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Application of a prediction model for work-related sensitization in bakery workers

E.Meijer, MD, PhD[1] ; E. Suarthana, MD, PhD[1,2] ; J. Rooijackers, MD, PhD[1,4]; D.E. Grobbee, MD, PhD[5] ; J.H. Jacobs, MSc[1]; T. Meijster PhD[1] ; J.G.R. de Monchy, MD, PhD[3]; E. van Otterloo[1]; G.B.G.J..van Rooy, MD[1,4]; J.J.G. Spithoven[1]; V.A.C. Zaat[4]; D.J.J. Heederik, PhD[1,5].

1. Institute for Risk Assessment Sciences, Division Environmental Epidemiology, Utrecht University, Utrecht, The Netherlands

2. Community Medicine Department, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

3. Department of Allergology, University Medical Center Groningen, Groningen, the Netherlands

4 . Netherlands Expertise Centre for Occupational Respiratory Disorders, Division Heart and Lungs, University Medical Center Utrecht, Utrecht, the Netherlands.

5. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

Address correspondence and requests for reprints to:

E. Meijer, MD, PhD: Institute for Risk Assessment Sciences, Division Environmental Epidemiology, Utrecht University. Jenalaan 18d, 3584 CK, Utrecht, The Netherlands. Phone +31(30) 2539536. Fax +31(30) 2539499. E-Mail: e.meijer@uu.nl

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ABSTRACT

Identification of work-related allergy, particularly work-related asthma in a (nationwide) medical surveillance program among bakery workers needs an effective and efficient strategy. Bakers at high risk for having work related allergy were indentified by the use of a questionnaire based prediction model for work related sensitization. The questionnaire was applied among 5,325 participating bakers. Sequential diagnostic investigations were performed only in those with an elevated risk. Performance of the model was evaluated in 674 randomly selected bakers who participated in the medical surveillance program and in the validation study. Clinical investigations were evaluated in the firstly referred 73 bakers at high risk. Ninety percent of bakers at risk of having asthma could be identified. Individuals at low risk showed 0.3% to 3.8% work related respiratory symptoms, medication use or absenteeism. Predicting flour sensitization by a simple questionnaire and score chart seems more effective in detecting work-related allergy than serology testing followed by clinical investigation in all IgE class II positive individuals. This prediction based stratification procedure appeared effective in detecting work-related allergy among bakers and can accurately be used for periodic examination, especially in small enterprises where delivery of adequate care is difficult. The approach may contribute to cost reduction.

Key words: amylase; medical surveillance; prediction model ; wheat; work-related asthma; questionnaire

INTRODUCTION

Exposure to high molecular weight flour allergens may result in allergic diseases, such as asthma, allergic rhinitis, conjunctivitis, and dermatitis.[1,2] Work-related asthma is the most serious outcome that accounts for acute morbidity, long term disability, and adverse social and economic impacts.[3,4]

To decrease respiratory allergy in bakery workers, the Dutch Government, in association with labour and industry organizations, agreed to a covenant in 2001. The main goals of this covenant were: dissemination of knowledge among employers and employees about reduction of exposure to workplace allergens, health risks and establishing a health surveillance program. Studies in the Dutch baking industry, flour mills and baking product industries have shown that exposure is high and needs to be reduced considerably to reduce the burden of disease. This can not be achieved over a short time period without structural changes to the production process making primary prevention not easily achievable.[5]

Besides, a "no-effect level" for work related allergy related to flour dust exposure can not be estimated.[6] This implies that even very low exposure levels will lead to the development of sensitization. Therefore, a combination of medical surveillance and exposure reduction in high risk workers seems to be the most (cost) effective alternative for intervention. For that reason we developed a secondary prevention program that aimed to first identify sensitized workers and perform sequential medical investigations only in these workers. However, to find all sensitized workers, all bakery workers (N = 8-10.000) would have to be investigated by skin prick tests or IgE serology, which is inefficient and results in high costs especially because these industries consist of more than 2500 traditional bakeries and about 80 industrial bakeries, flour mills and baking product industries spread all over the country. Sixty percent of the traditional bakeries have less than 5 employees and have a poor coverage by occupational health care services. Moreover, consultation of a company doctor occurs in only a minority of patients with work-related allergy.[7]

