

# Occupational allergy to bell pepper pollen in greenhouses in the Netherlands, an 8-year follow-up study

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**To cite this article:** Patiwaal JA, Jong NW, Burdorf A, Groot H, Gerth van Wijk R. Occupational allergy to bell pepper pollen in greenhouses in the Netherlands, an 8-year follow-up study. *Allergy* 2010; DOI: 10.1111/j.1398-9995.2010.02411.x.

## Keywords

bell pepper pollen; horticulture; longitudinal study; occupational allergy; risk factors.

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Accepted for publication 21 April 2010

DOI:10.1111/j.1398-9995.2010.02411.x

Edited by: Hans-Uwe Simon

## Abstract

**Background:** Pollen from bell pepper plants cultivated in greenhouses are known to cause occupational allergic disease. A cross-sectional study among 472 bell pepper employees in 1999 estimated prevalences for sensitization to bell pepper pollen of 28% and for work-related allergic symptoms of 54%. There is scarce information on the incidence of work-related allergy and its risk factors. Aims of the present study were to estimate the cumulative incidence of work-related symptoms and sensitization to bell pepper pollen, and to determine risk factors for the onset of these symptoms and sensitization.

**Methods:** Bell pepper employees who participated in a cross-sectional survey in 1999 were asked to take part in a follow-up study in 2007. Information on demographic characteristics, job characteristics and allergic symptoms was gathered by means of a questionnaire. Furthermore, skin tests were performed with *a.o.* bell pepper pollen.

**Results:** In total, 280 of 472 employees were available for questionnaires and in 250 employees allergy tests were performed. During the 8-year follow-up, the cumulative incidence of sensitization to bell pepper pollen was 9% and of work-related rhinitis 19%. Atopy [odds ratio (OR) 5.60] and smoking (OR 3.53) were significantly associated with development of rhinitis. The cumulative incidence of work-related asthma symptoms was 8%. Again atopy (OR 5.03) and smoking (OR 11.85) were significant risk factors.

**Conclusion:** Cumulative incidences for sensitization to bell pepper pollen, work-related rhinitis and asthma symptoms were 9%, 19% and 8%, respectively. Atopy and smoking are risk factors for developing work-related symptoms among workers in bell pepper horticulture.

The prevalence of occupational allergy and asthma has increased over the past few decades and an estimated 10–25% of all adult onset asthma can be attributed to the work place (1).

Occupational asthma and rhinitis may lead to substantial consequences for work, most notably productivity loss at work, sickness absence, and work disability (2–4). Employees in horticulture are at risk for developing an occupational allergy (5). The European Farmers' project demonstrated that working in a greenhouse was a risk factor for developing respiratory symptoms (5–7). Kronqvist et al. (8) showed that upper and/or lower airway symptoms were present in 38% of workers in Swedish greenhouse cucumber and tomato growers.

Greenhouses for crop growing in the Netherlands, approximately 9000 in total, host a large workforce. The bell pepper cultivation in the Netherlands is an important branch of horticulture under glass with a size of 1 184 ha and the current workforce (2008) consists of approximately 9800 employees (Commodity Board of Horticulture, market and innovation). Furthermore, the bell pepper greenhouse is an environment characterized by a high prevalence of upper and lower airway symptoms. In a cross-sectional study among 472 employees from 85 greenhouses – nearly 10% of the bell pepper workforce at that time – work-related allergic symptoms were found in 54% of workers (9). These symptoms consisted of rhinitis, conjunctivitis, and asthma in 49%, 30%, and 13%

of individuals, respectively. Further analysis demonstrated sensitization to the bell pepper plant in 35% of workers and 23% was sensitized to predatory mites which were used as a biological control of the crops (9, 10). Work-related symptoms among bell pepper employees were associated with sensitization to substances of the bell pepper plant (bell pepper pollen being the most important), age and atopy.

In the general (unexposed) population the prevalence rates reported for rhinitis range from 19% to 30% (11, 12) and for both conjunctivitis and asthma prevalence rates of 15–20% are found (13, 14). It can thus be concluded that the prevalence of work-related symptoms (mainly rhinitis and conjunctivitis) and allergy among greenhouse workers is high. Up to present, studies have been cross-sectional of nature and no longitudinal studies on the natural course of occupational allergy in greenhouse horticulture have been performed. Therefore, there is no information available on the cumulative incidences of work-related symptoms or allergy and its risk factors. To identify greenhouse employees who are at risk of developing sensitization and symptoms, more insight into these factors is needed. The obtained knowledge can be used to develop tools to detect occupational allergy in these employees in an early stage.

