

Occupational Exposure Among Bakery Workers: Impact on the Occurrence of Work-Related Symptoms as Compared With Allergic Characteristics

Jos Droste, MD

Paul Vermeire, MD

Marc Van Sprundel, MD, PhD

Peter Bulat, MD, PhD

Lutgart Braeckman, MD, PhD

Katrien Myny, MD

Michel Vanhoorne, MD, PhD

Objective: The aim of the study is to examine the relationship between exposure to occupational allergens, sensitization, and atopy and several outcome variables and the independent associations of these interrelated risk factors to work-related symptoms in particular. **Methods:** Data were collected by questionnaire, skin prick tests, lung function tests, and exposure measurements among 246 workers from 74 bakeries and analyzed using logistic and linear regression analyses. **Results:** Exposure levels were associated with respiratory symptoms, sensitization to baker's allergens, and lung function. High exposure and sensitization to common and bakers' allergens were independent risk factors for work-related symptoms. However, allergy determinants performed best in predicting work-related symptoms. **Conclusions:** Current exposure to occupational allergens is a risk factor for work-related symptoms, but sensitization to occupational allergens and atopy are more adequate and easier obtainable predictors of work-related symptoms. (J Occup Environ Med. 2005;47:458–465)

Baker's asthma is one of the most common types of occupational asthma.^{1–3} Furthermore, exposure to flour dust is one of the occupational exposures that have the strongest association with adult-onset asthma.⁴ In the past decade, many studies have reported on prevalence of work-related respiratory symptoms and sensitization to occupational allergens.^{5–7} Exposure to specific allergens occurring in bakeries, for example, wheat antigen and α -amylase, have been recognized as important risk factors for work-related respiratory symptoms.^{8–10} Several occupational studies have therefore been focused on exposure to these allergens and their effects on the health of bakery workers.^{11–15} They show that exposure, sensitization to specific bakers' allergens, and atopy are important risk factors for the occurrence of work-related symptoms. However, many of these risk factors are also interrelated.^{9,16,17} It is not well known to what extent these various determinants independently contribute to the occurrence of work-related symptoms. To identify or follow-up effectively workers at risk of respiratory or allergic symptoms, it is important to know which determinants are the most appropriate in predicting work-related symptoms. Therefore, this also may have practical relevance for occupational health practice as information on these various data are not equally easy to obtain.

From the Department of Epidemiology and Community Health, University of Antwerp, Belgium (Dr Droste, Prof Van Sprundel); Department of Respiratory Medicine, University of Antwerp, Belgium (Prof Vermeire); Section of Occupational and Environmental Health, Ghent University, Belgium (Prof Bulat, Prof Braeckman, Dr Myny, Prof Vanhoorne); and Institute of Occupational and Radiological Health, University of Belgrade, Yugoslavia (Prof Bulat).

Supported by Grant no. 3.0062.96 of the Fund of Scientific Research of Flanders.

Address correspondence to: J. H. J. Droste, MD, University of Antwerp, Dept. of Epidemiology and Community Health, Universiteitsplein 1, 2610 Antwerp, Belgium; E-mail: jos.droste@ua.ac.be.

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DOI: 10.1097/01.jom.0000161729.38843.38

The aim of the present study is to examine the relationships between exposure to dust, wheat, and α -amylase allergens and several outcome variables, including sensitization to occupational allergens, respiratory symptoms, and lung function, among workers from industrial and traditional bakeries. In addition, the risk for work-related symptoms will be assessed from information on exposure levels, basic questionnaire data, and results from allergy testing as the main predictive factors.

