What is the best strategy to reduce the burden of occupational asthma and allergy in bakers?

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ABSTRACT

Rationale Insight into the effectiveness of intervention strategies will help realise a decrease in the occupational disease burden from (allergic) respiratory diseases in the bakery population.

Objectives To use a simulation model to assess the impact of different intervention strategies on the disease burden of the bakery population over time.

Methods A recently developed dynamic population based model was used to prospectively evaluate the impact on disease burden resulting from different intervention strategies. We distinguished interventions based on exposure reductions for flour dust and fungal α-amylase, health surveillance combined with reduction in exposure, and pre-employment screening.

Main Results The impact of most interventions on disease burden was limited, generally less than 50% for lower respiratory symptoms and disabling occupational asthma. Only the rigorous health surveillance strategy, identifying workers who are sensitised or report upper respiratory symptoms and decreasing their individual exposures by 90% shortly after diagnosis, resulted in a decrease of almost 60% in disease burden after 20 years.

Conclusions This study demonstrates that different intervention strategies have substantially different impacts on the burden of disease. The time window during which changes occur differs considerably between strategies. This information can assist policy makers in their choice of intervention and gives guidance for achievable reductions in disease burden.

INTRODUCTION

Occupational exposure causes approximately 10–15% of adult cases of asthma, making it the most important respiratory occupational disease.[1 2] Workers exposed to flour dust are among the populations at high risk of developing occupational respiratory disease.[3] At present the burden of disease in flour exposed subjects is considerable, as has been described in various surveys.[4 5] In the Netherlands approximately 12 000 workers are potentially exposed to flour dust and thus are at risk of developing (allergic) respiratory disease.[4 6] There is an urgent need for effective interventions to reduce the occupational disease burden related to flour dust exposure.[7] However, only limited information is available on the effectiveness of various intervention strategies and no science based rationale for choosing between specific strategies exists. Health surveillance and exposure reduction are the most prominent approaches, but their relative effectiveness in reducing disease burden has not yet been established.[8–10]

What this paper adds

- Little work has been done in the field of occupational health regarding quantitative evaluation of the impact of intervention strategies.
- This paper describes one of the first studies to perform a quantitative health impact assessment to predict the effect of sector-wide intervention strategies on the disease burden of occupational respiratory symptoms.
- This study provides quantitative insight into how a particular intervention might lead to substantial differences in the occurrence of new cases and overall change in disease burden and the rate with which changes occur.
- This information can assist policy makers in their choice of intervention program and guide discussions on achievable reductions in disease burden related to occupational exposures.

A recently conducted large scale dissemination and education program on exposure control in the Dutch baking industry resulted in a small reduction in exposure to dust and allergens. The decrease in disease burden in the bakery population as a result of this exposure reduction has not been quantified but is expected to be small.[11] This implies that more rigorous approaches for intervention are needed to significantly reduce the disease burden of occupational asthma. Since both exposure and time to diagnosis (early identification) determine the prognosis of occupational asthma, both should be considered in designing an effective intervention strategy.[12] As a result, intervention scenarios might be complex and several intervention options may be considered when dealing with (allergic) respiratory diseases.[13–15]

Quantitative health impact assessment can be a powerful methodology to prospectively evaluate the impact of different intervention strategies, thereby helping to provide the evidence base necessary to gain widespread stakeholder support for implementing health policies.[16] To perform quantitative health impact assessment related to occupational exposure and respiratory diseases in bakery workers, a dynamic population based model was recently developed.[17] This model describes the onset and progression of work-related sensitisation and respiratory symptoms as well as work disability, in relation to occupational exposure over time.

The main objective of this study was to evaluate the potential impact of different intervention strategies on the health of bakery workers. Three main strategies were included in the evaluation: (1) hygienic intervention, aimed at reducing exposure levels in the whole population; (2) health surveillance, identifying 'high risk' workers combined with tailored exposure control for these individuals; and (3) pre-employment screening for atopy.