A longitudinal study was conducted based on follow-up of all participants in a previous cross-sectional study among bell pepper greenhouse workers (9). Although only bell pepper employees were subject of study, this branch of industry may serve as a model for many other kinds of horticulture characterized by pollen exposure.

The aims of this study were twofold: (1) to estimate the cumulative incidence of sensitization to bell pepper pollen and work-related rhinitis and asthma symptoms, and (2) to establish risk factors for the onset of work-related symptoms and occupational allergy.

## Material and methods

From March until September 2007, a follow-up study among bell pepper employees was performed. As many employees as possible of the 472 who participated in the first study were included in the follow-up study (9). Bell pepper greenhouses who participated in the cross-sectional survey in 1999 were approached by telephone and asked to take part in a second survey. Subsequently, the investigators paid a visit to the greenhouses. Subjects that had left the job were traced and also asked for participation. If they agreed to take part, the investigators paid a visit to their new workplace or made a home visit. During the visits the former and current employees gave their informed consent. A questionnaire was administered on gender, age, smoking habit, current job characteristics, work history, atopic complaints, and allergic symptoms at work, i.e. work-related rhinitis and asthma symptoms. Questions did not specifically focus on the flowering season. Subjects were labelled as having work-related rhinitis symptoms if they reported any of the following items: sneezing, rhinorrhoea, nasal itching or nasal obstruction after occupational exposure (9). Similarly, if subjects reported either wheezing, coughing, sputum, or shortness of breath after occupational exposure, they were labelled as having work-related asthma

symptoms (9). Sensitization to occupational allergens and common inhalant allergens was determined by means of skin prick tests. The study was approved by our Hospital Medical Ethical Committee. Confidentiality was maintained.

In this follow-up study, the cumulative incidence of sensitization to bell pepper pollen, work-related rhinitis and work-related asthma incidence were primary outcome measures. Work-related rhinitis and asthma incidence were defined, respectively, as newly reported rhinitis and asthma symptoms at work during follow-up that were not mentioned in the first study in 1999.

## Skin tests

Skin prick tests were carried out according to international guidelines (15, 16) and performed by a skilled allergy nurse. In addition, reactions were expressed in mean wheal diameter of the longest diameter and the orthogonal diameter. A diameter of 3 mm or more was considered positive (17).

## Allergens

*Home made extracts: bell pepper pollen and Amblyseius cucumeris*

As the bell pepper pollen appeared to be the substance of the bell pepper plant most strongly associated with allergic complaints, only pollen were used for skin prick testing during the follow-up study (9). Pollen from bell pepper plants were collected in a greenhouse in the period February–March 2007. The flowers were in full blossom, and biological control by predatory mites (*Amblyseius cucumeris*) was not used yet. A 10% (w/v) extract was made in phosphate-buffered saline (PBS) pH 7.4, containing 0.03% human serum albumin and 0.5% phenol (18). The protein concentration, determined by the method of Watanabe et al. (19) was 0.62 g/l. Predatory mites (*Amblyseius cucumeris*) were kindly supplied by Koppert Biological Systems (Berkel en Rodenrijs, the Netherlands) and extracted according to Groenewoud et al. (10). The protein concentration was 1.05 g/l (19). Appropriate aliquots were stored at –20°C, defrosted 1 h before skin test and mixed.

## Botrytis cinerea and common inhalant allergens

In addition, skin prick tests were performed with *Botrytis cinerea* (ALK Abello, SQ 412), one of the moulds found in greenhouses and with six common inhalant allergens from ALK Abelló (Nieuwegein, the Netherlands). The common inhalant allergens comprised *Dermatophagoides pteronyssinus* (SQ-503), grassmix (SQ-293) and tree mix (SQ-108), mugwort (SQ-312) and animal dander (dog, SQ-553 and cat, SQ-555). Dilution buffer served as a negative control, histamine chloride (10 mg/ml) as a positive control.