Subjects and Methods

Subjects

The current study was designed as a cross-sectional study among workers from small traditional bakeries and larger industrial bakeries in the provinces of Antwerp and East-Flanders in the northwest of Belgium. All workers involved in the baking process who were working for at least 4 hours a day were eligible for participation in the study. The population under study consisted of 246 workers from 74 participating bakeries. Of these, four were industrial bakeries with a total of 102 workers, whereas the remaining 144 workers came from 70 small traditional bakeries. The participation rate of the approached bakeries was 36%; the participation was lower among industrial bakeries than among traditional bakeries. The main reason for nonresponse was concern on interference with production routine. All participants gave their written consent. Data collection was conducted between January 1997 and December 1999.

Questionnaire

Data on respiratory, asthma-, and allergy-related symptoms were collected by means of a validated respiratory questionnaire,¹⁸ supplemented with questions on work-related symptoms and demographic and occupational characteristics. Questions on smoking history were derived from the European Community Re-

spiratory Health Survey questionnaire.¹⁹

Respiratory symptoms used in the current analyses were chronic cough, shortness of breath, wheeze ever, wheeze in the last 2 years lasting for more than 1 week, and work-related allergic symptoms during or after work. Respiratory symptoms already present before bakery employment were defined as previous history of respiratory symptoms. Work-related allergic symptoms were defined as sneezing or a running nose, itchy or watering eyes, shortness of breath, or eczema, during or shortly after contact with work-related substances.

Smoking status was categorized as never smoker, ex-smoker, or current smoker. Current smokers were defined as those who smoked at least one cigarette daily or one cigar weekly for a period of 1 year and who were still smoking within 1 month before the examination. Ex-smokers were all smokers who quit smoking at least 1 month before the examination. All other subjects were considered never-smokers.

Skin Prick Testing

Skin prick testing with 10 common aeroallergens and specific bakers' allergens was conducted according to standard procedures. The allergens tested for were *Dermatophagoides pteronyssinus* and *D. farinae* (house dust mite), storage mites (*Lepidoglyphus destructor*, *Tyrophagus putrescentiae*, *Acarus siro*), cat, dog, mixed grass pollen (timothy grass, foxtail grass, rye-grass, meadow grass, cocksfoot), mixed trees pollen (alder, birch, hazel), wheat pollen, wheat flour, rye flour, and fungal α -amylase using histamine chloride and allergen diluent as positive and negative controls, respectively (ALK Laboratory, Copenhagen, Denmark). Wheal diameters were recorded 15 minutes after application of the antigens. Mean diameters were calculated as the mean of the widest diameter and the perpendicular diameter measured at their midpoint. A mean wheal diameter of

at least 2 mm was considered a positive response. Responders to the negative control (>1 mm, $n = 0$) and non-responders to the positive control (< 2 mm, $n = 2$) were excluded from the analyses. Atopy was defined as having one or more positive responses (skin test positivity).

Spirometry

Baseline spirometry was performed in the bakeries during working hours by trained assistants using European Community for Steel and Coal guidelines.²⁰ Flow-volume measurements were performed with a Vicatest VCT-5 (Jaeger GmbH, Hoechberg, Germany). All forced expiratory maneuvers were performed standing up using a plastic mouthpiece without toothgrips. Lung function parameters forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), peak expiratory flow (PEF), and forced expiratory flow between 25% and 75% of vital capacity (MMEF) were recorded from at least three of as many as eight technically satisfactory maneuvers. Subjects were asked not to interrupt medication, and type and time of medication use was recorded if appropriate. Subjects were instructed not to smoke within 1 hour before spirometry.

Lung function parameters were expressed as percentages of predicted normal values (%FVC, %FEV₁, and %MMEF), according to European Community for Steel and Coal reference values.²⁰ Subjects with technically unsatisfactory spirometry or concomitant lower respiratory infections ($n = 38$) were excluded from this analysis.