METHODOLOGY

Disease model

The dynamic model simulates a population of workers which is followed over time and tracks the development of work related symptoms in each individual worker related to their occupational exposure.[17] Model parameters came from a series of recently published surveys. The model follows the classic disease model for development of occupational asthma.[18] Two mechanisms are taken into account: (1) allergic sensitisation which precedes development of respiratory symptoms[19] (sensitisation was defined as having a positive serological test against wheat flour or fungal α-amylase)[4]; and (2) a non-allergic pathway, where irritant mechanisms cause onset of nasal and lower respiratory symptoms.[18] Work-related upper respiratory symptoms were defined as having at least two of the following symptoms: sneezing, a running nose or itchy/teary eyes during work. Work-related lower respiratory symptoms were defined as having at least two of the following symptoms: asthma attacks, wheezing, shortness of breath or tightness of the chest during work.[4] We assumed that rhinitis symptoms generally precede the development of lower respiratory symptoms, although not in every case.[17 20] Eventually some workers develop work disabling asthmatic symptoms.[21 22] The model includes both the 'natural' turnover of workers in the population not necessarily related to the health status of the worker and workers leaving the population due to work-disabling asthma. A distribution for the working lifespan in the population was used to model turnover of workers.[17]

Figure 1 provides a simplified version of the flow diagram of the multi-stage disease model with the boxes and arrows representing the different disease stages and main transition routes, respectively. The numbers depicted around the transition arrows show the mean annual transition probability per unit exposure (mg/m^3 for flour dust and ng/m^3 for fungal α-amylase). Annual transition probabilities were estimated from a recent survey among bakers providing information on symptoms and exposure for a large number of individual workers.[4] Separate probabilities were estimated for atopic and non-atopic subjects. Multiplicative risk factors were estimated for the development of symptoms in sensitised workers; these were approximately a factor of 3 higher for workers sensitised to wheat and a factor of 2 higher for workers sensitised to fungal α-amylase. The full diagram and a detailed description of the model is given by Warren *et al*.[17]

The model simulates a fixed worker population of 10 000 individuals. The worker population is dynamic with a continual process of workers leaving the workforce (possibly through ill-health) and being replaced with new recruits. Each new worker is assigned a working lifetime (mean 20 years) and enters with a certain probability of being atopic (30%) and already sensitised to the occupational allergens (1% for amylase and 3% for wheat allergens) based on general population data.[23] The disease state of workers is updated yearly. An individual worker leaves the population when he/she comes to the end of their natural working life, or becomes disabled. Although it was acknowledged that workers can recover from several disease states depending upon changes in their exposure, no reliable information was available on the probability of recovery. Consequently, this mechanism was not included in the model.

Simulation of interventions

The impact of various interventions was evaluated over a period of 20 years. The specific changes in model input parameters used to simulate health impact resulting from the intervention are presented in table 1. Prevalence and incidence ratios were extracted from the simulation logs for the baseline year and year 20. The baseline figures are based upon running the model with the default exposure values (table 2) as presented by Warren *et al*.[17] We also used the simulation logs to count the number of individual interventions that would result from our health surveillance scenarios. This was done by counting the number of identified high risk workers in the year of the health surveillance (for a detailed description of the scenarios see the Results section).

Uncertainty was calculated as 2.5% upper and lower confidence intervals of the estimated prevalence and incidence values using a two-dimensional Monte Carlo simulation with 20 inner loops to correct for stochastic variability and 100 runs (outer loops) varying model parameters randomly according to input distributions chosen to represent parameter uncertainty.[17] Within this routine baseline and intervention simulations were paired in order that they shared the same 'uncertain' model parameters to reduce uncertainty in the estimates of intervention impact.

The impact of the various simulated interventions was presented as the relative change in disease parameters for four aggregated disease states: (1) work related sensitisation, (2) upper respiratory symptoms, (3) lower respiratory symptoms, and (4) work disabling asthma. A trend plot of the change in the prevalence of lower respiratory symptoms over time was created to illustrate the time effects of the different interventions.

