581	118842	1346	875	134	-25 (-325; 374)	4
*65 %	4	1325880	0	30024	751539	20701	2128143	49577	33136	81783	75612 (66466; 89011)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Section II: Scenarios with high symptomatic proportion (65% children, and 55% adults assumed to be symptomatic), with extra mixing

A. Seasonal influenza

i. Epidemiology (R_eff = 1.2, 1.3, 1.4)

Table S25: Seasonal influenza with R_eff=1.2: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	71294	16 %	10657 (9068; 12415)	513 (216; 1011)	51 (21; 102)	108 (57; 161)	638913 (0.35)
	1	31213	7 %	4666 (3970; 5435)	225 (95; 443)	22 (9; 45)	47 (25; 71)	649335 (0.37)
	1.5	15754	3 %	2355 (2004; 2743)	113 (48; 223)	11 (5; 23)	24 (13; 36)	621482 (0.4)
	2	4829	1 %	722 (614; 841)	35 (15; 68)	3 (1; 7)	7 (4; 11)	598475 (0.42)
80%	0.5	105817	23 %	15817 (13459; 18427)	762 (321; 1501)	76 (31; 152)	160 (84; 239)	667907 (0.31)
	1	58665	13 %	8769 (7462; 10216)	423 (178; 832)	42 (17; 84)	89 (47; 133)	695081 (0.33)
	1.5	40361	9 %	6033 (5134; 7028)	291 (122; 572)	29 (12; 58)	61 (32; 91)	668195 (0.35)
	2	27432	6 %	4100 (3489; 4777)	198 (83; 389)	20 (8; 39)	42 (22; 62)	644651 (0.38)
	4	21694	5 %	3243 (2759; 3778)	156 (66; 308)	15 (6; 31)	33 (17; 49)	585898 (0.42)
90%	0.5	128267	28 %	19173 (16315; 22336)	924 (389; 1819)	92 (38; 184)	195 (102; 290)	677796 (0.29)
	1	76687	17 %	11463 (9754; 13354)	552 (233; 1088)	55 (23; 110)	116 (61; 173)	718493 (0.31)
	1.5	56592	12 %	8459 (7198; 9855)	408 (172; 803)	40 (17; 81)	86 (45; 128)	693566 (0.33)
	2	42355	9 %	6331 (5387; 7376)	305 (128; 601)	30 (12; 61)	64 (34; 96)	670606 (0.35)
	4	36020	8 %	5384 (4581; 6273)	259 (109; 511)	26 (11; 52)	55 (29; 81)	608001 (0.39)
*65%	4	456443		68227 (58056; 79485)	3288 (1384; 6474)	326 (134; 654)	692 (363; 1032)	546922 (0.46)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S26: Seasonal influenza with R_eff=1.3: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	67060	10 %	10024 (8530; 11678)	483 (203; 951)	48 (20; 96)	102 (53; 152)	1005905 (0.34)
	1	29264	4 %	4374 (3722; 5096)	211 (89; 415)	21 (9; 42)	44 (23; 66)	982392 (0.36)
	1.5	14755	2 %	2206 (1877; 2569)	106 (45; 209)	11 (4; 21)	22 (12; 33)	926555 (0.39)
	2	4538	1 %	678 (577; 790)	33 (14; 64)	3 (1; 7)	7 (4; 10)	883268 (0.41)
80%	0.5	101309	15 %	15143 (12886; 17642)	730 (307; 1437)	72 (30; 145)	154 (81; 229)	1092363 (0.3)
	1	56147	8 %	8393 (7142; 9777)	404 (170; 796)	40 (17; 81)	85 (45; 127)	1079587 (0.32)
	1.5	38731	6 %	5789 (4926; 6745)	279 (117; 549)	28 (11; 56)	59 (31; 88)	1018827 (0.34)
	2	26478	4 %	3958 (3368; 4611)	191 (80; 376)	19 (8; 38)	40 (21; 60)	970668 (0.37)
	4	21048	3 %	3146 (2677; 3665)	152 (64; 299)	15 (6; 30)	32 (17; 48)	876239 (0.41)
90%	0.5	123878	18 %	18517 (15756; 21572)	892 (376; 1757)	88 (36; 178)	188 (99; 280)	1139258 (0.28)
	1	73971	11 %	11057 (9409; 12881)	533 (224; 1049)	53 (22; 106)	112 (59; 167)	1136626 (0.3)
	1.5	54701	8 %	8177 (6958; 9526)	394 (166; 776)	39 (16; 78)	83 (44; 124)	1074089 (0.32)
	2	41086	6 %	6141 (5226; 7155)	296 (125; 583)	29 (12; 59)	62 (33; 93)	1023763 (0.34)
	4	35051	5 %	5239 (4458; 6104)	252 (106; 497)	25 (10; 50)	53 (28; 79)	921201 (0.38)
*65%	4	673222		100631 (85629; 117235)	4849 (2041; 9549)	481 (198; 965)	1021 (535; 1522)	802573 (0.45)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S27: Seasonal influenza with R_eff=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	62521	7 %	9345 (7952; 10887)	450 (190; 887)	45 (18; 90)	95 (50; 141)	1315011 (0.33)
	1	27189	3 %	4064 (3458; 4735)	196 (82; 386)	19 (8; 39)	41 (22; 61)	1261461 (0.35)
	1.5	13695	2 %	2047 (1742; 2385)	99 (42; 194)	10 (4; 20)	21 (11; 31)	1181272 (0.38)
	2	4198	0 %	628 (534; 731)	30 (13; 60)	3 (1; 6)	6 (3; 9)	1120465 (0.4)
80%	0.5	95720	11 %	14308 (12175; 16669)	689 (290; 1358)	68 (28; 137)	145 (76; 216)	1452959 (0.29)
	1	52978	6 %	7919 (6738; 9226)	382 (161; 751)	38 (16; 76)	80 (42; 120)	1404068 (0.31)
	1.5	36611	4 %	5472 (4657; 6375)	264 (111; 519)	26 (11; 52)	56 (29; 83)	1313546 (0.34)
	2	25118	3 %	3755 (3195; 4374)	181 (76; 356)	18 (7; 36)	38 (20; 57)	1243902 (0.36)
	4	20032	2 %	2994 (2548; 3488)	144 (61; 284)	14 (6; 29)	30 (16; 45)	1118640 (0.4)
90%	0.5	117838	14 %	17614 (14988; 20520)	849 (357; 1671)	84 (35; 169)	179 (94; 266)	1533426 (0.27)
	1	70231	8 %	10498 (8933; 12230)	506 (213; 996)	50 (21; 101)	107 (56; 159)	1491065 (0.29)
	1.5	51971	6 %	7768 (6610; 9050)	374 (158; 737)	37 (15; 75)	79 (41; 117)	1395318 (0.31)
	2	39141	5 %	5851 (4978; 6816)	282 (119; 555)	28 (12; 56)	59 (31; 88)	1320905 (0.33)
	4	33444	4 %	4999 (4254; 5824)	241 (101; 474)	24 (10; 48)	51 (27; 76)	1183713 (0.37)
*65%	4	855061		127811 (108758; 148901)	6159 (2593; 12128)	610 (251; 1226)	1297 (680; 1933)	1014696 (0.45)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_eff = 1.2, 1.3, 1.4)

Table S28: Seasonal influenza with R_eff=1.2: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	14412	3227	730	5697	757	10455	1110	277	1004	688 (411; 1195)	4
	1	29471	2411	319	2494	332	28736	486	121	193	54 (-66; 276)	12
	1.5	23405	1757	161	1259	167	23574	245	61	5	-65 (-126; 47)	13
	2	17892	1234	49	386	51	18640	75	19	-115	-136 (-155; -102)	14
80 %	0.5	1135	5276	1083	8518	1124	-4314	1677	410	1721	1224 (824; 1991)	2
	1	24260	4456	600	4722	623	22770	930	228	698	422 (200; 849)	6
	1.5	20476	3799	413	3249	429	20184	640	156	434	244 (91; 536)	9
	2	16265	3274	281	2208	291	16759	435	106	264	135 (31; 334)	11
	4	-2109	2034	222	1734	230	-2261	338	84	361	265 (180; 419)	10
90 %	**0.5	-9299	6721	1313	10325	1363	-15578	2033	498	2192	1587 (1103; 2521)	1
	1	19493	5901	785	6173	815	17621	1215	297	1036	675 (386; 1231)	3
	1.5	17429	5244	579	4555	601	16938	897	219	724	460 (244; 868)	5
	2	14259	4719	434	3409	450	14685	671	164	521	323 (163; 631)	8
	4	-4251	3479	369	2878	383	-4401	561	140	606	447 (305; 702)	7
*65 %	4	212975	0	4672	36306	4854	258807	7121	1774	10898	8876 (7121; 12147)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S29: Seasonal influenza with R_eff=1.3: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	56415	3227	686	5359	713	52884	1044	259	504	205 (-53; 684)	4
	1	58600	2411	300	2338	311	58062	455	113	-137	-267 (-379; -59)	12
	1.5	41983	1757	151	1179	157	42253	230	57	-201	-266 (-324; -162)	13
	2	28811	1234	46	363	48	29588	71	18	-231	-251 (-269; -218)	14
80 %	0.5	54754	5276	1037	8155	1077	49762	1605	392	1097	620 (237; 1358)	2
	1	64107	4456	575	4519	597	62872	889	217	248	-15 (-229; 392)	8
	1.5	48655	3799	396	3118	411	48529	613	150	119	-63 (-210; 218)	10
	2	35949	3274	271	2131	281	36540	419	102	47	-77 (-178; 116)	11
	4	5343	2034	215	1682	224	5256	327	81	274	182 (97; 332)	7
90 %	**0.5	51612	6721	1268	9971	1316	45778	1962	479	1496	913 (444; 1815)	1
	1	66240	5901	757	5954	786	64643	1172	286	512	166 (-115; 700)	3
	1.5	51821	5244	560	4403	581	51521	866	211	341	86 (-123; 482)	6
	2	39649	4719	421	3307	436	40204	651	159	241	50 (-108; 348)	9
	4	8061	3479	359	2801	372	8009	545	135	464	311 (169; 560)	5
*65 %	4	312373	0	6891	53549	7165	379978	10498	2611	16075	13092 (10504; 17919)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S30: Seasonal influenza with R_eff=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	93396	3227	640	4996	665	90322	973	241	51	-228 (-468; 219)	5
	1	83976	2411	278	2173	289	83647	423	105	-430	-551 (-656; -357)	14
	1.5	58084	1757	140	1094	146	58461	213	53	-383	-443 (-497; -346)	13
	2	38241	1234	43	335	45	39052	65	16	-333	-350 (-368; -320)	12
80 %	0.5	102721	5276	980	7705	1017	98295	1516	369	513	63 (-299; 761)	2
	1	99337	4456	542	4264	563	98423	839	204	-165	-414 (-614; -29)	10
	1.5	73515	3799	375	2947	389	73603	580	141	-171	-343 (-481; -77)	11
	2	53318	3274	257	2022	267	54047	398	97	-154	-270 (-366; -88)	9
	4	12106	2034	205	1601	213	12121	312	77	188	101 (20; 243)	4
90 %	**0.5	106581	6721	1206	9485	1253	101358	1866	455	832	279 (-167; 1133)	1
	1	107878	5901	719	5653	746	106661	1112	271	24	-305 (-571; 205)	6
	1.5	82429	5244	532	4183	552	82406	823	200	-18	-259 (-458; 119)	7
	2	62235	4719	401	3151	416	62987	620	151	-23	-205 (-355; 80)	8
	4	19274	3479	342	2673	355	19383	520	129	322	177 (42; 415)	3
*65 %	4	394786	0	8752	68013	9108	480658	13328	3309	20415	16628 (13343; 22761)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

B. Moderate pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S31: Moderate pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	90898	8 %	13587 (11562; 15829)	655 (276; 1289)	65 (27; 130)	138 (72; 205)	2566950 (0.19)
	1	39369	3 %	5885 (5007; 6856)	284 (119; 558)	28 (12; 56)	60 (31; 89)	2541953 (0.19)
	1.5	19791	2 %	2958 (2517; 3446)	143 (60; 281)	14 (6; 28)	30 (16; 45)	2447516 (0.2)
	2	6073	1 %	908 (772; 1058)	44 (18; 86)	4 (2; 9)	9 (5; 14)	2374564 (0.21)
80%	0.5	146006	13 %	21824 (18571; 25426)	1052 (443; 2071)	104 (43; 209)	221 (116; 330)	2874579 (0.16)
	1	82429	7 %	12321 (10484; 14354)	594 (250; 1169)	59 (24; 118)	125 (66; 186)	2886734 (0.17)
	1.5	58242	5 %	8706 (7408; 10142)	419 (177; 826)	42 (17; 84)	88 (46; 132)	2789728 (0.17)
	2	41358	4 %	6182 (5260; 7202)	298 (125; 587)	30 (12; 59)	63 (33; 93)	2712492 (0.18)
	4	33904	3 %	5068 (4312; 5904)	244 (103; 481)	24 (10; 49)	51 (27; 77)	2545418 (0.19)
90%	0.5	183121	16 %	27372 (23292; 31889)	1319 (555; 2597)	131 (54; 263)	278 (146; 414)	3045716 (0.15)
	1	111482	10 %	16664 (14180; 19414)	803 (338; 1581)	80 (33; 160)	169 (89; 252)	3091439 (0.15)
	1.5	84255	7 %	12594 (10717; 14672)	607 (255; 1195)	60 (25; 121)	128 (67; 190)	2996658 (0.16)
	2	65184	6 %	9743 (8291; 11351)	469 (198; 925)	47 (19; 93)	99 (52; 147)	2919377 (0.17)
	4	56762	5 %	8485 (7220; 9885)	409 (172; 805)	41 (17; 81)	86 (45; 128)	2739108 (0.18)
*65%	4	1128247		168646 (143505; 196473)	8126 (3421; 16002)	806 (332; 1618)	1711 (897; 2551)	2230644 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S32: Moderate pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	75874	5 %	11341 (9651; 13213)	546 (230; 1076)	54 (22; 109)	115 (60; 172)	3519915 (0.18)
	1	32696	2 %	4887 (4159; 5694)	235 (99; 464)	23 (10; 47)	50 (26; 74)	3418511 (0.19)
	1.5	16399	1 %	2451 (2086; 2856)	118 (50; 233)	12 (5; 24)	25 (13; 37)	3267365 (0.2)
	2	5029	0 %	752 (640; 876)	36 (15; 71)	4 (1; 7)	8 (4; 11)	3153834 (0.2)
80%	0.5	123630	8 %	18480 (15725; 21529)	890 (375; 1753)	88 (36; 177)	187 (98; 279)	4032109 (0.15)
	1	69502	5 %	10389 (8840; 12103)	501 (211; 986)	50 (20; 100)	105 (55; 157)	3948116 (0.16)
	1.5	49111	3 %	7341 (6247; 8552)	354 (149; 697)	35 (14; 70)	74 (39; 111)	3779794 (0.17)
	2	34922	2 %	5220 (4442; 6081)	252 (106; 495)	25 (10; 50)	53 (28; 79)	3651586 (0.17)
	4	28685	2 %	4288 (3649; 4995)	207 (87; 407)	20 (8; 41)	44 (23; 65)	3415584 (0.19)
90%	0.5	156304	10 %	23364 (19881; 27219)	1126 (474; 2217)	112 (46; 224)	237 (124; 353)	4340679 (0.14)
	1	94619	6 %	14143 (12035; 16477)	681 (287; 1342)	68 (28; 136)	143 (75; 214)	4277640 (0.15)
	1.5	71445	5 %	10679 (9087; 12441)	515 (217; 1013)	51 (21; 102)	108 (57; 162)	4101838 (0.15)
	2	55299	4 %	8266 (7034; 9630)	398 (168; 784)	39 (16; 79)	84 (44; 125)	3966540 (0.16)
	4	48193	3 %	7204 (6130; 8392)	347 (146; 684)	34 (14; 69)	73 (38; 109)	3708027 (0.17)
*65%	4	1495049		223474 (190160; 260349)	10768 (4533; 21205)	1067 (440; 2144)	2267 (1189; 3380)	2954750 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S33: Moderate pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	63318	4 %	9465 (8054; 11026)	456 (192; 898)	45 (19; 91)	96 (50; 143)	4214823 (0.17)
	1	27196	2 %	4065 (3459; 4736)	196 (82; 386)	19 (8; 39)	41 (22; 61)	4054260 (0.18)
	1.5	13634	1 %	2038 (1734; 2374)	98 (41; 193)	10 (4; 20)	21 (11; 31)	3860499 (0.19)
	2	4174	0 %	624 (531; 727)	30 (13; 59)	3 (1; 6)	6 (3; 9)	3716690 (0.2)
80%	0.5	104183	6 %	15573 (13251; 18142)	750 (316; 1478)	74 (31; 149)	158 (83; 236)	4884145 (0.15)
	1	58376	3 %	8726 (7425; 10166)	420 (177; 828)	42 (17; 84)	89 (46; 132)	4723586 (0.15)
	1.5	41230	2 %	6163 (5244; 7180)	297 (125; 585)	29 (12; 59)	63 (33; 93)	4500929 (0.16)
	2	29351	2 %	4387 (3733; 5111)	211 (89; 416)	21 (9; 42)	45 (23; 66)	4334097 (0.17)
	4	24132	1 %	3607 (3069; 4202)	174 (73; 342)	17 (7; 35)	37 (19; 55)	4046934 (0.18)
90%	0.5	132427	8 %	19795 (16844; 23061)	954 (402; 1878)	95 (39; 190)	201 (105; 299)	5300189 (0.14)
	1	79800	5 %	11928 (10150; 13896)	575 (242; 1132)	57 (23; 114)	121 (63; 180)	5148743 (0.14)
	1.5	60206	3 %	8999 (7658; 10484)	434 (183; 854)	43 (18; 86)	91 (48; 136)	4910441 (0.15)
	2	46596	3 %	6965 (5927; 8114)	336 (141; 661)	33 (14; 67)	71 (37; 105)	4730772 (0.16)
	4	40627	2 %	6073 (5167; 7075)	293 (123; 576)	29 (12; 58)	62 (32; 92)	4413875 (0.17)
*65%	4	1761641		263324 (224068; 306773)	12688 (5342; 24986)	1258 (518; 2526)	2672 (1401; 3982)	3476939 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S34: Moderate pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	66065	3227	930	7264	968	60130	1435	368	822	418 (67; 1069)	3
	1	90391	2411	403	3146	419	88834	621	159	-284	-460 (-611; -179)	12
	1.5	67974	1757	203	1581	211	67736	312	80	-378	-466 (-543; -325)	13
	2	49758	1234	62	485	65	50380	96	24	-418	-443 (-468; -400)	14
80 %	0.5	68887	5276	1494	11753	1555	59362	2345	589	1740	1056 (500; 2115)	2
	1	115175	4456	844	6635	878	111275	1323	332	188	-194 (-512; 403)	8
	1.5	98112	3799	596	4688	620	96007	935	234	-44	-312 (-538; 112)	10
	2	82998	3274	423	3329	440	82079	663	166	-174	-357 (-525; -59)	11
	4	30933	2034	347	2709	361	29550	534	136	233	91 (-51; 334)	6
90 %	**0.5	63569	6721	1874	14740	1950	51726	2941	739	2414	1563 (858; 2893)	1
	1	126251	5901	1141	8974	1187	120850	1789	449	557	43 (-389; 852)	4
	1.5	113537	5244	862	6782	897	110240	1352	339	228	-152 (-490; 455)	7
	2	101125	4719	667	5247	694	99237	1046	262	34	-254 (-520; 220)	9
	4	48020	3479	581	4536	604	45778	894	228	428	190 (-49; 596)	5
*65 %	4	851961	0	11548	89742	12038	965289	17961	4701	34441	29478 (25108; 37499)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S35: Moderate pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	159501	3227	777	6063	809	155080	1193	301	-388	-727 (-1019; -187)	5
	1	150950	2411	335	2613	348	150065	514	130	-1016	-1160 (-1287; -927)	11
	1.5	105594	1757	168	1310	175	105698	258	65	-820	-891 (-956; -774)	7
	2	70950	1234	51	402	54	71677	79	20	-652	-671 (-695; -634)	6
80 %	0.5	211016	5276	1265	9951	1317	203758	1977	490	-100	-677 (-1151; 222)	2
	1	219546	4456	711	5594	741	216955	1111	275	-1101	-1421 (-1690; -916)	14
	1.5	176060	3799	503	3953	523	174880	785	194	-999	-1216 (-1416; -861)	9
	2	142041	3274	357	2811	372	141775	558	137	-888	-1037 (-1186; -783)	8
	**4	65738	2034	294	2292	306	64881	450	113	-212	-323 (-454; -114)	3
90 %	0.5	237762	6721	1600	12582	1666	228637	2500	619	168	-556 (-1159; 583)	1
	1	259836	5901	968	7616	1008	256144	1512	373	-1100	-1520 (-1905; -838)	13
	1.5	218491	5244	731	5751	761	216493	1142	282	-1066	-1375 (-1674; -858)	12
	2	185534	4719	566	4451	589	184647	883	218	-1000	-1230 (-1474; -827)	10
	4	106155	3479	493	3851	513	104776	756	189	-312	-500 (-719; -150)	4
*65 %	4	1128365	0	15302	118918	15980	1278566	23754	6175	45669	39101 (33299; 49714)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S36: Moderate pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	231499	3227	648	5060	675	228343	992	248	-1336	-1617 (-1862; -1166)	5
	1	196719	2411	278	2173	290	196388	426	106	-1577	-1693 (-1802; -1497)	8
	1.5	133799	1757	140	1089	145	134182	214	53	-1155	-1211 (-1268; -1112)	4
	2	86693	1234	43	334	45	87506	65	16	-827	-841 (-865; -808)	2
80 %	0.5	322418	5276	1066	8386	1111	317131	1661	406	-1573	-2057 (-2457; -1299)	7
	1	299841	4456	597	4699	622	298377	930	227	-2113	-2374 (-2609; -1953)	13
	1.5	235808	3799	422	3319	440	235427	657	160	-1744	-1921 (-2095; -1622)	10
	2	187177	3274	300	2363	313	187475	467	114	-1445	-1562 (-1699; -1345)	6
	**4	92734	2034	247	1928	257	92335	377	93	-564	-648 (-778; -467)	1
90 %	0.5	375729	6721	1355	10660	1412	369023	2111	516	-1652	-2253 (-2778; -1296)	9
	1	363572	5901	817	6423	851	361381	1271	310	-2414	-2758 (-3093; -2178)	14
	1.5	299624	5244	616	4846	642	298764	959	234	-2088	-2336 (-2606; -1896)	12
	2	250616	4719	477	3751	497	250611	742	181	-1814	-1992 (-2223; -1648)	11
	4	151458	3479	416	3247	433	150842	635	157	-903	-1045 (-1261; -740)	3
*65 %	4	1327750	0	18031	140123	18861	1504766	27943	7221	53809	46074 (39234; 58557)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

C. Severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S37: Severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	90898	8 %	18132 (15839; 20620)	1789 (1093; 2741)	303 (182; 471)	203 (107; 303)	2566946 (0.15)
	1	39369	3 %	7853 (6860; 8931)	775 (473; 1187)	131 (79; 204)	88 (46; 131)	2541949 (0.15)
	1.5	19791	2 %	3948 (3449; 4489)	389 (238; 597)	66 (40; 103)	44 (23; 66)	2447512 (0.16)
	2	6073	1 %	1211 (1058; 1378)	120 (73; 183)	20 (12; 31)	14 (7; 20)	2374560 (0.17)
80%	0.5	146006	13 %	29124 (25442; 33120)	2873 (1755; 4404)	487 (293; 756)	327 (171; 487)	2874575 (0.18)
	1	82429	7 %	16442 (14363; 18698)	1622 (991; 2486)	275 (165; 427)	184 (97; 275)	2886730 (0.16)
	1.5	58242	5 %	11618 (10149; 13212)	1146 (700; 1757)	194 (117; 302)	130 (68; 194)	2789724 (0.17)
	2	41358	4 %	8250 (7207; 9382)	814 (497; 1247)	138 (83; 214)	93 (49; 138)	2712488 (0.17)
	4	33904	3 %	6763 (5908; 7691)	667 (408; 1023)	113 (68; 176)	76 (40; 113)	2545414 (0.18)
90%	0.5	183121	16 %	36527 (31909; 41540)	3604 (2201; 5523)	611 (367; 949)	410 (215; 611)	3045713 (0.19)
	1	111482	10 %	22237 (19426; 25289)	2194 (1340; 3362)	372 (224; 577)	249 (131; 372)	3091435 (0.19)
	1.5	84255	7 %	16806 (14682; 19113)	1658 (1013; 2541)	281 (169; 436)	188 (99; 281)	2996654 (0.19)
	2	65184	6 %	13002 (11358; 14787)	1283 (784; 1966)	217 (131; 338)	146 (76; 217)	2919373 (0.2)
	4	56762	5 %	11322 (9891; 12876)	1117 (682; 1712)	189 (114; 294)	127 (67; 189)	2739105 (0.21)
*65%	4	1128247		225053 (196600; 255935)	22204 (13563; 34028)	3764 (2264; 5844)	2524 (1324; 3762)	2230640 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S38: : Severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	75874	5 %	15135 (13221; 17212)	1493 (912; 2288)	253 (152; 393)	170 (89; 253)	3519910 (0.18)
	1	32696	2 %	6522 (5697; 7417)	643 (393; 986)	109 (66; 169)	73 (38; 109)	3418506 (0.19)
	1.5	16399	1 %	3271 (2858; 3720)	323 (197; 495)	55 (33; 85)	37 (19; 55)	3267360 (0.2)
	2	5029	0 %	1003 (876; 1141)	99 (60; 152)	17 (10; 26)	11 (6; 17)	3153828 (0.2)
80%	0.5	123630	8 %	24661 (21543; 28045)	2433 (1486; 3729)	412 (248; 640)	277 (145; 412)	4032104 (0.15)
	1	69502	5 %	13864 (12111; 15766)	1368 (836; 2096)	232 (139; 360)	155 (82; 232)	3948111 (0.16)
	1.5	49111	3 %	9796 (8558; 11141)	967 (590; 1481)	164 (99; 254)	110 (58; 164)	3779789 (0.17)
	2	34922	2 %	6966 (6085; 7922)	687 (420; 1053)	117 (70; 181)	78 (41; 116)	3651581 (0.17)
	4	28685	2 %	5722 (4998; 6507)	565 (345; 865)	96 (58; 149)	64 (34; 96)	3415578 (0.19)
90%	0.5	156304	10 %	31178 (27236; 35457)	3076 (1879; 4714)	521 (314; 810)	350 (183; 521)	4340674 (0.14)
	1	94619	6 %	18874 (16488; 21464)	1862 (1137; 2854)	316 (190; 490)	212 (111; 315)	4277635 (0.15)
	1.5	71445	5 %	14251 (12449; 16207)	1406 (859; 2155)	238 (143; 370)	160 (84; 238)	4101833 (0.15)
	2	55299	4 %	11031 (9636; 12544)	1088 (665; 1668)	184 (111; 286)	124 (65; 184)	3966535 (0.16)
	4	48193	3 %	9613 (8398; 10932)	948 (579; 1453)	161 (97; 250)	108 (57; 161)	3708022 (0.17)
*65%	4	1495049		298219 (260516; 339142)	29422 (17973; 45090)	4988 (3000; 7744)	3344 (1754; 4985)	2954745 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S39: Severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	63318	4 %	12630 (11033; 14363)	1246 (761; 1910)	211 (127; 328)	142 (74; 211)	4214817 (0.17)
	1	27196	2 %	5425 (4739; 6169)	535 (327; 820)	91 (55; 141)	61 (32; 91)	4054254 (0.18)
	1.5	13634	1 %	2720 (2376; 3093)	268 (164; 411)	45 (27; 71)	30 (16; 45)	3860493 (0.19)
	2	4174	0 %	833 (727; 947)	82 (50; 126)	14 (8; 22)	9 (5; 14)	3716684 (0.2)
80%	0.5	104183	6 %	20781 (18154; 23633)	2050 (1252; 3142)	348 (209; 540)	233 (122; 347)	4884140 (0.15)
	1	58376	3 %	11644 (10172; 13242)	1149 (702; 1761)	195 (117; 302)	131 (69; 195)	4723580 (0.15)
	1.5	41230	2 %	8224 (7184; 9353)	811 (496; 1243)	138 (83; 214)	92 (48; 137)	4500923 (0.16)
	2	29351	2 %	5855 (5114; 6658)	578 (353; 885)	98 (59; 152)	66 (34; 98)	4334091 (0.17)
	4	24132	1 %	4814 (4205; 5474)	475 (290; 728)	81 (48; 125)	54 (28; 80)	4046928 (0.18)
90%	0.5	132427	8 %	26415 (23076; 30040)	2606 (1592; 3994)	442 (266; 686)	296 (155; 442)	5300183 (0.14)
	1	79800	5 %	15918 (13905; 18102)	1570 (959; 2407)	266 (160; 413)	178 (94; 266)	5148737 (0.14)
	1.5	60206	3 %	12009 (10491; 13657)	1185 (724; 1816)	201 (121; 312)	135 (71; 201)	4910435 (0.15)
	2	46596	3 %	9295 (8119; 10570)	917 (560; 1405)	155 (93; 241)	104 (55; 155)	4730766 (0.16)
	4	40627	2 %	8104 (7079; 9216)	800 (488; 1225)	136 (82; 210)	91 (48; 135)	4413869 (0.17)
*65%	4	1761641		351396 (306970; 399616)	34669 (21178; 53131)	5878 (3534; 9125)	3940 (2067; 5873)	3476933 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S40: Severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	66060	3228	1241	20709	1016	46322	1593	542	1120	727 (356; 1388)	3
	1	90384	2411	537	8969	440	82848	690	235	-155	-325 (-487; -38)	12
	1.5	67968	1757	270	4509	221	64725	347	118	-313	-398 (-480; -255)	13
	2	49754	1235	83	1384	68	49454	106	36	-398	-423 (-449; -378)	14
80 %	0.5	68872	5275	1993	33366	1632	37156	2601	869	2223	1559 (962; 2624)	2
	1	115161	4455	1125	18837	921	98732	1468	490	461	88 (-251; 687)	7
	1.5	98097	3799	795	13310	651	87140	1036	345	148	-110 (-356; 310)	10
	2	82982	3274	565	9451	462	75778	736	245	-37	-217 (-395; 83)	11
	4	30960	2034	463	7724	379	24428	592	200	343	208 (55; 454)	8
90 %	**0.5	63541	6720	2500	41848	2047	23867	3262	1090	3019	2192 (1438; 3522)	1
	1	126224	5900	1522	25476	1246	103879	1985	662	925	433 (-40; 1234)	4
	1.5	113510	5244	1150	19254	942	97408	1499	499	506	136 (-222; 748)	6
	2	101098	4719	890	14896	728	89303	1159	386	249	-33 (-316; 441)	9
	4	48064	3480	775	12932	634	37203	992	336	612	385 (130; 798)	5
*65 %	4	851968	0	15404	257088	12638	1137098	19969	6934	38201	33462 (28809; 41566)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S41: Severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	159488	3228	1036	17286	849	143545	1322	444	-142	-471 (-781; 80)	4
	1	150938	2411	446	7449	366	145088	570	191	-910	-1050 (-1184; -813)	14
	1.5	105585	1757	224	3736	183	103199	286	96	-767	-836 (-905; -716)	7
	2	70944	1235	69	1146	56	70908	88	29	-636	-654 (-679; -617)	6
80 %	0.5	210998	5275	1688	28252	1383	184949	2190	722	304	-255 (-764; 644)	2
	1	219528	4455	949	15883	777	206373	1230	405	-874	-1181 (-1475; -682)	13
	1.5	176040	3799	671	11223	549	167396	869	286	-838	-1051 (-1264; -695)	12
	2	142021	3274	477	7981	391	136447	618	203	-774	-918 (-1078; -665)	8
	4	65773	2034	392	6535	321	60560	498	166	-119	-226 (-366; -15)	3
90 %	**0.5	237726	6720	2134	35719	1749	204844	2769	912	680	-16 (-672; 1112)	1
	1	259801	5900	1292	21623	1058	241728	1675	551	-790	-1203 (-1610; -514)	9
	1.5	218456	5244	975	16327	799	205599	1264	415	-833	-1135 (-1452; -615)	11
	2	185498	4719	755	12637	618	176206	978	321	-819	-1042 (-1302; -640)	10
	4	106211	3480	658	10979	539	97515	837	279	-157	-337 (-572; 14)	5
*65 %	4	1128377	0	20412	340670	16776	1506235	26393	9107	50631	44341 (38182; 55091)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S42: Severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	231480	3228	864	14425	709	218709	1099	365	-1132	-1403 (-1663; -944)	5
	1	196703	2411	371	6196	304	192242	472	157	-1489	-1602 (-1719; -1404)	9
	1.5	133788	1757	186	3106	153	132101	236	79	-1111	-1164 (-1226; -1064)	4
	2	86686	1235	57	951	47	86865	72	24	-813	-828 (-852; -794)	3
80 %	0.5	322398	5275	1422	23808	1166	301276	1838	599	-1234	-1704 (-2135; -950)	7
	1	299820	4455	797	13340	653	289484	1029	335	-1923	-2178 (-2429; -1756)	13
	1.5	235786	3799	563	9422	461	229138	727	236	-1610	-1782 (-1969; -1484)	10
	2	187154	3274	401	6707	328	182991	517	168	-1349	-1463 (-1610; -1246)	8
	**4	92774	2034	329	5498	270	88710	417	138	-487	-570 (-703; -384)	1
90 %	0.5	375687	6720	1808	30263	1482	348854	2336	761	-1222	-1800 (-2368; -845)	6
	1	363531	5900	1089	18236	893	349212	1406	458	-2155	-2490 (-2848; -1911)	14
	1.5	299583	5244	822	13759	674	289572	1061	345	-1892	-2133 (-2421; -1694)	12
	2	250574	4719	636	10648	521	243488	820	266	-1663	-1836 (-2081; -1488)	11
	4	151524	3480	555	9256	455	144739	703	232	-773	-913 (-1135; -602)	2
*65 %	4	1327765	0	24051	401417	19801	1773034	31031	10650	59633	52215 (44964; 64891)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