We therefore, developed a questionnaire based prediction model to estimate the individual probability of the presence of IgE sensitization to wheat and/or α-amylase allergens. We used IgE sensitization to flour allergens as an outcome because it is strongly associated with already established allergic (asthmatic) diseases as well as subclinical illness.[8,9,10] This model enables risk stratification. Clinical evaluation can therefore, be restricted to workers with an elevated sensitization risk, leaving a considerable number of workers with low risk in which no or less far reaching medical investigations are needed.[11,12]

This paper describes the results of the application of a prediction model among 5,325 workers exposed to flour dust (from baking, milling, and bakery-ingredient industries). Performance of the model was evaluated in 674 traditional and industrial bakers who participated both in the health surveillance program as in a validation study among 890 randomly selected bakers. Results of clinical investigations in 73 firstly referred bakers, at high risk, are reported.

METHODS

The prediction model

The individual probability of sensitization to wheat and/or fungal α-amylase allergens (IgE class 2) was estimated with a questionnaire based prediction model. The model was previously developed with data from a survey among 390 Dutch bakers.[13] For practical application the model, was transformed into a score chart to calculate sum scores. (*Sum score = (asthma attacks*2) + (rhinitis symptoms*2) + (conjunctivitis symptoms*1) + (during work symptoms*1.5).* Each predictor is valued as 1 when present and 0 when absent. Risk groups were calculated using the following cut-off points 0 to 1: low score; 1.5 to 3.0: intermediate score; 3.5 or higher: high score. The model development and the score chart are described more extensively in the Online Depository.

1. Risk stratification. (fig 1)

A short questionnaire with 19 questions, containing the four predictors, was distributed to the bakery workers by instructed consultants who visited all companies. The workers were asked to complete the questionnaire and return it by regular mail. On the basis of their response, every worker was classified into: low, intermediate and high risk of being sensitized to wheat and/or fungal α-amylase.

2. Advice and referral

The results of the scores were communicated by a letter to every worker individually and to the occupational physician. Workers with a low sum score were informed about a low sensitization risk and that no action was indicated. Workers with intermediate scores were invited for diagnostic work-up by their occupational physician. Workers with high sum score were directly referred to the specialized clinic for occupational respiratory diseases.

3. Evaluation of the risk stratification

The accuracy and the impact of the risk stratification were evaluated in data from randomly selected traditional and industrial bakeries. This so-called validation study was based on a random sample of 674 exposed bakers who participated in the Health Surveillance program.[14]

4. Clinical evaluation

Results of advanced medical investigations are described in 73 firstly referred bakers. All bakers visiting the clinic underwent clinical history taking, physical examination, serology tests, spirometry, and non-specific bronchial hyper responsiveness (NSBHR) to histamine. Peak expiratory flow recordings (PEFR) and NSBHR were measured after a continuous period of at least two weeks both at and off from work. Workers with an established diagnosis were referred back to their occupational physician.

Statistical Analyses

All statistical analyses were performed with SPSS 15.0 for Windows (Statistical Products and Service Solution, Inc, Chicago). Prevalence rates were compared using the χ^2 test. Differences between means were compared using Student's t test or ANOVA. Discrimination was assessed by calculating the area under the Receiver Operating Characteristic curve (ROC area). The diagnostic model was developed using methods described by Harrell.[15] Statistical significance was defined as p-value of less than 0.05 (two tailed).

RESULTS

Between November 2004 and November 2006, 6714 workers from 1637 traditional bakeries and 1760 workers from 74 industrial bakeries were registered for participation in the program (Table 1). They covered almost all industrial and half of the traditional enterprises throughout the country. Of 1637 registered traditional bakeries, 1189 (72.7 %) participated in the program whereas all of the registered industrial bakeries participated. A short questionnaire, specifically developed for this purpose, was handed out to 8,396 bakery workers and received back from 5,325 (63.4%). Sixty percents of the workers in the traditional and 80% of the workers from the industrial bakeries sent back the short questionnaire. In the flour milling (n=10) and baking products companies (n=13) almost sixty percent of the workers joined the program. The highest rate of workers with low scores (60%) were found in traditional bakers and the highest rate of high scores (21%) in industrial bakers participating in the program (Table 2). A small non-participation study among 86 bakers showed that two third of them either did not receive the questionnaire, or forgot to send it back to the institute. The percentage of workers worried that the results could be used in an unfavourable way by their employer was 3%.