## Statistical analysis

In the statistical analysis, baseline characteristics of subjects which were included in follow-up were compared to those lost to follow-up: Differences between continuous variables

were tested with the unpaired Student *t*-test and the differences between frequencies of categorical variables were tested with the chi-square test ( $\chi^2$ ).

A logistic regression model was used to study risk factors for primary dichotomous outcomes measures i.e. onset of work-related rhinitis, work-related asthma symptoms and sensitization to bell pepper pollen during the follow-up period. For all three primary outcome measures the following independent variables from the baseline study were used; individual characteristics (gender, age, smoking), job characteristics (years of exposure, job classification) and atopy. Atopy was defined by the presence of a positive skin prick test result to at least one of the common inhalant allergens.

For the analysis, univariate associations were investigated and variables with a significance level of  $P < 0.10$  were considered for inclusion in the multivariate models. In the final multivariate models, only variables with a *P*-level below 0.05 were retained. The odds ratio (OR) was used as measure of association.

The statistical analysis was executed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

## Results

In total, 280 of 472 employees who participated in the first study were available for questionnaires and 250 of these 280

employees were available for both questionnaires and allergy testing. Among another 42 subjects it was possible to gather information on current employment status. Therefore, in total 322 subjects were included in the follow-up study (Fig. 1).

Information from the first study in 1999 on individual characteristics, job characteristics, allergy symptoms and allergy test results was compared between the (former and current) employees included in the follow-up study in 2007 and those lost to follow-up (Table 1). No difference was found for gender, work-related rhinitis, work-related asthma symptoms, atopy, and sensitization for bell pepper pollen or for any of the occupational allergens between the two groups. There was a clear overlap between atopy and sensitization to bell pepper pollen.

Owners were statistically more likely to be included in the follow-up study, compared to employees. The follow-up group had a smaller proportion of smokers compared to those lost to follow-up. This, however, appeared to be associated with job classification, because owners were less often smoker than employees. The mean age of the follow-up group was higher (38 vs 34 years) and also the mean duration of employment was higher in the follow-up group (8.89 vs 7.51 years).

Reasons for the owners to refuse participation (in the questionnaire survey and/or allergy tests) were lack of time