Exposure Measurements

Inhalable dust was collected individually during shift periods of usually 5 to 7 hours in 227 workers from 68 bakeries. Inhalable dust was sampled by personal dust samplers (Gillair 5) using Teflon filters (Millipore, pore size 1.0 μ m) and PAS-6 sampling heads at a flow rate of 2 L/min. After sampling, dust filters were

weighed in a preconditioned room of 18°C to 22°C with 45% to 55% humidity. Detection limit was 0.17 mg/mL. Wheat antigens and α -amylase allergens were recovered from the filters by extraction with 2.5 mL of phosphate-buffered saline. Wheat flour antigens were measured using enzyme-linked immunosorbent assay inhibition and an antiwheat IgG4 serum pool.²¹ Detection limit of this method was 50 ng/mL. α -Amylase allergens were measured using a sandwich enzyme immunoassay with affinity-purified polyclonal rabbit IgG antibodies,²² using a detection limit of 100 pg/mL. All samples were analyzed in duplicate on two different days and the mean value was used for statistical analysis. Measurements below detection limit were replaced by the values of the analytic limit of detection divided by the square root of 2 and by the volume of air drawn through the sample.²³ The laboratory analyses were conducted at the Department of Environmental Sciences at the Wageningen University, the Netherlands.

Data Analysis

All bakery workers were classified into seven categories according to type of bakery and main job task. Warehouse workers and technicians ($n = 6$), sandwich makers ($n = 5$), and workers with missing job tasks ($n = 8$) were excluded because of their small numbers. The remaining five job groups were ordered by their mean levels of inhalable dust exposure, according to the results already shown in a previous study on exposure in this study population.²⁴ Large variation (geometric SD between 2 and 3) in exposure existed within each job group, therefore the job groups were also aggregated into three job exposure groups: 1) low exposure group, consisting of industrial packers, 2) medium exposure group, including industrial bakers and traditional pastry bakers, and 3) high exposure group, including traditional bread bakers and traditional

bread + pastry bakers. Each of these three categorizations of bakery workers, according to type of bakery (two subgroups), type of bakery + job title (five subgroups) and aggregated job titles (three subgroups), were examined by analysis of variance of the log-transformed exposure levels to dust, wheat and α -amylase allergens. For each type of exposure the aggregated categorization into three subgroups gave the best discrimination between exposure levels and was used in subsequent analyses. However, to analyze the association between exposure and lung function measurements exposure also was categorized into three subgroups according to the tertiles of the log-transformed individual exposure levels.

The prevalence of respiratory symptoms, skin test results and lung function measurements was compared among the three exposure levels using 3×2 tables. Associations between exposure levels and symptoms and skin test results were tested by χ^2 tests for linear trend, between exposure levels and lung function parameters (normally distributed) by analysis of variance. In multivariate analyses these associations were examined using logistic and linear regression models. Potential confounding variables included in the regression models were age, smoking status and parental allergy.

Logistic regression models were applied to estimate the independent effect of the various predictive variables on the main outcome variable work-related symptoms. The first model included basic person characteristics (age, smoking, parental allergy, work duration) from the questionnaire ("basic model") and occupational exposure levels; the second model consisted of the basic model and allergy test results (baker's and common allergens); the third (full) model contained all predictive variables simultaneously. Regression models were evaluated by loglikelihood and Hosmer and Lemeshow goodness of fit tests.²⁵

The Hosmer and Lemeshow goodness of fit tests the null-hypothesis of no difference between observed and predicted values of the model, therefore a large P -value corresponds with a good fit between predicted and observed values. The predicted probability of work-related symptoms, calculated from the regression models for each subject, were used to construct receiver operating characteristic curves to calculate the area under curve (AUC). The AUC can be used as a statistical parameter to assess the ability of the regression models in correctly discriminating between subjects with or without work-related symptoms.²⁶ A value of 0.5 indicates no discriminating ability (purely by chance) and a value of 1.0 indicates absolute discriminative ability.

All tests were two-sided, P values <0.05 were considered to be statistically significant, as well as odds ratios with 95% confidence intervals not including the value 1 and linear regression coefficients not including the value 0. Statistical analyses were performed using SPSS-PC + V11.0 (SPSS, Chicago, IL).