Table 3 outlines predicted and observed sensitization rates across different scores in workers participating in the validation study. The predicted mean probability of sensitization to wheat and/or fungal α-amylase in these workers was lower (18.7%) than the observed sensitization

rate (20.1%). The predicted sensitization rate to wheat and/or fungal α-amylase in the high score group was somewhat higher (42.7%) than the observed rate (41.5%) and lower in the low score group (9.3% compared to 12.9%). Wheat sensitization was 5.9 times higher (46/135: 34.1%) in workers with high scores compared to workers with low scores, and showed 16.3 % (22/135) α-amylase sensitization (2.0 times higher than individuals with low scores). Workers sensitized to wheat allergens had 75.3% (64/85) intermediate and high scores, leaving 24.7% (21/85) reporting low scores. Table 4 shows the distribution of asthma related symptoms, work-related symptoms, absenteeism, and inhalation medication across different scores. Workers with low scores were statistically significantly older (mean 41.6 years) than workers with intermediate and high scores. On average they also worked longer (16.3 years) in their current job than bakers with intermediate and high scores. About 70% of workers reporting asthma attacks in the last 12 months and about 60 % reporting inhalation medication (corticosteroids & long acting β2 mimetics or short acting β2 mimetics) had high scores. Only 9.1% of bakers reporting wheezing had low scores. No low scores were identified in workers reporting asthma attacks during or after work. A finding understandably attributed to the fact that one of the questions was a predictor of the diagnostic rule. Bakers with work related eye or nasal symptoms showed high scores in 69 % respectively 61 % individuals, leaving only 5% respectively 10% of these symptoms in the low score group. Absenteeism was only detected in high and intermediate score bakers. And a change in job or task due to work related allergy was in 7 of the 8 cases found in bakers with high scores. Results in the low score group (low predicted probability of IgE sensitization to flour allergens) were analysed to evaluate the extent of misclassifying flour sensitization and the impact on detecting respiratory allergy. Table 5 shows the distribution of wheezing symptoms, work-related eye and nasal symptoms, medication use for bronchial asthma, across sensitization to flour allergens in workers with low scores. In the low score group 12.9% (47/365) bakers were sensitized to wheat and/or α-amylase allergens. Of the 47 bakers, 29

(61.7%) were sensitized to α-amylase and 21 (44.1%) to wheat. Only 6 bakers (1.6%) with low scores used inhalation medication (corticosteroids & long acting β2 mimetics and or short acting β2 mimetics). Symptoms reported during daily work, that improved if not working, including wheeze, conjunctivitis, or rhinitis were not reported in sensitized bakers with low scores.

Clinical evaluation was completed in 73 (69 traditional and 4 industrial bakers) firstly referred individuals (Table 6). Bakers with high scores, as calculated from the screening questionnaire, were advised to contact the clinic directly. Bakers with intermediate scores were first evaluated by their occupational physician and, if necessary, referred to the clinic. Two bakers with low scores visited the clinic on their own initiative. Of 73, 39.7% were wheat and 9.6% α-amylase sensitized. Rye serology was only assessed in workers reporting symptoms related to rye exposure (n=14). Eight out of 14 (57.1%) bakers were sensitized. Of these 8 workers, 75% (6) were also sensitized to wheat allergens. Rhinitis and conjunctivitis either isolated or in combination, was diagnosed in 69.9% (51/73) of the individuals of whom 58.8% (30/51) reported their rhinitis to be associated with their work. Bronchial asthma (general and work-related), was diagnosed in 25 (34.3 %) bakers attending the clinic, 10 (13.7 %) bakers had occupational asthma, and 3 (4.1 %) cases could be assigned as having work-exacerbated asthma. Most of the asthma cases (80%) were detected in the high score group. The prevalence of work-related rhino-conjunctivitis in bakers with work-related asthma was 83% (10/12) and 31% (4/13) in bakers with asthma diagnosed as not work-related (data not shown). In 8 (11%) bakers no clinical disease could be diagnosed. Five of them presented themselves with an intermediate sore, while none of them was sensitized to specific as well as common allergens. In three bakers COPD, hypertension, and hyperventilation were diagnosed.