D. Very severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S43: Very severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	90898	8 %	22680 (20187; 25353)	3151 (2198; 4364)	786 (540; 1103)	634 (332; 943)	2566939 (0.19)
	1	39369	3 %	9823 (8743; 10981)	1365 (952; 1890)	340 (234; 478)	274 (144; 409)	2541942 (0.19)
	1.5	19791	2 %	4938 (4395; 5520)	686 (479; 950)	171 (118; 240)	138 (72; 205)	2447504 (0.2)
	2	6073	1 %	1515 (1349; 1694)	211 (147; 292)	52 (36; 74)	42 (22; 63)	2374553 (0.21)
80%	0.5	146006	13 %	36429 (32426; 40723)	5062 (3531; 7010)	1262 (867; 1772)	1018 (533; 1515)	2874568 (0.16)
	1	82429	7 %	20566 (18306; 22991)	2858 (1993; 3957)	712 (489; 1000)	575 (301; 855)	2886723 (0.17)
	1.5	58242	5 %	14532 (12935; 16244)	2019 (1408; 2796)	503 (346; 707)	406 (213; 604)	2789717 (0.17)
	2	41358	4 %	10319 (9185; 11535)	1434 (1000; 1986)	357 (246; 502)	288 (151; 429)	2712481 (0.18)
	4	33904	3 %	8459 (7530; 9456)	1175 (820; 1628)	293 (201; 411)	236 (124; 352)	2545406 (0.19)
90%	0.5	183121	16 %	45690 (40668; 51075)	6349 (4428; 8792)	1583 (1087; 2222)	1277 (669; 1900)	3045706 (0.15)
	1	111482	10 %	27815 (24758; 31094)	3865 (2696; 5352)	964 (662; 1353)	777 (407; 1157)	3091428 (0.15)
	1.5	84255	7 %	21022 (18712; 23500)	2921 (2037; 4045)	728 (500; 1022)	587 (308; 874)	2996647 (0.16)
	2	65184	6 %	16264 (14476; 18181)	2260 (1576; 3130)	563 (387; 791)	454 (238; 676)	2919366 (0.17)
	4	56762	5 %	14162 (12606; 15832)	1968 (1373; 2725)	491 (337; 689)	396 (207; 589)	2739097 (0.18)
*65%	4	1128247		281504 (250567; 314683)	39116 (27282; 54168)	9752 (6699; 13692)	7866 (4120; 11707)	2230632 (0.23)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S44: Very severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	75874	5 %	18931 (16850; 21162)	2630 (1835; 3643)	656 (451; 921)	529 (277; 787)	3519901 (0.18)
	1	32696	2 %	8158 (7261; 9119)	1134 (791; 1570)	283 (194; 397)	228 (119; 339)	3418496 (0.19)
	1.5	16399	1 %	4092 (3642; 4574)	569 (397; 787)	142 (97; 199)	114 (60; 170)	3267350 (0.2)
	2	5029	0 %	1255 (1117; 1403)	174 (122; 241)	43 (30; 61)	35 (18; 52)	3153819 (0.2)
80%	0.5	123630	8 %	30846 (27456; 34482)	4286 (2990; 5936)	1069 (734; 1500)	862 (451; 1283)	4032095 (0.15)
	1	69502	5 %	17341 (15435; 19385)	2410 (1681; 3337)	601 (413; 843)	485 (254; 721)	3948102 (0.16)
	1.5	49111	3 %	12253 (10907; 13698)	1703 (1188; 2358)	424 (292; 596)	342 (179; 510)	3779780 (0.17)
	2	34922	2 %	8713 (7756; 9740)	1211 (844; 1677)	302 (207; 424)	243 (128; 362)	3651571 (0.17)
	4	28685	2 %	7157 (6371; 8001)	994 (694; 1377)	248 (170; 348)	200 (105; 298)	3415569 (0.19)
90%	0.5	156304	10 %	38999 (34713; 43595)	5419 (3780; 7504)	1351 (928; 1897)	1090 (571; 1622)	4340665 (0.14)
	1	94619	6 %	23608 (21013; 26391)	3280 (2288; 4543)	818 (562; 1148)	660 (346; 982)	4277625 (0.15)
	1.5	71445	5 %	17826 (15867; 19927)	2477 (1728; 3430)	618 (424; 867)	498 (261; 741)	4101824 (0.15)
	2	55299	4 %	13797 (12281; 15424)	1917 (1337; 2655)	478 (328; 671)	386 (202; 574)	3966525 (0.16)
	4	48193	3 %	12024 (10703; 13442)	1671 (1165; 2314)	417 (286; 585)	336 (176; 500)	3708012 (0.17)
*65%	4	1495049		373023 (332028; 416989)	51832 (36152; 71778)	12922 (8877; 18143)	10423 (5459; 15514)	2954735 (0.22)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S45 Very severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 65% of children and 55% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	63318	4 %	15798 (14062; 17660)	2195 (1531; 3040)	547 (376; 768)	441 (231; 657)	4214806 (0.17)
	1	27196	2 %	6786 (6040; 7585)	943 (658; 1306)	235 (161; 330)	190 (99; 282)	4054243 (0.18)
	1.5	13634	1 %	3402 (3028; 3803)	473 (330; 655)	118 (81; 165)	95 (50; 141)	3860482 (0.19)
	2	4174	0 %	1041 (927; 1164)	145 (101; 200)	36 (25; 51)	29 (15; 43)	3716673 (0.2)
80%	0.5	104183	6 %	25994 (23137; 29058)	3612 (2519; 5002)	900 (619; 1264)	726 (380; 1081)	4884129 (0.15)
	1	58376	3 %	14565 (12964; 16282)	2024 (1412; 2803)	505 (347; 708)	407 (213; 606)	4723570 (0.15)
	1.5	41230	2 %	10287 (9157; 11500)	1429 (997; 1979)	356 (245; 500)	287 (151; 428)	4500912 (0.16)
	2	29351	2 %	7323 (6518; 8186)	1018 (710; 1409)	254 (174; 356)	205 (107; 305)	4334080 (0.17)
	4	24132	1 %	6021 (5359; 6731)	837 (584; 1159)	209 (143; 293)	168 (88; 250)	4046917 (0.18)
90%	0.5	132427	8 %	33041 (29410; 36936)	4591 (3202; 6358)	1145 (786; 1607)	923 (484; 1374)	5300173 (0.14)
	1	79800	5 %	19911 (17722; 22257)	2767 (1930; 3831)	690 (474; 968)	556 (291; 828)	5148726 (0.14)
	1.5	60206	3 %	15022 (13371; 16792)	2087 (1456; 2891)	520 (357; 731)	420 (220; 625)	4910424 (0.15)
	2	46596	3 %	11626 (10348; 12996)	1615 (1127; 2237)	403 (277; 565)	325 (170; 484)	4730755 (0.16)
	4	40627	2 %	10137 (9023; 11331)	1409 (982; 1951)	351 (241; 493)	283 (148; 422)	4413858 (0.17)
*65%	4	1761641		439539 (391234; 491346)	61075 (42599; 84577)	15227 (10460; 21378)	12282 (6433; 18280)	3476922 (0.21)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S46: Very severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	66066	3226	1552	39055	1064	27622	2544	1690	2263	1933 (1454; 2630)	4
	1	90396	2409	672	16915	461	74757	1101	731	339	198 (-12; 500)	12
	1.5	67977	1756	338	8503	232	60661	553	367	-65	-135 (-241; 16)	13
	2	49761	1234	104	2609	71	48211	170	113	-322	-342 (-376; -296)	14
80 %	0.5	68876	5277	2492	62736	1709	7217	4126	2709	4053	3494 (2742; 4627)	2
	1	115167	4456	1407	35418	965	81834	2326	1525	1492	1178 (748; 1819)	6
	1.5	98104	3799	994	25025	682	75203	1642	1076	875	655 (347; 1107)	9
	2	82991	3274	706	17771	484	67304	1165	762	478	324 (101; 646)	11
	4	30913	2033	579	14567	397	17404	944	624	766	649 (460; 918)	10
90 %	**0.5	63552	6722	3126	78683	2144	-13678	5175	3396	5314	4622 (3664; 6040)	1
	1	126237	5901	1903	47901	1305	81029	3145	2062	2319	1899 (1310; 2763)	3
	1.5	113525	5244	1438	36202	986	80142	2375	1556	1558	1241 (790; 1898)	5
	2	101114	4718	1113	28008	763	75948	1836	1202	1061	819 (466; 1327)	8
	4	47988	3477	969	24388	664	25444	1580	1045	1321	1124 (808; 1574)	7
*65 %	4	851966	0	19259	482073	13234	1366532	32093	21601	52664	48727 (42834; 57333)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S47: Very severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	159509	3226	1295	32600	889	127951	2101	1384	796	521 (121; 1106)	3
	1	150958	2409	558	14048	383	138378	905	596	-506	-622 (-797; -372)	12
	1.5	105600	1756	280	7046	192	99838	454	299	-564	-621 (-710; -496)	13
	2	70954	1234	86	2161	59	69882	139	92	-574	-590 (-620; -550)	14
80 %	0.5	211006	5277	2110	53121	1448	159603	3456	2249	1828	1355 (716; 2311)	2
	1	219538	4456	1186	29863	814	192130	1940	1261	-19	-282 (-650; 258)	8
	1.5	176052	3799	838	21102	575	157336	1369	890	-235	-419 (-682; -37)	10
	2	142033	3274	596	15005	409	129297	973	631	-346	-473 (-669; -200)	11
	4	65714	2033	490	12325	336	54597	789	518	233	139 (-33; 369)	6
90 %	**0.5	237745	6722	2668	67160	1831	172807	4367	2842	2605	2013 (1198; 3225)	1
	1	259821	5901	1615	40656	1108	222343	2640	1716	372	17 (-489; 754)	5
	1.5	218477	5244	1220	30698	837	190966	1992	1294	44	-221 (-612; 337)	7
	2	185520	4718	944	23761	648	164886	1540	1000	-142	-340 (-655; 96)	9
	4	106114	3477	823	20706	564	87498	1327	870	434	277 (-11; 663)	4
*65 %	4	1128369	0	25520	638799	17568	1810256	42313	28370	69650	64413 (56625; 75829)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S48: Very severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 65% of children and 55% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	231511	3226	1081	27205	742	205709	1739	1138	-359	-585 (-922; -103)	5
	1	196730	2409	464	11685	319	186671	746	488	-1157	-1252 (-1400; -1043)	11
	1.5	133807	1756	233	5858	160	129313	374	245	-945	-990 (-1067; -885)	7
	2	86698	1234	71	1793	49	86018	114	75	-763	-775 (-802; -740)	6
80 %	0.5	322409	5277	1778	44765	1221	279921	2887	1867	33	-366 (-904; 437)	2
	1	299832	4456	996	25083	684	277525	1616	1043	-1215	-1435 (-1745; -983)	14
	1.5	235800	3799	704	17716	483	220697	1140	736	-1111	-1262 (-1491; -943)	10
	2	187169	3274	501	12611	344	176986	811	523	-994	-1096 (-1270; -861)	8
	4	92706	2033	412	10368	283	83675	658	429	-195	-269 (-423; -68)	3
90 %	**0.5	375711	6722	2260	56901	1552	321719	3669	2371	388	-113 (-813; 911)	1
	1	363556	5901	1362	34288	935	332871	2208	1425	-1187	-1482 (-1922; -861)	13
	1.5	299609	5244	1028	25869	706	277250	1664	1074	-1163	-1378 (-1724; -902)	12
	2	250601	4718	795	20021	546	233956	1287	830	-1099	-1255 (-1541; -879)	9
	4	151412	3477	693	17456	476	136264	1109	722	-281	-406 (-665; -70)	4
*65 %	4	1327752	0	30070	752708	20735	2131265	49646	33177	81900	75719 (66559; 89137)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Section III: Scenarios with low symptomatic proportion (35% children, and 25% adults assumed to be symptomatic), without assuming extra mixing

A. Seasonal influenza

i. Epidemiology (R_eff = 1.2, 1.3, 1.4)

Table S49: Seasonal influenza with R_eff=1.2: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	21168	13 %	3164 (2692; 3686)	152 (64; 300)	15 (6; 30)	32 (17; 48)	231460 (0.4)
	1	9297	6 %	1390 (1183; 1619)	67 (28; 132)	7 (3; 13)	14 (7; 21)	232881 (0.43)
	1.5	4706	3 %	703 (599; 820)	34 (14; 67)	3 (1; 7)	7 (4; 11)	223381 (0.46)
	2	1450	1 %	217 (184; 253)	10 (4; 21)	1 (0; 2)	2 (1; 3)	215745 (0.49)
80%	0.5	30777	19 %	4600 (3915; 5360)	222 (93; 437)	22 (9; 44)	47 (24; 70)	244870 (0.36)
	1	16952	11 %	2534 (2156; 2952)	122 (51; 240)	12 (5; 24)	26 (13; 38)	250016 (0.38)
	1.5	11580	7 %	1731 (1473; 2017)	83 (35; 164)	8 (3; 17)	18 (9; 26)	240089 (0.41)
	2	7771	5 %	1162 (988; 1353)	56 (24; 110)	6 (2; 11)	12 (6; 18)	231823 (0.44)
	4	6078	4 %	909 (773; 1058)	44 (18; 86)	4 (2; 9)	9 (5; 14)	212613 (0.48)
90%	0.5	37052	23 %	5538 (4713; 6452)	267 (112; 526)	26 (11; 53)	56 (29; 84)	251376 (0.34)
	1	21984	14 %	3286 (2796; 3828)	158 (67; 312)	16 (6; 32)	33 (17; 50)	259646 (0.36)
	1.5	16101	10 %	2407 (2048; 2804)	116 (49; 228)	11 (5; 23)	24 (13; 36)	249798 (0.39)
	2	11950	7 %	1786 (1520; 2081)	86 (36; 169)	9 (4; 17)	18 (10; 27)	241336 (0.41)
	4	10079	6 %	1507 (1282; 1755)	73 (31; 143)	7 (3; 14)	15 (8; 23)	220600 (0.45)
*65 %	4	161436		24131 (20534; 28113)	1163 (490; 2290)	115 (47; 231)	245 (128; 365)	199201 (0.53)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S50: Seasonal influenza with R_eff=1.3: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	20313	8 %	3036 (2584; 3537)	146 (62; 288)	15 (6; 29)	31 (16; 46)	407271 (0.39)
	1	8906	3 %	1331 (1133; 1551)	64 (27; 126)	6 (3; 13)	14 (7; 20)	394594 (0.42)
	1.5	4491	2 %	671 (571; 782)	32 (14; 64)	3 (1; 6)	7 (4; 10)	373047 (0.45)
	2	1375	1 %	206 (175; 239)	10 (4; 20)	1 (0; 2)	2 (1; 3)	356648 (0.47)
80%	0.5	30150	11 %	4507 (3835; 5250)	217 (91; 428)	22 (9; 43)	46 (24; 68)	445416 (0.35)
	1	16658	6 %	2490 (2119; 2901)	120 (51; 236)	12 (5; 24)	25 (13; 38)	433907 (0.37)
	1.5	11447	4 %	1711 (1456; 1993)	82 (35; 162)	8 (3; 16)	17 (9; 26)	409391 (0.4)
	2	7757	3 %	1159 (987; 1351)	56 (24; 110)	6 (2; 11)	12 (6; 18)	390515 (0.42)
	4	6114	2 %	914 (778; 1065)	44 (19; 87)	4 (2; 9)	9 (5; 14)	355611 (0.47)
90%	0.5	36620	14 %	5474 (4658; 6377)	264 (111; 519)	26 (11; 53)	56 (29; 83)	468005 (0.32)
	1	21804	8 %	3259 (2773; 3797)	157 (66; 309)	16 (6; 31)	33 (17; 49)	458047 (0.35)
	1.5	16044	6 %	2398 (2041; 2794)	116 (49; 228)	11 (5; 23)	24 (13; 36)	432007 (0.37)
	2	11986	4 %	1792 (1525; 2087)	86 (36; 170)	9 (4; 17)	18 (10; 27)	411741 (0.4)
	4	10177	4 %	1521 (1294; 1772)	73 (31; 144)	7 (3; 15)	15 (8; 23)	373426 (0.44)
*65%	4	266712		39867 (33924; 46445)	1921 (809; 3783)	190 (78; 382)	404 (212; 603)	327228 (0.52)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S51: Seasonal influenza with R_eff=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	19242	5 %	2876 (2447; 3351)	139 (58; 273)	14 (6; 28)	29 (15; 43)	557257 (0.38)
	1	8415	2 %	1258 (1070; 1465)	61 (26; 119)	6 (2; 12)	13 (7; 19)	531830 (0.41)
	1.5	4241	1 %	634 (539; 739)	31 (13; 60)	3 (1; 6)	6 (3; 10)	499550 (0.44)
	2	1298	0 %	194 (165; 226)	9 (4; 18)	1 (0; 2)	2 (1; 3)	475380 (0.46)
80%	0.5	28983	8 %	4332 (3686; 5047)	209 (88; 411)	21 (9; 42)	44 (23; 66)	617943 (0.34)
	1	16051	5 %	2399 (2042; 2795)	116 (49; 228)	11 (5; 23)	24 (13; 36)	591107 (0.36)
	1.5	11063	3 %	1654 (1407; 1927)	80 (34; 157)	8 (3; 16)	17 (9; 25)	553533 (0.39)
	2	7556	2 %	1129 (961; 1316)	54 (23; 107)	5 (2; 11)	11 (6; 17)	525160 (0.41)
	4	5974	2 %	893 (760; 1040)	43 (18; 85)	4 (2; 9)	9 (5; 14)	476368 (0.46)
90%	0.5	35449	10 %	5299 (4509; 6173)	255 (107; 503)	25 (10; 51)	54 (28; 80)	655287 (0.31)
	1	21126	6 %	3158 (2687; 3679)	152 (64; 300)	15 (6; 30)	32 (17; 48)	628440 (0.34)
	1.5	15603	4 %	2332 (1985; 2717)	112 (47; 221)	11 (5; 22)	24 (12; 35)	587794 (0.36)
	2	11698	3 %	1749 (1488; 2037)	84 (35; 166)	8 (3; 17)	18 (9; 26)	556959 (0.39)
	4	9969	3 %	1490 (1268; 1736)	72 (30; 141)	7 (3; 14)	15 (8; 23)	503047 (0.43)
*65%	4	356072		53224 (45290; 62007)	2565 (1080; 5050)	254 (105; 511)	540 (283; 805)	434619 (0.51)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_eff = 1.2, 1.3, 1.4)

Table S52: Seasonal influenza with R_eff=1.2: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	6626	3227	217	1692	225	7721	330	83	251	158 (75; 307)	3
	1	10185	2411	95	743	99	11659	145	36	26	-15 (-51; 51)	12
	1.5	7817	1757	48	376	50	9100	73	18	-19	-40 (-59; -6)	13
	2	5803	1234	15	116	15	6892	23	6	-48	-54 (-60; -43)	14
80 %	0.5	4275	5276	315	2477	327	6432	488	120	423	278 (162; 501)	2
	1	9821	4456	174	1365	180	12559	269	66	141	61 (-3; 185)	5
	1.5	7909	3799	119	932	123	10535	184	45	76	22 (-22; 106)	10
	2	6136	3274	80	626	82	8622	123	30	35	-1 (-31; 55)	11
	4	43	2034	62	486	65	1465	95	24	80	53 (29; 96)	9
90 %	**0.5	2281	6721	379	2982	393	5247	588	145	535	361 (220; 630)	1
	1	9248	5901	225	1770	233	12921	349	86	217	114 (31; 274)	4
	1.5	7706	5244	165	1296	171	11319	255	63	140	65 (3; 182)	6
	2	6128	4719	122	962	127	9637	190	47	91	36 (-10; 122)	8
	4	-103	3479	103	805	107	2361	157	39	133	89 (49; 160)	7
*65 %	4	77809	0	1652	12841	1715	94017	2522	632	3844	3127 (2506; 4285)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S53: Seasonal influenza with R_eff=1.3: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	24396	3227	208	1623	216	25577	316	79	56	-35 (-113; 109)	4
	1	22741	2411	91	712	95	24254	139	35	-109	-148 (-183; -84)	14
	1.5	15890	1757	46	359	48	17195	70	17	-105	-125 (-143; -93)	13
	2	10614	1234	14	110	15	11710	21	5	-98	-104 (-110; -94)	12
80 %	0.5	26897	5276	309	2427	320	29117	478	117	181	39 (-74; 257)	2
	1	26834	4456	171	1341	177	29602	264	65	-38	-116 (-179; 5)	9
	1.5	19957	3799	117	921	122	22596	181	44	-49	-102 (-146; -19)	10
	2	14572	3274	79	624	82	17060	123	30	-51	-87 (-117; -31)	11
	4	3124	2034	63	489	65	4542	95	24	49	22 (-2; 66)	5
90 %	**0.5	28026	6721	375	2948	389	31036	581	142	264	92 (-46; 358)	1
	1	29149	5901	223	1755	232	32840	346	85	11	-91 (-174; 67)	6
	1.5	22352	5244	164	1291	170	25970	254	62	-10	-85 (-147; 31)	7
	2	16942	4719	123	965	127	20447	190	46	-19	-74 (-121; 13)	8
	4	4977	3479	104	813	108	7431	158	39	83	39 (-3; 111)	3
*65 %	4	127726	0	2730	21215	2835	154506	4165	1041	6354	5171 (4145; 7083)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S54: Seasonal influenza with R_eff=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	40373	3227	197	1538	205	41661	300	75	-125	-211 (-285; -74)	6
	1	33921	2411	86	672	89	35484	131	33	-231	-268 (-301; -208)	14
	1.5	23045	1757	43	339	45	24375	66	16	-183	-201 (-218; -170)	11
	2	14853	1234	13	104	14	15957	20	5	-143	-147 (-154; -138)	8
80 %	0.5	47498	5276	297	2333	308	49836	459	112	-49	-186 (-295; 25)	4
	1	42165	4456	164	1292	171	44993	254	62	-205	-280 (-341; -163)	13
	1.5	30808	3799	113	891	118	33486	175	43	-166	-218 (-260; -138)	10
	2	22159	3274	77	608	80	24668	120	29	-132	-167 (-196; -112)	7
	**4	5959	2034	61	477	63	7391	93	23	18	-8 (-32; 35)	2
90 %	0.5	51616	6721	363	2853	377	54744	562	137	3	-163 (-297; 94)	3
	1	47210	5901	216	1701	225	50970	335	82	-185	-283 (-365; -130)	12
	1.5	35625	5244	160	1256	166	39288	247	60	-153	-226 (-286; -112)	9
	2	26756	4719	120	942	124	30290	185	45	-124	-177 (-223; -92)	5
	4	9690	3479	102	797	106	12165	155	39	31	-12 (-52; 60)	1
*65 %	4	169550	0	3645	28322	3787	205305	5558	1387	8486	6908 (5538; 9453)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

B. Moderate pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S55: Moderate pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	28133	6 %	4205 (3578; 4899)	203 (85; 399)	20 (8; 40)	43 (22; 64)	1076456 (0.22)
	1	12265	3 %	1833 (1560; 2136)	88 (37; 174)	9 (4; 18)	19 (10; 28)	1053779 (0.23)
	1.5	6175	1 %	923 (785; 1075)	44 (19; 88)	4 (2; 9)	9 (5; 14)	1012289 (0.24)
	2	1884	0 %	282 (240; 328)	14 (6; 27)	1 (1; 3)	3 (1; 4)	980937 (0.25)
80%	0.5	44537	9 %	6657 (5665; 7756)	321 (135; 632)	32 (13; 64)	68 (35; 101)	1219745 (0.19)
	1	25243	5 %	3773 (3211; 4396)	182 (77; 358)	18 (7; 36)	38 (20; 57)	1203434 (0.2)
	1.5	17842	4 %	2667 (2269; 3107)	129 (54; 253)	13 (5; 26)	27 (14; 40)	1157635 (0.21)
	2	12635	3 %	1889 (1607; 2200)	91 (38; 179)	9 (4; 18)	19 (10; 29)	1122532 (0.22)
	4	10336	2 %	1545 (1315; 1800)	74 (31; 147)	7 (3; 15)	16 (8; 23)	1054556 (0.23)
90%	0.5	55533	12 %	8301 (7063; 9671)	400 (168; 788)	40 (16; 80)	84 (44; 126)	1305850 (0.17)
	1	33934	7 %	5072 (4316; 5909)	244 (103; 481)	24 (10; 49)	51 (27; 77)	1296232 (0.18)
	1.5	25661	5 %	3836 (3264; 4469)	185 (78; 364)	18 (8; 37)	39 (20; 58)	1248656 (0.19)
	2	19823	4 %	2963 (2521; 3452)	143 (60; 281)	14 (6; 28)	30 (16; 45)	1211813 (0.2)
	4	17252	4 %	2579 (2194; 3004)	124 (52; 245)	12 (5; 25)	26 (14; 39)	1137472 (0.21)
*65%	4	472571		70638 (60108; 82294)	3404 (1433; 6703)	337 (139; 678)	717 (376; 1068)	923389 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S56: Moderate pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23911	4 %	3574 (3041; 4164)	172 (73; 339)	17 (7; 34)	36 (19; 54)	1536654 (0.21)
	1	10397	2 %	1554 (1322; 1811)	75 (32; 147)	7 (3; 15)	16 (8; 24)	1481925 (0.22)
	1.5	5229	1 %	782 (665; 911)	38 (16; 74)	4 (2; 7)	8 (4; 12)	1415092 (0.23)
	2	1603	0 %	240 (204; 279)	12 (5; 23)	1 (0; 2)	2 (1; 4)	1365492 (0.24)
80%	0.5	38383	6 %	5737 (4882; 6684)	276 (116; 544)	27 (11; 55)	58 (31; 87)	1771175 (0.18)
	1	21735	3 %	3249 (2765; 3785)	157 (66; 308)	16 (6; 31)	33 (17; 49)	1715061 (0.19)
	1.5	15399	2 %	2302 (1959; 2682)	111 (47; 218)	11 (5; 22)	23 (12; 35)	1637765 (0.2)
	2	10938	2 %	1635 (1391; 1905)	79 (33; 155)	8 (3; 16)	17 (9; 25)	1580026 (0.21)
	4	8976	1 %	1342 (1142; 1563)	65 (27; 127)	6 (3; 13)	14 (7; 20)	1480115 (0.22)
90%	0.5	48157	7 %	7198 (6125; 8386)	347 (146; 683)	34 (14; 69)	73 (38; 109)	1918403 (0.16)
	1	29392	4 %	4393 (3738; 5118)	212 (89; 417)	21 (9; 42)	45 (23; 66)	1863824 (0.17)
	1.5	22247	3 %	3325 (2830; 3874)	160 (67; 316)	16 (7; 32)	34 (18; 50)	1780683 (0.18)
	2	17229	3 %	2575 (2191; 3000)	124 (52; 244)	12 (5; 25)	26 (14; 39)	1718213 (0.19)
	4	15009	2 %	2243 (1909; 2614)	108 (46; 213)	11 (4; 22)	23 (12; 34)	1607837 (0.2)
*65%	4	655087		97920 (83322; 114077)	4718 (1986; 9291)	468 (193; 939)	993 (521; 1481)	1282188 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S57: Moderate pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20231	3 %	3024 (2573; 3523)	146 (61; 287)	14 (6; 29)	31 (16; 46)	1875814 (0.2)
	1	8773	1 %	1311 (1116; 1528)	63 (27; 124)	6 (3; 13)	13 (7; 20)	1421509 (0.24)
	1.5	4406	1 %	659 (560; 767)	32 (13; 62)	3 (1; 6)	7 (4; 10)	1663384 (0.23)
	2	1353	0 %	202 (172; 236)	10 (4; 19)	1 (0; 2)	2 (1; 3)	1292273 (0.27)
80%	0.5	32770	4 %	4898 (4168; 5707)	236 (99; 465)	23 (10; 47)	50 (26; 74)	1904160 (0.19)
	1	18536	2 %	2771 (2358; 3228)	134 (56; 263)	13 (5; 27)	28 (15; 42)	1535194 (0.22)
	1.5	13145	2 %	1965 (1672; 2289)	95 (40; 186)	9 (4; 19)	20 (10; 30)	1604236 (0.22)
	2	9360	1 %	1399 (1191; 1630)	67 (28; 133)	7 (3; 13)	14 (7; 21)	1329505 (0.25)
	4	7686	1 %	1149 (978; 1338)	55 (23; 109)	5 (2; 11)	12 (6; 17)	1700244 (0.22)
90%	0.5	41299	5 %	6173 (5253; 7192)	297 (125; 586)	29 (12; 59)	63 (33; 93)	2214420 (0.16)
	1	25159	3 %	3761 (3200; 4381)	181 (76; 357)	18 (7; 36)	38 (20; 57)	1747129 (0.19)
	1.5	19046	2 %	2847 (2423; 3317)	137 (58; 270)	14 (6; 27)	29 (15; 43)	1802544 (0.19)
	2	14779	2 %	2209 (1880; 2574)	106 (45; 210)	11 (4; 21)	22 (12; 33)	1482638 (0.22)
	4	12882	2 %	1926 (1639; 2243)	93 (39; 183)	9 (4; 18)	20 (10; 29)	1887420 (0.2)
*65 %	4	788750		117899 (100323; 137353)	5681 (2392; 11187)	563 (232; 1131)	1196 (627; 1783)	1543947 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S58: Moderate pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	39715	3227	288	2248	300	40106	446	116	37	-88 (-197; 112)	3
	1	41059	2411	126	980	131	42233	194	51	-236	-290 (-338; -203)	14
	1.5	29349	1757	63	493	66	30484	98	25	-213	-240 (-264; -196)	10
	2	20311	1234	19	151	20	21356	30	8	-188	-195 (-204; -182)	7
80 %	0.5	51917	5276	456	3585	474	52678	718	183	181	-26 (-197; 296)	2
	1	58528	4456	258	2032	269	60425	407	104	-209	-326 (-424; -142)	8
	1.5	47571	3799	183	1436	190	49561	288	73	-218	-298 (-370; -170)	12
	2	38890	3274	129	1017	135	40883	204	52	-213	-269 (-321; -176)	11
	4	17144	2034	106	826	110	18137	164	42	-21	-63 (-108; 12)	4
90 %	**0.5	58093	6721	568	4470	591	59185	896	228	292	35 (-179; 437)	1
	1	68718	5901	347	2731	361	71179	547	139	-179	-333 (-468; -87)	6
	1.5	58487	5244	263	2066	273	61130	413	105	-210	-323 (-428; -136)	9
	2	50206	4719	203	1596	211	52915	319	81	-220	-306 (-389; -161)	13
	4	27626	3479	177	1379	184	29367	273	70	-26	-97 (-172; 28)	5
*65 %	4	353389	0	4837	37589	5034	400849	7563	2015	14249	12167 (10343; 15533)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S59: Moderate pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	79499	3227	245	1911	255	80316	377	96	-442	-547 (-640; -378)	5
	1	67826	2411	106	831	111	69189	164	42	-542	-586 (-628; -511)	8
	1.5	46225	1757	54	418	56	47455	82	21	-401	-423 (-445; -385)	4
	2	30062	1234	16	128	17	31135	25	6	-292	-298 (-307; -285)	2
80 %	0.5	112034	5276	393	3090	409	113418	616	154	-541	-719 (-866; -440)	7
	1	103854	4456	222	1750	232	106106	349	87	-733	-832 (-918; -674)	12
	1.5	81632	3799	158	1240	164	83870	247	62	-608	-675 (-739; -563)	10
	2	64859	3274	112	880	117	67024	175	44	-508	-553 (-603; -472)	6
	**4	32045	2034	92	717	96	33174	141	36	-197	-229 (-276; -162)	1
90 %	0.5	131722	6721	493	3876	514	133561	773	193	-589	-810 (-999; -460)	9
	1	126402	5901	301	2366	313	129323	471	118	-848	-975 (-1097; -761)	14
	1.5	104030	5244	228	1791	237	107019	357	89	-735	-828 (-926; -665)	13
	2	86989	4719	176	1387	184	89961	276	69	-641	-708 (-792; -581)	11
	4	52487	3479	154	1199	160	54453	236	60	-319	-373 (-450; -261)	3
*65 %	4	490524	0	6705	52107	6990	556325	10461	2766	19797	16907 (14381; 21582)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S60: Moderate pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	110428	3227	207	1617	216	111616	318	80	-820	-908 (-988; -764)	10
	1	64386	2411	90	701	94	65912	138	35	-534	-572 (-607; -508)	7
	1.5	57056	1757	45	352	47	58369	69	17	-526	-543 (-563; -511)	6
	**2	27672	1234	14	108	14	28770	21	5	-272	-277 (-284; -266)	1
80 %	0.5	130317	5276	335	2638	350	132270	524	129	-825	-977 (-1104; -737)	11
	1	89774	4456	190	1492	198	92349	296	73	-646	-730 (-803; -595)	9
	1.5	80299	3799	135	1058	140	82765	210	52	-634	-691 (-746; -594)	8
	2	50866	3274	96	753	100	53191	149	37	-393	-431 (-474; -363)	3
	4	40505	2034	79	614	82	41765	120	30	-305	-330 (-376; -269)	2
90 %	0.5	171447	6721	423	3324	441	173981	660	163	-1114	-1298 (-1466; -998)	14
	1	117496	5901	258	2025	269	120845	402	99	-831	-940 (-1044; -756)	13
	1.5	107828	5244	195	1533	204	111141	304	75	-829	-907 (-994; -766)	12
	2	71049	4719	151	1190	158	74270	236	58	-522	-580 (-650; -471)	5
	4	68532	3479	132	1029	138	70713	202	50	-519	-560 (-638; -457)	4
*65 %	4	590564	0	8073	62738	8429	669804	12573	3304	23861	20379 (17341; 26010)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

C. Severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S61: Severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	28133	6 %	5612 (4902; 6382)	554 (338; 848)	94 (56; 146)	63 (33; 94)	1076454 (0.22)
	1	12265	3 %	2447 (2137; 2782)	241 (147; 370)	41 (25; 64)	27 (14; 41)	1053777 (0.23)
	1.5	6175	1 %	1232 (1076; 1401)	122 (74; 186)	21 (12; 32)	14 (7; 21)	1012287 (0.24)
	2	1884	0 %	376 (328; 427)	37 (23; 57)	6 (4; 10)	4 (2; 6)	980935 (0.25)
80%	0.5	44537	9 %	8884 (7761; 10103)	876 (535; 1343)	149 (89; 231)	100 (52; 148)	1219743 (0.19)
	1	25243	5 %	5035 (4399; 5726)	497 (303; 761)	84 (51; 131)	56 (30; 84)	1203432 (0.2)
	1.5	17842	4 %	3559 (3109; 4047)	351 (214; 538)	60 (36; 92)	40 (21; 59)	1157633 (0.21)
	2	12635	3 %	2520 (2202; 2866)	249 (152; 381)	42 (25; 65)	28 (15; 42)	1122530 (0.22)
	4	10336	2 %	2062 (1801; 2345)	203 (124; 312)	34 (21; 54)	23 (12; 34)	1054554 (0.23)
90%	0.5	55533	12 %	11077 (9677; 12597)	1093 (668; 1675)	185 (111; 288)	124 (65; 185)	1305848 (0.17)
	1	33934	7 %	6769 (5913; 7698)	668 (408; 1023)	113 (68; 176)	76 (40; 113)	1296230 (0.18)
	1.5	25661	5 %	5119 (4471; 5821)	505 (308; 774)	86 (51; 133)	57 (30; 86)	1248654 (0.19)
	2	19823	4 %	3954 (3454; 4497)	390 (238; 598)	66 (40; 103)	44 (23; 66)	1211811 (0.2)
	4	17252	4 %	3441 (3006; 3914)	340 (207; 520)	58 (35; 89)	39 (20; 58)	1137470 (0.21)
*65%	4	472571		94264 (82347; 107200)	9300 (5681; 14253)	1577 (948; 2448)	1057 (555; 1576)	923387 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S62: Severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention				Median (0.25; 0.75 percentiles) relative to baseline				Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23911	4 %	4770 (4167; 5424)	471 (287; 721)	80 (48; 124)	53 (28; 80)	1536651 (0.21)
	1	10397	2 %	2074 (1812; 2358)	205 (125; 314)	35 (21; 54)	23 (12; 35)	1481923 (0.22)
	1.5	5229	1 %	1043 (911; 1186)	103 (63; 158)	17 (10; 27)	12 (6; 17)	1415090 (0.23)
	2	1603	0 %	320 (279; 364)	32 (19; 48)	5 (3; 8)	4 (2; 5)	1365490 (0.24)
80%	0.5	38383	6 %	7656 (6688; 8707)	755 (461; 1158)	128 (77; 199)	86 (45; 128)	1771173 (0.18)
	1	21735	3 %	4336 (3787; 4930)	428 (261; 656)	73 (44; 113)	49 (26; 72)	1715059 (0.19)
	1.5	15399	2 %	3072 (2683; 3493)	303 (185; 464)	51 (31; 80)	34 (18; 51)	1637762 (0.2)
	2	10938	2 %	2182 (1906; 2481)	215 (131; 330)	36 (22; 57)	24 (13; 36)	1580023 (0.21)
	4	8976	1 %	1790 (1564; 2036)	177 (108; 271)	30 (18; 46)	20 (11; 30)	1480112 (0.22)
90%	0.5	48157	7 %	9606 (8391; 10924)	948 (579; 1452)	161 (97; 249)	108 (57; 161)	1918401 (0.16)
	1	29392	4 %	5863 (5122; 6667)	578 (353; 886)	98 (59; 152)	66 (34; 98)	1863821 (0.17)
	1.5	22247	3 %	4438 (3877; 5047)	438 (267; 671)	74 (45; 115)	50 (26; 74)	1780681 (0.18)
	2	17229	3 %	3437 (3002; 3908)	339 (207; 520)	57 (35; 89)	39 (20; 57)	1718211 (0.19)
	4	15009	2 %	2994 (2615; 3405)	295 (180; 453)	50 (30; 78)	34 (18; 50)	1607834 (0.2)
*65%	4	655087		130671 (114150; 148602)	12892 (7875; 19757)	2186 (1314; 3393)	1465 (769; 2184)	1282185 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S63: Severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20231	3 %	4035 (3525; 4589)	398 (243; 610)	67 (41; 105)	45 (24; 67)	1875811 (0.2)
	1	8773	1 %	1750 (1529; 1990)	173 (105; 265)	29 (18; 45)	20 (10; 29)	1421506 (0.24)
	1.5	4406	1 %	879 (768; 999)	87 (53; 133)	15 (9; 23)	10 (5; 15)	1663381 (0.23)
	2	1353	0 %	270 (236; 307)	27 (16; 41)	5 (3; 7)	3 (2; 5)	1292270 (0.27)
80%	0.5	32770	4 %	6537 (5710; 7434)	645 (394; 988)	109 (66; 170)	73 (38; 109)	1904157 (0.19)
	1	18536	2 %	3697 (3230; 4205)	365 (223; 559)	62 (37; 96)	41 (22; 62)	1535191 (0.22)
	1.5	13145	2 %	2622 (2291; 2982)	259 (158; 396)	44 (26; 68)	29 (15; 44)	1604234 (0.22)
	2	9360	1 %	1867 (1631; 2123)	184 (113; 282)	31 (19; 48)	21 (11; 31)	1329502 (0.25)
	4	7686	1 %	1533 (1339; 1744)	151 (92; 232)	26 (15; 40)	17 (9; 26)	1700241 (0.22)
90%	0.5	41299	5 %	8238 (7196; 9368)	813 (496; 1246)	138 (83; 214)	92 (48; 138)	2214417 (0.16)
	1	25159	3 %	5018 (4384; 5707)	495 (302; 759)	84 (50; 130)	56 (30; 84)	1747127 (0.19)
	1.5	19046	2 %	3799 (3319; 4320)	375 (229; 574)	64 (38; 99)	43 (22; 64)	1802541 (0.19)
	2	14779	2 %	2948 (2575; 3353)	291 (178; 446)	49 (30; 77)	33 (17; 49)	1482635 (0.22)
	4	12882	2 %	2570 (2245; 2922)	254 (155; 389)	43 (26; 67)	29 (15; 43)	1887417 (0.2)
*65%	4	788750		157333 (137442; 178923)	15523 (9482; 23789)	2632 (1582; 4086)	1764 (926; 2630)	1543944 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S64: Severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	39711	3228	384	6409	314	35831	496	171	131	9 (-107; 215)	3
	1	41055	2411	167	2794	137	40367	216	75	-196	-248 (-299; -160)	14
	1.5	29347	1757	84	1407	69	29544	109	38	-192	-218 (-244; -174)	13
	2	20309	1235	26	429	21	21068	33	11	-182	-189 (-198; -175)	12
80 %	0.5	51912	5275	608	10178	498	45903	798	270	330	126 (-54; 453)	2
	1	58523	4455	345	5769	282	56582	452	153	-125	-238 (-343; -55)	8
	1.5	47565	3799	244	4077	199	46843	319	108	-158	-237 (-313; -107)	10
	2	38884	3274	173	2887	141	38957	226	76	-171	-225 (-281; -133)	11
	4	17155	2034	141	2355	116	16578	182	62	13	-27 (-76; 48)	5
90 %	**0.5	58083	6720	758	12691	621	50734	995	337	477	227 (-2; 631)	1
	1	68708	5900	463	7755	379	66011	607	205	-66	-215 (-359; 31)	6
	1.5	58477	5244	350	5864	287	57219	459	155	-124	-235 (-347; -49)	7
	2	50195	4719	271	4530	222	49892	355	120	-154	-237 (-327; -93)	9
	4	27643	3480	236	3930	193	26764	303	104	30	-37 (-117; 89)	4
*65 %	4	353389	0	6452	107683	5285	472808	8422	2972	15843	13847 (11912; 17264)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S65: Severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	79493	3228	326	5447	268	76679	419	142	-363	-466 (-564; -294)	4
	1	67820	2411	142	2369	116	67604	182	62	-507	-550 (-595; -475)	9
	1.5	46221	1757	71	1191	59	46657	92	31	-384	-405 (-428; -367)	5
	2	30059	1235	22	365	18	30889	28	10	-287	-292 (-301; -280)	3
80 %	0.5	112027	5275	524	8771	430	107577	683	227	-414	-588 (-746; -309)	6
	1	103847	4455	297	4967	243	102795	386	128	-662	-758 (-850; -600)	13
	1.5	81624	3799	210	3519	172	81521	274	91	-558	-623 (-691; -511)	10
	2	64851	3274	149	2500	122	65354	194	64	-472	-515 (-569; -434)	8
	**4	32059	2034	123	2045	100	31825	157	53	-168	-199 (-247; -131)	1
90 %	0.5	131708	6720	657	11005	539	126227	857	285	-431	-643 (-847; -294)	7
	1	126388	5900	401	6717	329	124841	522	174	-751	-875 (-1005; -662)	14
	1.5	104016	5244	304	5084	249	103623	395	131	-661	-751 (-856; -589)	12
	2	86975	4719	235	3937	193	87328	306	101	-585	-650 (-738; -521)	11
	4	52510	3480	205	3419	168	52197	262	88	-270	-323 (-403; -208)	2
*65 %	4	490525	0	8944	149272	7338	656078	11642	4080	21996	19236 (16545; 23959)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S66: Severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	110419	3228	276	4609	227	108535	352	118	-755	-840 (-925; -693)	12
	1	64381	2411	120	1999	98	64575	153	51	-506	-542 (-580; -478)	6
	1.5	57051	1757	60	1004	49	57695	77	26	-512	-528 (-549; -496)	7
	**2	27669	1235	18	308	15	28562	24	8	-268	-272 (-280; -261)	2
80 %	0.5	130310	5275	447	7489	368	127281	580	190	-718	-865 (-1002; -627)	10
	1	89768	4455	253	4236	208	89525	328	108	-585	-666 (-746; -532)	8
	1.5	80292	3799	179	3004	147	80759	232	76	-591	-646 (-706; -550)	9
	2	50860	3274	128	2139	105	51762	165	54	-363	-399 (-445; -330)	3
	4	40521	2034	105	1751	86	40613	133	44	-281	-305 (-353; -242)	1
90 %	0.5	171432	6720	564	9438	463	167687	731	240	-979	-1159 (-1338; -860)	14
	1	117483	5900	343	5749	282	117008	445	146	-748	-854 (-967; -671)	11
	1.5	107814	5244	260	4352	214	108232	337	110	-767	-842 (-935; -702)	13
	2	71037	4719	202	3377	166	72012	261	85	-473	-530 (-605; -420)	4
	4	68559	3480	176	2935	145	68783	223	74	-478	-518 (-598; -413)	5
*65 %	4	590566	0	10769	179729	8849	789912	13984	4873	26498	23174 (19932; 28853)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

D. Very severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S67: Very severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	28133	6 %	7019 (6248; 7847)	975 (680; 1351)	243 (167; 341)	196 (103; 292)	1076450 (0.22)
	1	12265	3 %	3060 (2724; 3421)	425 (297; 589)	106 (73; 149)	86 (45; 127)	1053773 (0.23)
	1.5	6175	1 %	1541 (1371; 1722)	214 (149; 296)	53 (37; 75)	43 (23; 64)	1012284 (0.24)
	2	1884	0 %	470 (418; 525)	65 (46; 90)	16 (11; 23)	13 (7; 20)	980932 (0.25)
80%	0.5	44537	9 %	11112 (9891; 12422)	1544 (1077; 2138)	385 (264; 540)	310 (163; 462)	1219739 (0.19)
	1	25243	5 %	6298 (5606; 7041)	875 (610; 1212)	218 (150; 306)	176 (92; 262)	1203429 (0.2)
	1.5	17842	4 %	4452 (3962; 4976)	619 (431; 857)	154 (106; 217)	124 (65; 185)	1157630 (0.21)
	2	12635	3 %	3152 (2806; 3524)	438 (306; 607)	109 (75; 153)	88 (46; 131)	1122526 (0.22)
	4	10336	2 %	2579 (2295; 2883)	358 (250; 496)	89 (61; 125)	72 (38; 107)	1054551 (0.23)
90%	0.5	55533	12 %	13856 (12333; 15489)	1925 (1343; 2666)	480 (330; 674)	387 (203; 576)	1305845 (0.17)
	1	33934	7 %	8467 (7536; 9465)	1176 (821; 1629)	293 (201; 412)	237 (124; 352)	1296227 (0.18)
	1.5	25661	5 %	6403 (5699; 7157)	890 (621; 1232)	222 (152; 311)	179 (94; 266)	1248650 (0.19)
	2	19823	4 %	4946 (4402; 5529)	687 (479; 952)	171 (118; 241)	138 (72; 206)	1211808 (0.2)
	4	17252	4 %	4304 (3831; 4812)	598 (417; 828)	149 (102; 209)	120 (63; 179)	1137467 (0.21)
*65%	4	472571		117909 (104951; 131806)	16384 (11427; 22688)	4085 (2806; 5735)	3295 (1726; 4904)	923383 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S68: Very severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23911	4 %	5966 (5310; 6669)	829 (578; 1148)	207 (142; 290)	167 (87; 248)	1536646 (0.21)
	1	10397	2 %	2594 (2309; 2900)	360 (251; 499)	90 (62; 126)	72 (38; 108)	1481918 (0.22)
	1.5	5229	1 %	1305 (1161; 1458)	181 (126; 251)	45 (31; 63)	36 (19; 54)	1415085 (0.23)
	2	1603	0 %	400 (356; 447)	56 (39; 77)	14 (10; 19)	11 (6; 17)	1365485 (0.24)
80%	0.5	38383	6 %	9577 (8524; 10706)	1331 (928; 1843)	332 (228; 466)	268 (140; 398)	1771168 (0.18)
	1	21735	3 %	5423 (4827; 6062)	754 (526; 1044)	188 (129; 264)	152 (79; 226)	1715054 (0.19)
	1.5	15399	2 %	3842 (3420; 4295)	534 (372; 739)	133 (91; 187)	107 (56; 160)	1637757 (0.2)
	2	10938	2 %	2729 (2429; 3051)	379 (264; 525)	95 (65; 133)	76 (40; 114)	1580018 (0.21)
	4	8976	1 %	2240 (1993; 2504)	311 (217; 431)	78 (53; 109)	63 (33; 93)	1480107 (0.22)
90%	0.5	48157	7 %	12015 (10695; 13432)	1670 (1164; 2312)	416 (286; 584)	336 (176; 500)	1918396 (0.16)
	1	29392	4 %	7333 (6528; 8198)	1019 (711; 1411)	254 (175; 357)	205 (107; 305)	1863816 (0.17)
	1.5	22247	3 %	5551 (4941; 6205)	771 (538; 1068)	192 (132; 270)	155 (81; 231)	1780676 (0.18)
	2	17229	3 %	4299 (3826; 4805)	597 (417; 827)	149 (102; 209)	120 (63; 179)	1718206 (0.19)
	4	15009	2 %	3745 (3333; 4186)	520 (363; 721)	130 (89; 182)	105 (55; 156)	1607829 (0.2)
*65%	4	655087		163448 (145485; 182713)	22711 (15841; 31451)	5662 (3890; 7950)	4567 (2392; 6798)	1282181 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S69: Very severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and no extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20231	3 %	5048 (4493; 5643)	701 (489; 971)	175 (120; 246)	141 (74; 210)	1875806 (0.2)
	1	8773	1 %	2189 (1948; 2447)	304 (212; 421)	76 (52; 106)	61 (32; 91)	1421501 (0.24)
	1.5	4406	1 %	1099 (979; 1229)	153 (107; 212)	38 (26; 53)	31 (16; 46)	1663376 (0.23)
	2	1353	0 %	338 (300; 377)	47 (33; 65)	12 (8; 16)	9 (5; 14)	1292265 (0.27)
80%	0.5	32770	4 %	8176 (7278; 9140)	1136 (792; 1573)	283 (195; 398)	228 (120; 340)	1904152 (0.19)
	1	18536	2 %	4625 (4117; 5170)	643 (448; 890)	160 (110; 225)	129 (68; 192)	1535186 (0.22)
	1.5	13145	2 %	3280 (2919; 3666)	456 (318; 631)	114 (78; 160)	92 (48; 136)	1604228 (0.22)
	2	9360	1 %	2335 (2079; 2611)	325 (226; 449)	81 (56; 114)	65 (34; 97)	1329497 (0.25)
	4	7686	1 %	1918 (1707; 2144)	266 (186; 369)	66 (46; 93)	54 (28; 80)	1700235 (0.22)
90%	0.5	41299	5 %	10304 (9172; 11519)	1432 (999; 1983)	357 (245; 501)	288 (151; 429)	2214411 (0.16)
	1	25159	3 %	6277 (5587; 7017)	872 (608; 1208)	217 (149; 305)	175 (92; 261)	1747122 (0.19)
	1.5	19046	2 %	4752 (4230; 5312)	660 (461; 914)	165 (113; 231)	133 (70; 198)	1802536 (0.19)
	2	14779	2 %	3687 (3282; 4122)	512 (357; 710)	128 (88; 179)	103 (54; 153)	1482630 (0.22)
	4	12882	2 %	3214 (2861; 3593)	447 (312; 618)	111 (76; 156)	90 (47; 134)	1887411 (0.2)
*65%	4	788750		196797 (175169; 219993)	27345 (19073; 37868)	6817 (4683; 9572)	5499 (2880; 8185)	1543938 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S70: Very severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	39716	3226	480	12087	329	30045	797	533	490	390 (239; 606)	3
	1	41061	2409	209	5270	144	37847	347	232	-39	-81 (-148; 12)	12
	1.5	29351	1756	105	2653	72	28276	175	117	-114	-135 (-169; -88)	13
	2	20312	1234	32	809	22	20682	53	36	-158	-164 (-175; -149)	14
80 %	0.5	51913	5277	760	19137	521	36772	1273	842	898	729 (497; 1075)	2
	1	58525	4456	431	10846	295	51409	720	476	196	101 (-32; 298)	7
	1.5	47568	3799	305	7666	209	43187	509	336	68	1 (-94; 141)	10
	2	38887	3274	216	5429	148	36368	360	237	-11	-58 (-127; 42)	11
	4	17137	2033	176	4441	121	14432	291	194	144	109 (49; 192)	8
90 %	**0.5	58087	6722	948	23861	650	39349	1586	1049	1185	976 (683; 1409)	1
	1	68713	5901	579	14581	397	59057	968	640	366	238 (56; 504)	4
	1.5	58482	5244	438	11026	300	51962	731	483	201	106 (-33; 307)	6
	2	50201	4718	338	8517	232	45832	564	372	97	24 (-86; 180)	9
	4	27614	3477	294	7412	202	23183	486	324	249	192 (91; 329)	5
*65 %	4	353397	0	8067	201918	5534	568916	13624	9257	22024	20394 (17899; 24010)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S71: Very severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	79503	3226	408	10273	280	71767	668	443	-64	-148 (-277; 34)	4
	1	67830	2409	177	4467	122	65473	290	192	-377	-413 (-470; -333)	11
	1.5	46227	1756	89	2247	61	45586	146	97	-319	-336 (-366; -296)	7
	2	30063	1234	27	689	19	30562	45	30	-267	-272 (-282; -258)	6
80 %	0.5	112030	5277	655	16492	450	99710	1082	709	65	-81 (-281; 217)	2
	1	103851	4456	371	9339	255	98342	612	400	-391	-472 (-589; -304)	14
	1.5	81629	3799	263	6617	181	78368	433	283	-366	-423 (-508; -303)	9
	2	64856	3274	187	4700	128	63115	307	201	-336	-375 (-439; -288)	8
	4	32035	2033	153	3857	105	29953	249	164	-56	-84 (-141; -11)	3
90 %	**0.5	131716	6722	822	20692	565	116359	1357	888	170	-11 (-268; 363)	1
	1	126396	5901	502	12629	345	118822	827	541	-385	-494 (-655; -263)	13
	1.5	104024	5244	380	9559	261	99069	625	409	-385	-465 (-593; -289)	12
	2	86983	4718	294	7403	202	83803	484	316	-371	-429 (-534; -291)	10
	4	52470	3477	256	6449	176	49067	417	275	-84	-130 (-225; -8)	5
*65 %	4	490533	0	11182	279903	7684	789302	18781	12710	30493	28221 (24779; 33235)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S72: Very severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and no extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	110434	3226	345	8692	238	104384	559	368	-505	-577 (-686; -421)	13
	1	64390	2409	150	3769	103	62777	242	159	-398	-428 (-476; -361)	8
	1.5	57059	1756	75	1893	52	56796	122	80	-457	-472 (-498; -437)	11
	2	27673	1234	23	581	16	28287	37	24	-251	-255 (-264; -243)	3
80 %	0.5	130313	5277	559	14081	385	120566	914	593	-316	-440 (-611; -186)	5
	1	89771	4456	316	7965	218	85729	516	335	-358	-428 (-526; -284)	7
	1.5	80296	3799	224	5648	154	78069	366	237	-431	-479 (-552; -376)	9
	2	50864	3274	160	4022	110	49846	260	168	-248	-282 (-336; -207)	2
	**4	40494	2033	131	3302	90	39004	211	138	-187	-209 (-262; -143)	1
90 %	0.5	171441	6722	705	17745	485	159227	1151	747	-473	-628 (-849; -306)	12
	1	117490	5901	429	10810	296	111856	700	454	-441	-533 (-672; -336)	10
	1.5	107823	5244	325	8184	224	104334	530	343	-534	-602 (-712; -450)	14
	2	71045	4718	252	6350	174	68987	410	266	-293	-344 (-432; -226)	4
	4	68514	3477	220	5535	151	66085	354	231	-320	-357 (-446; -246)	6
*65 %	4	590573	0	13464	337014	9266	950317	22511	15182	36659	33907 (29785; 39945)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Section IV: Scenarios with low symptomatic proportion (35% children, and 25% adults assumed to be symptomatic), with extra mixing

A. Seasonal influenza

i. Epidemiology (R_eff = 1.2, 1.3, 1.4)

Table S73: Seasonal influenza with R_eff=1.2: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	17945	11 %	2682 (2282; 3125)	129 (54; 255)	13 (5; 26)	27 (14; 41)	238836 (0.4)
	1	7892	5 %	1180 (1004; 1374)	57 (24; 112)	6 (2; 11)	12 (6; 18)	236903 (0.43)
	1.5	3986	2 %	596 (507; 694)	29 (12; 57)	3 (1; 6)	6 (3; 9)	226116 (0.46)
	2	1232	1 %	184 (157; 215)	9 (4; 17)	1 (0; 2)	2 (1; 3)	217639 (0.48)
80%	0.5	25877	16 %	3868 (3291; 4506)	186 (78; 367)	18 (8; 37)	39 (21; 58)	256515 (0.36)
	1	14189	9 %	2121 (1805; 2471)	102 (43; 201)	10 (4; 20)	22 (11; 32)	256992 (0.38)
	1.5	9645	6 %	1442 (1227; 1680)	69 (29; 137)	7 (3; 14)	15 (8; 22)	245180 (0.41)
	2	6433	4 %	962 (818; 1120)	46 (20; 91)	5 (2; 9)	10 (5; 15)	235675 (0.44)
	4	5001	3 %	748 (636; 871)	36 (15; 71)	4 (1; 7)	8 (4; 11)	215703 (0.48)
90%	0.5	31068	19 %	4644 (3952; 5410)	224 (94; 441)	22 (9; 45)	47 (25; 70)	266234 (0.33)
	1	18343	11 %	2742 (2333; 3194)	132 (56; 260)	13 (5; 26)	28 (15; 41)	268862 (0.36)
	1.5	13389	8 %	2001 (1703; 2332)	96 (41; 190)	10 (4; 19)	20 (11; 30)	256646 (0.39)
	2	9872	6 %	1476 (1256; 1719)	71 (30; 140)	7 (3; 14)	15 (8; 22)	246685 (0.41)
	4	8304	5 %	1241 (1056; 1446)	60 (25; 118)	6 (2; 12)	13 (7; 19)	224932 (0.45)
*65 %	4	162646		24312 (20687; 28323)	1171 (493; 2307)	116 (48; 233)	247 (129; 368)	200628 (0.53)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S74: Seasonal influenza with R_eff=1.3: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	Mean workdays lost (proportion lost to caregiving)
65%	0.5	17154	6 %	2564 (2182; 2987)	124 (52; 243)	12 (5; 25)	26 (14; 39)	414674 (0.39)
	1	7519	3 %	1124 (956; 1309)	54 (23; 107)	5 (2; 11)	11 (6; 17)	398675 (0.42)
	1.5	3803	1 %	568 (484; 662)	27 (12; 54)	3 (1; 5)	6 (3; 9)	375805 (0.45)
	2	1175	0 %	176 (149; 205)	8 (4; 17)	1 (0; 2)	2 (1; 3)	358581 (0.47)
80%	0.5	25288	9 %	3780 (3216; 4404)	182 (77; 359)	18 (7; 36)	38 (20; 57)	457241 (0.34)
	1	13941	5 %	2084 (1773; 2428)	100 (42; 198)	10 (4; 20)	21 (11; 32)	440965 (0.37)
	1.5	9542	4 %	1426 (1214; 1662)	69 (29; 135)	7 (3; 14)	14 (8; 22)	414533 (0.4)
	2	6434	2 %	962 (818; 1120)	46 (20; 91)	5 (2; 9)	10 (5; 15)	394429 (0.42)
	4	5057	2 %	756 (643; 881)	36 (15; 72)	4 (1; 7)	8 (4; 11)	358719 (0.47)
90%	0.5	30656	11 %	4582 (3899; 5338)	221 (93; 435)	22 (9; 44)	46 (24; 69)	483185 (0.32)
	1	18183	7 %	2718 (2313; 3166)	131 (55; 258)	13 (5; 26)	28 (14; 41)	467434 (0.34)
	1.5	13344	5 %	1995 (1697; 2324)	96 (40; 189)	10 (4; 19)	20 (11; 30)	438982 (0.37)
	2	9934	4 %	1485 (1264; 1730)	72 (30; 141)	7 (3; 14)	15 (8; 22)	417174 (0.4)
	4	8401	3 %	1256 (1069; 1463)	61 (25; 119)	6 (2; 12)	13 (7; 19)	377827 (0.44)
*65%	4	267991		40058 (34087; 46668)	1930 (813; 3801)	191 (79; 384)	406 (213; 606)	328700 (0.52)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S75: Seasonal influenza with R_eff=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	16209	5 %	2423 (2062; 2823)	117 (49; 230)	12 (5; 23)	25 (13; 37)	564444 (0.38)
	1	7094	2 %	1060 (902; 1235)	51 (22; 101)	5 (2; 10)	11 (6; 16)	535802 (0.4)
	1.5	3585	1 %	536 (456; 624)	26 (11; 51)	3 (1; 5)	5 (3; 8)	502240 (0.44)
	2	1102	0 %	165 (140; 192)	8 (3; 16)	1 (0; 2)	2 (1; 2)	477284 (0.46)
80%	0.5	24283	7 %	3630 (3089; 4229)	175 (74; 344)	17 (7; 35)	37 (19; 55)	629516 (0.33)
	1	13422	4 %	2006 (1707; 2337)	97 (41; 190)	10 (4; 19)	20 (11; 30)	598014 (0.36)
	1.5	9226	3 %	1379 (1173; 1607)	66 (28; 131)	7 (3; 13)	14 (7; 21)	558548 (0.39)
	2	6274	2 %	938 (798; 1093)	45 (19; 89)	4 (2; 9)	10 (5; 14)	528991 (0.41)
	4	4968	1 %	743 (632; 865)	36 (15; 70)	4 (1; 7)	8 (4; 11)	479390 (0.46)
90%	0.5	29644	8 %	4431 (3771; 5162)	214 (90; 420)	21 (9; 43)	45 (24; 67)	670253 (0.31)
	1	17631	5 %	2635 (2243; 3070)	127 (53; 250)	13 (5; 25)	27 (14; 40)	637645 (0.33)
	1.5	12991	4 %	1942 (1652; 2262)	94 (39; 184)	9 (4; 19)	20 (10; 29)	594621 (0.36)
	2	9710	3 %	1451 (1235; 1691)	70 (29; 138)	7 (3; 14)	15 (8; 22)	562274 (0.38)
	4	8263	2 %	1235 (1051; 1439)	60 (25; 117)	6 (2; 12)	13 (7; 19)	507324 (0.43)
*65%	4	357358		53417 (45453; 62230)	2574 (1084; 5069)	255 (105; 512)	542 (284; 808)	436069 (0.5)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_eff = 1.2, 1.3, 1.4)

Table S76: Seasonal influenza with R_eff=1.2: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	9650	3227	184	1434	190	11069	280	70	167	88 (17; 214)	3
	1	11509	2411	81	631	84	13124	123	31	-11	-46 (-76; 11)	12
	1.5	8488	1757	41	319	42	9844	62	16	-38	-56 (-71; -27)	13
	2	6035	1234	13	98	13	7145	19	5	-54	-59 (-64; -50)	14
80 %	0.5	9057	5276	265	2083	275	11711	411	101	291	170 (72; 358)	2
	1	12441	4456	145	1142	151	15459	225	55	68	1 (-53; 104)	7
	1.5	9663	3799	99	776	102	12485	153	38	26	-19 (-56; 51)	10
	2	7303	3274	66	518	68	9926	102	25	1	-29 (-54; 18)	11
	4	878	2034	51	400	53	2408	78	19	53	32 (12; 67)	8
90 %	**0.5	8293	6721	318	2501	330	11865	493	121	372	226 (109; 452)	1
	1	12772	5901	188	1476	195	16814	291	72	120	34 (-36; 167)	4
	1.5	10199	5244	137	1078	142	14087	212	52	69	6 (-45; 103)	6
	2	7955	4719	101	795	105	11674	157	38	38	-8 (-46; 63)	9
	4	1305	3479	85	664	88	3948	129	32	89	53 (20; 112)	5
*65 %	4	78363	0	1665	12937	1728	94693	2541	636	3873	3151 (2526; 4317)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S77: Seasonal influenza with R_eff=1.3: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	27437	3227	176	1371	182	28936	267	67	-28	-104 (-170; 18)	5
	1	24078	2411	77	601	80	25731	117	29	-145	-178 (-208; -125)	14
	1.5	16549	1757	39	304	40	17923	59	15	-124	-140 (-155; -113)	13
	2	10839	1234	12	94	12	11955	18	5	-104	-108 (-114; -100)	11
80 %	0.5	31765	5276	259	2036	268	34478	401	98	49	-70 (-165; 115)	2
	1	29477	4456	143	1122	148	32520	221	54	-111	-176 (-229; -74)	12
	1.5	21715	3799	98	768	101	24548	151	37	-99	-144 (-180; -74)	10
	2	15748	3274	66	518	68	18370	102	25	-85	-115 (-140; -68)	8
	4	3948	2034	52	404	54	5473	79	20	23	1 (-19; 37)	4
90 %	0.5	34177	6721	314	2468	325	37792	486	119	101	-43 (-159; 179)	1
	1	32738	5901	186	1464	193	36796	288	71	-87	-172 (-241; -40)	9
	1.5	24889	5244	137	1074	142	28781	212	52	-82	-144 (-196; -47)	7
	2	18788	4719	102	800	105	22500	158	39	-72	-117 (-156; -45)	6
	**4	6405	3479	86	671	89	9037	131	33	39	3 (-32; 63)	3
*65 %	4	128298	0	2743	21316	2849	155206	4185	1046	6385	5196 (4165; 7117)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S78: Seasonal influenza with R_eff=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	43340	3227	166	1295	172	44934	252	63	-206	-277 (-340; -162)	9
	1	35227	2411	73	567	75	36923	110	28	-266	-297 (-325; -246)	12
	1.5	23688	1757	37	286	38	25084	56	14	-200	-215 (-230; -189)	8
	2	15078	1234	11	88	12	16201	17	4	-148	-152 (-158; -144)	3
80 %	0.5	52281	5276	249	1955	258	55096	385	94	-177	-291 (-383; -114)	7
	1	44760	4456	137	1080	143	47855	213	52	-275	-338 (-389; -240)	13
	1.5	32527	3799	94	743	98	35391	146	36	-215	-257 (-293; -191)	10
	2	23314	3274	64	505	67	25952	99	24	-165	-194 (-219; -148)	5
	**4	6760	2034	51	397	53	8293	77	19	-7	-28 (-49; 7)	1
90 %	0.5	57704	6721	303	2386	315	61421	470	115	-157	-296 (-408; -81)	4
	1	50737	5901	180	1419	187	54851	279	68	-280	-362 (-430; -234)	14
	1.5	38116	5244	133	1046	138	42044	206	50	-223	-283 (-333; -188)	11
	2	28565	4719	99	782	103	32301	154	38	-176	-219 (-258; -149)	6
	4	11081	3479	85	660	88	13727	129	32	-11	-47 (-81; 13)	2
*65 %	4	170114	0	3658	28425	3801	205998	5578	1392	8517	6933 (5559; 9487)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