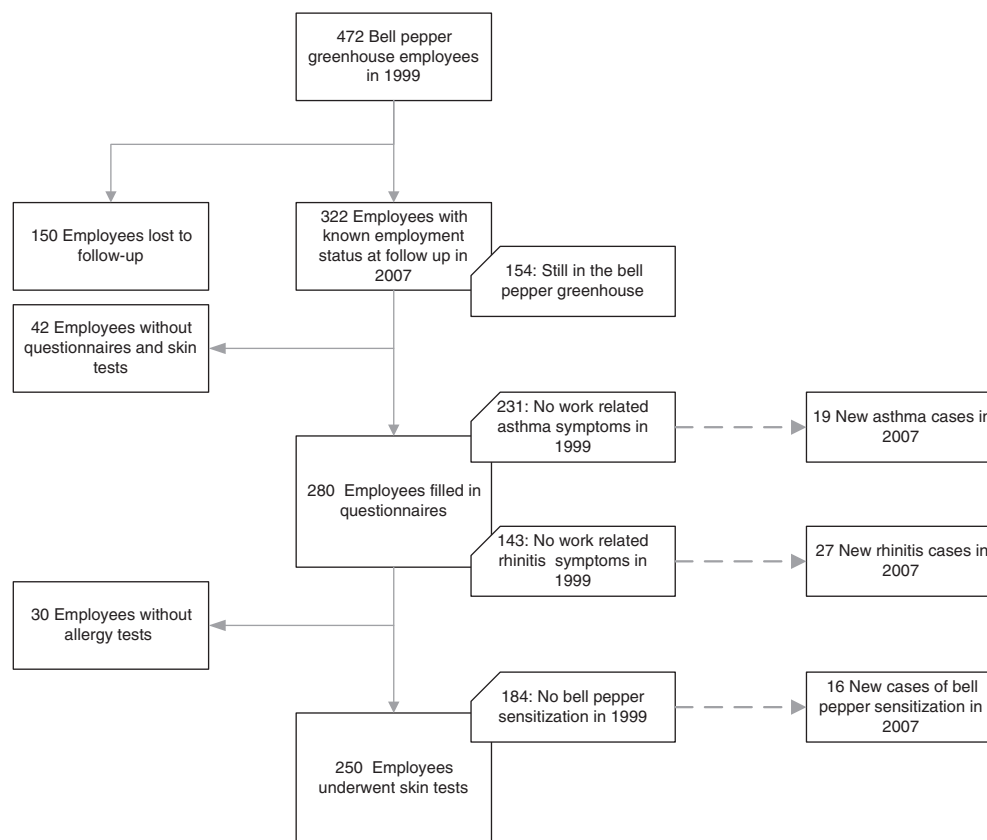


**Figure 1** Overview of bell pepper employees at baseline (1999) and during follow-up in 2007: (participants and non-participants).

**Table 1** Individual and job characteristics and allergy (symptoms) at baseline (1999) of the group follow-up vs lost to follow-up in 2007

|                                                        | Participant<br>2007 ( <i>n</i> = 322) | Non-participant<br>2007 ( <i>N</i> = 150) |
|--------------------------------------------------------|---------------------------------------|-------------------------------------------|
| Determinants                                           |                                       |                                           |
| Gender (male)                                          | 263 (82%)                             | 124 (83%)                                 |
| Age (mean years)*                                      | 37.7                                  | 34.3                                      |
| Smoking*                                               | 94 (29%)                              | 59 (39%)                                  |
| Job classification<br>(owner)*                         | 116 (36%)                             | 17 (11%)                                  |
| Duration of employment<br>(mean years)*                | 8.98                                  | 7.51                                      |
| Atopy                                                  | 113 (35%)                             | 64 (42%)                                  |
| Sensitization to one of the<br>occupational allergens† | 133 (41%)                             | 72 (48%)                                  |
| Sensitization to the bell<br>pepper plant‡             | 112 (35%)                             | 55 (36%)                                  |
| Work-related rhinitis<br>symptoms                      | 156 (48%)                             | 77 (51%)                                  |
| Work-related asthma<br>symptoms                        | 43 (13%)                              | 20 (13%)                                  |

\**P* < 0.05.†Occupational allergens: bell pepper plant, *amblyseius cucumeris*, *botrytis cinerea*.

‡Bell pepper plant: bell pepper stem, leaf, pollen, juice, stamen.

or interest (*n* = 5) and the fact that they had quit the bell pepper cultivation or had changed to other crop growing (*n* = 9). Some owners could not be reached by telephone (*n* = 6) and one owner had died. Consequently, this hampered the recruitment of the (formerly) enlisted employees.

The cumulative incidence of sensitization to bell pepper pollen, work-related rhinitis and asthma symptoms was 9%, 19%, and 8%, respectively (Table 2). There was a clear overlap among these incidences. Of the 27 workers who developed work-related rhinitis, seven workers also developed work-related asthma symptoms, and 12 workers developed sensitization to bell pepper pollen. Furthermore, of the 19 workers who developed work-related asthma symptoms, all workers developed work-related rhinitis and 10 of 19 were also newly sensitized to bell pepper pollen. Finally, of the 16 workers who developed a bell pepper pollen sensitization, 13 also developed work-related rhinitis of which three developed work-related asthma symptoms as well.

At baseline, work-related allergy symptoms were also strongly interrelated with 93.3% of subjects with asthmatic complaints also reporting rhinitis. Furthermore, atopy at baseline was associated with sensitization to occupational allergens at baseline, with 65% of the atopic subjects also being sensitized to the bell pepper plant and 80% of the atopic subjects to at least one of the occupational allergens (i.e. either to the bell pepper plant, to *botrytis cinerea* or to *amblyseius cucumeris*) (data not shown).

The cumulative incidence of sensitization to bell pepper pollen during 8-year follow-up was 9% (*n* = 16) (Table 2). With increasing age (OR 0.95) the risk of developing sensitization to bell pepper pollen decreased (Tables 3 and 4).