DISCUSSION

Prediction models for various outcomes have been developed in the last decades for clinical diagnosis in a comprehensive and scientific way. The essence of diagnosis concerns the level of probability with which the outcome (illness) is known to be present or absent in a particular person at a particular time.[16,17] The development of diagnostic prevalence/probability functions for a given outcome, in a given domain, makes it possible to find a small number of predictors to constitute the best possible knowledge base for diagnosis. However, few prediction models have been developed for occupational respiratory medicine purposes or found an application in surveillance programs.[18-20] This is surprising, because with the use of prediction models risk groups may be identified easily in occupational health practice or medical surveillance programs specifically aiming at secondary prevention. Our study demonstrates that with a simple short questionnaire, developed to predict flour sensitization, work related allergy can accurately be identified.

In this medical surveillance program among all eligible bakers in the Netherlands, a diagnostic rule was applied to predict the presence of wheat and/or fungal α-amylase sensitization. We stratified bakers into risk groups to inform them about the probability of having an allergic disease and to assist in clinical referral. Risk stratification resulted into a high score group for clinical investigation, an intermediate score group for medical follow up by occupational physicians, and a low score group comprising about 57% of the workforce in which medical investigations were supposed not indicated. Allergic diseases were diagnosed more specifically in an outpatient clinic specialised in occupational respiratory disorders. Given the large number of bakeries spread all over the country, we presented the questionnaire to the individual baker by trained consultants visiting the bakery. With this approach we attained a rather satisfactory overall response rate of about 63%, with the highest rate in industrial bakers (79%). This is comparable to other sector wide surveillance programs

which for instance exist in the construction industry (personal communication). Surprisingly, only 3 % of the non-responding bakers were worried that the results could be used in an unfavourable way by their employer.

In general, most prediction models show a reduced accuracy when applied in new populations [12]. We have not assessed this so-called external validation of our model. We have, however, validated the model internally. Differences in sensitization rate may still be expected for the total population (predicted 18.7 % versus observed 20.1 %) as well across different scores (table 3). Furthermore, our study also showed that the model discriminated wheat sensitization more accurately than sensitization to α-amylase allergens. In bakers with a high score, 34.1% wheat sensitization was found compared to 16.3 % α-amylase.

Stratification and misclassification

The choice of cut off points to classify workers into high, intermediate, or low risk (probability) groups is crucial and determines referral policy and misclassification rate. A balance must be sought between an acceptable proportion of missed cases and unnecessary referrals. Although the used model was developed with the best available knowledge, derived from a well-designed appropriate study, failures and difficulties for various reasons can be expected. One might wonder whether it is acceptable to miss 35.6% (47/132) flour sensitized individuals at the gain of minimizing the number of individuals (56%) to be evaluated by occupational physicians and clinical pulmonologists.

Misclassification of workers in the high score group wrongly assigned as “sensitized” is less dramatic because they present respiratory health complaints that need to be evaluated further, as is presented in the clinical evaluation. However, on the basis of our validation sample we estimated that 12.9% of the workers with a low calculated sensitisation probability are wrongly assigned as “not- sensitized” to flour allergens . This is a serious problem because no further medical investigation was advised. These workers may be asymptomatic, or deny

symptoms due to poor perception. When bakers were re-investigated as part of the validation study, the low score group showed very low prevalence's of reported wheezing (2.7 %), work-related wheezing (0.3%), work-related conjunctivitis (1.0%), and work-related rhinitis (3.8%). Although, asthma attacks were not reported in the low score group, the non-detection of current asthmatics is a serious problem especially in sensitized workers. However, we found 6 (1.6%) bakers treated with inhalation medication (corticosteroids & long acting β2 mimetics and/or short acting β2 mimetics) in the low score group, that may indicate respiratory problems. Three of them were sensitized to flour allergens. None of the sensitized bakers reported work-related asthma attacks, work-related wheezing or work-related upper respiratory symptoms. Therefore, it seems rational to conclude that they belong to a group of sensitized workers with their respiratory disorder (asthma or COPD) well treated (no respiratory symptoms) and/or their exposures optimally controlled. If we extrapolate these findings to all investigated traditional and industrial bakers,0.9% (1.6% x 55.2%) individuals with possible bronchial asthma or COPD are not detected because of having low scores, comprising 41 (0.9 x 4612) individuals.