B. Moderate pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S79: Moderate pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23680	5 %	3540 (3012; 4124)	171 (72; 336)	17 (7; 34)	36 (19; 54)	1091116 (0.22)
	1	10333	2 %	1545 (1314; 1799)	74 (31; 147)	7 (3; 15)	16 (8; 23)	1061697 (0.23)
	1.5	5204	1 %	778 (662; 906)	37 (16; 74)	4 (2; 7)	8 (4; 12)	1017659 (0.24)
	2	1589	0 %	238 (202; 277)	11 (5; 23)	1 (0; 2)	2 (1; 4)	984651 (0.25)
80%	0.5	37330	8 %	5580 (4748; 6501)	269 (113; 529)	27 (11; 54)	57 (30; 84)	1245270 (0.19)
	1	21139	4 %	3160 (2689; 3681)	152 (64; 300)	15 (6; 30)	32 (17; 48)	1218871 (0.2)
	1.5	14921	3 %	2230 (1898; 2598)	107 (45; 212)	11 (4; 21)	23 (12; 34)	1169108 (0.21)
	2	10551	2 %	1577 (1342; 1837)	76 (32; 150)	8 (3; 15)	16 (8; 24)	1131404 (0.22)
	4	8612	2 %	1287 (1095; 1500)	62 (26; 122)	6 (3; 12)	13 (7; 19)	1061981 (0.23)
90%	0.5	46457	10 %	6944 (5909; 8090)	335 (141; 659)	33 (14; 67)	70 (37; 105)	1340091 (0.17)
	1	28380	6 %	4242 (3610; 4942)	204 (86; 403)	20 (8; 41)	43 (23; 64)	1317712 (0.18)
	1.5	21436	5 %	3204 (2727; 3733)	154 (65; 304)	15 (6; 31)	33 (17; 48)	1265068 (0.19)
	2	16549	3 %	2474 (2105; 2882)	119 (50; 235)	12 (5; 24)	25 (13; 37)	1224889 (0.2)
	4	14382	3 %	2150 (1829; 2504)	104 (44; 204)	10 (4; 21)	22 (11; 33)	1148600 (0.21)
*65%	4	473995		70851 (60289; 82542)	3414 (1437; 6723)	338 (139; 680)	719 (377; 1072)	926266 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S80: Moderate pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20039	3 %	2995 (2549; 3490)	144 (61; 284)	14 (6; 29)	30 (16; 45)	1549468 (0.21)
	1	8717	1 %	1303 (1109; 1518)	63 (26; 124)	6 (3; 12)	13 (7; 20)	1488845 (0.22)
	1.5	4384	1 %	655 (558; 763)	32 (13; 62)	3 (1; 6)	7 (3; 10)	1419784 (0.23)
	2	1337	0 %	200 (170; 233)	10 (4; 19)	1 (0; 2)	2 (1; 3)	1368766 (0.24)
80%	0.5	32035	5 %	4788 (4075; 5579)	231 (97; 454)	23 (9; 46)	49 (25; 72)	1793787 (0.18)
	1	18150	3 %	2713 (2309; 3161)	131 (55; 257)	13 (5; 26)	28 (14; 41)	1728624 (0.19)
	1.5	12830	2 %	1918 (1632; 2234)	92 (39; 182)	9 (4; 18)	19 (10; 29)	1647863 (0.2)
	2	9113	1 %	1362 (1159; 1587)	66 (28; 129)	7 (3; 13)	14 (7; 21)	1587809 (0.21)
	4	7466	1 %	1116 (950; 1300)	54 (23; 106)	5 (2; 11)	11 (6; 17)	1486605 (0.22)
90%	0.5	40148	6 %	6001 (5107; 6991)	289 (122; 569)	29 (12; 58)	61 (32; 91)	1948913 (0.16)
	1	24504	4 %	3663 (3117; 4267)	176 (74; 348)	17 (7; 35)	37 (19; 55)	1882840 (0.17)
	1.5	18532	3 %	2770 (2357; 3227)	133 (56; 263)	13 (5; 27)	28 (15; 42)	1795168 (0.18)
	2	14344	2 %	2144 (1824; 2498)	103 (43; 203)	10 (4; 21)	22 (11; 32)	1729747 (0.19)
	4	12494	2 %	1868 (1589; 2176)	90 (38; 177)	9 (4; 18)	19 (10; 28)	1617602 (0.2)
*65%	4	656378		98113 (83487; 114302)	4728 (1990; 9310)	469 (193; 941)	995 (522; 1484)	1284702 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S81: Moderate pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	16883	2 %	2524 (2147; 2940)	122 (51; 239)	12 (5; 24)	26 (13; 38)	1886851 (0.2)
	1	7331	1 %	1096 (932; 1277)	53 (22; 104)	5 (2; 11)	11 (6; 17)	1802061 (0.21)
	1.5	3683	0 %	551 (468; 641)	27 (11; 52)	3 (1; 5)	6 (3; 8)	1714030 (0.22)
	2	1131	0 %	169 (144; 197)	8 (3; 16)	1 (0; 2)	2 (1; 3)	1649393 (0.23)
80%	0.5	27246	3 %	4073 (3466; 4745)	196 (83; 386)	19 (8; 39)	41 (22; 62)	2200452 (0.17)
	1	15426	2 %	2306 (1962; 2686)	111 (47; 219)	11 (5; 22)	23 (12; 35)	2104744 (0.18)
	1.5	10926	1 %	1633 (1390; 1903)	79 (33; 155)	8 (3; 16)	17 (9; 25)	2000221 (0.19)
	2	7776	1 %	1162 (989; 1354)	56 (24; 110)	6 (2; 11)	12 (6; 18)	1923166 (0.2)
	4	6390	1 %	955 (813; 1113)	46 (19; 91)	5 (2; 9)	10 (5; 14)	1798067 (0.21)
90%	0.5	34289	4 %	5125 (4361; 5971)	247 (104; 486)	24 (10; 49)	52 (27; 78)	2402402 (0.16)
	1	20909	3 %	3125 (2659; 3641)	151 (63; 297)	15 (6; 30)	32 (17; 47)	2301410 (0.17)
	1.5	15831	2 %	2366 (2014; 2757)	114 (48; 225)	11 (5; 23)	24 (13; 36)	2186747 (0.17)
	2	12265	2 %	1833 (1560; 2136)	88 (37; 174)	9 (4; 18)	19 (10; 28)	2101984 (0.18)
	4	10691	1 %	1598 (1360; 1862)	77 (32; 152)	8 (3; 15)	16 (9; 24)	1962808 (0.19)
*65%	4	789919		118074 (100472; 137557)	5689 (2395; 11204)	564 (232; 1133)	1198 (628; 1786)	1546131 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S82: Moderate pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	46742	3227	242	1892	252	47583	376	98	-110	-214 (-306; -46)	4
	1	44083	2411	106	826	110	45453	164	43	-300	-345 (-385; -271)	9
	1.5	30851	1757	53	416	55	32084	83	21	-245	-267 (-288; -230)	7
	2	20797	1234	16	127	17	21872	25	7	-198	-204 (-211; -192)	6
80 %	0.5	63938	5276	382	3005	397	65430	602	154	-65	-239 (-382; 32)	2
	1	65234	4456	216	1702	225	67547	341	87	-348	-445 (-528; -292)	12
	1.5	52208	3799	153	1201	159	54495	240	61	-315	-382 (-442; -273)	10
	2	42127	3274	108	849	112	44332	170	43	-282	-327 (-372; -250)	8
	**4	19675	2034	88	688	92	20841	136	35	-76	-110 (-149; -47)	3
90 %	0.5	73763	6721	476	3739	494	75775	749	191	-24	-238 (-417; 99)	1
	1	78088	5901	290	2284	302	81112	457	116	-370	-497 (-611; -290)	14
	1.5	65389	5244	219	1725	228	68461	345	88	-353	-446 (-535; -289)	13
	2	55438	4719	169	1332	176	58480	266	68	-330	-399 (-472; -279)	11
	4	31977	3479	147	1149	153	34007	228	59	-119	-175 (-241; -71)	5
*65 %	4	354496	0	4852	37702	5050	402100	7585	2020	14294	12205 (10376; 15582)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S83: Moderate pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	85707	3227	205	1601	213	86915	316	81	-570	-658 (-736; -516)	6
	1	70493	2411	89	697	93	72025	138	35	-597	-633 (-669; -570)	7
	1.5	47556	1757	45	350	47	48872	69	18	-429	-447 (-466; -415)	4
	2	30511	1234	14	107	14	31611	21	5	-301	-306 (-314; -295)	2
80 %	0.5	122785	5276	328	2579	341	124814	514	129	-759	-907 (-1031; -673)	10
	1	109802	4456	186	1461	193	112417	291	73	-855	-936 (-1010; -804)	11
	1.5	85761	3799	131	1033	137	88259	206	51	-694	-749 (-804; -655)	8
	2	67729	3274	93	734	97	70079	146	36	-569	-603 (-648; -536)	5
	**4	34275	2034	76	597	79	35556	118	30	-245	-270 (-313; -212)	1
90 %	0.5	145799	6721	411	3232	427	148450	644	161	-870	-1049 (-1211; -759)	13
	1	134773	5901	251	1972	261	138190	393	98	-1016	-1121 (-1225; -942)	14
	1.5	110178	5244	190	1492	197	113544	297	74	-861	-936 (-1021; -799)	12
	2	91654	4719	147	1155	153	94919	230	57	-738	-790 (-866; -683)	9
	4	56345	3479	128	998	133	58565	197	50	-401	-442 (-513; -346)	3
*65 %	4	491494	0	6718	52209	7004	557425	10481	2771	19837	16940 (14410; 21625)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S84: Moderate pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	115807	3227	173	1349	180	117333	265	67	-931	-1003 (-1071; -882)	7
	1	90622	2411	75	586	78	92293	115	29	-826	-854 (-888; -801)	6
	1.5	60213	1757	38	294	39	61599	58	15	-570	-584 (-602; -556)	3
	**2	37810	1234	12	90	12	38931	18	4	-379	-382 (-391; -371)	1
80 %	0.5	168768	5276	279	2193	290	171282	436	108	-1311	-1436 (-1542; -1238)	12
	1	144208	4456	158	1242	164	147099	247	61	-1254	-1321 (-1385; -1207)	10
	1.5	111582	3799	112	879	116	114273	175	43	-991	-1033 (-1086; -953)	8
	2	87419	3274	80	626	83	89905	124	31	-793	-819 (-865; -758)	5
	4	45642	2034	65	511	68	47031	100	25	-379	-397 (-442; -342)	2
90 %	0.5	202456	6721	351	2760	365	205701	548	135	-1550	-1699 (-1841; -1448)	14
	1	178778	5901	214	1683	223	182560	334	82	-1528	-1611 (-1709; -1456)	13
	1.5	144865	5244	162	1274	169	148505	253	62	-1262	-1318 (-1404; -1197)	11
	2	119663	4719	126	987	131	123139	196	48	-1060	-1099 (-1177; -1000)	9
	4	75366	3479	109	854	114	77768	168	42	-625	-655 (-730; -563)	4
*65 %	4	591411	0	8085	62831	8442	670769	12591	3308	23896	20409 (17366; 26048)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

C. Severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S85: Severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23680	5 %	4723 (4126; 5372)	466 (285; 714)	79 (48; 123)	53 (28; 79)	1091114 (0.22)
	1	10333	2 %	2061 (1801; 2344)	203 (124; 312)	34 (21; 54)	23 (12; 34)	1061695 (0.23)
	1.5	5204	1 %	1038 (907; 1180)	102 (63; 157)	17 (10; 27)	12 (6; 17)	1017657 (0.24)
	2	1589	0 %	317 (277; 360)	31 (19; 48)	5 (3; 8)	4 (2; 5)	984649 (0.25)
80%	0.5	37330	8 %	7446 (6505; 8468)	735 (449; 1126)	125 (75; 193)	84 (44; 124)	1245268 (0.19)
	1	21139	4 %	4217 (3684; 4795)	416 (254; 638)	71 (42; 109)	47 (25; 70)	1218869 (0.2)
	1.5	14921	3 %	2976 (2600; 3385)	294 (179; 450)	50 (30; 77)	33 (18; 50)	1169106 (0.21)
	2	10551	2 %	2105 (1839; 2393)	208 (127; 318)	35 (21; 55)	24 (12; 35)	1131402 (0.22)
	4	8612	2 %	1718 (1501; 1954)	169 (104; 260)	29 (17; 45)	19 (10; 29)	1061979 (0.23)
90%	0.5	46457	10 %	9267 (8095; 10538)	914 (558; 1401)	155 (93; 241)	104 (55; 155)	1340089 (0.17)
	1	28380	6 %	5661 (4945; 6438)	559 (341; 856)	95 (57; 147)	63 (33; 95)	1317710 (0.18)
	1.5	21436	5 %	4276 (3735; 4863)	422 (258; 647)	72 (43; 111)	48 (25; 71)	1265066 (0.19)
	2	16549	3 %	3301 (2884; 3754)	326 (199; 499)	55 (33; 86)	37 (19; 55)	1224887 (0.2)
	4	14382	3 %	2869 (2506; 3262)	283 (173; 434)	48 (29; 74)	32 (17; 48)	1148598 (0.21)
*65%	4	473995		94548 (82595; 107523)	9328 (5698; 14296)	1581 (951; 2455)	1060 (556; 1580)	926264 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S86: Severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention				Median (0.25; 0.75 percentiles) relative to baseline				Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20039	3 %	3997 (3492; 4546)	394 (241; 604)	67 (40; 104)	45 (24; 67)	1549465 (0.21)
	1	8717	1 %	1739 (1519; 1977)	172 (105; 263)	29 (17; 45)	19 (10; 29)	1488842 (0.22)
	1.5	4384	1 %	874 (764; 994)	86 (53; 132)	15 (9; 23)	10 (5; 15)	1419781 (0.23)
	2	1337	0 %	267 (233; 303)	26 (16; 40)	4 (3; 7)	3 (2; 4)	1368763 (0.24)
80%	0.5	32035	5 %	6390 (5582; 7267)	630 (385; 966)	107 (64; 166)	72 (38; 107)	1793784 (0.18)
	1	18150	3 %	3620 (3163; 4117)	357 (218; 547)	61 (36; 94)	41 (21; 61)	1728621 (0.19)
	1.5	12830	2 %	2559 (2236; 2910)	252 (154; 387)	43 (26; 66)	29 (15; 43)	1647861 (0.2)
	2	9113	1 %	1818 (1588; 2067)	179 (110; 275)	30 (18; 47)	20 (11; 30)	1587806 (0.21)
	4	7466	1 %	1489 (1301; 1694)	147 (90; 225)	25 (15; 39)	17 (9; 25)	1486602 (0.22)
90%	0.5	40148	6 %	8008 (6996; 9107)	790 (483; 1211)	134 (81; 208)	90 (47; 134)	1948910 (0.16)
	1	24504	4 %	4888 (4270; 5559)	482 (295; 739)	82 (49; 127)	55 (29; 82)	1882837 (0.17)
	1.5	18532	3 %	3697 (3229; 4204)	365 (223; 559)	62 (37; 96)	41 (22; 62)	1795165 (0.18)
	2	14344	2 %	2861 (2499; 3254)	282 (172; 433)	48 (29; 74)	32 (17; 48)	1729744 (0.19)
	4	12494	2 %	2492 (2177; 2834)	246 (150; 377)	42 (25; 65)	28 (15; 42)	1617599 (0.2)
*65%	4	656378		130928 (114375; 148895)	12917 (7891; 19796)	2190 (1317; 3400)	1468 (770; 2188)	1284699 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S87: Severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	34289	4 %	3368 (2942; 3830)	332 (203; 509)	56 (34; 87)	38 (20; 56)	2402399 (0.2)
	1	20909	3 %	1462 (1277; 1663)	144 (88; 221)	24 (15; 38)	16 (9; 24)	2301407 (0.21)
	1.5	15831	2 %	735 (642; 835)	72 (44; 111)	12 (7; 19)	8 (4; 12)	2186744 (0.22)
	2	12265	2 %	226 (197; 257)	22 (14; 34)	4 (2; 6)	3 (1; 4)	2101981 (0.23)
80%	0.5	10691	1 %	5435 (4748; 6181)	536 (328; 822)	91 (55; 141)	61 (32; 91)	1962805 (0.17)
	1	27246	3 %	3077 (2688; 3499)	304 (185; 465)	51 (31; 80)	35 (18; 51)	2200449 (0.18)
	1.5	15426	2 %	2179 (1904; 2478)	215 (131; 330)	36 (22; 57)	24 (13; 36)	2104741 (0.19)
	2	10926	1 %	1551 (1355; 1764)	153 (93; 235)	26 (16; 40)	17 (9; 26)	2000218 (0.2)
	4	7776	1 %	1275 (1113; 1450)	126 (77; 193)	21 (13; 33)	14 (7; 21)	1923163 (0.21)
90%	0.5	6390	1 %	6840 (5975; 7778)	675 (412; 1034)	114 (69; 178)	77 (40; 114)	1798064 (0.16)
	1	16883	2 %	4171 (3643; 4743)	411 (251; 631)	70 (42; 108)	47 (25; 70)	1886848 (0.17)
	1.5	7331	1 %	3158 (2759; 3591)	312 (190; 477)	53 (32; 82)	35 (19; 53)	1802058 (0.17)
	2	3683	0 %	2447 (2137; 2782)	241 (147; 370)	41 (25; 64)	27 (14; 41)	1714027 (0.18)
	4	1131	0 %	2133 (1863; 2425)	210 (129; 322)	36 (21; 55)	24 (13; 36)	1649390 (0.19)
*65%	4	789919		157566 (137645; 179188)	15546 (9496; 23824)	2635 (1585; 4092)	1767 (927; 2634)	1546128 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S88: Severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	46739	3228	323	5395	264	43984	417	144	-31	-133 (-231; 39)	3
	1	44080	2411	141	2354	115	43880	182	63	-265	-309 (-352; -234)	9
	1.5	30849	1757	71	1186	58	31292	92	32	-227	-249 (-271; -211)	7
	2	20795	1235	22	362	18	21629	28	10	-193	-198 (-206; -187)	6
80 %	0.5	63933	5275	510	8531	417	59751	669	227	59	-111 (-263; 162)	2
	1	65229	4455	289	4831	236	64328	378	128	-278	-372 (-461; -218)	13
	1.5	52203	3799	204	3410	167	52221	267	90	-266	-331 (-395; -222)	10
	2	42121	3274	144	2411	118	42722	189	64	-247	-291 (-339; -214)	8
	4	19685	2034	118	1962	96	19543	151	52	-48	-80 (-122; -17)	4
90 %	**0.5	73753	6720	634	10617	519	68703	832	282	131	-76 (-270; 260)	1
	1	78078	5900	387	6486	317	76788	508	172	-275	-399 (-521; -193)	12
	1.5	65379	5244	293	4899	239	65192	383	129	-281	-372 (-467; -216)	14
	2	55427	4719	226	3782	185	55954	296	100	-275	-342 (-419; -221)	11
	4	31994	3480	196	3277	161	31840	253	87	-72	-125 (-196; -21)	5
*65 %	4	354496	0	6471	108007	5301	474275	8447	2980	15892	13890 (11949; 17317)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S89: Severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	85700	3228	274	4565	224	83865	351	119	-504	-590 (-673; -444)	5
	1	70487	2411	119	1986	97	70696	153	52	-568	-604 (-642; -540)	7
	1.5	47552	1757	60	999	49	48202	77	26	-415	-432 (-452; -400)	4
	2	30509	1235	18	305	15	31405	23	8	-297	-301 (-309; -290)	2
80 %	0.5	122778	5275	437	7321	358	119937	570	190	-653	-797 (-930; -565)	9
	1	109795	4455	248	4148	203	109651	323	107	-795	-874 (-953; -743)	12
	1.5	85753	3799	175	2932	143	86301	228	76	-652	-705 (-764; -611)	8
	2	67721	3274	124	2083	102	68686	162	54	-539	-572 (-620; -504)	6
	**4	34288	2034	102	1701	83	34436	130	44	-221	-245 (-289; -186)	1
90 %	0.5	145785	6720	548	9175	449	142334	714	238	-737	-913 (-1086; -621)	11
	1	134759	5900	335	5600	274	134451	436	145	-935	-1037 (-1149; -858)	14
	1.5	110164	5244	253	4235	207	110713	329	109	-800	-872 (-964; -735)	13
	2	91640	4719	196	3278	160	92725	255	84	-691	-742 (-822; -633)	10
	4	56367	3480	171	2846	140	56691	218	73	-360	-401 (-474; -303)	3
*65 %	4	491495	0	8961	149566	7353	657375	11664	4087	22040	19275 (16578; 24007)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S90: Severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	115798	3228	231	3846	189	114760	294	99	-876	-946 (-1019; -823)	7
	1	90614	2411	100	1670	82	91173	128	43	-802	-830 (-865; -776)	6
	1.5	60208	1757	50	839	41	61035	64	22	-558	-571 (-591; -543)	3
	2	37807	1235	15	258	13	38756	20	7	-376	-379 (-387; -368)	2
80 %	0.5	168761	5275	372	6226	305	167133	483	159	-1222	-1342 (-1458; -1145)	12
	1	144200	4455	211	3525	172	144746	273	90	-1203	-1267 (-1338; -1155)	10
	1.5	111573	3799	149	2497	122	112603	193	63	-955	-997 (-1052; -915)	8
	2	87410	3274	106	1777	87	88713	137	45	-767	-793 (-841; -732)	5
	**4	45658	2034	87	1456	71	46078	111	37	-359	-376 (-423; -321)	1
90 %	0.5	202439	6720	468	7836	383	200472	607	200	-1437	-1583 (-1735; -1334)	13
	1	178762	5900	285	4778	234	179364	370	121	-1459	-1540 (-1645; -1384)	14
	1.5	144848	5244	216	3618	177	146081	280	92	-1210	-1264 (-1356; -1143)	11
	2	119646	4719	167	2803	137	121257	217	71	-1020	-1057 (-1139; -957)	9
	4	75394	3480	146	2436	120	76172	186	62	-591	-620 (-698; -528)	4
*65 %	4	591413	0	10785	179995	8862	791055	14004	4879	26536	23208 (19961; 28896)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

D. Very severe pandemic

i. Epidemiology (R_0 = 1.4, 1.6, 1.8)

Table S91: Very severe pandemic influenza with R_0=1.4: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	23680	5 %	5908 (5259; 6605)	821 (573; 1137)	205 (141; 287)	165 (86; 246)	1091111 (0.22)
	1	10333	2 %	2578 (2295; 2882)	358 (250; 496)	89 (61; 125)	72 (38; 107)	1061692 (0.23)
	1.5	5204	1 %	1298 (1156; 1451)	180 (126; 250)	45 (31; 63)	36 (19; 54)	1017653 (0.24)
	2	1589	0 %	396 (353; 443)	55 (38; 76)	14 (9; 19)	11 (6; 16)	984645 (0.25)
80%	0.5	37330	8 %	9314 (8290; 10412)	1294 (903; 1792)	323 (222; 453)	260 (136; 387)	1245265 (0.19)
	1	21139	4 %	5274 (4695; 5896)	733 (511; 1015)	183 (126; 257)	147 (77; 219)	1218865 (0.2)
	1.5	14921	3 %	3723 (3314; 4162)	517 (361; 716)	129 (89; 181)	104 (54; 155)	1169102 (0.21)
	2	10551	2 %	2633 (2343; 2943)	366 (255; 507)	91 (63; 128)	74 (39; 109)	1131398 (0.22)
	4	8612	2 %	2149 (1913; 2402)	299 (208; 413)	74 (51; 105)	60 (31; 89)	1061975 (0.23)
90%	0.5	46457	10 %	11591 (10317; 12957)	1611 (1123; 2230)	402 (276; 564)	324 (170; 482)	1340086 (0.17)
	1	28380	6 %	7081 (6303; 7916)	984 (686; 1363)	245 (169; 344)	198 (104; 294)	1317707 (0.18)
	1.5	21436	5 %	5348 (4761; 5979)	743 (518; 1029)	185 (127; 260)	149 (78; 222)	1265062 (0.19)
	2	16549	3 %	4129 (3675; 4616)	574 (400; 795)	143 (98; 201)	115 (60; 172)	1224884 (0.2)
	4	14382	3 %	3588 (3194; 4011)	499 (348; 690)	124 (85; 175)	100 (53; 149)	1148594 (0.21)
*65%	4	473995		118264 (105267; 132204)	16433 (11462; 22757)	4097 (2814; 5752)	3305 (1731; 4919)	926260 (0.27)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S92: Very severe pandemic influenza with R_0=1.6: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention				Median (0.25; 0.75 percentiles) relative to baseline				Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	20039	3 %	5000 (4450; 5589)	695 (485; 962)	173 (119; 243)	140 (73; 208)	1549461 (0.21)
	1	8717	1 %	2175 (1936; 2431)	302 (211; 419)	75 (52; 106)	61 (32; 90)	1488837 (0.22)
	1.5	4384	1 %	1094 (974; 1223)	152 (106; 210)	38 (26; 53)	31 (16; 45)	1419776 (0.23)
	2	1337	0 %	334 (297; 373)	46 (32; 64)	12 (8; 16)	9 (5; 14)	1368758 (0.24)
80%	0.5	32035	5 %	7993 (7114; 8935)	1111 (775; 1538)	277 (190; 389)	223 (117; 332)	1793779 (0.18)
	1	18150	3 %	4529 (4031; 5062)	629 (439; 871)	157 (108; 220)	127 (66; 188)	1728616 (0.19)
	1.5	12830	2 %	3201 (2849; 3578)	445 (310; 616)	111 (76; 156)	89 (47; 133)	1647856 (0.2)
	2	9113	1 %	2274 (2024; 2542)	316 (220; 438)	79 (54; 111)	64 (33; 95)	1587801 (0.21)
	4	7466	1 %	1863 (1658; 2082)	259 (181; 358)	65 (44; 91)	52 (27; 77)	1486598 (0.22)
90%	0.5	40148	6 %	10017 (8916; 11198)	1392 (971; 1928)	347 (238; 487)	280 (147; 417)	1948905 (0.16)
	1	24504	4 %	6114 (5442; 6834)	850 (593; 1176)	212 (145; 297)	171 (89; 254)	1882833 (0.17)
	1.5	18532	3 %	4624 (4116; 5169)	642 (448; 890)	160 (110; 225)	129 (68; 192)	1795161 (0.18)
	2	14344	2 %	3579 (3186; 4001)	497 (347; 689)	124 (85; 174)	100 (52; 149)	1729739 (0.19)
	4	12494	2 %	3117 (2775; 3485)	433 (302; 600)	108 (74; 152)	87 (46; 130)	1617595 (0.2)
*65%	4	656378		163770 (145772; 183073)	22756 (15872; 31513)	5673 (3897; 7965)	4576 (2397; 6811)	1284694 (0.26)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

Table S93: Very severe pandemic influenza with R_0=1.8: number of avoided cases, GP-visits, hospitalizations, and deaths associated with each sick leave intervention, assuming 35% of children and 25% adults are symptomatic, and with extra mixing.

Intervention		Median (0.25; 0.75 percentiles) relative to baseline						Mean workdays lost (proportion lost to caregiving)
% on leave	Delay time	Symptomatic cases avoided	% Reduction in AR	GP-visits avoided	Hospital admissions avoided	ICU admissions avoided	Avoided Deaths	
65%	0.5	16883	2 %	4212 (3749; 4709)	585 (408; 811)	146 (100; 205)	118 (62; 175)	1886843 (0.2)
	1	7331	1 %	1829 (1628; 2045)	254 (177; 352)	63 (44; 89)	51 (27; 76)	1802052 (0.21)
	1.5	3683	0 %	919 (818; 1027)	128 (89; 177)	32 (22; 45)	26 (13; 38)	1714021 (0.22)
	2	1131	0 %	282 (251; 315)	39 (27; 54)	10 (7; 14)	8 (4; 12)	1649384 (0.23)
80%	0.5	27246	3 %	6798 (6051; 7599)	945 (659; 1308)	235 (162; 331)	190 (99; 283)	2200444 (0.17)
	1	15426	2 %	3849 (3426; 4303)	535 (373; 741)	133 (92; 187)	108 (56; 160)	2104735 (0.18)
	1.5	10926	1 %	2726 (2426; 3047)	379 (264; 525)	94 (65; 133)	76 (40; 113)	2000212 (0.19)
	2	7776	1 %	1940 (1727; 2169)	270 (188; 373)	67 (46; 94)	54 (28; 81)	1923157 (0.2)
	4	6390	1 %	1594 (1419; 1782)	222 (155; 307)	55 (38; 78)	45 (23; 66)	1798058 (0.21)
90%	0.5	34289	4 %	8555 (7615; 9564)	1189 (829; 1646)	296 (204; 416)	239 (125; 356)	2402394 (0.16)
	1	20909	3 %	5217 (4644; 5832)	725 (506; 1004)	181 (124; 254)	146 (76; 217)	2301401 (0.17)
	1.5	15831	2 %	3950 (3516; 4415)	549 (383; 760)	137 (94; 192)	110 (58; 164)	2186738 (0.17)
	2	12265	2 %	3060 (2724; 3421)	425 (297; 589)	106 (73; 149)	86 (45; 127)	2101975 (0.18)
	4	10691	1 %	2667 (2374; 2982)	371 (259; 513)	92 (63; 130)	75 (39; 111)	1962799 (0.19)
*65%	4	789919		197089 (175429; 220319)	27386 (19101; 37924)	6828 (4690; 9586)	5507 (2884; 8197)	1546122 (0.25)

* This is the baseline intervention; values are reported in absolute terms, and not in terms of avoided cases.

B.

ii. Costs and effects (R_0 = 1.4, 1.6, 1.8)

Table S94: Very severe pandemic influenza with R_0=1.4: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	46744	3226	404	10174	277	39115	671	449	272	188 (60; 370)	3
	1	44085	2409	176	4440	121	41758	293	196	-133	-169 (-226; -91)	12
	1.5	30853	1756	89	2236	61	30224	147	99	-161	-179 (-208; -139)	13
	2	20798	1234	27	683	19	21304	45	30	-172	-177 (-187; -165)	14
80 %	0.5	63935	5277	637	16040	436	52099	1067	706	535	394 (199; 684)	2
	1	65231	4456	361	9083	247	59997	603	399	-9	-88 (-201; 76)	7
	1.5	52206	3799	255	6411	174	49165	425	281	-76	-132 (-212; -14)	10
	2	42125	3274	180	4534	123	40562	300	198	-113	-152 (-211; -68)	11
	4	19667	2033	147	3700	101	17753	242	161	61	33 (-19; 102)	6
90 %	**0.5	73757	6722	793	19962	543	59181	1327	878	723	549 (302; 910)	1
	1	78083	5901	484	12194	332	70973	809	535	85	-21 (-173; 202)	5
	1.5	65385	5244	366	9211	251	60802	611	403	-9	-88 (-207; 80)	8
	2	55433	4718	282	7111	193	52565	471	311	-65	-124 (-220; 7)	9
	4	31965	3477	245	6179	168	28850	405	270	110	63 (-23; 178)	4
*65 %	4	354504	0	8091	202527	5551	570673	13662	9283	22090	20456 (17954; 24082)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Table S95: Very severe pandemic influenza with R_0=1.6: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits			Output measures	
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	85712	3226	342	8610	235	79751	560	372	-253	-323 (-432; -170)	4
	1	70497	2409	149	3745	102	68910	244	162	-459	-488 (-537; -421)	9
	1.5	47559	1756	75	1884	51	47305	123	81	-360	-374 (-400; -340)	7
	2	30513	1234	23	574	16	31134	37	25	-280	-284 (-293; -272)	6
80 %	0.5	122782	5277	547	13765	375	113373	903	592	-253	-374 (-542; -125)	5
	1	109799	4456	310	7799	212	105934	511	335	-569	-637 (-735; -495)	13
	1.5	85758	3799	219	5513	150	83675	361	236	-492	-539 (-612; -438)	10
	2	67726	3274	156	3916	107	66822	256	167	-425	-456 (-512; -383)	8
	**4	34265	2033	127	3208	87	32875	207	137	-128	-150 (-200; -87)	1
90 %	0.5	145793	6722	685	17251	470	134109	1132	741	-236	-387 (-602; -73)	3
	1	134768	5901	418	10529	287	129434	690	451	-630	-720 (-857; -527)	14
	1.5	110173	5244	316	7963	217	106921	521	341	-569	-634 (-743; -486)	12
	2	91649	4718	245	6163	168	89791	403	263	-513	-559 (-652; -440)	11
	4	56328	3477	213	5368	146	54078	347	229	-205	-242 (-325; -136)	2
*65 %	4	491502	0	11204	280455	7700	790861	18816	12732	30552	28274 (24826; 33299)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

h

Table S96: Very severe pandemic influenza with R_0=1.8: costs and benefits associated with each sick leave intervention relative to the baseline, assuming 35% of children and 25% of adults are symptomatic, and with extra mixing.

Intervention		Mean costs (1000 USD)						Mean benefits		Output measures		
% on leave	Max. days	Productivity losses	Cost of campaign	GP-visits avoided	Hospitali-sations avoided	Medication costs avoided	Total costs	QALYs saved	YPLL saved	Mean NHB (QALYs)	Median NHB (0.25; 0.75 percentile)	Rank
65 %	0.5	115814	3226	288	7254	198	111300	468	308	-667	-725 (-819; -597)	6
	1	90627	2409	125	3150	86	89675	203	134	-712	-735 (-778; -678)	7
	1.5	60216	1756	63	1582	43	60284	102	67	-513	-524 (-547; -494)	4
	2	37812	1234	19	486	13	38528	31	21	-362	-364 (-374; -353)	2
80 %	0.5	168765	5277	465	11707	319	161551	761	495	-887	-989 (-1134; -777)	10
	1	144205	4456	263	6628	181	141589	430	279	-1014	-1070 (-1156; -950)	11
	1.5	111578	3799	187	4695	128	110369	304	198	-821	-859 (-924; -771)	8
	2	87416	3274	133	3341	91	87125	216	140	-672	-695 (-749; -630)	5
	**4	45630	2033	109	2745	75	44733	176	115	-281	-297 (-347; -238)	1
90 %	0.5	202449	6722	585	14733	402	193451	957	622	-1016	-1143 (-1331; -874)	13
	1	178772	5901	357	8984	245	175087	583	378	-1203	-1275 (-1399; -1108)	14
	1.5	144859	5244	270	6802	185	142845	441	286	-1016	-1066 (-1170; -934)	12
	2	119657	4718	209	5270	144	118752	341	221	-870	-905 (-995; -797)	9
	4	75347	3477	182	4593	125	73923	294	192	-460	-487 (-571; -388)	3
*65 %	4	591419	0	13483	337514	9281	951697	22541	15201	36711	33955 (29827; 40001)	

*Baseline intervention; values reported as absolute gains and losses.
**optimal intervention.

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4;5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.Hansen.Edwards@fhi.no

SUPPLEMENTARY FILE 3: FIGURES

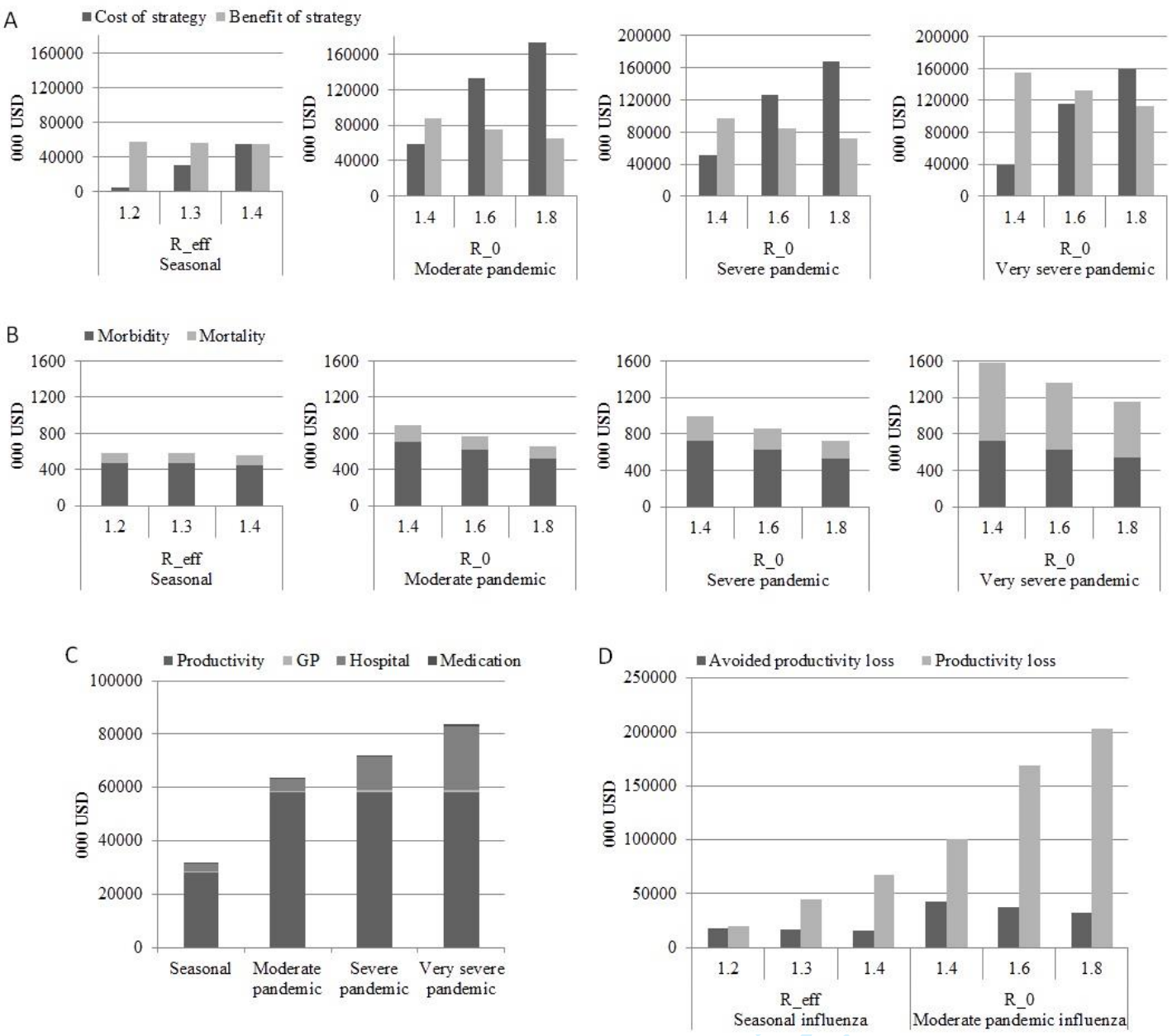


Figure S1: The effect transmissibility and pandemic severity on economic parameters for the intervention involving 90% of sick persons taking sick leave within 0.5 days of onset; no extra mixing assumed. A) Total monetary costs and benefits of the intervention under seasonal and pandemic scenarios. B) Benefits from avoided morbidity and mortality under seasonal and pandemic scenarios. C) Proportions of costs avoided due to avoided hospitalizations, GP-visits, medication use and productivity losses under seasonal and pandemic influenza. D) Baseline productivity losses and productivity losses avoided due to the sick leave intervention under seasonal and moderate pandemic influenza (the same pattern follows for more severe pandemic influenza scenarios.

