

SPT allergens

- *Dermatophagoides pteronyssinus*
- *Dermatophagoides farina*
- *Alternaria alternate*
- *Cladosporium herbarium*
- *Blatella germanica*
- Dog
- Cat
- Horse
- Timothy
- Mugwort
- Birch

Calculation of PD20

PD20 = $A + ((20-B)*(C-A)) / (D - B)$ where A = administered dose methacholine before 20 percent decrease in FEV₁, B = percent decrease in FEV₁ after A, C = administered dose methacholine after 20 percent decrease in FEV₁ and D = percent decrease in FEV₁ after C.

Definitions for definition according to GINA

To be considered as having controlled asthma the subject had to: have day time symptoms \leq 2/week, have no limitations in activities due to asthma, no night time symptoms, per required need (PRN) medication $<$ 3/week, FEV₁ % of predicted $>$ 80% and no exacerbations during the last 12 months. To be considered as having partly controlled asthma the subject had to have any one out of: day time symptoms \geq 3/week, limitations in activities due to asthma, night time symptoms, per required need (PRN) medication \geq 3/week, FEV₁ % of predicted $<$ 80% and at least one exacerbation during the last 12 months. To be considered as having uncontrolled asthma the subject had to have at least 3 out of: day time symptoms \geq 3/week, limitations in activities due to asthma, night time symptoms, per required need (PRN) medication \geq 3/week, FEV₁ % of predicted $<$ 80% and at least one exacerbation during the last 12 months.

Rationale behind definition of multi-symptom asthma

The questionnaire we used has been used in several studies in Sweden and other countries since 1985. Already in the late 1980s and early 1990s it was found that recurrent wheeze and attacks of shortness of breath, two of the core symptoms of multi-symptom asthma, correlated with impaired lung function (Lundbäck et al. *Tuber Lung Dis*, 1994 Apr;75(2):116-26), this was true particularly in subjects with asthma. Further the same symptoms correlated with hyper-reactivity particularly in asthmatics (Lundbäck et al. *Allergy*, 1993 Feb;48(2):117-24). This was also found in an Estonian study (Meren et al. *J Asthma*, 2005 Jun;42(5):357-65). In 2007-2008 a large interview study of 789 subjects (of totally 999 invited) with physician-diagnosed asthma derived from a population study in Stockholm, Sweden, underwent structured interviews, and different morbidity variables were considerably more common in

those reporting the above symptoms. The triggers exertion and cold were selected, because they are less biased compared with symptoms caused by irritants such as tobacco smoke, dust, strong smelling scents etc, which also strongly correlate with sensoric hyper reactivity without bronchial obstruction. Further, the large EMFUMOSA has shown that triggers connected to allergy, i.e. pollen and furry animals, are inappropriate to use in identifying severe asthma. We thus had strong evidence for our hypothesis that the selected questions would correlate with a more severe asthma than asthma in general.

Definitions

- *Physician-diagnosed asthma*: “Have you been diagnosed as having asthma by a doctor”.
- *Asthma medication*: “Do you currently use asthma medicine (permanently or as needed)”.
- *Attacks of shortness of breath*: “Do you presently have, or have you had in the last 10 years, asthma symptoms (intermittent breathlessness or attacks of shortness of breath; the symptoms may exist simultaneously with or without cough or wheezing)” and “Have you had these symptoms within the last year”.
- *Recurrent wheeze*: “Do you usually have wheezing or whistling in your chest when breathing”.
- *Any wheeze*: “Have you had whistling or wheezing in the chest at any occasion during the last 12 months”.
- *Dyspnoea*: “Do you get breathless when you walk on level ground with people of your own age”.
- *Breathlessness – exertion*: “Do you usually have breathlessness, wheeze or severe cough on exertion”.
- *Breathlessness – cold*: “Do you usually have breathlessness, wheeze or severe cough in cold weather”.
- *Breathlessness – exertion in cold*: “Do you usually have breathlessness, wheeze or severe cough on exertion in cold weather”.
- *Difficult breathing after use of pain-killer*: “Have you ever had any difficulty with your breathing within 3 hours after taking a pain killer”.
- *Chronic bronchitis ever*: “Have you ever had chronic bronchitis, COPD or emphysema”.
- *Chronic productive cough*: Sputum production for at least 3 months during two subsequent years, Sputum production was defined as answering yes to “Do you usually have phlegm when coughing or do you have phlegm in the chest which is difficult to bring up”.