Ideally, we would like to have information about the clinical evaluation of bakers with a low score that would give more accurate evidence of the existence of occupational allergic diseases, like work-related asthma etc. However, our approach to analyze the responses of 365 bakers with low scores gives sufficient indication that the number of false negatives is acceptable. We only found 6 bakers (1.6%) using some kind of inhalation medication that could be attributed to having asthma or COPD (or no-disease), and not a single worker indicated having (work-related) asthma. We therefore think that the evaluation of this group is rather robust. Besides, a clinical investigation of workers already informed to have a low probability and advised that no medical investigations were needed, would undoubtedly lead to substantial biased results. We therefore think our approach by calculating the expected prevalence of a proxy for asthma/COPD (use of inhalation medication) gives an acceptable

and sufficient accurate result also given the size of the group of bakers.

The alternative of not missing sensitized workers is to investigate all bakers (n=4612) by serological tests and refer only workers with positive IgE class II for clinical evaluation. An approach that would lead not only to high costs but would also result in undetected symptomatic bakers not sensitized to flour allergens. Again, if we look at cases reporting inhalation medication for their asthma, 5.5% (28/508) symptomatic bakers not sensitized to wheat and/or α-amylase allergens will be missed and excluded from advanced medical follow-up (data not shown). So, choosing for the alternative and investigate all bakers by serology would lead to a 6-times (5.5/0.9) higher number of non-detected possible asthma cases compared to our method by means of a prediction model for flour sensitization.

Clinical evaluation

Among the 73 referred bakers with intermediate and high scores one third had bronchial asthma. Eighty percent of these asthmatics reported high scores. Occupational asthma was diagnosed in 10 cases (40%) and work-exacerbated asthma in three cases (12%), leaving 12 cases diagnosed as "general" asthma (for definitions see Online Depository). Three "general" asthma cases were sensitized to wheat allergens. All three bakers reported work-related upper respiratory symptoms and use of respiratory medication. However, they were regarded as "general" asthma because diagnostic tests (*eg,* positive serial PEFR's or significant improvement of histamine response (at the end of a working period compared with a period away from work) could not be assessed appropriately. Nine "general" asthma cases were not sensitized to any of the workplace allergens (wheat, α-amylase, soya or rye). Unfortunately, serial PEFR's and work-related histamine response could not be assessed in all of them because of constraints put by the employer. So, it seems plausible that some cases may be more correctly classified as occupational asthma or work-exacerbated asthma and not as "general" asthma. These results point toward the well known difficulties in establishing a

proper diagnosis of asthma in the workplace. Especially for occupational asthma and work-exacerbated asthma where an improvement in symptoms during times away from work that worsen on days with regular exposures must be objectively assessed.

Work related asthma may be accompanied or preceded by symptoms of rhinitis or conjunctivitis. These symptoms showed to be present in 70% of these asthmatics. A clear association with their work could be established in about 40%. In bakers with occupational asthma or work-exacerbated asthma, work-related rhinitis and/or conjunctivitis were reported in the majority of cases (85%) while in "general" asthma these symptoms were found in 25% patients. Besides, about 50% (14 out of 30) patients with work-related rhinitis and/or conjunctivitis were found to have coexisting asthma. These findings stress the importance of work related rhinitis and/or conjunctivitis associated with work related asthma that are however, difficult to test objectively.

This surveillance program and its evaluation demonstrate that by applying a simple questionnaire model to predict the probability of flour sensitization, work related allergy can accurately be detected in bakers with an elevated risk. Ninety percent of bakery workers with asthma could effectively be identified in this way. The model discriminated wheat sensitization more accurately than sensitization to α-amylase allergens. Workers with a low sensitization probability showed very low rates (0.3% - 3.8%) of work related respiratory symptoms or other indicators of disease (medication use, absenteeism). Predicting flour sensitization by means of a simple questionnaire and a score chart is probably more effective in detecting work-related allergy than serology testing followed up by clinical investigation in all IgE class II positive individuals. Therefore, this model can fairly and straightforwardly be incorporated into the already existing and statutory-regulated periodic occupational health examinations among bakery workers, especially in small enterprises where delivery of adequate care is difficult. The approach is expected to contribute to costs reduction.