The cumulative incidence of work-related rhinitis symptoms during the 8-year follow-up was 19% (*n* = 27). In the univariate analyses, atopy (OR 4.29), smoking (OR 2.34) and age (OR 0.96) were associated with development of rhinitis symptoms (*P* < 0.10) (Table 3). In the final multivariate model only smoking (OR 3.53) and atopy (OR 5.60) were significantly associated with the development of rhinitis symptoms (*P* < 0.05) (Table 4).

The cumulative incidence of work-related asthma symptoms was 8% (*n* = 19). In the univariate analyses atopy (OR 2.75), smoking (OR 8.62) and job classification (owner) (OR 0.28) were associated (*P* < 0.10) with the development of asthma (Table 3). In the final multivariate model only smoking (OR 11.85) and atopy (OR 5.03) were significantly associated with the development of asthma symptoms (Table 4).

The duration of employment appeared not be a risk factor for either work-related rhinitis or work-related asthma symptoms.

At time of follow-up, 48% of workers was still employed in bell pepper horticulture. Job classification was the only determinant significantly associated with current employment in bell pepper horticulture. Compared to employees, owners were more likely to stay in the bell pepper greenhouse [OR (95% CI): 1.97 (1.21–3.20)]. Within the employee group who had left the greenhouse, rhinitis symptoms in 1999 were significantly (*P* < 0.05) more present than among the employees who stayed [61% (74/122) vs 38% (32/84)].

## Discussion

During the 8-year follow-up, the cumulative incidence of bell pepper pollen sensitization was 9% and the cumulative inci-

**Table 2** Prevalence at baseline (1999) and cumulative incidence during follow-up (2007) of the three primary outcomes i.e. sensitization to bell pepper pollen, work-related rhinitis and work-related asthma symptoms

|                                     | Prevalence at<br>baseline %<br>(95% CI) | Number of workers<br>for whom data<br>was available during<br>8-year follow-up | Population-at-risk<br>during 8-year<br>follow-up | New cases<br>during 8-year<br>follow-up | Cumulative<br>incidence %<br>(95% CI) |
|-------------------------------------|-----------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------|-----------------------------------------|---------------------------------------|
| Sensitization to bell pepper pollen | 27.3 (25.2–29.4)                        | 250                                                                            | 184                                              | 16                                      | 8.7 (7.5–9.9)                         |
| Work-related rhinitis symptoms      | 49.5 (46.2–52.5)                        | 280                                                                            | 143                                              | 27                                      | 18.8 (16.1–21.7)                      |
| Work-related asthma symptoms        | 13.3 (12.2–14.5)                        | 280                                                                            | 231                                              | 19                                      | 8.2 (7.2–9.2)                         |

**Table 3** Univariate analysis of individual and job characteristics and atopy at baseline (1999) on the cumulative incidence of sensitization to bell pepper pollen, work-related rhinitis symptoms and work-related asthma symptoms during follow-up in 2007

| Determinants<br>(baseline in 1999) | New cases of<br>sensitization to bell<br>pepper pollen: 16/184 (9%)<br>Odds ratio (95% CI) | New cases of<br>work-related rhinitis<br>symptoms: 27/143 (19%)<br>Odds ratio (95% CI) | New cases of work-<br>related asthma symptoms:<br>19/231 (8%)<br>Odds ratio (95% CI) |
|------------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Gender (male)                      | 1.67 (0.54–5.11)                                                                           | 0.74 (0.23–2.37)                                                                       | 1.81 (0.65–5.05)                                                                     |
| Age                                | 0.95 (0.91–1.00)**                                                                         | 0.96 (0.92–1.00)**                                                                     | 0.98 (0.94–1.02)                                                                     |
| Smoking                            | 1.50 (0.52–4.36)                                                                           | 2.34 (1.00–5.50)*                                                                      | 8.62 (2.96–25.07)**                                                                  |
| Job classification (owner)         | 1.3 (0.46–3.65)                                                                            | 0.80 (0.34–1.91)                                                                       | 0.28 (0.08–0.99)**                                                                   |
| Duration of employment             | 0.98 (0.90–1.07)                                                                           | 0.96 (0.90–1.03)                                                                       | 0.98 (0.90–1.06)                                                                     |
| Atopy                              | 1.86 (0.61–5.72)                                                                           | 4.29 (1.64–11.20)**                                                                    | 2.75 (1.07–7.10)**                                                                   |