- *Chronic rhinitis*: Yes to “Do you have a blocked nose more or less constantly” and/or “Do you have a runny nose more or less constantly”.
- *Allergic rhinitis*: “Have you now, or have you ever had, allergic rhinitis (hay-fever) or allergic eye catarrh”.
- *Occupational exposure*: “Have you been heavily exposed to gas, dust or fumes at work”.
- *Smokers* reported smoking during the year preceding the survey .
- *Ex-smokers* reported having quit smoking at least 12 months preceding the survey.
- *Ever smoker* were either smokers or ex-smokers.
- *Non-smokers* reported neither smoking nor ex-smoking.
- *Age at onset*: response to “How old were you when you developed asthma”.
- *Area of residence* was categorised according to population density and location. Metropolitan Gothenburg with more than 500 000 inhabitants and towns/villages in West Gothia according to size: towns with more than 10 000 inhabitants, towns with 2 000 - 10 000 inhabitants, villages with 500 – 2 000 inhabitants and villages and rural areas with less than 500 inhabitants.
- *Family history of asthma*: “Do any of your parents or sibling have, or have had, asthma?”;
- *Family history of allergy*: “Do any of your parents or sibling have, or have had, allergic rhinitis or allergic eye catarrh”;
- *Rural childhood*: “Did you live in country-side (i.e. not town or suburb) during your first five years of life”;
- *Farm childhood*: “Did your family live on a farm during your first five years of life”

Comparison between multinomial and binominal regression models

Independent variables		Dependant variables					
		Multi-symptom asthma vs. non-asthma		Multi-symptom asthma vs. other asthma		Other asthma vs. non-asthma	
Variable	Category	Binominal OR (95% CI)	Multinomial OR (95% CI)	Binominal OR (95% CI)	Multinomial OR (95% CI)	Binominal OR (95% CI)	Multinomial OR (95% CI)
Family history	Asthma-, Allergy-	1	1	1	1	1	1
	Asthma+, Allergy-	2.55 (1.64 - 3.97)	2.56 (1.65 - 3.98)	1.12 (0.69 - 1.82)	1.05 (0.65 - 1.69)	2.43 (1.95 - 3.03)	2.45 (1.97 - 3.05)
	Asthma-, Allergy+	2.73 (2.00 - 3.72)	2.77 (2.04 - 3.77)	1.55 (1.09 - 2.21)	1.5 (1.07 - 2.11)	1.84 (1.56 - 2.16)	1.85 (1.57 - 2.17)
	Asthma+, Allergy+	7.34 (5.53 - 9.74)	7.53 (5.69 - 9.96)	1.69 (1.24 - 2.31)	1.59 (1.17 - 2.17)	4.61 (3.94 - 5.38)	4.73 (4.05 - 5.52)
Smoking	Non-smokers	1	1	1	1	1	1
	Ex-smokers	1.13 (0.86 - 1.49)	1.15 (0.88 - 1.51)	0.78 (0.57 - 1.05)	0.81 (0.60 - 1.09)	1.43 (1.24 - 1.65)	1.42 (1.23 - 1.64)
	Smokers	1.31 (1.01 - 1.71)	1.31 (1.01 - 1.71)	1.25 (0.93 - 1.69)	1.29 (0.96 - 1.73)	1.05 (0.90 - 1.22)	1.02 (0.88 - 1.19)
Age (years)	16-30	1	1	1	1	1	1
	31-45	1.02 (0.75 - 1.38)	1.06 (0.78 - 1.43)	1.01 (0.72 - 1.41)	1.09 (0.75 - 1.44)	1.01 (0.87 - 1.18)	1.02 (0.88 - 1.19)
	46-60	1.19 (0.87 - 1.62)	1.22 (0.9 - 1.66)	1.62 (1.14 - 2.29)	1.64 (1.17 - 2.3)	0.74 (0.62 - 0.87)	0.74 (0.63 - 0.88)
	61-75	1.51 (1.09 - 2.11)	1.56 (1.13 - 2.16)	1.94 (1.33 - 2.82)	2.03 (1.41 - 2.93)	0.76 (0.63 - 0.92)	0.77 (0.64 - 0.92)
Occupational exposure	Yes	2.03 (1.61 - 2.56)	2.08 (1.65 - 2.63)	1.54 (1.18 - 1.99)	1.56 (1.20 - 2.01)	1.33 (1.16 - 1.52)	1.34 (1.17 - 1.53)
Sex	Women	1.56 (1.24 - 1.97)	1.61 (1.28 - 2.02)	1.38 (1.07 - 1.78)	1.47 (1.14 - 1.89)	1.09 (0.97 - 1.23)	1.1 (0.97 - 1.23)