Contributors

EM, DH, and ES developed the health surveillance program and study design of the validation study. EM, ES, VZ, EO, and JS took part in the acquisition of data. JR and FR were involved in the clinical evaluation. EM, DH and ES analysed and interpreted the data and drafted the manuscript.

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Figures:

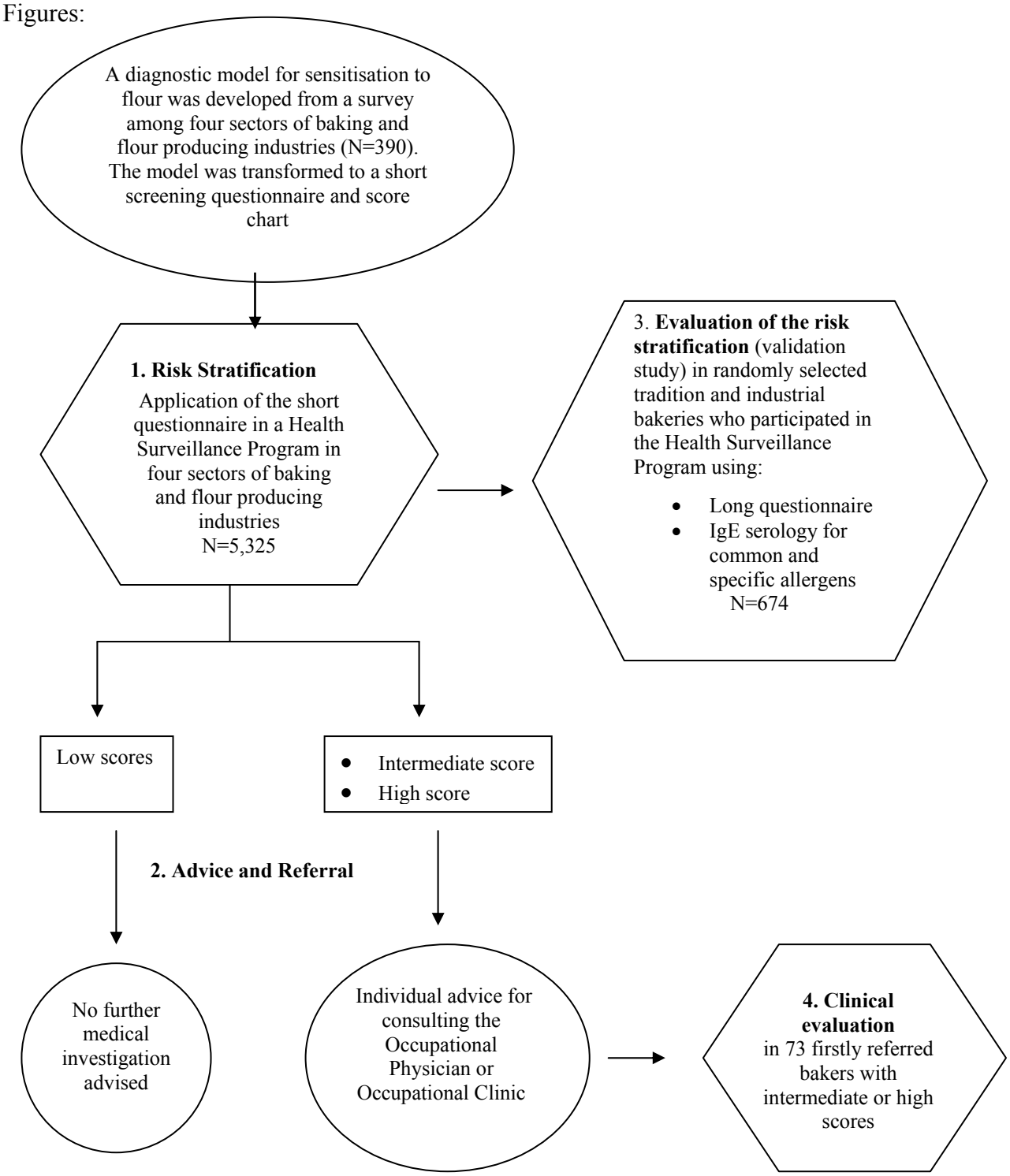

Fig 1. Design and participation in the Health Surveillance program and evaluation of the risk stratification in the validation study

Tables

Table 1. Participation among different industries enrolled in the health surveillance program.