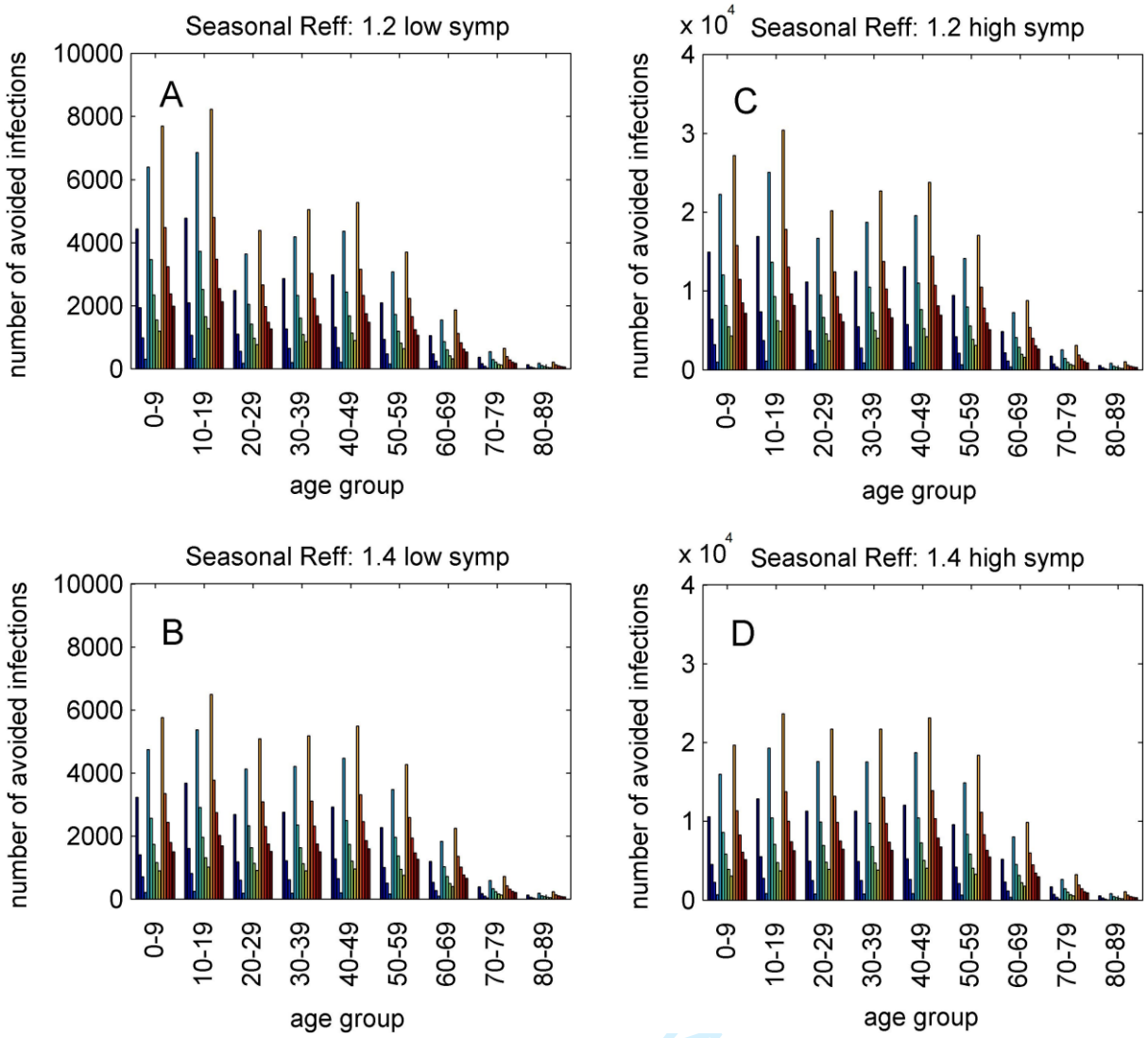


Figure S2: Absolute number of avoided clinical cases for selected seasonal scenarios, grouped according to median age, for all 14 interventions.
Interventions 1-4: Shades of blue: (65%; 0.5, 1, 1.5, and 2 days)
Interventions 5-9: Shades of green to yellow: (80%; 0.5, 1, 1.5, 2, and 4 days)
Interventions 10-14: Shades of orange to red: (90%; 0.5, 1, 1.5, 2, and 4 days)

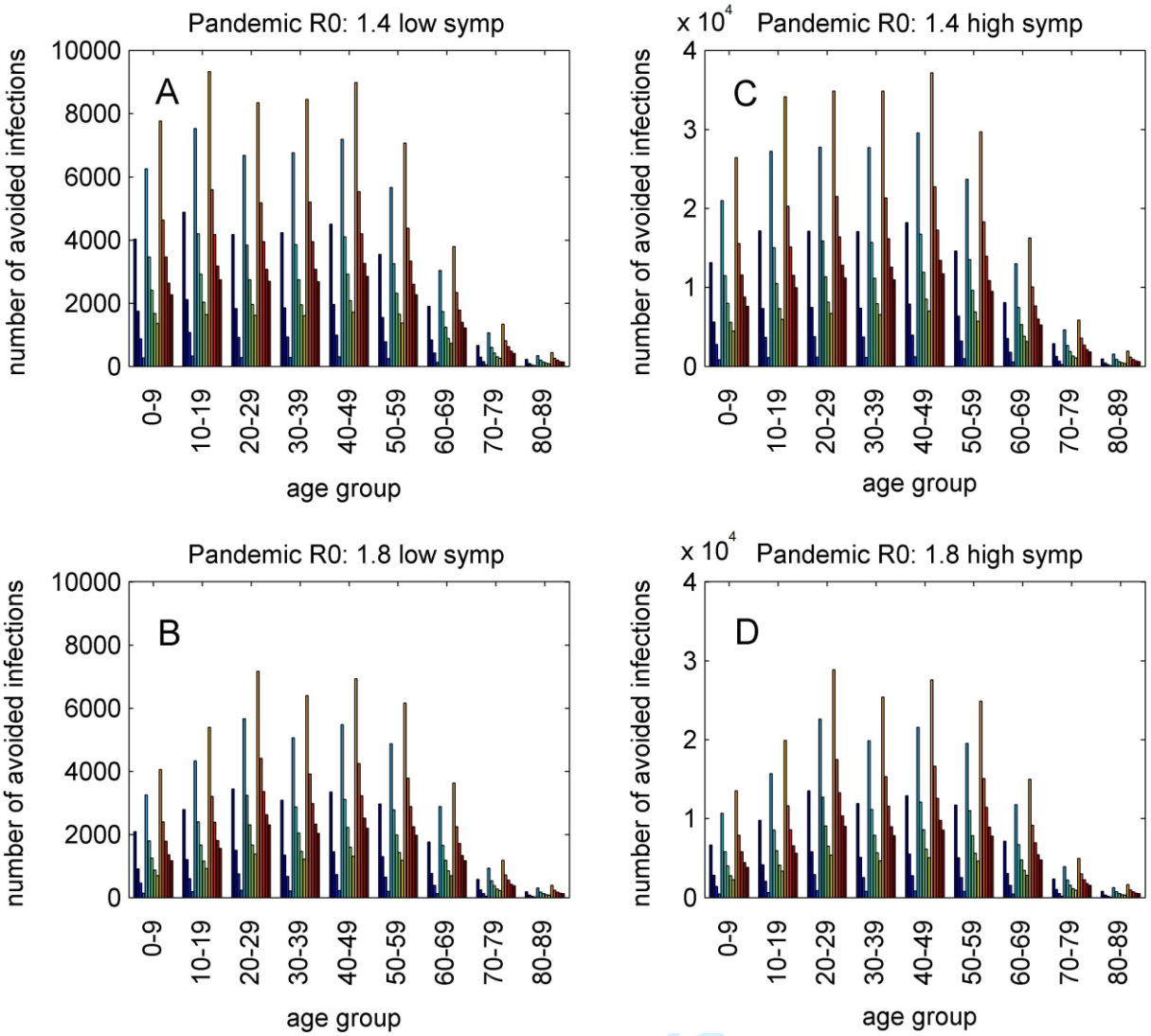
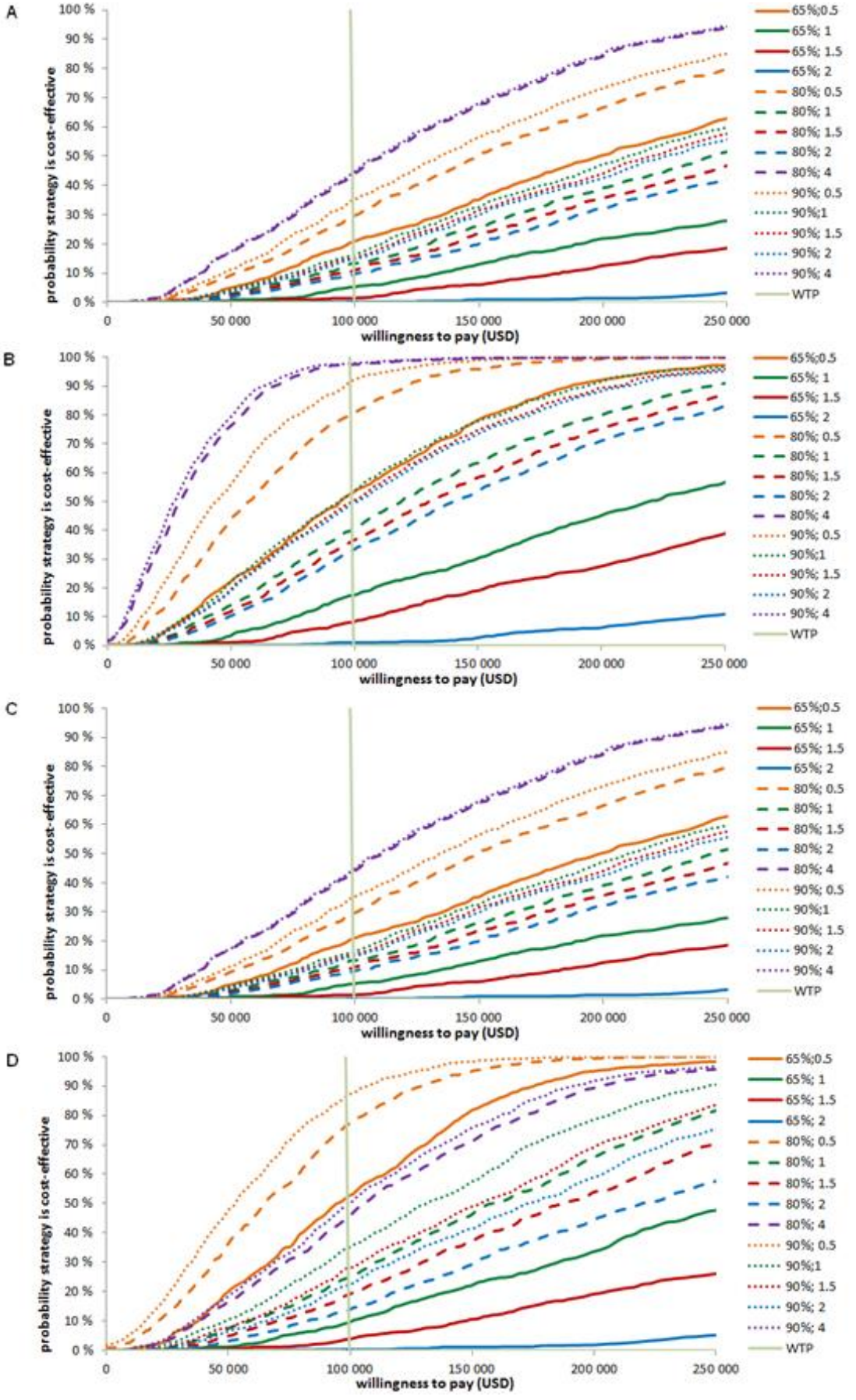


Figure S3: Absolute number of avoided clinical cases for selected pandemic scenarios, grouped according to median age, for all 14 interventions.
Interventions 1-4: Shades of blue: (65%; 0.5, 1, 1.5, and 2 days)
Interventions 5-9: Shades of green to yellow: (80%; 0.5, 1, 1.5, 2, and 4 days)
Interventions 10-14: Shades of orange to red: (90%; 0.5, 1, 1.5, 2, and 4 days)

Figure S4: Acceptability curves without extra mixing.

A) Seasonal influenza (R_eff=1.3), low symptomatic proportions(35% children and 25% adults symptomatic), without extra mixing, B) Seasonal influenza (R_eff=1.3), high symptomatic proportions(65% children and 55% adults symptomatic) without extra mixing, C) Pandemic influenza (R_0=1.6), low symptomatic proportions(35% children and 25% adults symptomatic), without extra mixing, D) Pandemic influenza (R_0=1.6), high symptomatic proportions(65% children and 55% adults symptomatic) without extra mixing.



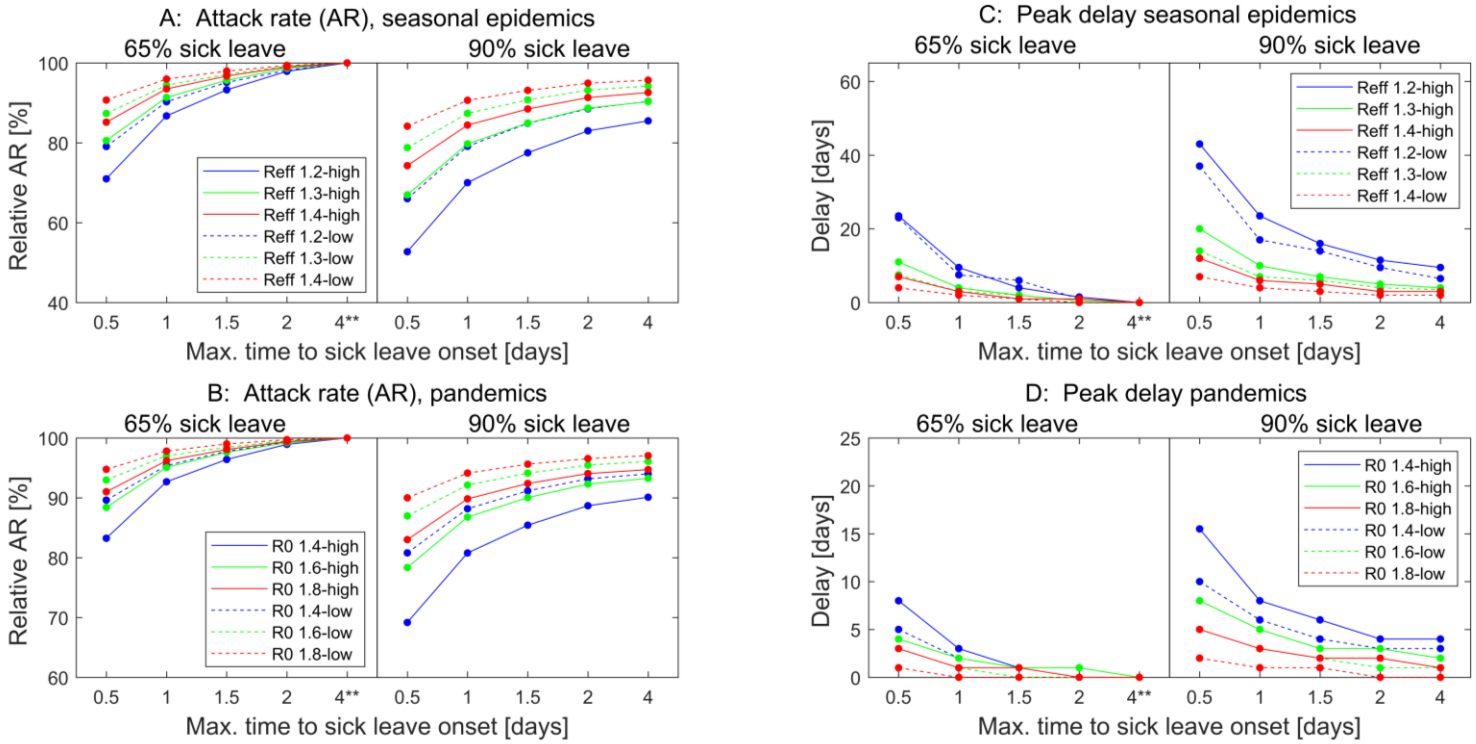


Figure S5: ***Impact of workplace-based interventions on clinical attack rate and timing of peak for seasonal epidemics (panels A and C) and for pandemics (panels B and D) with extra mixing*** in the households and the general population. Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted with stippled lines; scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted with solid lines. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility). The figure shows sick leave interventions with 65% and 90% adherence combined with absence onset within 0.5, 1, 1.5, 2, and 4 days. The baseline intervention (65% adherence and sick leave onset within 4 days of symptom onset) is indicated by **.

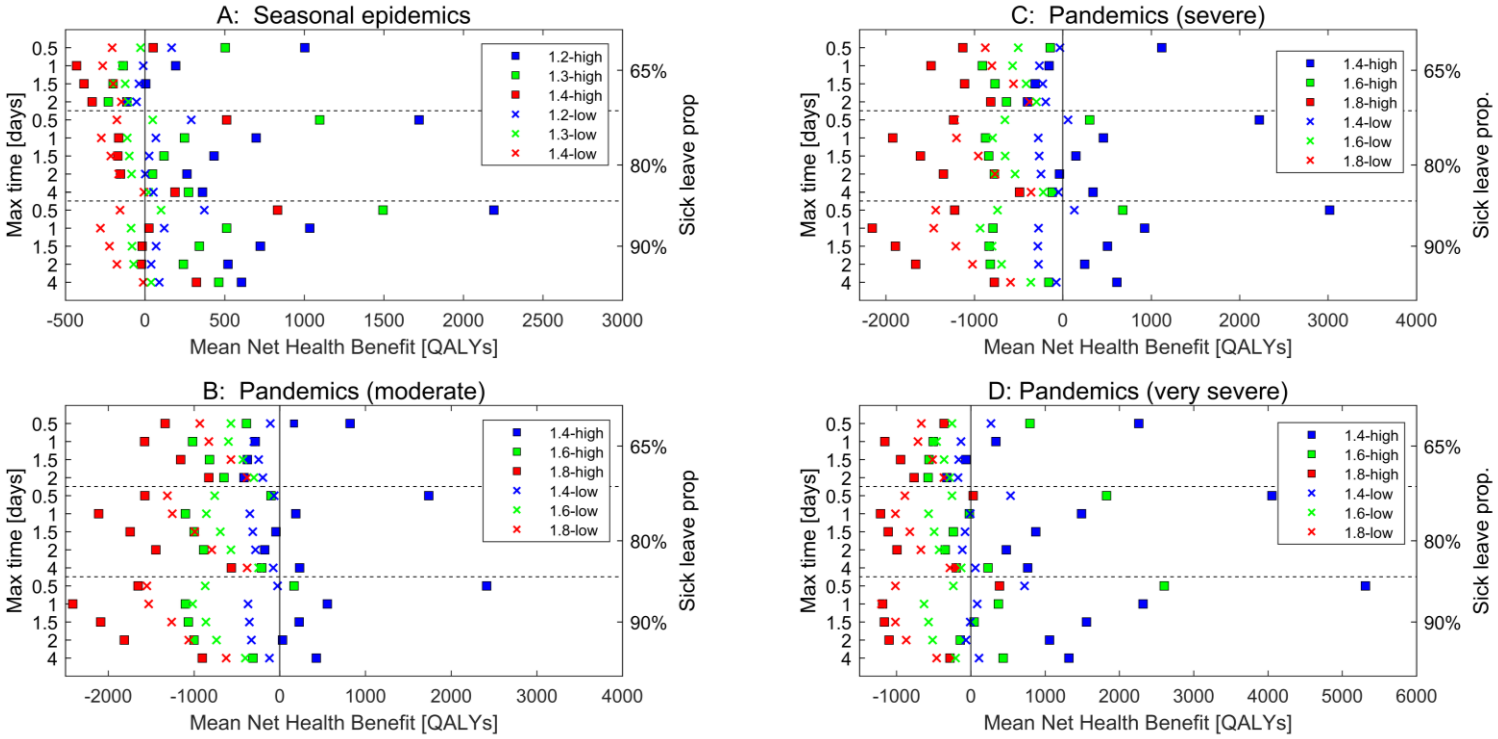
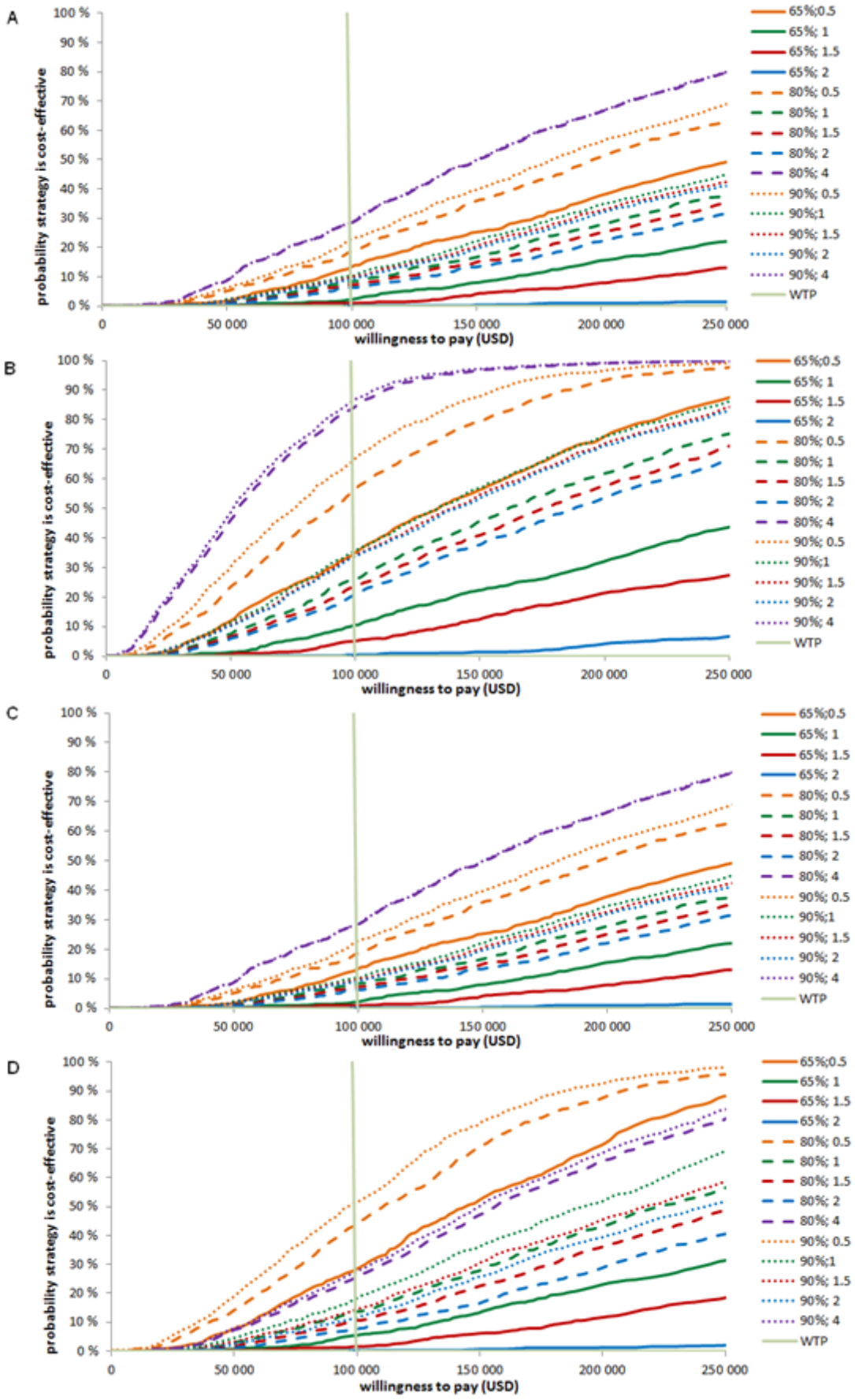


Figure S6: Mean Net Health Benefit (NHB) of workplace-based interventions for all scenarios assuming extra mixing in households and the general population; seasonal epidemics (A), moderate pandemics (B), severe pandemics (C), very severe pandemics (D).

Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted as crosses, and scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted as squares. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility)

Figure S7: Acceptability curves with mixing.

A) Seasonal influenza (R_eff=1.3), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, B) Seasonal influenza (R_eff=1.3), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing, C) Pandemic influenza (R_0=1.6), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, D) Pandemic influenza (R_0=1.6), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing.



CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2 & 3
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	5 & 6
		Present the study question and its relevance for health policy or practice decisions.	5 & 6
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	7 & 8
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6, 7, 8 & Supplementary file 1
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	10
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	6, 8 & 9
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	7,8 & 9
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Supplementary file 1
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	10 & Supplementary file 1
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	9, 10 & Supplementary file 1

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	9, 10 & Supplementary file 1
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	NA
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	9,10, & Supplementary file 1
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	10 & Supplementary file 1
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	9, 10 & Supplementary file 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	7-10 & Supplementary file 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	7-10 & Supplementary file 1

Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Supplementary file 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	11-15, Fig. 3 & Supplementary file 2
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	NA
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	14-16, Fig. 4 & Supplementary file 2, Supplementary file 3
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	17-19
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	16-20
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we	22

		recommend authors comply with International Committee of Medical Journal Editors recommendations.	

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

BMJ Open

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027832.R1
Article Type:	Research
Date Submitted by the Author:	16-Jan-2019
Complete List of Authors:	Hansen Edwards, Christina; Nasjonalt folkehelseinstitutt, Tomba, Gianpaolo; Universita degli Studi di Roma La Sapienza, Dept. of Mathematics Sonbo Kristiansen, Ivar; University of Oslo, Health Management and Health Economics White, Richard; Nasjonalt folkehelseinstitutt de Blasio, Birgitte; Nasjonalt folkehelseinstitutt
Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Health economics, Infectious diseases, Occupational and environmental medicine
Keywords:	Human influenza, Infection control < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, HEALTH ECONOMICS

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.Hansen.Edwards@fhi.no

Keywords: Human Influenza; Infection Control; Epidemiology; Public Health; Health Economics

Word count: 4287

Abstract

Objectives: To quantify population level health and economic consequences of sick leave among workers with influenza symptoms.

Interventions: Compared with current sick leave practice (baseline) we evaluated the health and cost consequences of: I) increasing the proportion of workers on sick leave from 65% (baseline) to 80% or 90%; II) shortening the maximum duration from symptom onset to sick leave from 4 days (baseline) to 2 days, 1.5 days, 1 day, and 0.5 days; and III) combinations of I and II.

Methods: A dynamic compartmental influenza model was developed using Norwegian population data and survey data on employee sick leave practices. The sick leave interventions were simulated under 12 different seasonal epidemic and 36 different pandemic influenza scenarios. These scenarios varied in terms of transmissibility, the proportion of symptomatic cases, and illness severity (risk of primary care consultations, hospitalizations and deaths). Using probabilistic sensitivity analyses, a net health benefit approach was adopted to assess the cost-effectiveness of the interventions from a societal perspective.

Results: Compared with current sick leave practice, sick leave interventions were cost-effective for 31 (65%) of the pandemic scenarios, and 11 (92%) of the seasonal scenarios. Economic benefits from sick leave interventions were greatest for scenarios with low transmissibility, high symptomatic proportions, and high illness severity. Overall, the health and economic benefits were greatest for the intervention involving 90% of sick workers taking sick leave within one-half day of symptoms. Depending on the influenza scenario, this intervention resulted in a 44.4–99.7% reduction in the attack rate. Interventions involving sick

leave onset beginning 2 days or later, after the onset of symptoms, resulted in economic losses.

Conclusions: Prompt sick leave onset and a high proportion of sick leave among workers with influenza symptoms may be cost-effective, particularly during influenza epidemics and pandemics with low transmissibility or high morbidity.

Article Summary

Strengths and limitations of this study

- Although national recommendations for flu management often advise sick leave from work, no systematic studies of health and cost consequences of such recommendations have been published, and no studies have evaluated the effects of sick leave interventions in detail.
- This study uses mathematical modelling to compare current sick leave practice with 14 alternative sick leave interventions, related to the proportion of ill employees taking sick leave and the timeliness of sick leave relative to symptoms, to investigate the epidemiological effects of these interventions and their economic consequences
- Some of the parameters used in the modelling and evaluation are not influenza-specific, such as the above current sick leave practice, but rather based on influenza-like illness (ILI), being derived from interviews unaccompanied by test results.
- All interventions were assessed for a variety of potential epidemic and pandemic influenza scenarios with varying characteristics.
- We have studied population-wide effects for the Norwegian setting and our findings may not be directly transferrable to other settings or sub-groups.

Introduction

Seasonal influenza affects 5–15% of the world's population annually. Globally, influenza epidemics are responsible for 250,000–500,000 deaths and 3–5 million cases of severe illness per year.[1] During an influenza pandemic the disease burden may increase substantially. The disease also imposes a considerable cost burden on the healthcare system, but the greatest proportion of costs are indirect costs resulting from lost workdays.[2]

When influenza-infected workers report to work, their co-workers are at risk of becoming infected. We recently conducted a literature review on influenza transmission in the workplace and assessed sick leave recommendations during influenza in 18 European countries.[3] We found that while pandemic preparedness plans of many European countries officially advise sick workers to be absent from work, only one study was identified that had assessed the effectiveness of sick leave interventions during seasonal influenza.[3] This was a modelling study indicating that liberal sick leave policies and increased payment compensations during sick leave would reduce workplace transmission up to 39%[3 4]. Norway is a western-European society with generous social welfare programs, so few workers lose income as a result of sick leave due to influenza-like symptoms.[5-7] No studies to date have ascertained whether sick leave during influenza is a cost-effective way of reducing the spread of influenza. In addition, countries that advise workers with influenza to take sick leave recommend diverse sick leave strategies.[3]

Influenza transmission depends on a complex interaction between the host, pathogen and the environment. Characteristics, such as the attack rate and disease severity of a particular influenza season, may affect which sick leave strategies are most cost-effective to implement. The effectiveness of sick leave as a mitigation intervention is limited by

asymptomatic transmission. The proportion of asymptomatic cases reported in the literature varies between 25% and 75%,[8-11] and asymptomatic cases may shed reduced amounts of the virus.[12] Moreover, in symptomatic individuals, virus shedding may begin 1–2 days prior to the onset of symptoms.[9 10] During the symptomatic phase, workers can either choose to be present at work while feeling ill ("presenteeism") or to remain at home ("absenteeism"). Studies have suggested that workplace presenteeism during influenza infection is widespread.[13 14] From a public health and socioeconomic perspective, incentivising sick leave during influenza infection may reduce disease transmission enough to reduce the overall costs to society[15]. From the perspective of an employer, however, the burden of work absenteeism may be considerable, as the value of the work employees would have produced is lost.[16 17]

Using a model framework, we attempted to quantify the costs and health consequences of increasing sick leave among workers with influenza symptoms. In our study we define sick leave as the period of time a worker is absent from paid work due to influenza symptoms. We simulated the effect of implementing different sick leave policies during an influenza outbreak in the Norwegian population. We conducted a survey to inform the model with local data on current influenza-related sick leave behaviour in Norway, and compared different sick leave interventions with current practice.

Material and methods

Modelling assumptions

We developed a model to quantify the number of mild, moderate and severe influenza cases. A scenario-based approach was applied to account for the fact that influenza, particularly pandemic influenza, varies in terms of transmissibility, likelihood of symptomatic infections, and illness severity (i.e. risk of primary care visits, hospitalizations and death). We differentiated between interventions (variation in sick leave behaviour) and scenarios (variations in influenza characteristics), and studied each sick leave intervention given each distinct influenza scenario. In total, we analysed current sick leave practice (baseline), and 14 alternative sick leave interventions combined with 48 influenza scenarios. The health outcomes from the disease model were used in an economic model to estimate costs and quality adjusted life years (QALYs). Because the parameters of the economic model (listed in Table SMM1, Supplementary File 1) were uncertain, we used Monte Carlo simulations to explore the consequences of the uncertainty. In this paper, we outline the main characteristics of the models and their input parameters. A detailed description of the survey and models is provided in Supplementary file 1.

Influenza-related sick leave

During epidemics, Norwegian health authorities advise that workers with symptoms of influenza remain at home until feeling well enough to work. During pandemics, sick leave is recommended until at least 24 hours following defervescence[3 18]. Lacking data on influenza-related absences, we conducted a web-based survey in a convenience sample of 490 Norwegian employees. In total, 46% (224/490) of the participants reported having experienced influenza-like symptoms during the previous influenza season. Based on expert

opinion, influenza-like symptoms, for the purposes of the survey, included: fever, cough, sore throat, headache, fatigue, muscle pain, and/or stuffy nose. Among participants reporting influenza-like-symptoms, 74% had taken sick leave. The duration of absence varied from 1–13 workdays (mean of 2.4 days) and individuals waited from 1–8 days (mean of 2.7 days) after the onset of symptoms to take leave (Figure SMM1, Supplementary File 1). Among those who took sick leave, 24% began on the first day that they experienced symptoms, 43% on the second day, 19% on the third day, while 14% waited at least four days before taking sick leave (Figure SMM2, Supplementary File 1).