\* $P < 0.10$ ; \*\* $P < 0.05$ .**Table 4** Multivariate analysis of individual and job characteristics and atopy at baseline (1999) on the cumulative incidence of sensitization to bell pepper pollen, work-related rhinitis symptoms and work-related asthma symptoms during follow-up in 2007

| Determinants<br>(baseline in 1999) | New cases of<br>sensitization to bell<br>pepper pollen: 16/184 (9%)<br>Odds ratio (95% CI) | New cases of<br>work-related rhinitis<br>symptoms: 27/143 (19%)<br>Odds ratio (95% CI) | New cases of<br>work-related asthma<br>symptoms: 19/231 (8%)<br>Odds ratio (95% CI) |
|------------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Gender (male)                      | n/a                                                                                        | n/a                                                                                    | n/a                                                                                 |
| Age                                | 0.95 (0.91–1.00)*                                                                          | 0.98 (0.94–1.02)                                                                       | n/a                                                                                 |
| Smoking                            | n/a                                                                                        | 3.53 (1.28–9.69)*                                                                      | 11.85 (3.59–39.11)*                                                                 |
| Job classification (owner)         | n/a                                                                                        | n/a                                                                                    | 0.47 (0.12–1.78)                                                                    |
| Duration of employment             | n/a                                                                                        | n/a                                                                                    | n/a                                                                                 |
| Atopy                              | n/a                                                                                        | 5.60 (1.77–17.75)*                                                                     | 5.03 (1.65–15.37)*                                                                  |

n/a, not applicable.

\* $P < 0.05$ .

dence of work-related rhinitis and asthma symptoms was 19% and 8%, respectively. Important individual risk factors were atopy and smoking.

The estimated prevalence of bell pepper pollen sensitization, work-related rhinitis and asthma symptoms in the baseline study may be assumed to be the cumulative incidence because of the average duration of exposure of about 8 years. On the basis of these prevalence figures, it was expected that the cumulative incidence for bell pepper pollen sensitization and for work-related rhinitis and asthma symptoms during the 8-year follow-up would be in the same range as the prevalence found at baseline. However, the observed cumulative incidence was lower for all three measures. This finding can be partly explained by the fact that the peak of onset of sensitization and symptoms apparently occurs during the first several years of exposure and not in a later phase of prolonged exposure. The fact that sensitization to an occupational allergen occurs in the first years of exposure is also described for other occupational groups with occupational allergy. In laboratory animal workers sensitization to occupational allergens and symptoms occur primarily in the first 2–3 years after starting exposure to laboratory animals (20). In baker apprentices, the peak incidence of skin reactivity and work-related rhinoconjunctivitis was reached about

1–2 years after entering an educational programme (21). Furthermore, one of the reasons for the cumulative incidence being lower than estimated is a healthy worker effect (HWE) (22). In our study, a HWE seems to have occurred since rhinitis symptoms in 1999 were significantly more present in the group that had left the greenhouse during follow-up compared to the group still employed in the greenhouse, indicating that rhinitis could be an expelling factor. Sixteen of 168 former employees explicitly mentioned that allergy symptoms were reason of their resignation. This points to a possible HWE and moreover it also indicates that work-related allergy possibly has economic consequences for both the industry and for the workers themselves. Another indication for a HWE was that at time of follow-up 8 years later, 48% of workers were still employed in bell pepper horticulture and owners were more likely to be still at work in the bell pepper greenhouse than employees. Another possible explanation for the lower cumulative incidence is the fact that the working environment in most bell pepper greenhouses has changed over the years, for example greenhouses are more spacious than before. It can be hypothesized that the pollen density nowadays is, therefore, less high. Personal sampling to measure pollen concentrations will be required to estimate the current exposure of the employees.

Taking the duration of the follow-up into account, the incidence of bell pepper pollen sensitization, work-related rhinitis and work-related asthma symptoms was 11, 24 and 10 cases per 1000 person-years, respectively. In 2001, the second Dutch National Study of General Practice reported an incidence of 'hay fever/allergic rhinitis' of 8.8 new cases per thousand individuals per year (23) and on the basis of data from five general practice data registration systems, the number of new asthma cases in the general population occurring in 2003 was 6.5 per thousand men and 7.9 per thousand women (23). Thus, compared to the incidence of rhinitis in the general population, the cumulative incidence of work-related rhinitis in this group of bell pepper employees is considerably higher. The cumulative incidence of work-related asthma symptoms found in our study is comparable to the incidence of asthma in the general population. It is known that adult onset asthma can mainly be attributed to the workplace.