	Traditional bakeries	Industrial bakeries	Flour mills	Bakery ingredients industries	Total
Registered employers n	1,637	74	†	†	1711
Participating employers n	1,189	74	10	13	1,286
Employees in participating industries n	5,398	1,760	686	552	8,396
Participating employee's n (%)	3,214 (59,5)	1,398 (79.4)	393 (57.0)	320 (58.0)	5,325 (63.4)

† Numbers not known in milling, and baking products industries

Data presented as column (%)

Table 2. Score distribution among different bakery industries enrolled in the health surveillance program.

	Traditional bakeries	Industrial bakeries	Flour mills	Bakery ingredients industries	Total
Low Score. n (%)	1,946 (60.5)	721 (51.6)	213 (54.2)	179 (55.9)	3,059 (57.4)
Intermediate Score. n (%)	706 (22.0)	379 (27.1)	109 (27.7)	88 (27.5)	1,282 (24.1)
High Score. n (%)	562 (17.5)	298 (21.3)	71 (18.1)	53 (16.6)	984 (18.5)

Data presented as column (%)

Table 3. Performance of the prediction model in 674 randomly selected traditional and industrial bakers.

	Low score	Intermediate Score	High score	Total
Predicted IgE sensitization (n)	**372**	**163**	**139**	**674**
Wheat and/or α-amylase allergens. Mean (SE)	9.3 (.0)	19.8 (.4)	42.7 (1.1)	18.7 (.6)
Observed IgE sensitization (n)	**365**	**158**	**135**	**658**
Wheat and/or α-amylase allergens. % (N)	12.9 (47)	18.4 (29)	41.5 (56)	20.1 (132)
Wheat (IgE ≥.7 kU/L). % (n)	6.0 (21)	11.4 (18)	34.1 (46)	12.9 (85)
α-amylase (IgE ≥.7 kU/L). % (n)	8.0 (29)	12.0 (19)	16.3 (22)	10.6 (70)

Data presented as column % (n), unless otherwise stated.

Table 4. Performance of the prediction model in 674 randomly selected traditional and industrial bakers. Prevalence of respiratory symptoms, medication use, absenteeism, and job change across different scores.

	Low score	Intermediate Score	High score	Total
	372 (55.2)	163 (24.2)	139 (20.6)	674
Age. mean (SD)	41.6 # (11.1)	36.9 (10.6)	38.8 (10.4)	39.9 (11.0)
Working years. mean (SD)	16.3 # (11.7)	12.1 (8.9)	14.0 (10.2)	14.8 (10.9)
Respiratory symptoms				
Wheezing last 12 months	10 (9.1)	37 (33.6)	63 (57.3)	110 (100.0)
Asthma attack last 12 months *	0 (.0)	7 (29.2)	17 (70.8)	24 (100.0)
Awakened by an asthma attack last 12 months	0 (.0)	4 (30.8)	9 (69.2)	13 (100.0)
Asthma attack after exercise last 12 months	0 (.0)	6 (33.3)	12 (66.7)	18 (100.0)
Work related respiratory symptoms and other characteristics				
During work asthma attacks that improve if not working	0 (.0)	4 (22.2)	14 (77.8)	18 (100.0)
After work asthma attacks	0 (.0)	1 (8.3)	11 (91.7)	12 (100.0)
During work wheezing that improves if not working *	1 (2.2)	7 (15.6)	37 (82.2)	45 (100.0)
During work eye symptoms that improves if not working *	4 (5.0)	21 (26.3)	55 (68.8)	80 (100.0)
During work running nose or sneezing that improve if not working *	14 (9.9)	41 (28.9)	87 (61.3)	142 (100.0)
Absenteeism due to asthma	0 (.0)	6 (50.0)	6 (50.0)	12 (100.0)
Change of job or task within the bakery due to work related allergy	0 (.0)	1 (12.5)	7 (87.5)	8 (100.0)
Medication use				
Use of medication for asthma in the last 12 months	6 (9.7)	16 (25.8)	40 (64.5)	62 (100.0)