RESULTS

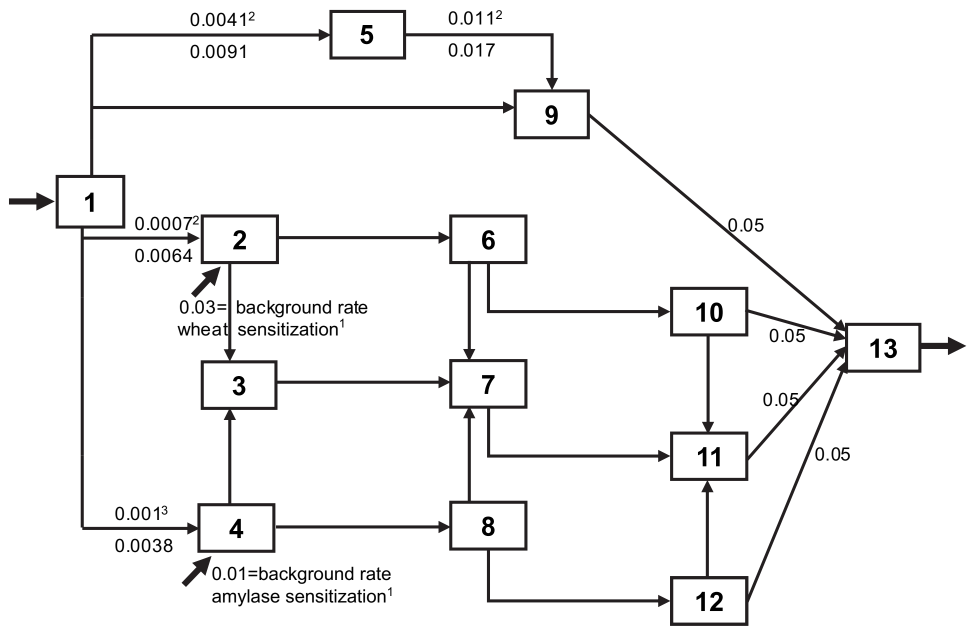
Intervention strategies

The baseline intervention scenario used in this study corresponds to the intervention program implemented as part of the Dutch covenant program described in an earlier paper (Meijster *et al*[11]). In this program, sector-wide training and education were provided to inform workers of the risk of occupational exposures and educate them with respect to a set of basic good exposure control practices. The intervention program ran for 6 years until the end of the covenant period. At the end of the covenant period, a 12% decrease in flour dust exposure and a 39% decrease in fungal α-amylase exposure was observed.[11]

The impact of this intervention scenario was compared with the impact of four other realistic but fictive intervention strategies proposed in this study:

a. Continuation of the present (covenant) intervention program in the future. This is predicted to result in a decrease in population exposure levels of 33% for flour dust and 81% for fungal α-amylase after 20 years.
b. Hygiene intervention, implementing rigorous exposure control measures throughout the whole bakery sector as described by Meijster *et al*.[24] This implies substantial investments in approximately 2500 small bakeries and 80 industrial bakeries. Implementation is assumed to be finished at the start of the simulation period. This is predicted to result in a decrease in population exposure levels of 32% for both flour dust and fungal α-amylase at the start of the simulation period as well as an approximately 20% decrease in exposure variability.

Figure 1 Causal diagram of dynamic population based health model showing all possible health transitions within the population relating to the development of sensitisation and respiratory symptoms (from Warren *et al*[17]).



Disease states	Box
Non-sensitised and non-symptomatic	1
Sensitised to wheat and non-symptomatic	2
Sensitised to wheat and a-amylase and non-symptomatic	3
Sensitised to a-amylase and non-symptomatic	4
Non-sensitised and moderate symptoms	5
Sensitised to wheat and moderate symptoms	6
Sensitised to wheat and a-amylase and moderate symptoms	7
Sensitised to a-amylase and moderate symptoms	8
Non-sensitised and severe symptoms	9
Sensitised to wheat and severe symptoms	10
Sensitised to wheat and a-amylase and severe symptoms	11
Sensitised to a-amylase and severe symptoms	12
Work-disabling asthmatic symptoms	13

Transition probabilities
0.001=non-atopics
0.004= atopics

[1]probability/year; [2] probability/mg exposure/year; [3] probability/ng exposure/year

c. Health surveillance, where high risk workers are identified and immediately after detection exposure is reduced by 90% for both flour dust and fungal α-amylase in these high risk workers and kept at this reduced level. Subsequently, health surveillance is repeated every 3 years during which new high risk workers are identified and their exposures reduced. We evaluated two scenarios; in the first scenario (Health surveillance intervention I) only sensitised workers are identified and labelled high risk. In the second scenario (Health surveillance intervention II) we included upper respiratory symptoms in the screening, so all workers with sensitisation or upper respiratory symptoms are labelled high risk.
d. Screening of new employees, where workers are screened for their atopic status prior to employment and those who are atopic are refused employment.