Results

Exposure Groups

After exclusion of sandwich makers, technicians, and warehouseworkers, 227 bakery workers with known job titles were included in the analysis. The distributions of population characteristics and main outcome variables among job title subgroups are listed in Table 1. Traditional bakers differ considerably from industrial bakers. Traditional bread bakers in particular were working more hours per week, had more often parental allergy and work-related symptoms, and more often were sensitized to baker's allergens as well as to common allergens.

These job titles were ordered by increasing geometrical mean levels of dust, wheat-, and α -amylase: industrial packer, industrial baker, tra-

TABLE 1Study Population Characteristics by Job Category, *n* (%) (unless stated otherwise)

Industrial Characteristic	Industrial Packer, <i>n</i> = 34	Industrial Baker, <i>n</i> = 49	Traditional Pastry Baker, <i>n</i> = 37	Traditional Bread Baker, <i>n</i> = 23	Bread + Pastry, <i>n</i> = 84	<i>P</i> (linear trend)
Gender						
Male	28 (82)	48 (98)	35 (95)	23 (100)	79 (94)	0.17
Female	6 (18)	1 (2)	2 (5)	0 (0)	5 (6)	
Age, mean years (SD)	34 (1.5)	32 (1.4)	32 (1.7)	28.9 (1.9)	34.1 (1.1)	0.77
No. hours/week working, mean (SE)	39 (0.3)	41 (1.6)	42 (2.6)	48 (3.6)	62 (2.5)	<0.01
No. years in bakery, mean (SE)	9.9 (1.7)	5.2 (0.9)	7.2 (1.2)	7.0 (1.5)	12.2 (1.3)	<0.01
Smoker						
Never	12 (35)	15 (40)	13 (35)	10 (53)	37 (48)	0.18
Ex	8 (24)	7 (18)	8 (23)	1 (5)	14 (18)	
Current	14 (41)	16 (42)	16 (43)	8 (42)	26 (34)	
Parental allergy	5 (16)	6 (19)	5 (16)	4 (24)	20 (29)	0.11
Previous history resp. symptoms	4 (12)	3 (8)	1 (3)	3 (16)	7 (9)	0.36
Work-related symptoms	2 (6)	7 (19)	7 (19)	8 (42)	30 (39)	<0.01
Bakers' allergens Positive	3 (9)	7 (14)	5 (14)	4 (18)	17 (21)	0.10
Atopy (common allergens)	7 (21)	13 (27)	9 (24)	8 (36)	30 (37)	0.05

TABLE 2

Exposure Levels for 3 Job Exposure Groups (low, medium, high)

Exposure group*	Dust (mg/mL)		Wheat (ng/mL)		α -Amylase (pg/mL)	
	<i>n</i>	GM (SEM)	<i>n</i>	GM (SEM)	<i>n</i>	GM (SEM)
Low	31	0.53 (1.14)	32	2.81 (1.15)	32	0.07 (1.16)
Medium	55	1.05 (1.15)	56	8.13 (1.23)	55	0.27 (1.31)
High	102	2.09 (1.07)	104	16.34 (1.14)	96	0.40 (1.20)
<i>P</i> (trend)		<0.01		<0.01		<0.01

*Low exposure: industrial packers; medium exposure: industrial bakers, traditional pastry bakers; high exposure: traditional bread bakers, traditional bread + pastry bakers

GM, Geometric Means (standard error of means).

ditional pastry baker, traditional bread baker, and traditional bread + pastry baker. On the basis of their mean levels of dust exposure, bakery job titles were aggregated into three exposure groups with low, medium, and high exposure. Log-transformed mean exposure levels of inhalable dust, wheat-, and α -amylase allergens for the three exposure groups are shown in Table 2.