The survey respondents were mostly public sector employees who have high job security. There is evidence that workers with lower job security are more likely to attend work despite feeling ill,[19] therefore we lowered the baseline sick leave rate in our model to 65% to make the results more representative of the general working population in Norway.

In the baseline sick leave setting, we assumed that symptomatic workers would stay at home for an average of 3.5 calendar days for seasonal influenza, adjusting for a working week of five days. For pandemic influenza, we increased this period to 6.5 calendar days, in line with the Norwegian national guidelines during the 2009 H1N1 pandemic that suggested one week of absence from the onset of symptoms. Consistent with the survey, we assumed that among those workers who take sick leave because of influenza, 24%, 43%, 19%, and 14% would initiate sick leave on the first, second, third, and fourth day relative to symptom onset, respectively. We found no data in the literature on the proportion of children absent from school or day-care due to influenza-like illness. Therefore, we assumed that 90% of children with influenza would remain at home, with cumulative withdrawal rates of 33%, 67%, and 100% on the first, second, and third day relative to symptom onset, respectively.

Interventions

We considered all combinations of the following interventions aimed at increasing the proportion of workers taking sick leave and/or reducing the delay from symptom onset to withdrawal from the workplace: I) proportion of symptomatic workers taking sick leave: 65%, 80% and 90%, and II) maximum time from symptom onset to sick leave: 0.5 days, 1 day, 1.5 days, 2 days and 4 days. These interventions were chosen based on the results from our survey on sick-leave behaviour, and on perceived feasibility. Interventions were compared to the baseline sick leave practice, defined as 65% of ill workers taking sick leave after a maximum of four days with symptoms. In children, the baseline pattern of sick leave was kept constant.

We simulated interventions with less than 4 days of maximum delay from symptoms onset to sick leave using a truncated variant of the baseline daily withdrawal proportions. For example, in the case of a maximum of 2 days delay, 24% would initiate sick leave when symptoms first appeared, 43% on the following day, and the remaining 33% on the next day.

Main features of the influenza model and the economic model

We developed an age-structured, deterministic simulation model (Fig 1) for the spread of influenza in Norway (population: 5.05 million in January 2013). The social mixing structure, representing mixing within households, schools, workplaces, and general society, was reconstructed from simulations based on real demographic data (Figure SMM3, Supplementary File 1). People at home with influenza illness were assumed to not mix with other people at work/school, or in the general population. We calibrated the model to a broad spectrum of seasonal and pandemic influenza scenarios: seasonal epidemics at an effective reproductive number (R_eff) of 1.2, 1.3, and 1.4, assuming 35% of children and 25% of adults would develop symptoms (low symptomatic proportions), or that 65% of children and 55% of

adults would develop symptoms (high symptomatic proportions). For pandemic influenza, we constructed scenarios at a basic reproductive number (R_0) of 1.4, 1.6, and 1.8, also assuming low or high symptomatic proportions as described above. The reproductive number is defined as the number of secondary cases that one influenza case would produce, and can be regarded as a measure of transmissibility.

We assumed that individuals become infectious prior to the onset of symptoms, and that their infectivity would peak approximately on the first day of symptoms and would last for seven days, according to a given infectivity profile (Figure SMM4, Supplementary File 1). Individuals with asymptomatic infection were assumed to be half as infectious as those with symptoms, but with a similar contour of infectivity.

We developed a probabilistic health economic model to translate the output from the infection model into costs of healthcare, costs of sick leave (productivity losses), and the intervention costs for each intervention. Productivity losses are highly relevant in sick leave intervention studies, and therefore we assessed cost-effectiveness from a societal perspective. To ease comparison between the interventions and scenarios, we used a net health benefit (NHB) approach assuming that the value of a QALY (λ) was NOK 570,807 ($98,060 USD[20]) in line with Norwegian guidelines.[21] By definition, NHB=QALY gains - (cost of intervention/ λ). This means that an intervention is cost-effective if NHB expressed as QALYs is greater than zero. All costs were measured in 2012 Norwegian Kroner (NOK) ($1.00 USD= NOK 5.82)[20].

The age-specific incidence of symptomatic influenza from simulations of the dynamic model was used as input data for the economic analyses. We used the estimates adopted in the 2014 Norwegian pandemic preparedness plan for the proportion of clinical cases that would

require healthcare (visit to a GP, hospitalisation, or intensive care treatment), and used estimates of mortality from the same source.[22] The plan includes three distinct morbidity/mortality estimates for moderate, severe, and very severe pandemics. The morbidity during seasonal influenza was assumed to be similar to that observed during a moderate pandemic.

The dynamic influenza model was developed in Matlab version R2013a using the ode45 solver. The economic model was developed in STATA-13 and Excel 2010.

Patient and public involvement

Public health officials were involved in the development of the study design and outcome measures. Patients were not involved in study development, and study findings were not disseminated to study participants, as these were anonymous.

Results

This section is organised as follows: First, we present the baseline disease burden and baseline economic costs for each of the main scenarios. Second, we describe the health impacts of the sick leave interventions. Third, we present the results of the cost-effectiveness analyses. Lastly, we present results from the sensitivity analyses, in which we have assumed extra mixing in the household and general population in individuals who are absent from work. We present the epidemiological results by reporting relative changes in the clinical attack rate (AR), which is defined as the proportion of the population that acquire a clinical infection. The comparative changes in GP visits, hospitalisations, and mortalities closely mimicked changes in the AR. We report the cost-effectiveness results in terms of mean NHB. Complete tables for all results related to the epidemiologic outcomes, direct and indirect costs in the

economic model, including probabilistic variation, are available upon request from the authors.

Baseline scenarios

Table 1 shows the key epidemiologic and economic results for each of the baseline scenarios for seasonal and pandemic influenza. In the absence of any intervention, the model produced clinical attack rates (ARs) ranging from 3.2–16.9% for seasonal influenza at an R_eff of 1.2–1.4, and 9.4–34.8% for pandemic influenza at an R_0 of 1.4–1.8. Visits to a GP and hospitalisations ranged from 478–2,521 and 23–122 per 100,000 people for seasonal epidemics, and from 1,398–8,688 and 67–1,207 per 100,000 for pandemics. The corresponding mortality ranged from 5–26 expected deaths per 100,000 people for seasonal influenza, and from 15–243 deaths for pandemic influenza.

Table 1: Key population baseline epidemiological and economic outcomes for seasonal epidemics and severe pandemics in each of the scenarios considered.

	Seasonal influenza R_eff[b]			Pandemic influenza severe (moderate; very severe)[a] R_0[c]		
Baseline outcomes in the total population	**1.2**	**1.3**	**1.4**	**1.4**	**1.6**	**1.8**
Low symptomatic proportions						
Clinical attack rate, AR (%)	3.2	5.3	7.0	9.4	13.0	15.6
Median number of GP visits per 100,000 population	478	789	1,053	1,866 (1,398; 2,334)	2,587 (1,939; 3,236)	3,115 (2,334; 3,896)
Median number of hospitalisations (per 100,000 population)	23	38	51	184 (67; 325)	255 (93; 450)	307 (112; 541)
Median number of deaths (per 100,000 population)	5	8	11	21 (15; 65)	30 (20; 90)	35 (24; 109)
Mean total costs (million USD)	94	155	205	473 (401; 569)	656 (557; 789)	790 (670; 950)
Productivity losses (% of total costs)	83	83	83	75 (88; 62)	75 (88; 62)	75 (88; 62)
High symptomatic proportions						
Clinical attack rate, AR (%)	9.0	13.3	16.9	22.3	29.5	34.8
Median number of GP visits per 100,000 population	1,342	1,983	2,521	3,329 (4,442; 5,557)	5,892 (4,415; 7,370)	6,946 (5,205; 8,688)
Median number of hospitalisations (per 100,000 population)	65	96	122	438 (160; 772)	581 (212; 1,024)	685 (251; 1,207)
Median number of deaths (per 100,000 population)	14	20	26	50 (34; 155)	66 (44; 1,024)	78 (53; 243)
Mean total costs (million USD)	257	378	479	1,134 (963; 1,363)	1,503 (1,276; 1,807)	1,770 (1,503; 2,128)
Productivity losses (% of total costs)	82	82	82	75 (88; 62)	75 (88; 62)	75 (88; 62)

a= moderate (severe; very severe) refers to illness severity in the influenza scenario, b=effective reproductive number, c= basic reproductive number, cd= 35% of children aged < 16 years, and 25% of adults aged 16+ years develop symptoms, e=65% of children aged < 16 years, and 55% of adults aged 16+ years develop symptoms

The mean total costs of influenza in Norway, including productivity losses and healthcare resource use ranged from $94–$479 million USD for seasonal epidemics, $401–1,503 million for moderate pandemics, $473–1,770 million for severe pandemics, and $569–2,128 million for very severe pandemics. Production losses made up the majority of the total costs. The proportion of the total costs owing to productivity losses was 82–83% during seasonal influenza, and 62–82% during pandemic influenza. The proportion was lowest during very severe pandemic influenza, where the healthcare costs increased substantially. (Fig S1).

Epidemiological impact of sick leave interventions in workplaces

Figures 2 and 3 display the intervention effects on the AR, the epidemic peak delay, and changes in the epidemic curves when compared to the baseline scenarios.

For the seasonal influenza scenarios, the AR was reduced by 44.4–98.8% (mean value of 85.4%) compared with the baseline values (Fig 2A). The interventions achieved the highest reduction at the lowest transmissibility of R_eff = 1.2 (blue) and at high symptomatic proportions (solid lines); the relative minimum AR was 60.3% assuming low symptomatic proportions (stippled lines). As expected, the interventions with a high proportion of workers on sick leave (90%) and early withdrawal from work/school (0.5 days) had the greatest effect. General trends in the pandemic scenarios were similar to those obtained in the seasonal epidemics. However, as the transmissibility in these scenarios was higher on average, the interventions were less effective. Overall, the interventions reduced the AR by 63.6–99.7% (mean AR of 91.0%) relative to their baseline values (Fig 2B). Pandemic scenarios with low symptomatic proportions had a relative minimum AR of 77.3%.

In the seasonal influenza scenarios, the interventions delayed the epidemic peak by 0 to 58 days. The delay was particularly pronounced at R_eff = 1.2 (Fig 2C and Fig 3, left column top panel). The scenarios assuming low symptomatic proportions had a maximum time delay of 43 days, and most cases exhibited a delay of 1–2 weeks. Pandemic scenarios resulted in shorter peak time delays than the seasonal scenarios, ranging from 0–20 days (Fig 2D and Fig 3, right column); the delay of time to peak was at most 10 days in scenarios with low symptomatic proportions.

The median age among avoided clinical cases was similar within each scenario, ranging from 26.7–33.6 years for the seasonal scenarios, and from 33.6–38.1 years for the pandemic scenarios (Fig S2 and Fig S3). More infections were avoided in younger individuals when transmissibility or symptomatic proportions were low.

Cost-effectiveness of sick leave interventions in workplaces

Figure 4 summarises the results of the cost-effectiveness analyses for seasonal influenza (Fig 4A), and for pandemics assuming moderate, severe, and very severe illness (Fig 4B–D, respectively).

In total, for 100% (6/6) of seasonal influenza scenarios, sick leave interventions were cost-effective compared to current sick leave practice; cost-effective interventions were obtained for 50% (3/6) of moderate, 50% (3/6) of severe, and 87% (5/6) of very severe pandemic scenarios. In general, the mean NHB was higher at low transmissibility (blue) compared to high transmissibility (red), assuming that all other factors remained equal (Fig 4). The mean NHB was larger at high symptomatic proportions (squares) compared to low symptomatic proportions (crosses), for similar transmissibility.

In the pandemic scenarios assuming low symptomatic proportions, interventions were cost-effective for R_0 < 1.6, except in the case of a very severe pandemic where interventions were also cost-effective for R_0 = 1.6 (Fig 4B-D). For pandemic influenza with high symptomatic proportions, all scenarios at R_0 < 1.8 produced cost-effective interventions. For very severe pandemic scenarios, cost-effective interventions were also found for R_0 = 1.8.

In 16 of the 17 scenarios for which interventions were cost-effective, the superior intervention was for 90% of ill workers to take sick leave within one-half day of the onset of symptoms. (Fig 4 and Fig S1). While in one scenario, a seasonal epidemic at R_eff = 1.4 with low symptomatic proportions, 90% of symptomatic workers taking sick leave at the baseline delay from symptom onset, was the most cost-effective intervention. In this particular case, the combination of 90% of symptomatic workers taking sick leave and sick leave onset within 0.5 days ranked third in terms of cost effectiveness. Generally, when symptomatic proportions were low, the only cost-effective interventions were those in which sick leave onset occurred within 0.5 days, or interventions solely increasing the adherence. In contrast, scenarios with high symptomatic proportions produced cost saving results for a variety of different interventions.

Among the cost-effective interventions, the largest mean NHB was in the range 31–535 quality adjusted life years (QALYs) for low symptomatic proportions and 1,506–2,898 QALYs for high symptomatic proportions in the seasonal scenarios. For pandemic scenarios with low symptomatic proportions, interventions were cost-effective for moderate and severe scenarios with low transmissibility (R_0=1.4), and for very severe scenarios with low and moderate transmissibility (R_0=1.4 and R_0=1.6). The largest mean NHBs were 292, 477, and 170–1,185 QALYs for assumptions of moderate, severe, and very severe

morbidity/mortality, respectively. For high symptomatic proportions, the QALY value varied from 345–3,749, 1,966–4,481, and 1,859–7,256 for moderate, severe, and very severe morbidity/mortality, respectively.

Notably, interventions that focused exclusively on increasing the proportion of symptomatic workers taking sick leave, had comparatively high probabilities of being cost-effective, as shown by the stochastic simulations and illustrated in acceptability curves (Fig S4). Conversely, interventions with sick leave starting later than one day after the onset of symptoms were generally not cost-effective, except for scenarios with high symptomatic proportions, or when combined with an increased proportion of symptomatic workers taking sick leave.

Sensitivity analyses: assuming extra mixing for individuals absent from work

In the sensitivity analyses where additional mixing in the household and the general population was assumed, the effectiveness of sick leave interventions was somewhat diminished compared with the main scenarios (Fig S5). However, on the whole, the cost-effectiveness and ranking of the different interventions under the various scenarios were retained (Fig S6 and Fig S7). The reduction in the AR relative to the baseline varied from 52.7–99.4% in the seasonal scenarios, and 69.1–99.7% in the pandemic scenarios (Fig S5). In total, 83% (5/6) of seasonal scenarios, and 33% (2/6) of moderate, 50% (3/6) of severe, and 67% (4/6) of very severe pandemic scenarios produced cost-saving interventions. Consistent with the results obtained in the main analyses, the best intervention for the scenarios with cost-effective results was 90% of symptomatic workers taking sick leave with withdrawal at 0.5 days after the onset of symptoms. For this intervention, the mean NHB varied from 101–

2,192 QALYs for seasonal epidemics, and from 168–2,414, 131–3,019, and 388–5,314 QALYs for moderate, severe, and very severe pandemics, respectively.

Discussion

We have shown that the effectiveness of sick leave during influenza on reducing the spread of the disease is dependent on: i) timing of absence onset, ii) the proportion of ill workers leaving work, and iii) the characteristics of the influenza epidemic (transmissibility, influenza severity, etc.). The results of our study indicate that the earlier the absence and the greater the proportion leaving work, the greater the effectiveness. Leaving work more than two days after onset of symptoms has minimal impact on the spread of the disease. Even when taking costs of lost production into account, early absence among high proportions of workers is cost-effective in most disease scenarios. Exceptions are pandemics with low transmissibility and general epidemics with low symptomatic proportions.

The modelling approach allowed us to simulate population level effects of different sick leave interventions under a range of possible influenza scenarios, providing information that would not readily be observed in real-life studies. The scenarios presented are largely consistent with those proposed in a recent review on pandemic influenza scenarios in Europe, in which the authors argued for the use of multiple scenarios based on the recent experience from the 2009 H1N1 pandemic[23]. Other studies address the effects of expanding the right to sick leave[4 24], but since access to paid sick leave is more or less universal in Norway, we have focused specifically on different sick leave interventions. Our study is the first to investigate epidemiological and economic outcomes of workplace-based interventions on a population

level. We are also the first, to our knowledge, to investigate the effects of the timeliness of sick leave initiation relative to symptom onset during influenza.

Our results indicate that early withdrawal is important for cost-effectiveness, but this result may depend on the ability to differentiate influenza from other illnesses with similar symptoms. Because influenza symptoms are non-specific, and it is unknown whether sick leave interventions are cost-effective for illnesses with influenza-like symptoms, e.g. respiratory syncytial virus (RSV), early withdrawal may not be as cost-effective in practice. Influenza surveillance data, which is available in many countries, could be used to restrict recommendations to apply only in geographic regions where influenza activity is rising. Another central question is how these sick leave recommendations can be communicated effectively to the working population and the costs of achieving the sick leave behaviours described. In our study, the cost-effective interventions were also assumed to be the most costly to implement, with a mean cost of $5.6 million; but the true cost is uncertain. A pilot study could be initiated to assess costs and feasibility of earlier sick leave and increased proportion of symptomatic workers taking sick leave.

Our study has several limitations. The profile of infectiousness assumed in our model was an influential variable. Although it was based on data from a household study, we acknowledge that there is uncertainty related to how infectiousness changes over time, and to the relative infectivity of an asymptomatic infection. The proportion of GP visits and hospital admissions, and the case-fatality rate assumed under different influenza scenarios were based on estimates proposed by Norwegian experts, and were not age-specific. A recent review reported lower estimates in other European countries,[23] but these values are likely country-specific. Another limitation of this study was that influenza illness has been shown to reduce

productivity at work,[25] however, this may vary depending on occupation. We assumed that 8% of workers would continue to work from home during their illness and while taking care of sick children, but information on this topic is scarce. A study from Sweden found that 60% of parents work from home when their children are sick[26] thus our assumption may underestimate the economic benefit of the intervention. The economic benefits from earlier onset of sick leave may also have been underestimated. It seems plausible that earlier sick leave onset could lead to a quicker recovery, however, we could not find any evidence of this in the literature; therefore, we assumed the recovery period to be constant, and independent of sick leave onset. Finally, influenza cases and workplace absences were modelled to occur randomly on a population level. In reality, absences may cluster in specific workplaces, which may cause understaffing for critical functions and a subsequent increase in cost.

We assumed that the number of days of sick leave was 3.5 calendar days for seasonal influenza and 6.5 calendar days for pandemic influenza. Because we found that the epidemiological benefits of sick leave were limited after 2 days of symptoms, we also explored the effect of assuming the same number of total absence days during pandemics as during epidemics (3.5 calendar days). This resulted in higher economic benefits for interventions involving early onset within one day, but lower benefits for other interventions.

Current recommendations on sick leave during influenza are typically focused on the duration of sick leave, but the present results suggest that recommendations may be improved by encouraging prompt initiation of sick leave. However, although sick leave can reduce the spread of influenza, our findings indicate that this effect is insufficient to offset an ongoing epidemic or pandemic so, ideally, sick leave interventions should be implemented in conjunction with existing strategies. Economic evaluations of mitigation interventions such as

vaccines, antivirals, and school closures, are common in the literature.[27-29] In contrast, studies on sick leave interventions are limited [28 29], which is somewhat surprising considering that this is a widespread recommendation in national pandemic preparedness plans.[3] Moreover, pharmaceutical interventions are limited by availability[30]; therefore non-pharmaceutical interventions can be considered as viable backup strategies. As a result, there is a need for quantitative modelling for policy planning and decision-making purposes. The present economic results are based on Norwegian demographic and economic assumptions, and several factors would need to be recalculated for use in other countries. Nevertheless, our model provides a structure for analysing this problem and provides a method, which could be applied in other settings.

The findings in this paper indicate that there are epidemiological and economic benefits from sick leaves during influenza, however further studies are needed to assess these effects in more detail and in other settings. Future studies should consider collecting additional data on influenza transmission pathways, sick leave practice and the behaviour of workers during sick leave. Ideally, such studies should also aim to test for influenza to establish aetiology, rather than relying on self-reported influenza status. Moreover, it is of importance to conduct studies to explore the effects of sick leave interventions within specific occupational groups. For example, influenza has been found to be less prevalent in janitors and technicians compared with other occupations.[31] Likewise, some workers may be more likely to spread influenza (e.g. a waiter in a restaurant), or be more likely to spread influenza to high-risk persons (e.g. healthcare workers). Finally, investigations into the cost-effectiveness of sick leave interventions for other communicable diseases, perhaps especially those with high illness severity or low transmissibility, are warranted.

Conclusion

Recommending early absence from work among all workers with influenza symptoms represents an effective intervention during influenza epidemics and pandemics. The intervention is also cost-effective in most influenza scenarios.

List of abbreviations

AR: Attack rate

QALY: Quality adjusted life year

R_0: Basic reproductive number

R_eff: Effective reproductive number

NHB: Net health benefit

GP: General practitioner

EQ-5D: EuroQol 5 D

Author contributions

The study was designed by BFdB, CHE, and ISK. The mathematical model was designed by BFdB and GST, and the economic model was developed by CHE, ISK, and RW. The data analysis was performed by CHE and BFdB. The manuscript was prepared by CHE and BFdB. All authors revised and accepted the final manuscript.

Acknowledgements

The authors wish to thank Siri Helene Hauge and Olav Hungnes of the Norwegian Institute of Public Health for their insightful comments and guidance on influenza and influenza-related policies. We would also like to thank Arna Desser for her assistance with proofreading the article.

Data sharing

The main sources of data have been provided in the text of the main article or in the supplementary files, however, additional information can be provided by the authors on request.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interests

All authors have completed the ICMJE uniform disclosure form and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

Ethical considerations

Informed consent was obtained from all survey participants of the survey. The study was reviewed by the Data Protection Official at the University of Oslo, and it was considered that approval from an ethical committee was not required due to the nature/content of the study.

References

1. World Health Organization. Influenza (seasonal) factsheet No211: World Health Organization; 2009 [08.10.2013]. Available from: http://www.who.int/mediacentre/factsheets/fs211/en/.

2. Xue Y, Kristiansen I, de Blasio B. Modeling the cost of influenza: the impact of missing costs of unreported complications and sick leave. *BMC public health* 2010;**10**(1):724. doi: 10.1186/1471-2458-10-724.

3. Edwards CH, Tomba GS, Blasio BFd. Influenza in workplaces: transmission, workers' adherence to sick leave advice and European sick leave recommendations *European Journal of Public Health* 2016;**1-8**. doi: 10.1093/eurpub/ckw031.

4. Kumar S, Grefenstette JJ, Galloway D, et al. Policies to reduce influenza in the workplace: impact assessments using an agent-based model. *American Journal of Public Health* 2013;**103**(8):1406-11. doi: 10.2105/AJPH.2013.301269.

5. National Insurance Act. Act 1997-02-28-19. Act relating to national insurance Avd I 1997 Nr. 5LOV-1997-02-28-19 [04.07.2014]. Available from: https://lovdata.no/dokument/NL/lov/1997-02-28-19.

6. Intensjonsavtale om et mer inkluderende arbeidsliv 4. mars 2014 - 31. desember 2018 (IA-avtalen) 2014 [04.07.2014]. Available from: https://www.regjeringen.no/globalassets/upload/asd/dokumenter/2014/ia_20142018/signert_ia_avtale.pdf.

7. Ose SO, Dyrstad K, Slettebak R, et al. Evaluering av IA-avtalen (2010-2013) 2013 [03.07.2014]. Available from: http://www.sintef.no/prosjekter/evaluering-av-ia-avtalen-2010-2013/.

8. Elder AG, O'Donnell B, McCruden EA, et al. Incidence and recall of influenza in a cohort of Glasgow healthcare workers during the 1993–4 epidemic: results of serum testing and questionnaire. *Bmj* 1996;**313**(7067):1241-42.

9. Carrat F, Vergu E, Ferguson NM, et al. Time lines of infection and disease in human influenza: a review of volunteer challenge studies. *American journal of epidemiology* 2008;**167**(7):775-85. doi: 10.1093/aje/kwm375.

10. Lau LLH, Cowling BJ, Fang VJ, et al. Viral shedding and clinical illness in naturally acquired influenza virus infections. *Journal of Infectious Diseases* 2010;**201**(10):1509-16. doi: 10.1086/652241

11. Suess T, Remschmidt C, Schink SB, et al. Comparison of shedding characteristics of seasonal influenza virus (sub) types and influenza A (H1N1) pdm09; Germany, 2007–2011. *PloS one* 2012;**7**(12):e51653. doi: 10.1371/journal.pone.0051653.

12. Patrozou E, Mermel LA. Does influenza transmission occur from asymptomatic infection or prior to symptom onset? *Public health reports* 2009;**124**(2):193.

13. Nichol KL, Heilly SJD, Greenberg ME, et al. Burden of Influenza-Like Illness and Effectiveness of Influenza Vaccination among Working Adults Aged 50–64 Years. *Clinical Infectious Diseases* 2009;**48**(3):292-98. doi: 10.1086/595842

14. Carrat F, Sahler C, Rogez S, et al. Influenza burden of illness: estimates from a national prospective survey of household contacts in France. *Archives of internal medicine* 2002;**162**(16):1842. doi: 10.1001/archinte.162.16.1842.

15. Liao S, Ma Y, Chen J, et al. Paid sick-leave: is it a good way to control epidemics? In: Glass K, Colbaugh R, Ormerod P, et al., eds. Complex Sciences: Second International Conference, COMPLEX 2012, Santa Fe, NM, USA, December 5-7, 2012, Revised Selected Papers. Cham: Springer International Publishing, 2013:213-27.

16. Keech M, Scott A, Ryan P. The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. *Occupational Medicine* 1998;**48**(2):85-90. doi: 10.1093/occmed/48.2.85.

17. Keech M, Beardsworth P. The impact of influenza on working days lost. *Pharmacoeconomics* 2008;**26**(11):911-24. doi: 10.2165/00019053-200826110-00004

18. Norwegian Institute of Public health. Reviderte råd for anbefalinger om sykefravær ved influensaliknende sykdom [Revised advice for recommendations on absenteeism due to influenza-like illness] [13.06.2013]. Available from: https://www.fhi.no/globalassets/migrering/dokumenter/pdf/rapport-om-anbefalinger-om-fravar-ved-sykdom-2009-11-18.pdf.pdf.

19. Johns G. Presenteeism in the workplace: A review and research agenda. *Journal of Organizational Behavior* 2010;**31**(4):519-42. doi: 10.1002/job.630.

20. Central bank of Norway. Exchange rate for USD. 2013. [14.08.2015]. Available from: http://www.norges-bank.no/Statistikk/Valutakurser/.

21. Norwegian Directorate of Health. Helseeffekter i samfunnsøkonomiske analyser. 2007 [20.06.2014]. Available from: https://helsedirektoratet.no/lists/publikasjoner/attachments/643/helseeffekter-i-samfunnsokonomiske-analyser-is-1435.pdf.

22. Ministry of Health and Care Services. Norwegian National Influenza Pandemic Preparedness Plan 2006 [17.07.2014]. Available from: https://www.regjeringen.no/no/dokumenter/nasjonal-beredskapsplan-for-pandemisk-in/id102132/.

23. Napoli C, Fabiani M, Rizzo C, et al. Assessment of human influenza pandemic scenarios in Europe. *Euro Surveill*: 2015;**20**(7).

24. Kumar S, Quinn SC, Kim KH, et al. The impact of workplace policies and other social factors on self-reported influenza-like illness incidence during the 2009 H1N1 pandemic. *American Journal of Public Health* 2012;**102**(1). doi: 10.2105/AJPH.2011.300307.

25. Brouwer WB, Van Exel N, Koopmanschap M, et al. Productivity costs before and after absence from work: as important as common? *Health Policy* 2002;**61**(2):173-87. doi: 10.1016/S0168-8510(01)00233-0.

26. Novus. Unionen – Privata tjänstemän om att vobba 2015: Unionen; 2015 [14.04.2015]. Available from: http://www.unionenopinion.se.

27. Lee VJ, Lye DC, Wilder-Smith A. Combination strategies for pandemic influenza response-a systematic review of mathematical modeling studies. *BMC medicine* 2009;**7**(1):76. doi: 10.1186/1741-7015-7-76.

28. Aledort JE, Lurie N, Wasserman J, et al. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;**7**(1):208. doi: 10.1186/1471-2458-7-208.

29. Crabtree A, Henry B. Non-pharmaceutical measures to prevent influenza transmission: the evidence for individuals protective measures: National Collaborating Center for Infectious Diseases, 2011.

30. Bell D, Nicoll A, Fukuda K, et al. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerging infectious diseases* 2006;**12**(1):81-87. doi: 10.3201/eid1201.051370.

31. Anderson NJ, Bonauto DK, Fan ZJ, et al. Distribution of influenza-like illness (ILI) by occupation in Washington State, September 2009–August 2010. *PloS one* 2012;**7**(11):e48806. doi: 10.1371/journal.pone.0048806.

Figure Legends

Figure 1: Schematic representation of our model. An age-stratified SEIR model is used to model influenza spread; following infection, susceptible individuals (*S*) enter the incubation state, divided into pre-infectious (*E1-E6*) (*E*) and infectious (*E7-E8*) compartments. A proportion of individuals develop asymptomatic infection (*Asym1-14*) followed by recovery; the remainder develop symptomatic infection, categorized into people at school/work (*Sym1-14*), or people at home (*Symh1-Symh14*). Infectious individuals (red box, collectively denoted by *I*) mix with susceptible individuals in school, workplace, general community, and household settings; people at home during illness experience reduced mixing outside their households. When the infectious period ends, individuals are moved to the Removed class (*R*), not participating in disease spread anymore. Influenza scenarios are defined by: initial proportions of susceptible persons, transmissibility, proportions of asymptomatic individuals, and severity (red arrows). Influenza interventions are modelled by varying the timing and proportion of workers who take sick leave (yellow arrow). Healthcare utilization and deaths were estimated based on the age-specific incidence of symptomatic infections. Direct costs and effects include healthcare/medication costs, and quality of life detriments due to morbidity and mortality (blue box). People who work during illness and people who stay home from work due to own illness or to provide caregiving incur indirect costs due to lost productivity (green box). See Supplementary File 1 for further details about the model structure.

Figure 2: Impact of workplace-based interventions on clinical attack rate and timing of peak for seasonal epidemics (panels A and C) and for pandemics (panels B and D). Scenarios

assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted with stippled lines; scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted with solid lines. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility). The figure shows sick leave interventions with 65% and 90% adherence combined with absence onset within 0.5, 1, 1.5, 2, and 4 days. The baseline intervention (65% adherence and sick leave onset within 4 days of symptom onset) is indicated by **.

Figure 3: Impact of workplace-based interventions on the epidemic and pandemic curves in all main scenarios. Daily incidence in baseline scenarios are depicted for seasonal epidemics at R_eff=1.2, 1.3 and 1.4 (left column) and for pandemic influenza at R0=1.4, 1.6 and 1.8 (right column). In each panel, the solid lines depict the baseline scenario (65% adherence and sick leave onset within 4 days of symptom onset) assuming low symptomatic proportions (35% children, 25% adults develop symptoms), and the stripled lines depict the baseline scenario assuming high symptomatic proportions (65% children, 55% adults develop symptoms). The shaded grey regions illustrate the range of curves obtained when introducing the 14 different workplace-based interventions.

Figure 4: Mean Net Health Benefit (NHB) of workplace-based interventions for all main scenarios; seasonal epidemics (A), moderate pandemics (B), severe pandemics (C), very severe pandemics (D). Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted with crosses, and scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted with

squares. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility).