Simulation results

The baseline figures for the prevalence of the different disease states are provided in table 2.

Table 3 gives the impact of the different intervention strategies presented as the (relative) change in prevalence for the three aggregated disease states over the 20-year simulation period. For disability the change in onset of new cases was evaluated. The confidence intervals in table 3 indicate that uncertainties around our estimates of the relative impact of interventions are fairly limited for both sensitisation and respiratory symptoms and somewhat larger for work disabling asthmatic symptoms. Figure 2 shows a plot with the trend lines for the change in prevalence of lower respiratory symptoms for all simulated intervention scenarios for the full 20-year period.

The baseline scenario shows a modest decrease in the prevalence of the different disease states, generally of less than 15%. With a continuation of the intervention program for the full 20-year period the health impact is substantially larger, especially for the respiratory symptoms. This intervention scenario requires continuous investment in training across the whole population over a 20-year period assuming this will have a constant decreasing effect on the population exposure levels.

The hygienic intervention reduces the disease burden by almost 50% for both severe symptoms and work disabling asthma. The impact levelled off at the end of the 20-year period (figure 2).

The two health surveillance scenarios exhibit substantial differences in terms of both their health impact and the number of individuals targeted. The reduction in lower respiratory symptoms and disabling asthma is approximately twice as high when upper respiratory symptoms are included in the screening. A consequence of the reduction in individuals progressing from upper respiratory symptoms to lower respiratory symptoms as a result of the individual interventions is an increased prevalence of upper respiratory symptoms. In the scenario based on screening for sensitisation, an initial 1100 individual interventions have to be performed at the start of the intervention

Table 1 Description of changes in input parameters in the dynamic population model to evaluate the impact of different intervention scenarios

		Change in model input parameters		
Intervention scenario	**Description of parameter change**	**Flour dust exposure**	**Fungal α-amylase**	**Population parameters***
No intervention	–	GM=1.19 GSD_{bw}=2.29 GSD_{ww}=2.27	GM=0.57 GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0.3
Covenant intervention	▸For first 6 years, population GM exposure decreases by 2% annually for flour dust and 8% annually for fungal α-amylase ▸After the 6-year level, exposures stay constant ▸Variability is assumed to stay the same	*Year t=1–6;* GM=GM (t−1)×0.98 *Year t=7–20*; GM=1.05 GSD_{bw}=2.29 GSD_{ww}=2.27	*Year t=1–6;* GM=GM (t−1)×0.92 *Year t=7–20*; GM=0.35 GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0.3
Continuation of covenant	▸Equal to the above described scenario ▸However, the decrease in the GM values for both exposures is continued for the full 20-year period	GM=GM(t−1)×0.98 GSD_{bw}=2.29 GSD_{ww}=2.27	GM=GM(t−1)×0.92 GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0.3
Hygiene intervention	▸Individual exposure estimates from the baseline measurement dataset are recalculated according to the reduction factors derived previously	GM=0.82 GSD_{bw}=2.03 GSD_{ww}=2.05	GM=0.39 GSD_{bw}=2.56 GSD_{ww}=4.44	Prob_atopy=0.3
Health surveillance intervention (I)	αExposures of high risk individuals (sensitised workers) are reduced by 90% ▸Individual workers can only receive an intervention once ▸The population variability of exposure is assumed to remain unchanged	*High risk individuals:* $GM_{post\text{-}int}=0.1\times GM_{pre\text{-}int}$ *Others:* $GM_{post\text{-}int}=GM_{pre\text{-}int}$ GSD_{bw}=2.29 GSD_{ww}=2.27	*High risk individuals:* $GM_{post\text{-}int}=0.1\times GM_{pre\text{-}int}$ *Others:* $GM_{post\text{-}int}=GM_{pre\text{-}int}$ GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0.3
Health surveillance intervention (II)	▸As above, but now non-sensitised workers with rhinitis symptoms are also included in the definition of high risk workers	*High risk individuals:* $GM_{post\text{-}int}=0.1\times GM_{pre\text{-}int}$ *Others:* $GM_{post\text{-}int}=GM_{pre\text{-}int}$ GSD_{bw}=2.29 GSD_{ww}=2.27	*High risk individuals:* $GM_{post\text{-}int}=0.1\times GM_{pre\text{-}int}$ *Others:* $GM_{post\text{-}int}=GM_{pre\text{-}int}$ GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0.3
Pre-employment screening	▸Exposure parameters are not affected ▸The probability of atopy for new employees is set to 0 assuming no atopic subjects enter the workforce	GM=1.19 GSD_{bw}=2.29 GSD_{ww}=2.27	GM=0.57 GSD_{bw}=2.77 GSD_{ww}=4.57	Prob_atopy=0