Exposure, Symptoms, Sensitization, and Lung Function

When examining the association between exposure and symptoms (Table 3, upper section), respiratory symptoms were generally more prev-

alent with increasing exposure level. However, this relationship was statistically significant only for work-related symptoms (high exposure odds ratio = 10.9). Among workers with low exposure 5.9% reported symptoms during or immediately after work compared with 18.9 and 39.6% among those with medium and high exposure, respectively.

Similar results were observed for the association between exposure and sensitization to allergens, particularly to bakers' allergens (Table 3, lower section). Higher exposure levels were accompanied by higher prevalence of skin test positivity (though not reaching statistical significance). Although sensitization for

wheat allergen was more prevalent in all three exposure levels, the association between sensitization and exposure was stronger for α -amylase than for wheat allergen (though both not statistically significant). By comparison, sensitization to the most prevalent common allergen, house dust mite, showed no association with occupational exposure level, whereas sensitization to any common allergen (atopy) was associated with the high exposure group only.

Table 4 shows the association between pulmonary function levels and exposure levels. Mean FVC, FEV₁, and MMEF of workers with medium and high exposure were only slightly lower than those of workers with low

TABLE 3Prevalence, *n* (%), of Respiratory Symptoms and Sensitization to Allergens by Group Exposure Levels

	Exposure Level			Odds Ratio (95% CI)	
	Low	Medium	High	Medium vs. Low	High vs. Low
Respiratory symptoms					
Chronic cough	1/34 (2.9)	11/75 (14.7)	12/95 (12.6)	5.6 (0.7–45.5)	5.2 (0.6–41.9)
Shortness of breath	2/34 (5.9)	6/74 (8.1)	14/95 (14.7)	1.5 (0.3–7.9)	3.2 (0.7–15.1)
Wheeze ever	5/34 (14.7)	9/70 (12.9)	30/94 (31.9)	0.9 (0.3–3.0)	3.2 (1.1–9.3)
Wheeze within 2 years*	1/28 (3.6)	6/71 (8.5)	12/96 (12.5)	2.5 (0.3–22.0)	3.7 (0.4–30.4)
Work-related symptoms	2/34 (5.9)	14/74 (18.9)	38/96 (39.6)	3.9 (0.8–18.2)	10.9 (2.5–48.7)
Sensitization					
wheat allergen	3/33 (9.1)	9/86 (10.5)	17/103 (16.5)	1.4 (0.3–5.7)	1.9 (0.5–7.5)
α-Amylase allergen	1/33 (3.0)	4/86 (4.7)	13/103 (12.6)	2.1 (0.2–20.2)	4.4 (0.5–37.2)
any bakers' allergen†	3/33 (9.1)	12/86 (14.0)	21/103 (20.4)	1.8 (0.4–7.2)	2.3 (0.6–8.8)
Housedust mite	7/33 (21.2)	18/86 (20.9)	28/103 (27.2)	0.6 (0.3–1.5)	1.1 (0.4–2.8)
Any common allergen‡	7/33 (21.2)	22/86 (25.6)	38/103 (36.9)	1.1 (0.4–3.2)	2.0 (0.8–5.4)

Odds ratios (95% confidence intervals) adjusted for age and smoking categories (and parental allergy with allergens). The low-exposure group is the reference category.

*Wheeze within last 2 years lasting >1 week.

†Wheat flour, rye flour, α-amylase.

‡Housedust mite, mixed grass pollen, mixed trees pollen, cat, dog.