In the cross-sectional survey in 1999, bell pepper pollen sensitization appeared to be the most important allergen (in the bell pepper greenhouse) associated with work-related symptoms (9). Therefore, during follow-up the cumulative incidence of bell pepper sensitization was studied and not the cumulative incidences of sensitization to other occupational allergens or to the common inhalant allergens (including pollen allergy). The onset of the other allergens is most likely less relevant and therefore the limitation resulting from this approach seems to be marginal.

### Risk factors

The cumulative incidence of bell pepper sensitization in our study decreased significantly by age. In general, it is known that the development of inhalant allergies diminishes when age increases (24, 25). This could also hold true for occupational allergies and our finding points into that direction.

Risk factors found in this study for the cumulative incidence of work-related rhinitis and asthma symptoms were smoking and atopy.

Whether smoking is associated with development of work-related allergic symptoms has been a matter of debate. Jeebhay et al. (26) demonstrated that smoking is indeed a risk factor for development of occupational asthma among salt water fish processing workers. Siracusa, however, showed that smoking was a negative determinant for development of asthma in working groups in British Colombia (27). A review from 2006 on studies on smoking and occupational asthma published from 1970 to 2005 showed that there is little support for the hypothesis that smoking is a risk factor for the development of occupational asthma (28). In general, tobacco smoke impairs the innate immune system and in a recently published review Cagnani et al. (29) have concluded that active smoking is associated with current rhinitis and asthma symptoms and that it seems to be a risk factor for development of new asthma in rhinitis patients. Our study clearly

showed that smoking is a risk factor for development of both work-related rhinitis and asthma symptoms in this particular branch.

Inhalant atopy as a whole (i.e. sensitization to at least one of the following common inhalant allergens: *Dermatophagoides pteronyssinus*, grass pollen, tree pollen, mugwort, dog or cat dander) appeared to be an important determinant of work-related symptoms and sensitization to the bell pepper plant in the previous cross-sectional study conducted in 1999 (9). Therefore, also in this longitudinal study the common inhalant allergens were not studied separately but grouped together as one possible risk factor. Furthermore, at baseline atopy and bell pepper pollen sensitization strongly overlapped and therefore it was not possible to estimate the separate role of these two factors (9). The proposed sequence of events in developing occupational allergy while working with high molecular weight allergens is first atopy, then development of sensitization to an occupational allergen, subsequently the development of occupational rhinitis, and finally the onset of occupational asthma (30–32). In our study, we found that atopy is indeed at the start of the series of events, because atopy was associated with the cumulative incidence of both work-related rhinitis and asthma symptoms in bell pepper employees. This finding corroborates earlier results showing that atopic people have an increased risk of developing work-related allergic symptoms while being exposed to high molecular weight antigens (30–32). Our study also seems to confirm the hypothesis that occupational rhinitis precedes occupational asthma (33, 34) because work-related rhinitis was associated with the onset of work-related asthma symptoms. However, this association was partly explained by the fact that rhinitis and asthma had similar risk factors. With two measurements over time, the study design did not allow us to investigate the sequence in more detail. However, the clear overlap among the cumulative incidence of sensitization to bell pepper pollen, work-related rhinitis, and work-related asthma symptoms indicates that these outcomes are clustered. During the field visits to the greenhouses it was established that almost all cultivations were sweet bell pepper and, hence, capsaicin from *Capsicum annuum* will not have played an important role in the onset of work-related symptoms.

In future research, the exact sequence of events should be disentangled to facilitate better targeted prevention and early treatment strategies. The fact that occupational allergy may have a profound effect on work performance through productivity loss at work as well as sick leave emphasises the need for these prevention and early treatment strategies.

### Conclusion

Cumulative incidences for sensitization to bell pepper pollen, work-related rhinitis and asthma symptoms were 9%, 19% and 8%, respectively. We found that smoking and atopy are risk factors for developing work-related rhinitis and asthma symptoms in bell pepper greenhouse workers.

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