*Only the probability of being atopic (Prob_atopy) is relevant for the evaluated intervention strategies.
GM, geometric mean exposure level; $GM_{pre\text{-}int}$, individual exposure estimate before receiving an individual intervention; $GM_{post\text{-}int}$, individual exposure estimate after receiving an individual intervention; GSD_{bw}, the between worker or inter-individual exposure variability; GSD_{ww}, the day-to-day or intra-individual exposure variability.

program and an estimated 200–250 individual interventions after each following health surveillance cycle (every 3 years). When upper respiratory symptoms are also considered as a risk factor, the number of interventions increases substantially; that is, 1800 individual interventions at the start and around 400 interventions after each following health surveillance cycle. For both health surveillance scenarios the disease burden levels off after 20 years, implying that additional reductions in disease burden from these approaches will be limited.

Screening for atopy among new employees has a limited impact on work related disease burden, with prevalences for respiratory symptoms and work disabling asthma decreasing by less than 20% after 20 years. The trend plot indicates that disease prevalence declines gradually and the effect does not seem to level off at the end of the simulation period.

No detailed data are presented here on changes in incidence for the different intervention scenarios. The magnitude of the change in incidence after a 20-year period for most scenarios is approximately similar to the decrease observed in disease prevalence. The only notable differences were observed for the scenario where the baseline intervention was assumed to continue, where the incidence figures showed a substantially larger reduction (up to 40% for lower airway symptoms). This observation is in line with the fact that the prevalence trend plot does not show a strong levelling off for this scenario. The other exception involves the upper airway symptoms for the health surveillance. The incidence does show a decrease over time of approximate 20% for both scenarios, whereas the prevalence shows only a very limited decrease or even an increase. This is to be expected, given that in both scenarios, individuals who are sensitised receive an exposure reduction. This causes the occurrence of new cases for upper airway symptoms to drop. It also causes workers who have developed upper airway symptoms to stay in this disease state longer since their disease does not progress to more severe symptoms. As a result the prevalence does not show a similar decrease over time.

DISCUSSION

This is one of the first quantitative health impact assessments for occupational respiratory symptoms that incorporates detailed information on occupational exposure and exposure–response relationships. It is also the first attempt to predict the effect of a range of different sector-wide intervention strategies

Table 2 Baseline disease figures for prevalence of the different disease states (per 1000 workers)

Disease state	Prevalence (97.5% CI)
Work related sensitisation	134 (106 to 163)
Upper respiratory symptoms	100 (80 to 123)
Lower respiratory symptoms	64 (41 to 110)
Work disabling asthmatic symptoms	3 (0.2 to 5)

on the occupational disease burden. As the results show, the choice for a particular intervention might lead to substantial differences in the occurrence of new cases and overall change in disease burden over time. Also, the rates at which these changes occur differ substantially. This information can assist policy makers in their choice of intervention program and may also guide discussions on achievable reductions in disease burden related to occupational exposures especially where exposure limits are missing, as is the case for most sensitising agents.

Complete cessation of exposure, often suggested as the only true effective measure for secondary prevention of (occupational) asthma, is in many occupational settings not possible.[8] However, to decrease the disease burden from occupational respiratory diseases, primary prevention should be the main focus. In the case of occupational asthma, significant workplace exposure reductions are likely to play an important role.[7 14] Estimating the extent to which risks can be controlled through exposure reductions requires detailed quantitative information on both exposure levels and exposure–response relationships.[25] Unfortunately detailed exposure response information is often lacking.[15] The fact that such information is available for the bakery sector, and is explicitly taken into account in our model, results in high resolution of the model and enables quantitative health impact assessment for a range of different intervention scenarios.