TABLE 4

Association Between Exposure Levels for Job Groups and Individual Exposure Groups and Lung Function Measurements

Exposure Level	FVC%pred	FEV ₁ %pred	MMEF%pred
By group exposure			
Medium vs. low	−4.1 (9.0, 0.8)	−0.4 (−5.3, 4.5)	3.8 (−5.2, 12.8)
High vs. low	−2.8 (−7.6, 2.0)	−1.9 (−6.7, 2.8)	−1.7 (−10.4, 7.1)
By individual exposure			
Medium vs. low	−0.8 (−5.3, 3.7)	−1.7 (−6.2, 2.8)	−2.4 (−10.6, 5.7)
High vs. low	−2.9 (−7.3, 1.4)	−4.1 (−8.5, 0.2)	−5.9 (−13.9, 2.0)

Regression coefficients (95% confidence interval limits) adjusted for smoking categories. The Low-exposure level is the reference category.

exposure. This relationship appeared more clearly when lung function levels were categorized based on individual measurements instead of exposure group by job title. Although individual regression coefficients were statistically not significant, a dose-response relationship could be noticed with all three lung function parameters.

Prediction of Work-Related Symptoms

To determine the independent effect of exposure on the risk of work-related symptoms and to compare the risk by exposure with coexisting risk factors, such as atopy and sensitization, to bakers' allergens, we examined the associations between several risk factors and work-related symptoms in different regression models

(Table 5). When exposure levels were entered (model 1) medium and high levels of exposure were associated with the occurrence of work-related symptoms; however, this relationship was statistically significant only among subjects with high exposure. With allergy testing results (model 2), sensitization to both bakers' allergens and to common allergens (atopy) were independent risk factors for work-related symptoms. In the full model, with adjustment of all questionnaire, allergy testing and exposure variables for one another (model 3), parental allergy, sensitization to bakers' allergens, atopy and high exposure level remained independent predictors for work-related symptoms, whereas a history of respiratory symptoms prior to working as a baker just fell

short of significance. First-order interactions between exposure and allergy variables did not appear statistically significant and were therefore not included in the model. Except for model 1 with exposure levels only, all models showed a satisfactory to good fit, particularly when allergy status was included.

Comparison of the predictive ability of the different models with that of the "basic" model (AUC 0.72) showed that inclusion of exposure levels improved the model only moderately (AUC model 1 0.76). Entering allergic sensitization to bakers' allergens and atopic status into the 'basic' model improved the model substantially (AUC model 2 0.80). Finally, the full model with both exposure and sensitization variables (model 3) had the best predic-

TABLE 5

Association Between Work-Related Symptoms and Exposure Level (Model 1), Sensitization for Baker's Allergens and Common Allergens (Atopy) (Model 2) and all Independent Predictors Simultaneously (Model 3)

Independent Variables	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
Age (years)	1.01 (0.97–1.05)	0.99 (0.95–1.03)	0.99 (0.95–1.04)
Smoking			
Never	1	1	1
Ex	1.3 (0.5–3.4)	0.8 (0.3–2.4)	1.0 (0.4–2.9)
Current	0.8 (0.3–1.6)	0.6 (0.3–1.3)	0.6 (0.3–1.5)
Parental allergy	2.2 (0.9–4.9)	2.6 (1.1–6.2)	2.4 (1.0–5.8)
Working duration (hours/day)	1.01 (0.99–1.03)	1.03 (1.01–1.05)	1.02 (0.99–1.04)
Previous history of resp. symptoms	4.2 (1.3–13.7)	2.3 (0.7–7.8)	2.7 (0.7–10.1)
Exposure level			
Low	1	—	1
Medium	4.7 (0.9–24.6)	—	5.0 (0.8–30.6)
High	9.4 (1.8–49.1)	—	8.5 (1.4–52.0)
Sensitization to bakers' allergens	—	5.9 (2.3–15.1)	3.2 (1.0–10.7)
Atopy (common allergens)	—	2.6 (1.2–5.5)	2.3 (1.0–5.2)
H-L (<i>P</i> value) [†]	0.15	0.83	0.88
AUC (95% CI) [‡]	0.76 (0.68–0.83)	0.80 (0.73–0.87)	0.82 (0.76–0.88)

All models are adjusted for basic characteristics. Associations estimated by odds ratios with 95% confidence interval.

[†]Hosmer–Lemeshow statistic, 'basic' model: *P* = 0.72.