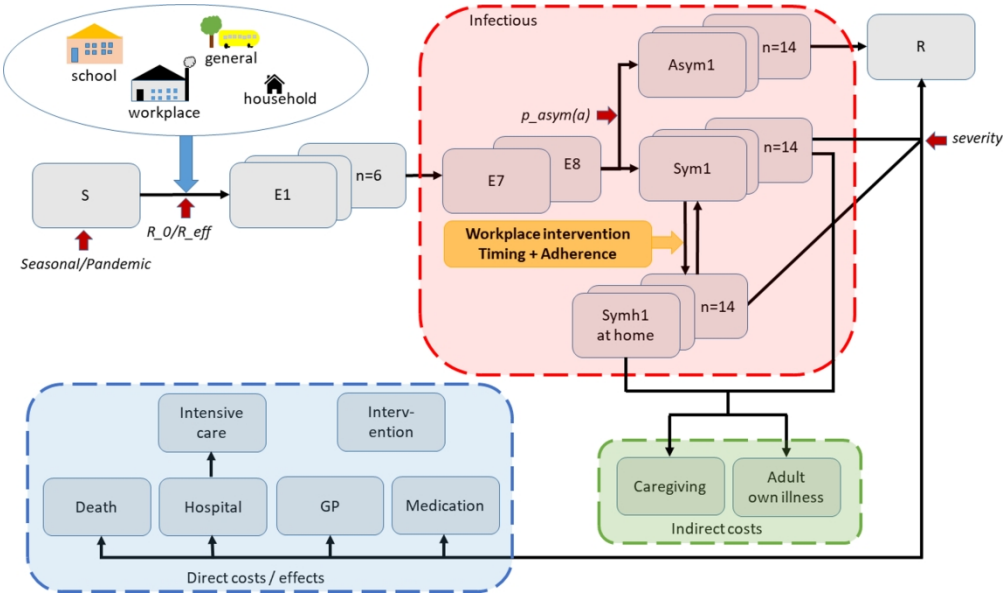


Fig 1

299x176mm (300 x 300 DPI)

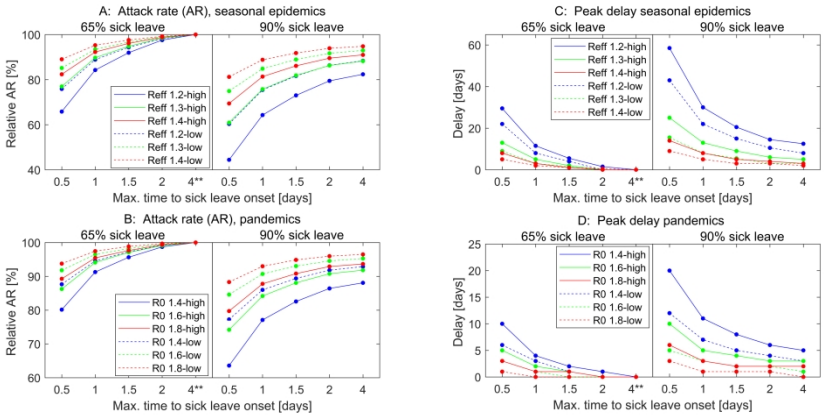


Fig 2

338x148mm (300 x 300 DPI)

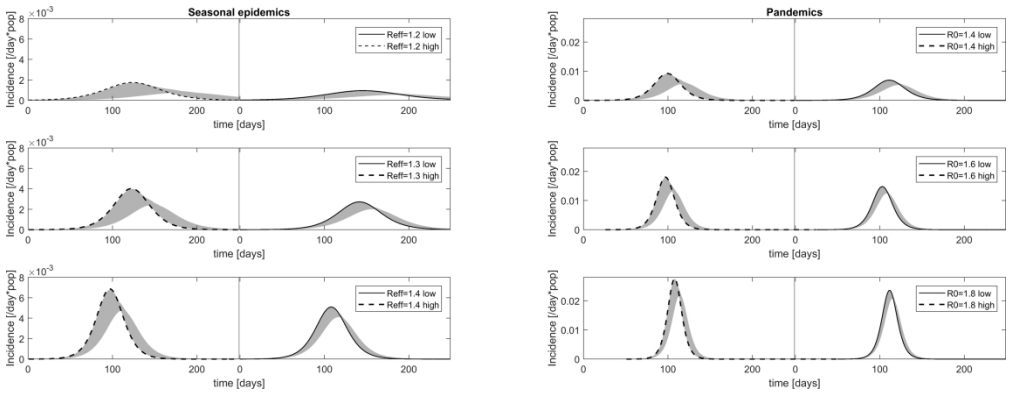
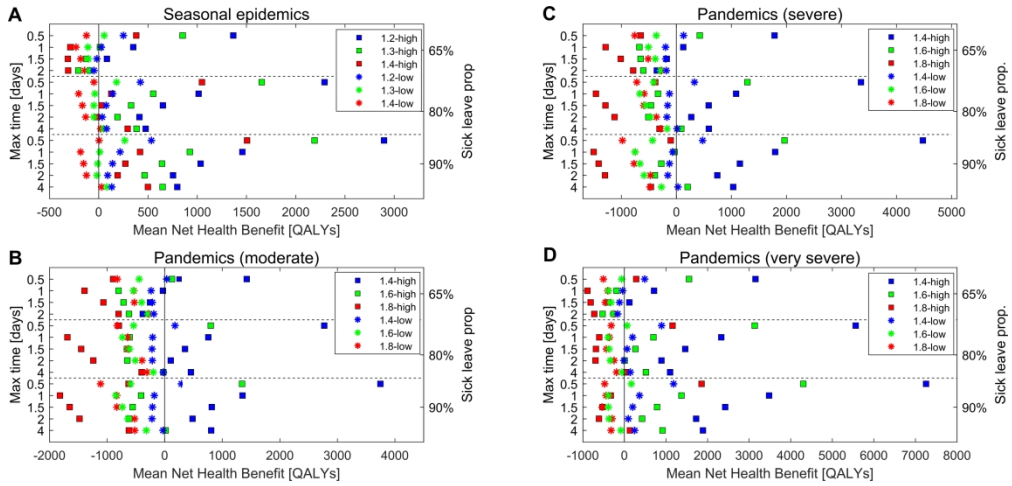


Fig 3

313x120mm (300 x 300 DPI)



Mean Net Health Benefit (NHB) of workplace-based interventions for all main scenarios; seasonal epidemics (A), moderate pandemics (B), severe pandemics (C), very severe pandemics (D). Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted with crosses, and scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted with squares. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility).

279x132mm (300 x 300 DPI)

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.hansen.edwards@fhi.no

SUPPLEMENTARY FILE 1: MATERIALS AND METHODS

SURVEY ON INFLUENZA-RELATED SICK LEAVE AMONG NORWEGIAN EMPLOYEES

A questionnaire consisting of 14 questions was issued either electronically via Questback©, or on paper via personal distribution to a convenience sample of Norwegian employees in the Oslo area between November 2013 and January 2014. The convenience sample was selected based on network recruitment, and consisted mainly of public sector employees. All data gathered on paper were folded and placed in an envelope, and were later entered into Questback©, and the original responses were destroyed. The data were stored in Questback© and analyzed in Excel 2013. Once analyses were completed the original data and any imported copies were deleted. The first 6 questions were concerning age, gender, inclusive work life status of employer, household size, the number of children below 12 years living in the household, and presence of influenza-like symptoms in the previous season (defined as August 2012 to April 2013). Questions 7-9 were only asked to the respondents who indicated having children below the age of 12 living in the household. The questions addressed: whether these children had experienced influenza-like symptoms in the previous winter, whether the children were sick simultaneously with the respondent, and if yes, the number of days of sickness overlap. The last 4 questions were asked to respondents who indicated having experienced influenza-like symptoms in the previous season. The respondents were asked to indicate the number of days of symptoms, the number of days spent at home from work during the symptomatic period (and which symptomatic days were spent at home), whether the days spent at home were GP-certified or self-certified, at what day of symptoms a physician was contacted, and on which days (if any) children below the age of 12 were sick simultaneously with the respondent.

A total of 490 employees completed the questionnaire. 72% of the respondents were females, and the remaining 28% were males. The age of the respondents ranged from 20 -70 years, with a mean age of 46. Most (96%) of the employees had employers with an inclusive

work life agreement (IW-agreement). There were no apparent differences between employees with and without IW–employers but the proportion of non-IW respondents was too small to meaningfully compare the two.

Among the 490 respondents, 224 reported having experienced symptoms of influenza last season. The number of days of symptoms varied from 1-20 days with a mean and median of approximately 6.5 and 5, respectively (Figure SMM1). Among the respondents that reported ILI symptoms, 161 respondents were absent from work, 58 respondents did not take time off work, the remaining 5 were missing. The duration of sick leave varied from 1-13 days, with a mean and median of 2.4 and 2 days, respectively.

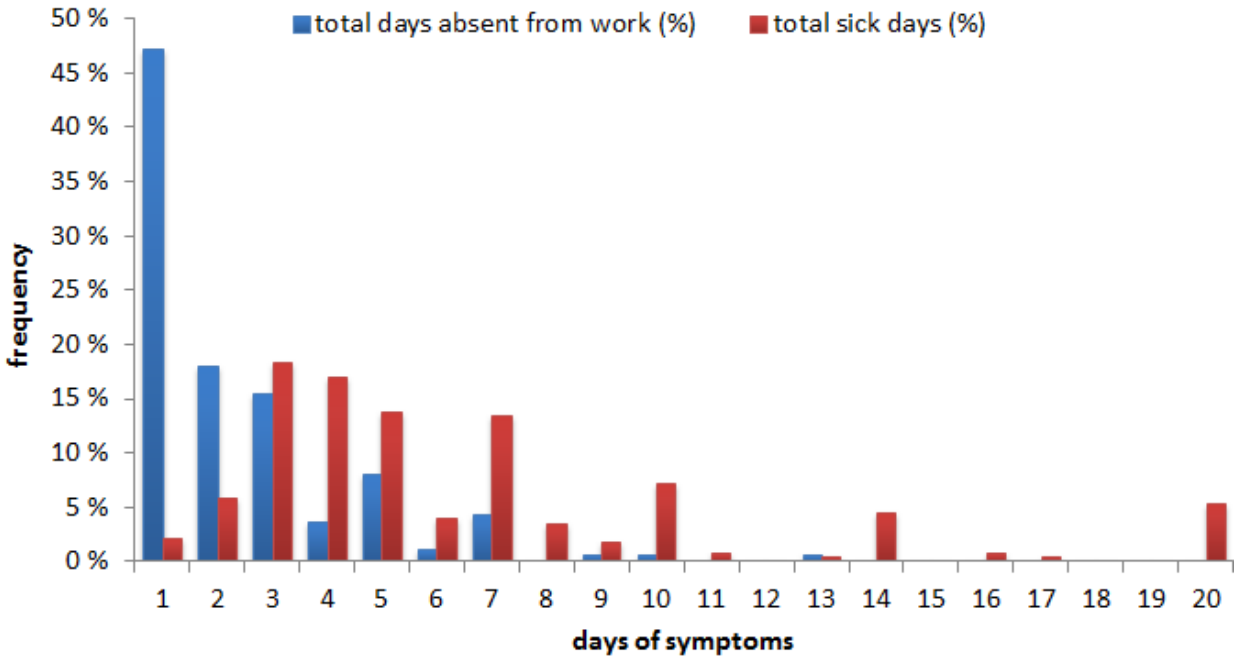


Figure SMM1: Frequency distributions showing the duration of symptoms (N=224) and the distribution of days absent from work (N=161) among respondents with ILI-symptoms.

Of the respondents that had influenza-like illness 20% reported visiting a GP for their symptoms, and 58% of these went on to take sick leave, while 42% continued to work. In total 14% of sick leaves were GP-certified, the remaining were self-certified.

Sick leave was initiated within 1-8 days after symptom onset. The shortest duration between sickness onset and sick leave was less than 1 day, and the longest duration was 7-8 days (Figure SMM2). We did not collect any information about which factors affected the likelihood of staying at home. We suspect that in addition to having mild symptoms at onset, possible explanatory factors for delayed onset of sick leave may be social pressure or deadlines at work. In our paper we truncated the final category into 4 days or later (simulated as 4 days maximum) such that 24% took sick leave on the first day following symptom onset, 43% on the second day, 19% on the third day, and the remaining 14% on the 4th day or later.

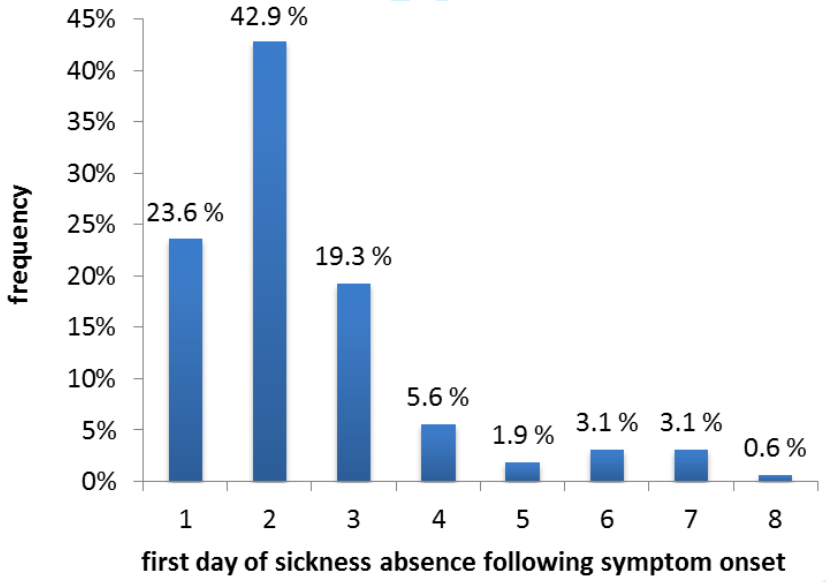


Figure SMM2: Frequency distribution showing the timing of sick leave onset counted in days from the time when symptom appeared (N=161)

The sick leave periods mainly occurred over consecutive days, with the exception of 5 respondents who reported intermittent sick leave histories. For the latter only the first sick leave period was counted. A total of 15 respondents reported being absent on one or more days without experiencing symptoms on these days; these sick leaves did not seem to be linked with sick children in the household.

Among the respondents, 155 said they had children <12 years in the household, 101/155 of the children had been ill in the past winter. The number of children was significantly correlated (p>0.01) with ILI symptoms in parents. The frequency of ILI symptoms in respondents was 16% higher when the household had one or more children <12 years. There was also a strong correlation (p>0.01) between experiencing ILI symptoms and having sick children. Although the correlation works from parent to child, and from child to parent, the latter is perhaps more correct as the sample of parents is non-random. If a child<12 in the household was ill, 74% of parents experienced ILI symptoms, otherwise 23% of parents experienced symptoms.

The survey was an attempt at providing a rough estimate of sick leave practice during influenza among the working population in Norway. Our sample is not representative of the Norwegian working population, and was largely made up of people working within health professions. Some respondents indicated that they had been on sick leave on days without symptoms (N = 6), this may be a result of measurement error or could reflect that the sick leave period was used in its full length as these sick leave periods were 7 days or longer. Since we were asking about past health states and sick leave behavior, recall bias may have been a problem. In the responses replies involving round numbers (10 days, 20 days) were relatively more common. This may have been a result of recall bias.

Survey on influenza-related sickness absence among Norwegian employees [August 2012 - April 2013]

Please enter or circle your response

1. Age:	
2. Gender:	F M

3. Do you have an employer with an agreement about inclusive worklife (IW-agreement)?	Yes No
4. How many people were living in your household last winter? (including yourself)	Yes No
5. How many children under the age of 12 years were living in your household last winter?	Yes No
6. Did you have flu-like symptoms last winter? Typical symptoms of flu are: fever / cough / sore throat / headache / fatigue / muscle pain / stuffy nose)	Yes No

(Questions 7-8 are only relevant if you had children under 12 years living in your household last winter)

7. Were any of the children (under 12 years living in the household) ill with flu-like symptoms in the previous winter?	Yes No
8. Were any children ill at the same time as you?	Yes No

(Questions 9 to 13 are only relevant if you experienced influenza-like symptoms last winter)

Please indicate the following by ticking the relevant day(s)	Symptom start Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	
9. On which days did you experience influenza-like symptoms? (for how long were you ill?)																					More than 14 days
10. On which days did you stay home from work?																					No days
11. Which absence days were GP-certified?																					No days
12. On which day did you visit a GP?																					I did not visit a GP
13. On which days were children less than 12 years living in your household experiencing symptoms as well?																					Not relevant

THE INFLUENZA MODEL

An age-stratified compartmental SEIR (*Susceptible-Exposed-Infected-Recovered*) model was developed to simulate the spread of influenza. Due to lack of local data, the social mixing patterns were adapted from published synthetic contact matrices, which were based on the simulation of an agent-based virtual population parameterized with detailed Norwegian census and social demographic data[1]. Mixing between age groups (Figure SMM3) were defined using four setting-specific contact matrices, accounting for contacts within households $\left(\mathbf{M}^{H}\right)$, contacts within schools $\left(\mathbf{M}^{S}\right)$, contacts within workplaces $\left(\mathbf{M}^{W}\right)$ and contacts in the general population $\left(\mathbf{M}^{GP}\right)$. Each matrix provides the relative frequency of contacts between different age classes. The overall contact matrix $\left(\mathbf{M}^{tot}\right)$ was obtained as a linear combination $\mathbf{M}_{ij}^{TOT} = \sum_{K} \alpha_K \mathbf{M}_{ij}^{K}$, where α_K accounts for the proportion of transmission occurring in the various settings, $K \in \{H, S, W, GP\}$. The weights, α_K ,were chosen at 0.3 for households, 0.18 for schools, 0.19 for workplaces and 0.33 for transmission occurring in the general community in accordance with empirical observations and previously published studies on influenza-like diseases[1-5]. Further details on the calculation of the mixing matrices are provided elsewhere[1].

The population was divided into 100 one-year age groups according to the size and age-distribution of the Norwegian population at 1 January 2013[6]. Newly infected individuals pass through an incubation phase which was modelled using 8 compartments ($E_1.E_2...E_8$). The mean incubation period was fixed at 1.9 days[7] including the E_1-E_8 compartments, and the average latency period was assumed at 1.425 days covering the first six compartments. The mean duration of the infectious phase was assumed at 7.475 days, consisting of E_7-E_8 compartments and 14 infectious compartments, all assumed to last for 0.5 days. The

infectious compartments were further split into three groups: people with asymptomatic infection ($Asym_1 ... Asym_{14}$), people with symptomatic infection ($Sym_1 ... Sym_{14}$) and people with symptomatic infection at home ($Symh_1 ... Symh_2$). The timing and the rates of flow between the two latter categories were modelled according to the type of intervention studied, as detailed in the main text. The variation of infectivity as a function of the duration of time since infection (the infectivity profile) was adapted from a study on household transmission[5], which is in alignment with data from the 2009 H1N1 pandemic where most transmission was found to occur early after and to peak around the time of symptom onset[7] (Figure SMM4).

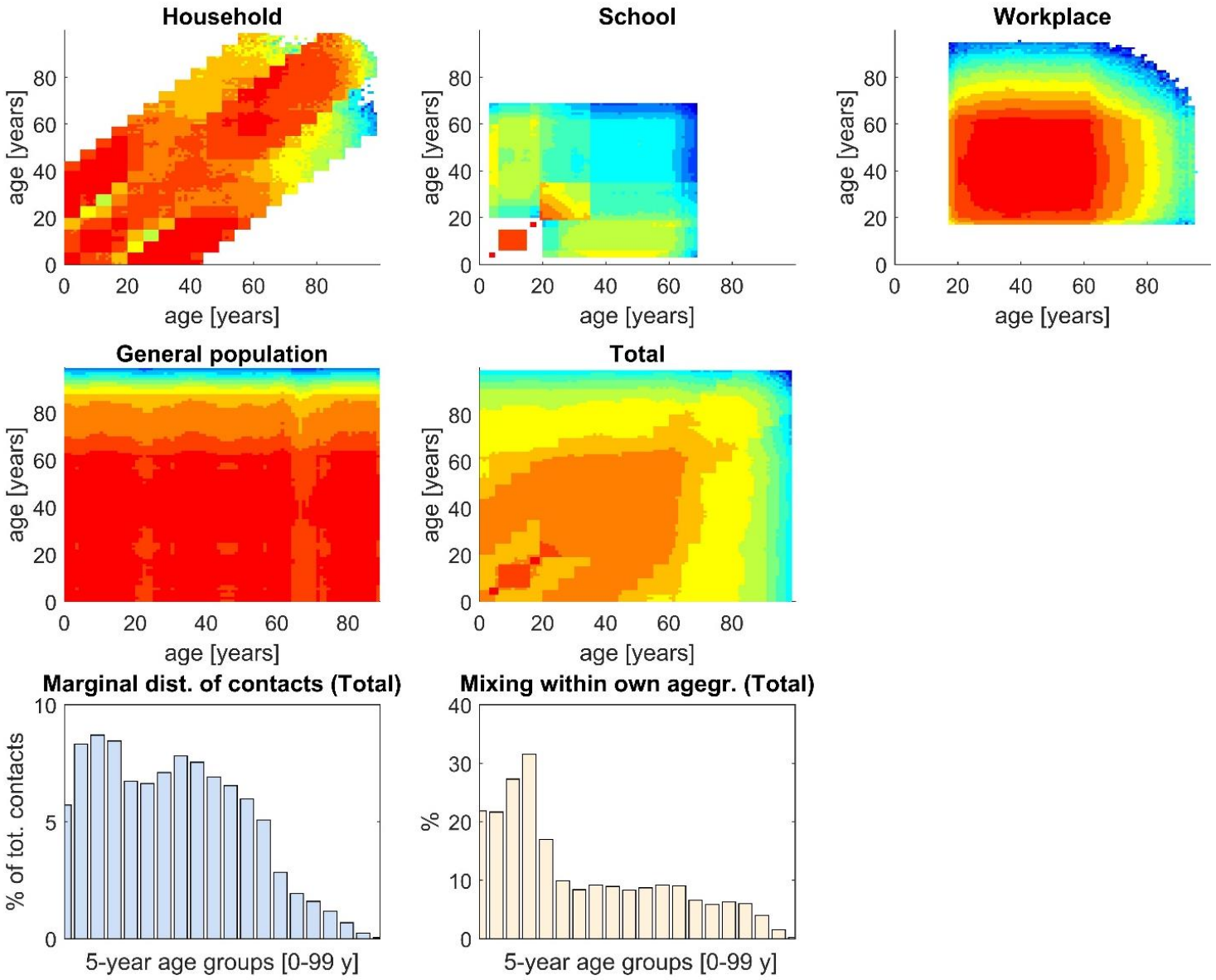


Figure SMM3: ***Mixing patterns by age assumed in the model:*** *Mixing matrices of the relative frequency of contacts among age classes in households, schools, workplace and the general population (top rows). The total mixing matrix was obtained as a weighted sum of the setting-specific matrices. The matrices are represented using a logarithmic scale (blue: low intensity; red: high intensity). The bottom row shows the marginal distribution of contacts (left) and the proportion of contacts with people of the same age (right) in the total matrix, aggregated into five-yearly age groups.*

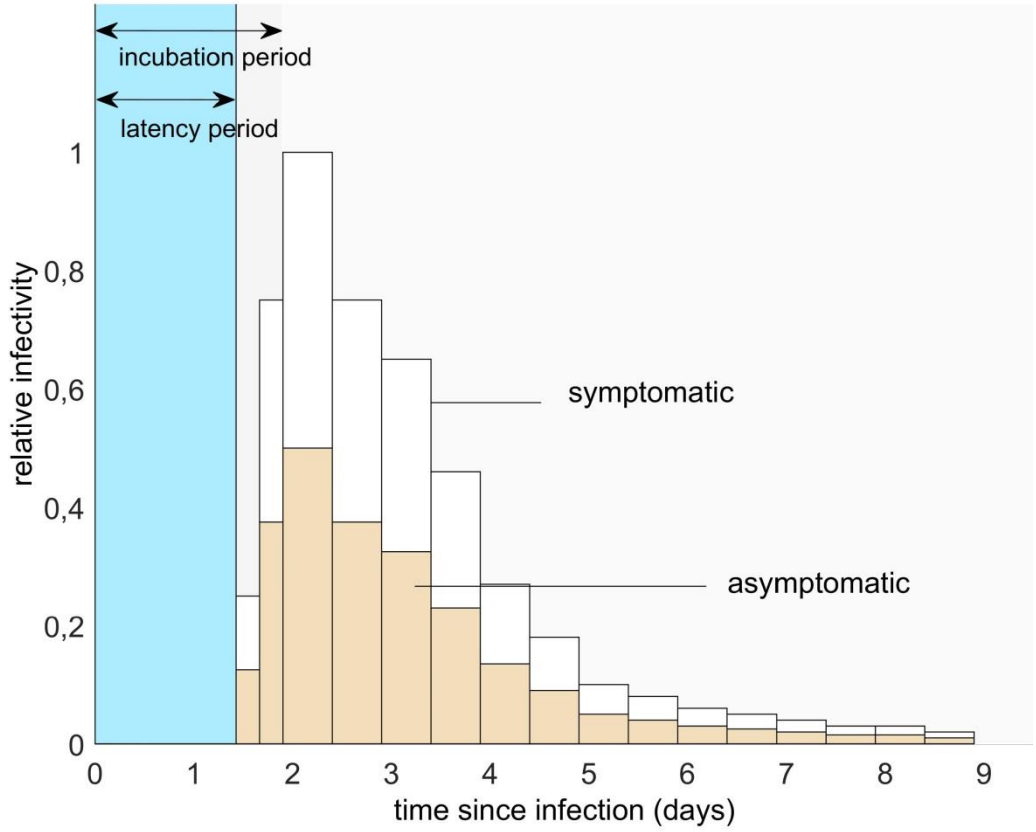


Figure SMM4: Schematic representation of the infectivity profile assumed in the model for individuals with symptomatic and asymptomatic influenza infection. The latency period is 1.5 days, the incubation period is 1.9 days, and infectivity peaks around 2 days after infection.

Recent analyses suggest that approximately 3 in 4 cases of seasonal and pandemic influenza are asymptomatic[8] and we assumed the baseline probability for symptomatic infection to be 0.35 for children <16 years and 0.25 for adults. However, in other scenarios we assumed that 50% of adults and 65% of children < 16 years develop symptoms in accordance with Longini et al.[9]. We assumed higher susceptibility and infectivity in children < 16 years of 1.05 and 1.30, respectively, compared to that of adults based on results from a Norwegian study using data from the 2009-H1N1 pandemic[10].

We modelled pandemic influenza by assuming a fully susceptible population at the simulation outset and using basic reproductive numbers: R_0=1.4, 1.6, or 1.8. For seasonal influenza we assumed that 0. 075, 0.20, and 0.40 of children < 16 years, adults 16-69 years,

and elderly 70+ years were fully immune at the simulation outset based on personal communication with experts at the Norwegian Institute of Public Health. In these simulations we considered effective reproductive numbers: R_eff=1.2, 1.3, and 1.4.

Sensitivity analyses

In the main scenarios we modelled sick leave by eliminating mixing at the workplace (0%) and in the general population (0%). There is lack of knowledge about how people behave during influenza sickness absence[11] , which impacts both their transmission potential and whom they will infect. We therefore performed sensitivity analyses by assuming that people during influenza sick leave would increase their likelihood of transmission in the household and in the general population. This was implemented in the model by adjusting the household mixing matrix (+10%) and the general population mixing matrix (-90%) compared to the mixing assumed in non-infected people at the same age.

COST-EFFECTIVENESS

We developed a probabilistic health economic model to capture the health consequences, healthcare costs, productivity losses from work absences, and campaign cost for each intervention. The age-specific incidence of clinical events was based on results from the dynamic model. The probabilities of clinical events leading to a healthcare encounter (general practitioner (GP) visit or hospitalization) or death were taken from the Norwegian Pandemic Preparedness Plan[12]. The plan includes distinct morbidity estimates for moderate, severe, and very severe pandemics. The morbidity during seasonal influenza was assumed similar to a moderate pandemic (Table SMM1).

Table SMM1: Parameters of the economic model. Mean values and distributions used for the cost-effectiveness analysis.

Parameter	Mean value	Distribution	Source
Probability of dying			
Seasonal /moderate pandemic	0.15%	$Tri(0.0015 \pm 0.0009)$	*
Severe pandemic	0.22%	$Tri(0.0022 \pm 0.00132)$	
Very severe pandemic	0.70%	$Tri(0.0070 \pm 0.0042)$	
Probability of hospitalization			
Seasonal / moderate	0.75%	$Beta(7.49, 992)$	**
Severe pandemic	2.00%	$Beta(19.98, 979)$	
Very severe pandemic	3.50%	$Beta(34.97, 964)$	
Probability of intensive care in hospital			
Seasonal / Moderate Pandemic	10.00%	$Beta(99, 899)$	**
Severe pandemic	17.00%	$Beta(169, 829)$	
Very severe pandemic	25.00%	$Beta(250, 749)$	
Probability of visiting a GP			
Seasonal / moderate Pandemic	15.00%	$Beta(150, 849)$	**
Severe pandemic	20.00%	$Beta(200, 799)$	
Very severe pandemic	25.00%	$Beta(250, 749)$	
Probability of working from home when ill	8.00%	$Beta(929, 10825)$	**[13]
Daily productivity loss adults	Age-specific (5-year)	Log Normal, mean (provided in ref. 6), 20% variation about mean	***[6]
Daily productivity loss caretakers	$ 337	$ln(337, 4543)$	***[6]
Productivity lost before and after (per absence)	5.00%	$ln(0.95, 0.0361)$	***[14]
Productivity when working from home/work	65.00%	$ln(0.65, 0.017)$	***[15-17]
Cost of a GP consultation	$ 68	$N(68, 185)$	#[18 19]
Cost of medications			
0-14 years (+5% severe+10% very severe)	$ 10.6	$N(10.6, 4.48)$	#[20 21]
15-64 years (+5% severe+10% very severe)	$ 10.4	$N(10.4, 4.32)$	#[20 21]
65+ years (+5% severe+10% very severe)	$ 14.0	$N(14.0, 7.90)$	#[20 21]
Cost of hospitalization			
Non-intensive care	$ 9 503	$Gamma(0.126, 75401)$	##[22]
Intensive care	$ 20 435	$Gamma(4.3, 4768)$	##[22]
National cost of campaign			
Cost of increasing adherence			
to 80%	$ 2 040 378	$N(2040378, 408076^2)$	
to 90%	$ 3 490 120	$N(3490120, 698024^2)$	
Cost of earlier onset of sick leave			#[23]
2 days of delay	$ 1 238 321	$N(1238321, 247664^2)$	
1.5 days of delay	$ 1 762 679	$N(1762679, 352535^2)$	
1 day of delay	$ 2 418 124	$N(2418124, 483625^2)$	
0.5 days of delay	$ 3 237 432	$N(3237432, 647486^2)$	
QALY losses (per case)			
QALY loss un-hospitalized cases	0.0078	$ln(0.0078, 0.000024)$	***[24 25]
QALY loss hospitalized cases	0.0170	$ln(0.017, 0.000012)$	
QALY loss influenza mortality	Age-specific (1-year)	Normal, 20% variation about the mean	PC

* Triangular distribution; Tri(a ± b) has mean a and standard deviation $b/\sqrt{6}$

** Beta distribution; Beta(a,b) has mean a/(a+b) and standard deviation $\sqrt{\frac{ab}{(a+b)^2(a+b+1)}}$

*** Log-normal distribution, parameters are mean and variance of this distribution, standard deviation is 20% of mean

Normal distribution, parameters are mean and variance of this distribution, standard deviation is 20% of mean

Gamma distribution; Gamma(a,b) has mean ab and standard deviation $b\sqrt{a}$

$PC\ mean = 0.94 - 0.002 \times age$. Personal communication with Kim Rand-Hendriksen (2014).

HEALTHCARE COSTS

We compared the number of GP visits, hospitalizations, and deaths as well as the health-related quality of life, under each sick leave intervention, with the baseline intervention (Table SMM1). The cost of an influenza-related hospitalization was estimated using data from the Norwegian Patient Registry, on patients admitted with ICD-10 diagnoses J10-J11 (influenza) and J12-J18 (pneumonia) and discharged with influenza-associated diagnoses. We estimated the average hospitalization cost per patient by identifying the DRG codes most commonly related to influenza and pneumonia. For intensive care patients we used the DRG for diseases in respiratory organs requiring ventilation support as an estimate for the cost per hospitalized case. Costs were computed using the DRG unit price, trim points and cost weights (for 2013).[22] The cost of a GP consultation was assumed at $68.[18 19]

MEDICATION COSTS

The types of medication and proportion of users was based on findings in Meier et al.[21], while use of throat drops and tissues was assumed. The cost of antibiotics was assumed equal to the cost of Fenoksymetylpenicillin[20] deducted VAT. Costs of over-the-counter drugs were based on the average cost at three pharmacies and four grocery stores in Oslo.

CAMPAIGN COSTS

Each intervention was assumed to involve a campaign to communicate recommendations. We assumed the cost of the baseline intervention (65% compliance, maximum of 4 days from symptom onset to sick leave) to be similar to the campaign cost associated with the 2009 H1N1 Pandemic in Norway ($USD 1.7 million), equally divided into costs associated with adherence and sick leave onset delay. The campaign costs were assumed to increase by a factor of 1.5 per 10% increase in the adherence, and by a factor of 1.25 per half day reduction in the maximum delay time to work absence. The costs were converted to 2012 monetary equivalents by adjusting for inflation.

HEALTH EFFECTS

Health related quality measures based on the EuroQol-5D[26] were used to compute QALYs (Quality Adjusted Life Years) associated with mortality and morbidity. QALYs associated with mortality were based on the expected value of remaining life years using age-dependent life-expectancies[27] with a yearly discount rate of 4%. The age distribution of deaths was based on those specified in a Norwegian study of seasonal influenza mortality[28].

INDIRECT COSTS

In the baseline intervention (65% compliance, 4 days of maximum delay from symptoms onset to sick leave) we assumed that symptomatic workers would stay at home for an average of 3 workdays for seasonal influenza and 5.21 workdays for pandemic influenza, corresponding to 3.5 and 6.5 calendar days respectively. The average number of workdays lost was higher for interventions that reduced the delay from symptom onset to sick leave, following the implementation of interventions in the dynamic model.

Productivity losses were valued using a human capital approach. Labor costs were based on full-time equivalent wages and the value of labor not returned to the worker. For sick adults, 5-year age-specific wage rates for ages 16-74[6] were used, and for caretakers the average population wage was used. In Norway, all employees have a right to at least 3 days of

self-certified leave with full salary, while self-employed workers (8%) may take out insurance and their income loss during work absenteeism will depend on their insurance policy.[29] About 60% of employees have an inclusive-work life (IW) employer with more flexible sick leave arrangements and a right to 8 days of self-certified leave. Once the self-certified sick leave period ends, additional sick leave days require a GP certificate. The first 16 days are covered by the employer, and additional days by the state.[30-32] For each sick leave event, we included a productivity loss equal to 5% of the labor cost to account for productivity losses before and after the sick leave period[14]. We assumed that 8% of adults on sick leave worked from home, guided by the proportion working from home from a 2009 survey.[13] Sick persons working from home, and workers going to work despite feeling ill were assumed to work at 65% of full capacity[15-17] In Norway, parental leave is 1 year and parents have the right to care benefits during child sickness when the child <12 years.[33] Therefore all ill children between 1 and 12 years of age were assumed to require parental care. We assumed that 15% of parents were homemakers[34] with no associated productivity loss. Overlap between parental and child sickness absences, which was found to be 37.5% in our sick leave survey, was also adjusted for.

SENSITIVITY ANALYSES

For each epidemiological scenario (seasonal influenza R_eff = 1.2-1.4 with moderate morbidity; pandemic influenza R_0= 1.4-1.8 with moderate, severe, or very severe morbidity) we performed a probabilistic sensitivity analysis using Monte Carlo sampling (10 000 draws) of the parameters listed in Table SMM1.

REFERENCES

1. Fumanelli L, Ajelli M, Manfredi P, et al. Inferring the Structure of Social Contacts from Demographic Data in the Analysis of Infectious Diseases Spread. *PLOS Computational Biology* 2012;8(9):e1002673.
2. Merler S, Ajelli M, Pugliese A, et al. Determinants of the Spatiotemporal Dynamics of the 2009 H1N1 Pandemic in Europe: Implications for Real-Time Modelling. *PLoS Comput Biol* 2011;7(9):e1002205. doi: 10.1371/journal.pcbi.1002205
3. Ferguson NM, Cummings DA, Fraser C, et al. Strategies for mitigating an influenza pandemic. *Nature* 2006;442(7101):448-52.
4. Cauchemez S, Valleron A-J, Boelle P-Y, et al. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-54. doi: http://www.nature.com/nature/journal/v452/n7188/suppinfo/nature06732_S1.html
5. Ferguson NM, Cummings DA, Cauchemez S, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature* 2005;437(7056):209-14.
6. Statistics Norway. 2014 [Available from: http://www.ssb.no/].
7. Ghani A, Baguelin M, Griffin J, et al. The early transmission dynamics of H1N1pdm influenza in the United Kingdom. *PLoS currents* 2009;1
8. Hayward AC, Fragaszy EB, Bermingham A, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. *The Lancet Respiratory Medicine* 2014
9. Longini IM, Nizam A, Xu S, et al. Containing pandemic influenza at the source. *Science* 2005;309(5737):1083-87.
10. de Blasio BF, Iversen BG, Tomba GS. Effect of Vaccines and Antivirals during the Major 2009 A (H1N1) Pandemic Wave in Norway–And the Influence of Vaccination Timing. *PloS one* 2012;7(1):e30018.