As this study shows, the impact of any intervention scenario will be modest for work related respiratory symptoms. Nevertheless, a reduction of almost 60% in the disease burden from lower respiratory symptoms and work disabling asthma, predicted for the extensive health surveillance program, is a substantial improvement compared to what was achieved with the most recent intervention approach based on education and dissemination only. The limited effect predicted for most scenarios may be surprising, but a more detailed consideration of recent epidemiological studies in which a 'no effect level' for work related allergy and respiratory symptoms could not be estimated and estimated exposure–response relationships appear to be relatively steep, indicates that our predictions seem plausible.[26 27] Our results together with recent epidemiological insights imply that even (very) low exposures will lead to the development of sensitisation and respiratory symptoms, although at a relatively low rate. A substantial reduction in disease burden would require a reduction in exposure levels among exposed workers of more than 90%. This is clearly challenging and extremely expensive given the current state of intervention research and efficacy values for most control measures.[28] In order to achieve such goals more ambitious health policies and rigorous interventions are needed in the future.

A reduction in exposure might also have another effect; workers with moderate symptoms might stay in the workforce longer. In this case the number of healthy work years will increase even though the chance of getting a disease within one's working life might stay approximately the same for an individual worker. This shows that it is important to take into account different aspects of disease burden (prevalence, time

Table 3 Change in the prevalence of work related sensitisation, upper respiratory symptoms, lower respiratory symptoms and work disability for the different intervention scenarios

		Prevalence	
Scenario	Disease state	Change*	2.5% CI
Covenant intervention	Work related sensitisation	−13%	−17% to −10%
	Upper respiratory symptoms	−6%	−8% to −3%
	Lower respiratory symptoms	−13%	−16% to −10%
	Work disabling asthmatic symptoms†	−13%	−29% to +3%
Continuation of covenant	Work related sensitisation	−21%	−26% to −17%
	Upper respiratory symptoms	−14%	−17% to −10%
	Lower respiratory symptoms	−25%	−30% to −20%
	Work disabling asthmatic symptoms	−24%	−38% to −12%
Hygienic intervention	Work related sensitisation	−21%	−25% to −17%
	Upper respiratory symptoms	−21%	−26% to −16%
	Lower respiratory symptoms	−46%	−52% to −40%
	Work disabling asthmatic symptoms	−46%	−57% to −33%
Health surveillance intervention (I)	Work related sensitisation	3%	−1% to 8%
	Upper respiratory symptoms	−4%	−8% to 0%
	Lower respiratory symptoms	−31%	−40% to −22%
	Work disabling asthmatic symptoms	−30%	−45% to −15%
Health surveillance intervention (II)	Work related sensitisation	−2%	−6% to 2%
	Upper respiratory symptoms	18%	7% to 28%
	Lower respiratory symptoms	−58%	−66% to −50%
	Work disabling asthmatic symptoms	−59%	−71% to −45%
Pre-employment screening	Work related sensitisation	−21%	−31% to −13%
	Upper respiratory symptoms	−14%	−23% to −4%
	Lower respiratory symptoms	−18%	−26% to −6%
	Work disabling asthmatic symptoms	−16%	−35% to 4%

*Difference between pre- and post-intervention period over a 20-year period.
†For work disabling asthma the figures reflect the change in onset of new cases; since disabled workers leave the workforce in the year they become disabled no prevalence figures can be estimated for this stage.

until occurrence, etc), since the impact on each worker might differ substantially according to the characteristics of the disease(s) modelled (ie, aetiological characteristics) and types of intervention.

The number of individual interventions (approximately 400 after each health surveillance cycle every 3 years in a population of 10 000) resulting from the more extensive health surveillance strategy seems feasible to implement. New high risk workers are identified at each health surveillance cycle since both new recruits and existing workers will keep progressing through to the high risk disease states. In contrast, the hygienic intervention would involve several thousands of companies within