[‡]Area Under Curve, derived from ROC curve, "basic" model = 0.71 (0.63–0.79).

tive ability, although its AUC of 0.82 was only slightly higher than the model with the allergy testing variables only. However, 95% confidence levels of AUCs were overlapping one another more or less. As a result, the mean predicted probability of work-related symptoms estimated by the regression models among bakery workers with high exposure levels, atopy, and sensitization to bakers' allergens were 34%, 44%, and 45%, respectively, according to model 2, and 39%, 44%, and 45%, respectively, according to model 3.

Discussion

The results of our study consistently showed positive associations between exposure levels and respiratory symptoms, sensitization to wheat- and α -amylase allergens, and an inverse relationship with lung function measurements. However, only the association between work-related symptoms and high exposure level was statistically significant. Furthermore, high exposure level and allergic predisposition (according to sensitization to common or bakers' allergens) were both strong independent risk factors for work-

related symptoms. However, as compared to questionnaire- or exposure data only, allergic sensitization performed best in predicting work-related symptoms, according to the good predictive ability of the regression models which included sensitization to bakers' and common allergens (atopy).

The associations between the main risk factors tested in our models, exposure to inhalable dust, wheat, and α -amylase allergens and sensitization to occupational allergens, and work-related symptoms among bakery workers have been well documented in a comprehensive review by Houba et al.² However, our study is the first to assess the independent contributions of these risk factors, including questionnaire, exposure measurements and allergy testing, to the predictability of work-related symptoms among bakery workers. Our results agree with earlier findings of positive relationships between symptoms and exposure or sensitization to flour dust, wheat, and α -amylase among bakery workers.^{7–16,27,28} Associations between exposure and symptoms appear to be the strongest among bakers sensitized for bakers' allergens; however, nonsensi-

tized bakery workers also report symptoms during working hours.^{9,10} Our study shows that both exposure and sensitization to bakers' or common allergens are independent risk factors for work-related symptoms. This finding corresponds with a previous study of our population of bakers in which atopy was a risk factor in the exposed bakers' population, whereas no association between symptoms and atopy was found among a (unexposed) control population. Furthermore, the independent effects of sensitization for bakers' and common allergens (atopy) appeared to be additive to the risk of work-related symptoms.¹⁷ Similar exposure–response relationships have been found in workers exposed to other occupational allergens, like rat urinary allergen among laboratory animal workers.^{29,30}

The importance of allergic sensitization on the occurrence of work-related symptoms has been illustrated by the good predictability of regression models which included allergy variables. The AUC of the full model of 0.82 corresponds with a good predictability on a scale ranging from 0.5 (no predictive value) to 1.0 (perfect predictive value).²⁶

However, the model with allergy determinants only (model 2) has only marginally less predictability for the risk of work-related symptoms (AUC 0.80, with largely overlapping confidence intervals). This finding may have implications for occupational health services when monitoring employees working in bakeries. For efficiency reasons, it is useful to identify primarily bakery workers at risk of developing work-related symptoms. These workers should be followed more closely than workers with minor risk of work-related symptoms. According to our results, determination of easily obtainable personal characteristics indicative of an allergic predisposition, for example, a history of chronic respiratory symptoms, parental allergy and allergic sensitization to bakers' allergens and common allergens, is adequate to distinguish between high risk and low risk bakery workers. For this purpose, the level of *current* exposure is of less importance. This does not mean that exposure to occupational allergens by itself is not an important issue concerning occupational health and workplace safety. Exposure to occupational allergens is a prerequisite for the development of allergic work-related symptoms, but work-related symptoms can also be no-allergic. In addition, sensitization to occupational allergens does not only reflect current occupational exposure, but may also be the result of any past exposure. Thus, level of current exposure is a well-established risk factor for the development of work-related symptoms, and it still is essential to reduce workplace exposure for reasons of prevention. However, when compared to personal allergic characteristics, it adds only little to the predictability of work-related symptoms.