Long acting β2 mimetics	0 (.0)	2 (100.0)	0 (.0)	2 (100.0)
Inhalation corticosteroids & Long acting β2 mimetics	5 (9.8)	14 (27.5)	32 (62.7)	51 (100.0)
Short acting β2 mimetics	5 (12.2)	13 (31.7)	23 (56.1)	41 (100.0)

Data presented as row (%), unless otherwise stated.

*: Questions identical to a predictor in the model

Statistically significantly different from Intermediate and High score ($p < 0.03$)

Table 5. Performance of the prediction model in bakers with low scores.

	Not Sensitized to wheat or α-amylase	Sensitized to wheat or α-amylase	Total
Bakers n (%)	318 (87.1)	47 (12.9)	365* (100.0)
Age	41.5 (11.4)	41.6 (9.2)	41.5 (11.2)
Working years	16.4 (11.9)	15.7 (11.2)	16.3 (11.8)
Questionnaire responses			
Wheezing last 12 months	9 (2.9)	1 (2.2)	10 (2.8)
During work wheezing that improves if not working	1 (.3)	0 (.0)	1 (.3)
During work eye symptoms that improve if not working	4 (1.3)	0 (0.0)	4 (1.1)
During work running nose or sneezing that improve if not working	13 (4.1)	0 (0.0)	13 (3.6)
Use of medication for asthma in the last 12 months	3 (1.0)	3 (6.4)	6 (1.6)
Inhalation corticosteroids & Long acting β2 mimetics	3 (1.0)	2 (4.7)	5 (1.4)
Short acting β2 mimetics	2 (.7)	3 (7.0)	5 (1.4)

* 372 individuals with low scores. From 7 individuals no blood was drawn.

Data presented as column (%)

Table 6. Results of the clinical evaluation

	Low score	Intermediate score	High score	Total
Sensitization	2	25	46	73
Wheat allergens (IgE ≥.7 kU/L)	1 (50.0)	9 (36.0)	19 (41.3)	29 (39.7)
α-amylase allergens (IgE ≥.7 kU/L)	0 (0.0)	0 (0.0)	7 (15.2)	7 (9.6)
Rye allergens (IgE ≥.7 kU/L)[†]	0/1 (0.0)	2/3 (67.0)	6/10 (60.0)	8/14 (57.1)
Soya allergens (IgE ≥.7 kU/L)	0 (0.0)	2 (8.0)	1 (2.2)	3 (4.1)
Phadiatop (IgE ≥.35 kU/L))	2 (100.0)	8 (32.0)	24 (52.2)	34 (46.6)
Non specific bronchial hyper responsiveness				
Histamine PD $_{20\ (\leq 2.5\ mg)}$	0/2 (0.0)	8/25 (32.0)	20/42 (47.6)	28/69 (40.6)
Clinical diagnoses				
No clinical disease	0 (0.0)	5 (20.0)	3 (6.5)	8 (11.0)
COPD, Hypertension, Hyperventilation	0 (0.0)	0 (0.0)	3 (6.5)	3 (4.1)
Asthma (general and work-related)	0 (0.0)	5 (20.0)	20 (43.5)	25 (34.3)
Occupational asthma	-	2 (8.0)	8 (17.4)	10 (13.7)
Work-exacerbated asthma	0 (0.0)	0 (0.0)	3 (6.5)	3 (4.1)
Rhinitis, rhinoconjunctivitis	1 (50.0)	16 (64.0)	34 (73.9)	51 (69.9)
Work-related allergic rhinitis or rhino conjunctivitis	1 (50.0)	9 (36.0)	20 (43.5)	30 (41.1)

[†] Only in workers reporting symptoms when exposed to rye. n=14
Data presented as n (column %).