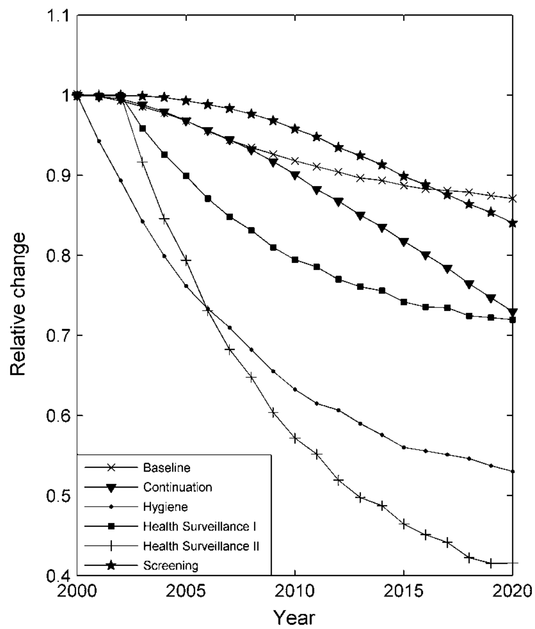


Figure 2 Trend plot of the change in the prevalence of lower respiratory symptoms for the six intervention scenarios for the 20-year simulation period.

a short time period. This would introduce a high burden on the resources of occupational health services and large associated costs. Although the health surveillance scenario would also lead to a substantial logistical burden, the fact that the exposure reduction effort is targeted at those workers at high risk of developing severe respiratory symptoms means it will lead to a greater reduction in the disease burden. Overall, a combination of health surveillance and substantial exposure reduction focussing on high risk workers seems to be the most effective choice for an intervention strategy.

Besides the fact that pre-screening of workers only resulted in a limited decrease in disease burden, there are also strong ethical reasons to oppose such intervention measures. In general, it is not believed to be ethical to exclude a substantial section of the (working) population because of differences in susceptibility (atopy) when exposure interventions are possible and other risk factors exist as well. In many countries screening of new employees and excluding workers at high risk from entering a working population are prohibited.

The intervention scenarios evaluated contain some assumptions that do not fully reflect real life. For example, complete and effective implementation of state-of-the-art control measures is unlikely to be achieved in the near future, but the simulation does provide an illustrative insight in the possible impact given the current state-of-the-art of controls. Screening of workers within the health surveillance system before they have developed symptoms will often prove to be difficult without delays, especially when based on serological evaluations. Alternative approaches such as the use of predictive diagnostic questionnaires, may reduce costs at the expense of a somewhat higher disease misclassification.[29] Furthermore, they are generally based upon symptom related questions, so only workers who have already developed certain (mild) symptoms will be identified. These simulations assume that diagnostic tests used are 100% accurate. Here misclassification is not easily estimated since a gold standard does not exist. All these assumptions have to be taken into account when making final decisions with respect to the preferred strategy.

In addition, we assume in this study that the outcome of an intervention would be the same for the population as a whole (eg, percentage reduction in exposure). This is, in our opinion, a valid assumption. However, the manner in which these exposure reductions could be achieved might differ substantially per sector or even per company. These differences will have to be taken explicitly into account if these health impact assessment results are to be translated into cost–benefit analysis. We emphasised the performance of quantitative health impact assessment to compare different intervention scenarios. Future work should include further refinement of intervention scenarios to better reflect real world situations. This should also include obtaining a better evidence base regarding the effectiveness of interventions and specific control measures within the bakery sector. In addition, the robustness of the results should be explored using comprehensive uncertainty analyses.

With respect to the dynamic model, sensitivity analysis performed during the development phase indicated the approach is fairly robust to moderate changes and therefore uncertainty in input parameters.[11] Nevertheless, there is a need for longitudinal epidemiological studies, especially for work related (allergic) respiratory diseases, to enable more thorough estimation of transition probabilities and to improve our mechanistic insights. Epidemiological studies should also focus on obtaining information on exposure–response relationships at low exposures instead of extrapolating.[30] This will lead to better insight into the potential of exposure reduction to reduce the onset of new cases and stop or delay the progression of disease in those already ill.

Although improvements to the model are possible, overall we believe our model has a reliable and strong scientific basis given the use of high quality exposure and epidemiological data to estimate most model input parameters. In addition, the impact of uncertainty in model parameters on our results is both quantified and probably limited since we compare the relative difference in health impact between intervention scenarios. Since both pre- and post-intervention simulations share the same 'uncertain' model parameters, the uncertainty in the relative difference is expected to be limited.

In conclusion, this paper provides valuable information on changes in disease burden related to various intervention programs. Besides health impact, the final decision in favour of a certain intervention strategy will generally be highly influenced by factors such as the associated cost–benefit ratio, practical limitations, and support among employers and employees. A final decision on a preferred intervention strategy can only be made after careful weighing of all these factors.

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