Results from cross-sectional epidemiology studies may be influenced by low response rates or misclassification on outcome or explanatory variables. In theory, a response rate of 36% of the bakeries contacted may have induced a non-response bias through a greater

readiness of symptomatic subjects to participate, leading to an overestimation of relative risks. Conversely, bakeries with high dust or allergen exposures may have responded less, which may have led to an underestimation of relative risks. However, the reasons for non-response most frequently mentioned were not related to symptoms or disease but to organizational problems, particularly interference with work routine. Also, in most cases the owner/baker alone decided whether to participate or not, resulting in a response of either none or all workers. As a result, the individual response rate was much higher, between 90% and 100%. The opposite effect can be encountered through the "healthy worker effort," by which workers abandoned their occupation because of serious work-related health problems. As this is more likely among more highly exposed workers, that is, traditional bread bakers, relative risks of work-related symptoms may be underestimated because of this selection bias. Because of the strong positive linear trend in the prevalence of work-related symptoms among the job titles in our study population it seems unlikely that these selection biases would have had a major effect on our results.

Differences in sampling strategy and equipment used as well as differences in laboratory measurement methods may lead to different results of exposure assessment. Moreover, the categorization of exposure data into distinctive exposure groups may affect results of exposure studies, in particular those concerning dose-response relationships. Studies on the variability of dust exposure levels have shown that categorization of bakery workers according to job titles is the best way of studying exposure-response relationships.^{31,32} This was confirmed by and large in our study. However, a dose-response relationship with lung function measurements only existed when exposure levels were categorized according to the tertiles of the individual scores; hence, categorization according to job titles apparently

may lead to some misclassification in exposure level assessment. Further comparisons between different ways of categorizing exposure data may be useful to understand exposure-response relationships but would exceed the scope of the present study.

Finally, measurement of self-reported work-related symptoms by means of a questionnaire may lead to misclassification on the outcome variable. Nonetheless, the reason why we used work-related symptoms as outcome variable instead of, for example, a more objective allergy parameter like sensitization to bakers' allergens, is that bakery workers are not likely to report ill or quit their jobs because they are sensitized to bakers' allergens (which they are usually unaware of) but because of their work-related symptoms. To account for confounding attributable to information bias among symptomatic bakery workers the regression models were adjusted for a personal history of chronic respiratory symptoms already existing before working as a baker. Accordingly, we intended to adjust also for pre-existing allergy symptoms, like allergic rhinitis, but it did not appear possible to distinguish reliably between pre-existing (nonwork-related) and work-related allergy symptoms; therefore, accounting for this feature would have lead to an overadjustment of the associations between predictive and outcome variables.

Conclusion

Among bakery workers exposure to inhalable dust, wheat flour and α -amylase is associated with respiratory and work-related symptoms, with sensitization to bakers' allergens and, though only moderately, with decreased pulmonary function. In addition, exposure to high levels of bakery dust, wheat- and α -amylase allergens, parental allergy, sensitization to bakers' allergens and atopy are all independent risk factors for work-related symptoms. Of these, sensitization to occupational allergens and atopy appear to be the

most adequate predictors of work-related symptoms, whereas current exposure levels add only little to their prediction. Therefore, on behalf of good occupational health practice it seems useful to identify bakery workers at risk of work-related symptoms primarily on their allergic status, regarding bakers' as well as common allergens. In addition, special attention is needed for traditional (bread or bread + pastry) bakers since they are likely to have the highest prevalence of sensitization to bakers' allergens and atopy, whereas this category of bakery workers participates the least in periodic occupational health care.

Acknowledgments

We are thankful for the cooperation of the owners, bakers, and employees of the bakeries who participated in the study. We also thank Ms. K. Possel and Ms. K. Van Leemput for the data collection, and the Belgian Federation of Bakers for their contribution to the organization of the study.

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