11. Edwards CH, Tomba GS, de Blasio BF. Influenza in workplaces: transmission, workers' adherence to sick leave advice and European sick leave recommendations. *The European Journal of Public Health* 2016;26(3):478-85.

12. Ministry of Health and Care Services. Norwegian National Influenza Pandemic Preparedness Plan 2006.

13. Statistics Norway. Level of living 2009 - Cross sectional study - Working conditions 2012-10-09 ed: Norwegian Social Science Data Services (NSD), 2009.

14. Brouwer WB, Van Exel N, Koopmanschap M, et al. Productivity costs before and after absence from work: as important as common? *Health Policy* 2002;61(2):173-87.

15. Keech M, Scott A, Ryan P. The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. *Occupational Medicine* 1998;48(2):85-90.

16. Palmer LA, Rousculp MD, Johnston SS, et al. Effect of influenza-like illness and other wintertime respiratory illnesses on worker productivity: The child and household influenza-illness and employee function (CHIEF) study. *Vaccine* 2010;28(31):5049-56.

17. Smith A. A review of the effects of colds and influenza on human performance. *Occupational Medicine* 1989;39(2):65-68.

18. Den norske legeforening. Normaltariff for fastleger og legevakt 2013-2014 [Available from: http://normaltariffen.legeforeningen.no/pdf/Fastlegetariff_2013.pdf], accessed 07.07.2014.

19. Romøren TI, Torjesen DO, Landmark B. Promoting coordination in Norwegian health care. *International Journal of Integrated Care* 2011;11(Special 10th Anniversary Edition)

20. Foreningen for utgivelse av norsk legemiddelhåndbok. Norsk legemiddel håndbok for helsepersonell 2013. Oslo: Fagbokforlaget 2013.

21. Meier CR, Napalkov PN, Wegmüller Y, et al. Population-Based Study on Incidence, Risk Factors, Clinical Complications and Drug Utilisation Associated with Influenza in the United Kingdom. *EJCMID* 2000;19(11):834-42. doi: 10.1007/s100960000376

22. Norwegian Directorate of Health. Innsatsstyrt finansiering 2013, 2012.

23. Norwegian Directorate for Civil Protection Rapport Ny influensa A (H1N1) 2009 Gjennomgang av erfaringene i Norge. 2. edition ed, 2010.

24. Baguelin M, Jit M, Miller E, et al. Health and economic impact of the seasonal influenza vaccination programme in England. *Vaccine* 2012;30(23):3459-62.

25. Van Hoek AJ, Underwood A, Jit M, et al. The impact of pandemic influenza H1N1 on health-related quality of life: a prospective population-based study. *PLoS One* 2011;6(3):e17030.

26. EuroQol Research Foundation. EQ-5D 2015 [Available from: http://www.euroqol.org/].

27. Survey on Living Conditions, Health, Care and Social Contact 2012. *Data collected by Statistics Norway Second NSD edition, Bergen 2014*

28. Gran JM, Kacelnik O, Grjibovski AM, et al. Counting pandemic deaths: comparing reported numbers of deaths from influenza A (H1N1) pdm09 with estimated excess mortality. *Influenza and other respiratory viruses* 2013;7(6):1370-79.

29. Norwegian Labour and Welfare Administration. Sickness benefits for self-employed and freelancers. 2015

30. National Insurance Act. Act 1997-02-28-19. Act relating to national insurance. In: Affairs MoLaS, ed. Avd I 1997 Nr. 5, LOV-1997-02-28-19.

31. Intensjonsavtale om et mer inkluderende arbeidsliv 4. mars 2014 - 31. desember 2018 (IA-avtalen), 2014.

32. Ose SO, Dyrstad K, Slettebak R, et al. Evaluering av IA-avtalen (2010-2013), 2013:348.

33. Arbeids- og sosialdepartementet. Working Environment act. Act 2005-06-17-62. Act relating to working environment, working hours an employment protection, etc. as subsequently amended, last by act 23 February 2007-10. 2005

34. Ministry of Children Equality and Social Inclusion. Meld.St.6 En helhetlig integreringspolitikk Mangfold og fellesskap, 2013.

Evaluating costs and health consequences of sick leave strategies against pandemic and seasonal influenza in Norway using a dynamic model

Christina Hansen Edwards[1], Gianpaolo Scalia Tomba[2], Ivar Sønbø Kristiansen[3], Richard White[4], Birgitte Freiesleben de Blasio[4,5]

[1]Department of Health and Inequality, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[2]Department of Mathematics, University of Rome Tor Vergata, Via Ricerca Scientifica 00133 Roma, Italy.

[3]Department of Health Management and Health Economics, Institute for Health and Society, University of Oslo. P.O.Box 1130. 0318 Blindern, Oslo, Norway.

[4]Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, P.O. Box 0403. 4403 Nydalen, Oslo, Norway.

[5]Oslo Centre for Biostatistics and Epidemiology. Department of Biostatistics. Institute of Basic Medical Sciences. University of Oslo. P.O.Box 1122. 0317 Blindern, Oslo, Norway.

Correspondence to: CH Edwards Christina.Hansen.Edwards@fhi.no

SUPPLEMENTARY FILE 2: FIGURES

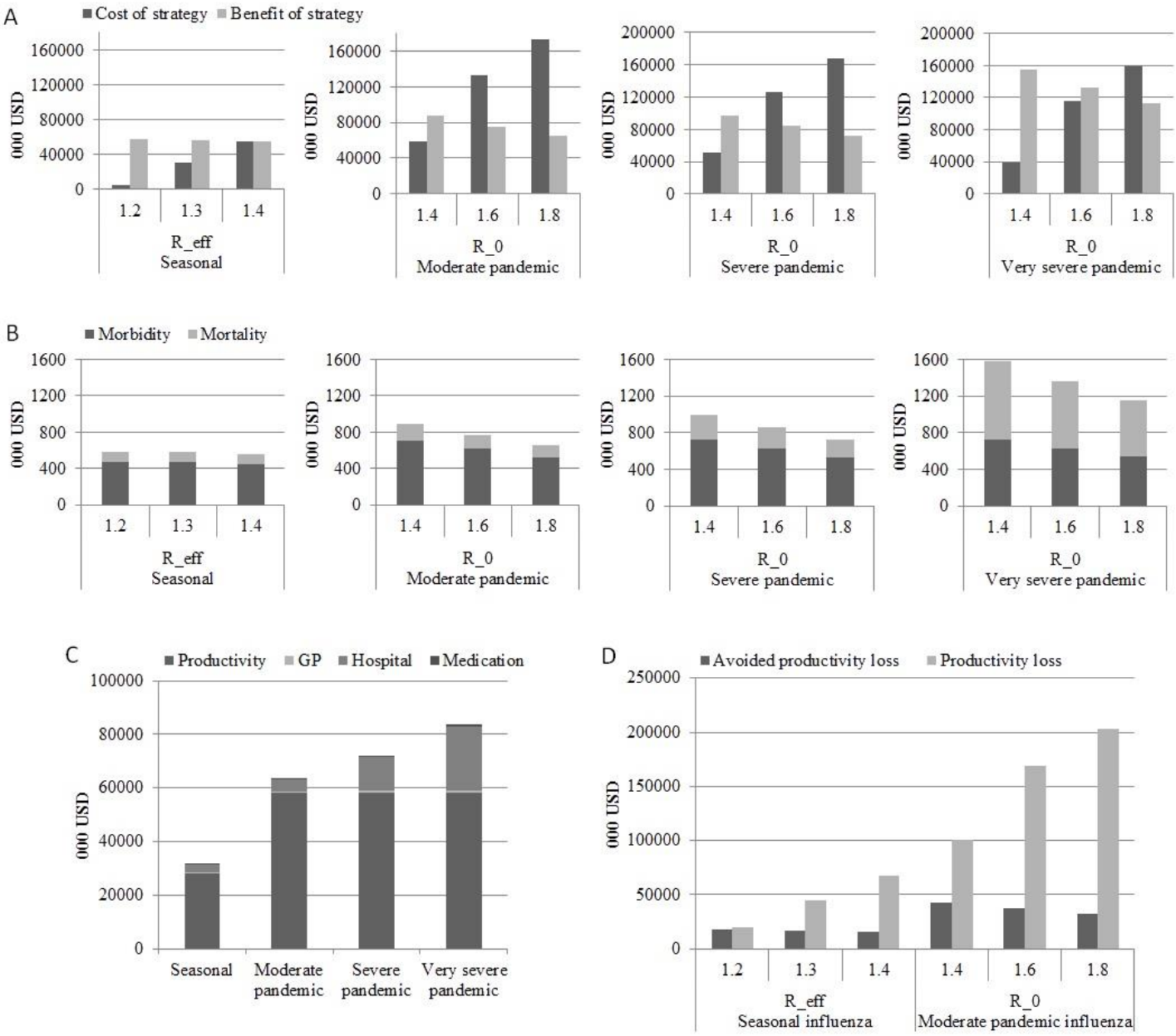


Figure S1: The effect transmissibility and pandemic severity on economic parameters for the intervention involving 90% of sick persons taking sick leave within 0.5 days of onset; no extra mixing assumed. A) Total monetary costs and benefits of the intervention under seasonal and pandemic scenarios. B) Benefits from avoided morbidity and mortality under seasonal and pandemic scenarios. C) Proportion of costs avoided due to avoided hospitalizations, GP-visits, medication use and productivity losses under seasonal and pandemic influenza. D) Baseline productivity losses and productivity losses avoided due to the sick leave intervention under seasonal and moderate pandemic influenza (the same pattern follows for more severe pandemic influenza scenarios.

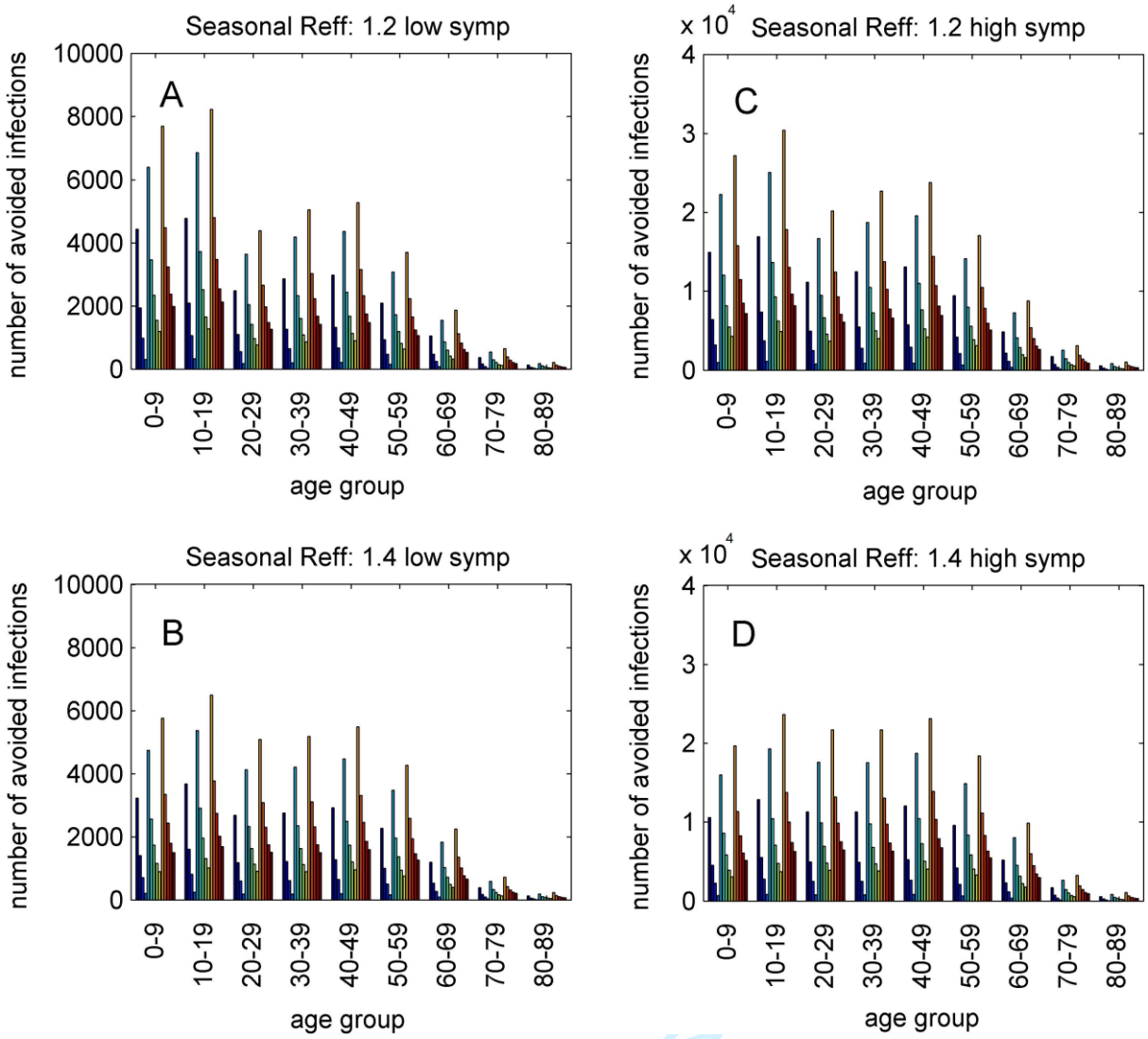


Figure S2: Absolute number of avoided clinical cases for selected seasonal scenarios, grouped according to median age, for all 14 interventions.
Interventions 1-4: Shades of blue: (65%; 0.5, 1, 1.5, and 2 days)
Interventions 5-9: Shades of green to yellow: (80%; 0.5, 1, 1.5, 2, and 4 days)
Interventions 10-14: Shades of orange to red: (90%; 0.5, 1, 1.5, 2, and 4 days)

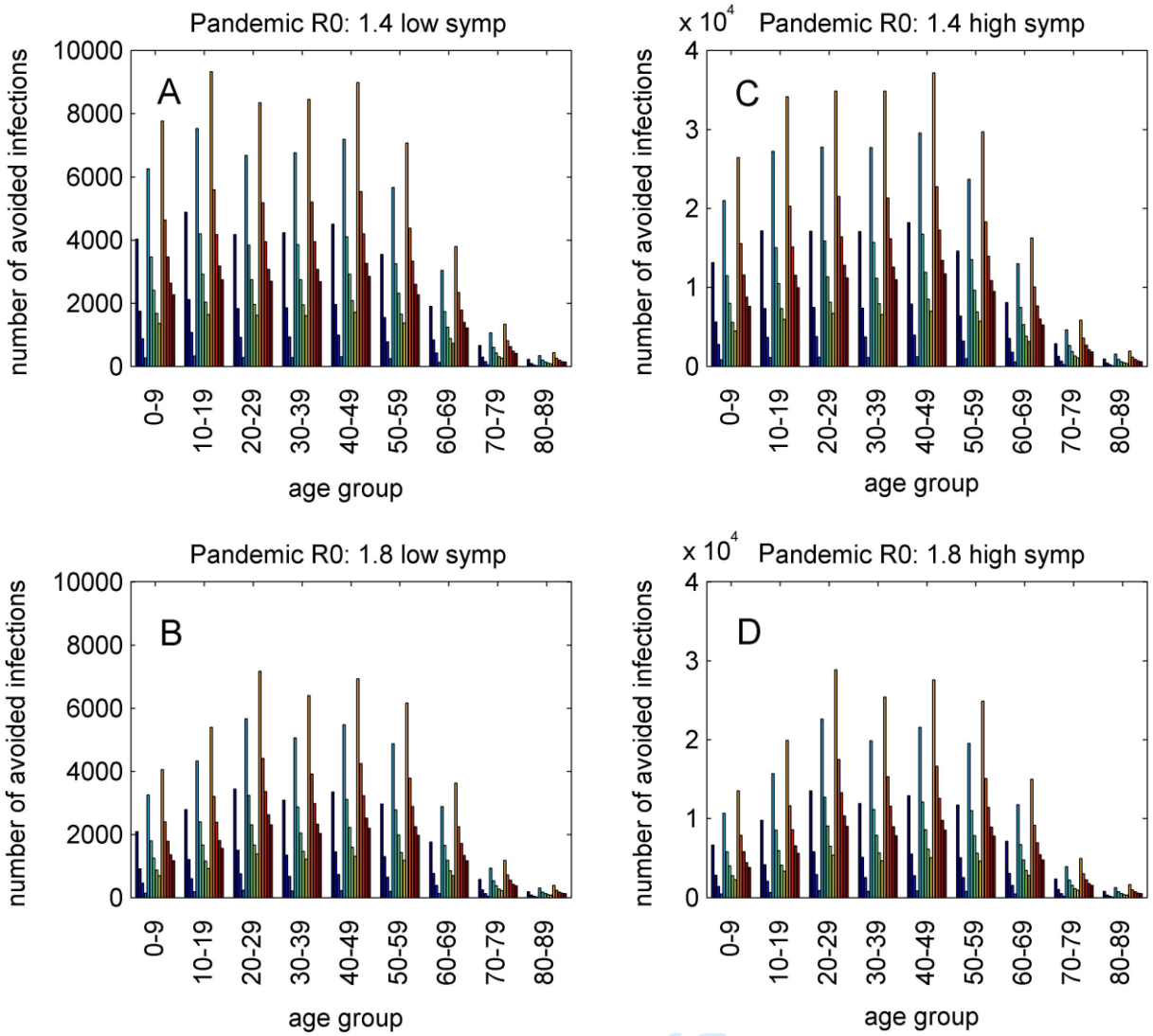
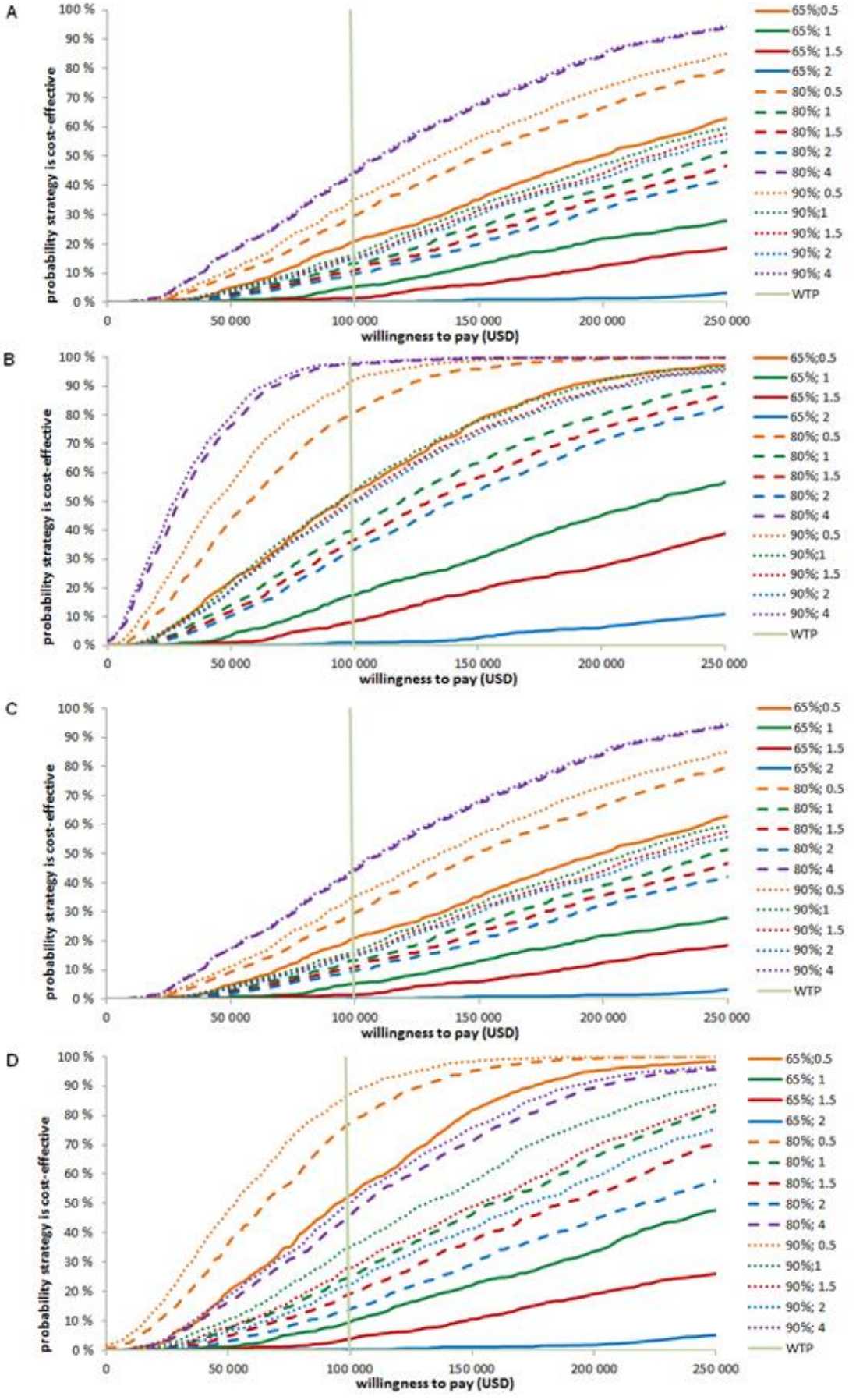


Figure S3: Absolute number of avoided clinical cases for selected pandemic scenarios, grouped according to median age, for all 14 interventions.
Interventions 1-4: Shades of blue: (65%; 0.5, 1, 1.5, and 2 days)
Interventions 5-9: Shades of green to yellow: (80%; 0.5, 1, 1.5, 2, and 4 days)
Interventions 10-14: Shades of orange to red: (90%; 0.5, 1, 1.5, 2, and 4 days)

Figure S4: Acceptability curves without extra mixing.

A) Seasonal influenza (R_eff=1.3), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, B) Seasonal influenza (R_eff=1.3), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing, C) Pandemic influenza (R_0=1.6), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, D) Pandemic influenza (R_0=1.6), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing.



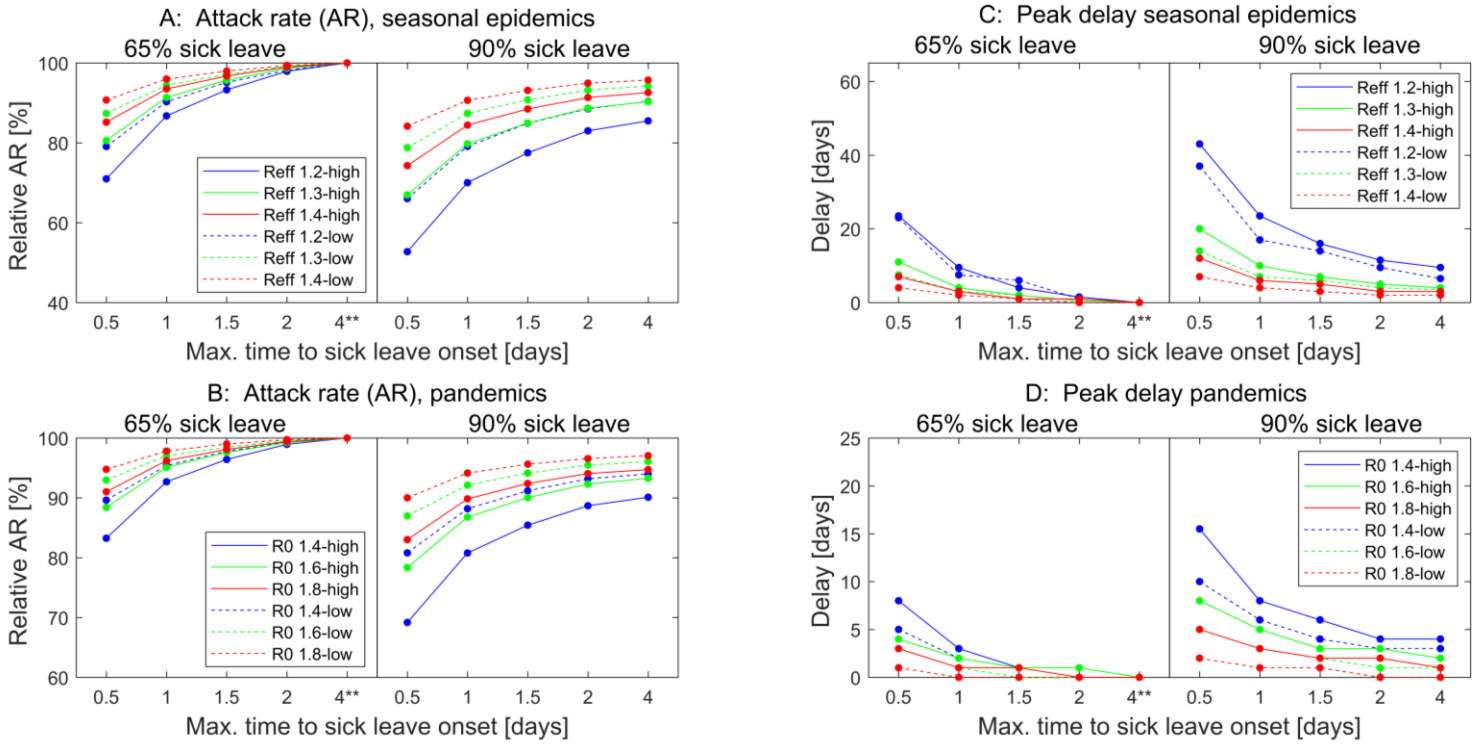


Figure S5: Impact of workplace-based interventions on clinical attack rate and timing of peak for seasonal epidemics (panels A and C) and for pandemics (panels B and D) with extra mixing in the households and the general population. Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted with stippled lines; scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted with solid lines. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility). The figure shows sick leave interventions with 65% and 90% adherence combined with absence onset within 0.5, 1, 1.5, 2, and 4 days. The baseline intervention (65% adherence and sick leave onset within 4 days of symptom onset) is indicated by **.

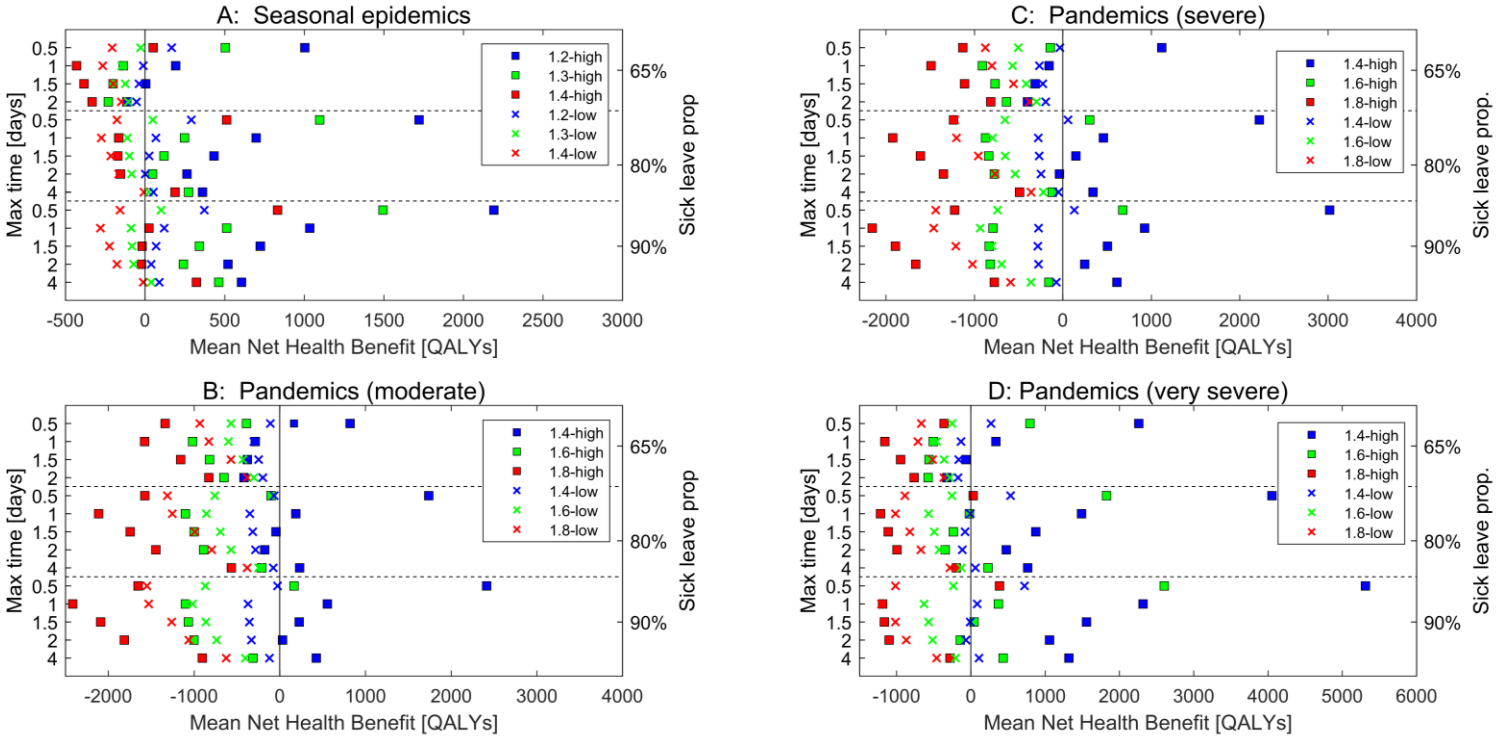
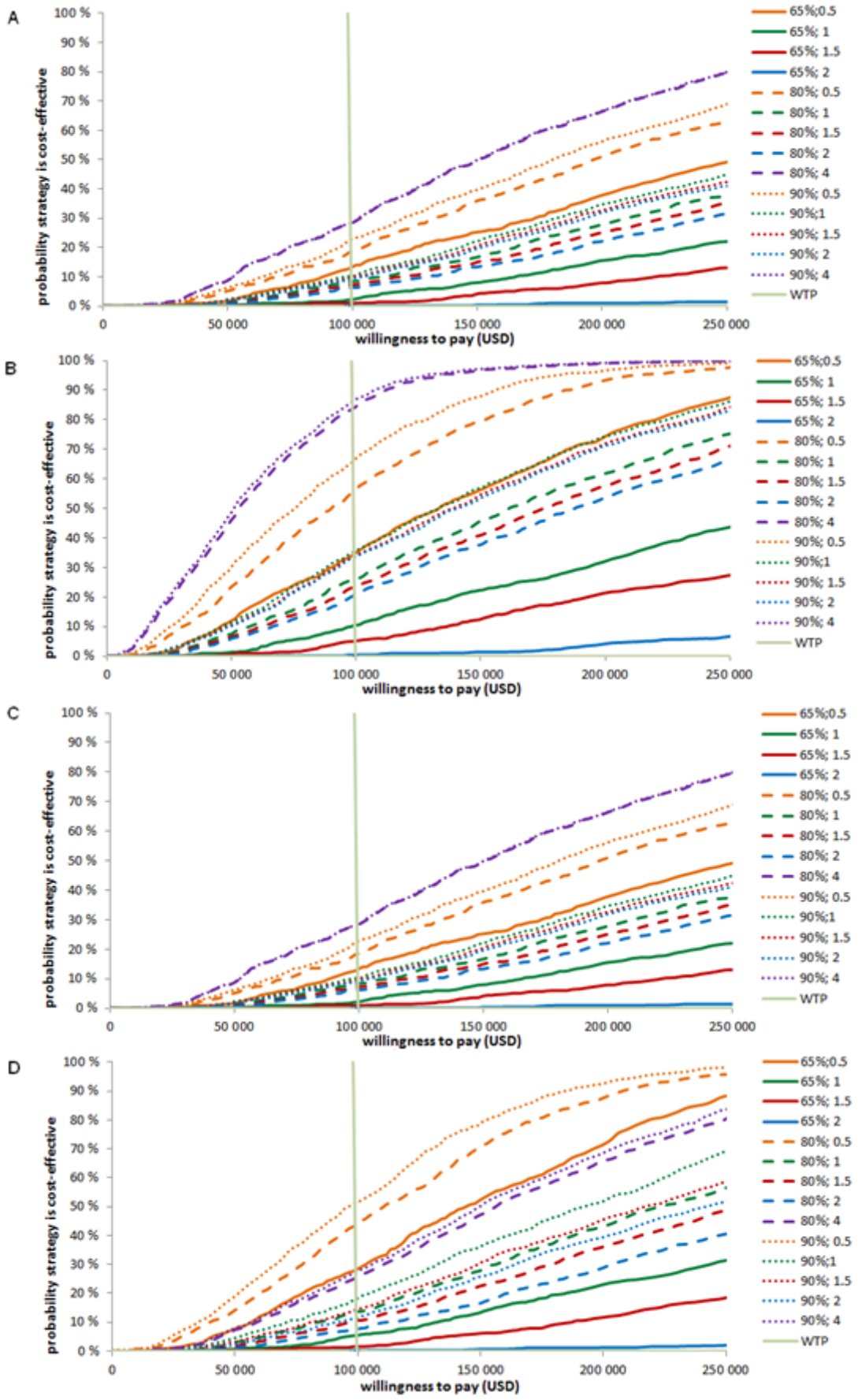


Figure S6: Mean Net Health Benefit (NHB) of workplace-based interventions for all scenarios assuming extra mixing in households and the general population; seasonal epidemics (A), moderate pandemics (B), severe pandemics (C), very severe pandemics (D).

Scenarios assuming low symptomatic proportions (35% children, 25% adults develop symptoms) are depicted as crosses, and scenarios assuming high symptomatic proportions (65% children, 55% adults develop symptoms) are depicted as squares. Each level of transmissibility has a unique colour (blue = lowest transmissibility, green = medium transmissibility, and red = highest transmissibility)

Figure S7: Acceptability curves with mixing.

A) Seasonal influenza (R_eff=1.3), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, B) Seasonal influenza (R_eff=1.3), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing, C) Pandemic influenza (R_0=1.6), low symptomatic proportions (35% children and 25% adults symptomatic), without extra mixing, D) Pandemic influenza (R_0=1.6), high symptomatic proportions (65% children and 55% adults symptomatic) without extra mixing.



CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2 & 3
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	5 & 6
		Present the study question and its relevance for health policy or practice decisions.	5 & 6
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	7 & 8
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6, 7, 8 & Supplementary file 1
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	10
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	6, 8 & 9
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	7,8 & 9
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Supplementary file 1
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	10 & Supplementary file 1
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	9, 10 & Supplementary file 1

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	9, 10 & Supplementary file 1
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	NA
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	9,10, & Supplementary file 1
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	10 & Supplementary file 1
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	9, 10 & Supplementary file 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	7-10 & Supplementary file 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	7-10 & Supplementary file 1

Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Supplementary file 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	11-15, Fig. 3 & Supplementary file 2
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	NA
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	14-16, Fig. 4 & Supplementary file 2, Supplementary file 3
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	17-19
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	16-20
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we	22

		recommend authors comply with International Committee of Medical Journal Editors recommendations.	

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist