

COHORT PROFILE

Cohort profile: The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort

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Summary

The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort was set up in The Netherlands with two main aims: to investigate the effect of mite-allergen avoidance on the incidence of childhood asthma (Intervention study) and to assess lifestyle and environmental risk factors for childhood asthma (Natural History study). The baseline study population consisted of 3963 children born in 1996–1997. Questionnaires were completed by parents during pregnancy, when the child was 3 months old, then annually from 1 up to 8 years and by parents as well as children at 11 and 14 years. Data were obtained on child and family characteristics, a wide range of environmental and lifestyle exposures and on asthma and other allergic and respiratory outcomes. Home visits and clinical examinations were conducted in sub-groups at the ages of 1, 4, 8 and 12 years to obtain objective measures. These included anthropometric measures, measurements of lung function, bronchial hyper-responsiveness and blood pressure, house dust and blood samples, which were used to determine total and specific IgEs, cholesterol and HbA1c and to extract DNA. More information on the data available in the PIAMA study can be found at <http://www.birthcohorts.net/> and <http://www.enrieco.dk/Default.asp> and researchers interested in collaboration are invited to contact the principal investigators via alet.wijga@rivm.nl.

Why was the cohort set up?

In the 1980s and early 1990s, the prevalence of asthma in The Netherlands substantially increased, especially in children. This rising trend and the lack of understanding of its causes were reasons for major concern among public health policymakers. In 1992, the Public Health Council of The Netherlands issued a report entitled *Indoor Allergens, Allergy and the Development of Chronic Respiratory Diseases*. The report addressed the question whether reduction of exposure to indoor allergens early in life would prevent or delay the development of inhalant allergies and asthma in children. The Council recommended that an intervention trial should be set up to evaluate the effectiveness of measures to reduce early postnatal exposure to indoor allergens. In conjunction with the proposed Intervention study, a Natural History study was set up to investigate the many questions surrounding the development of inhalant allergy and asthma in the general population.

The intervention part and the natural history part were integrated into one study: the PIAMA birth cohort study with two main aims: (i) to investigate the effect of mite-allergen avoidance on the incidence of asthma and allergy in childhood (Intervention study); and (ii) to investigate lifestyle and environmental (indoor and outdoor) risk factors for childhood asthma and allergy (Natural History study).

The intervention consisted of application of mattress and pillow covers onto the bed of the infant and the parents' bed. Participants of the intervention study were randomly allocated to receive either 'active' (mite-impermeable) covers or 'placebo' (standard cotton) covers. No intervention was applied in the Natural History study. At the start of the study, the length of follow-up was planned to be 8 years to allow sufficient time for allergic sensitization and symptoms to develop. The original design of the PIAMA study has been described in detail in 2002.¹

In the course of the study genetic and genomic studies were incorporated also. Already in the early years of the study it became apparent that not only asthma, but also overweight was increasing in children in The Netherlands and childhood overweight rapidly developed into a major public health problem. In the PIAMA study, weight and height data had been collected annually since birth together with a wide range of environmental and lifestyle factors. Thus, a substantial number of overweight-related study questions could be addressed in addition to the questions that the study was originally designed to answer.

The study was highly successful both in terms of follow-up rates and in terms of the wealth of data obtained. These success factors in combination with new research questions that came up during the course of the study were reason for the investigators to extend the follow-up beyond the age of 8 years and also to broaden the scope of the health outcomes investigated. Three years after the originally planned 8 years of follow-up had been completed, the remaining participants were invited to participate in 2 more waves of data collection at the age of 11–12 years and at the age of 14–15 years. When the study was thus extended to follow the children up into early adolescence, early markers of cardiometabolic risk, such as blood pressure, serum cholesterol concentrations and HbA1c, were included in the study as health outcomes besides asthma and allergy.

Who is in the cohort?

The planned sample size of the intervention arm of the cohort was 800 'high risk' children (children of allergic mothers, defined as mothers with at least one of the following: asthma ever, pet allergy, house dust mite allergy or nasal allergy such as hayfever). Of these 800 high risk children, 400 were to be allocated to the intervention group and 400 to the placebo group. The Natural History arm of the cohort was planned to consist of 400 high risk children, who received neither an active nor a placebo intervention, and of 2500 low risk children (children of non-allergic mothers). A validated screening questionnaire was used to identify allergic and non-allergic mothers.² Recruitment of participants from the general population took place in 1996–1997 through 52 antenatal clinics in three different regions of The Netherlands.

A total number of 10 819 pregnant women completed screening questionnaires of which 10 232 were usable; 29% of these women were classified as 'allergic'. For the Intervention study, 2015 allergic women were invited to participate in the study and 855 (42%) agreed. For the Natural History study, 764 allergic and 5083 non-allergic women were invited and 472 (62%) and 2819 (55%) agreed to participate, respectively. All participants gave written informed consent. When recruitment was completed, the total study population of the PIAMA cohort thus consisted of 4146 pregnant women (31% allergic); the total number of children at baseline was 3963. The difference between the number of pregnant women and the number of children in the study ($n=183$; 4.4%) was partly due to miscarriages and stillbirths and partly due to mothers being lost to follow-up without ever having completed a postnatal questionnaire. Characteristics of the study population are shown in Table 1.

Participants were recruited from the general population. We compared the baseline characteristics of the study population with available information on the general population of The Netherlands. According to data from Statistics Netherlands, 22% of adults in The Netherlands were highly educated in 2001³ and 15% of children born in 1997 in The Netherlands had at least one non-Western parent.⁴ In the PIAMA population, more parents are highly educated and fewer parents are from non-Western countries (see Table 1), reflecting the common phenomenon that in research involving lengthy questionnaires, more highly educated native speakers are likely to participate than the lower educated and non-native speakers. The PIAMA population was similar to the general population in the mid-nineties with respect to maternal age at childbirth⁵ and with respect to breastfeeding,⁶ but the prevalence of low birthweight (<2500 g) was lower in PIAMA than in the general population (7%).⁷ No comparison could be made for smoking prevalence as the PIAMA questionnaires specifically asked about parental smoking in the home. Maternal allergy was used to define children at high risk for asthma and allergy and to allocate children to different study arms (active intervention, placebo intervention and natural history).

Frequency of follow-up

Questionnaires for parental completion were administered during pregnancy, at the child's ages of 3 months and 1 year and then annually up to the child's age of 8 years. At the child's age of 11 years parents were again asked to complete a questionnaire and for the first time the children themselves completed a questionnaire also. Collection of questionnaire data from parents and children at the age of 14 years is currently (2011–2012) ongoing.

Table 1 Characteristics of the study population

Characteristic	<i>n</i>	%
Sex	3963	
Male		51.9
Female		48.2
Region^a	3963	
North		31.1
Central		40.0
West		28.9
Urbanization (addresses per km²)	3961	
<500		14.2
500–1000		18.1
1000–1500		22.6
1500–2500		30.7
≥2500		14.3
Home country of parents	3669	
Dutch (both parents)		91.8
Western, non-Dutch (at least 1 parent)		4.6
Non-Western (at least 1 parent)		3.6
Older siblings present	3937	50.7
Maternal allergy^b	3963	31.2
Paternal allergy^b	3957	30.8
Maternal education^c	3807	
Low		23.5
Intermediate		41.6
High		35.0
Paternal education^c	3761	
Low		25.9
Intermediate		34.4
High		39.7
Maternal age (at birth of child)	3920	
<25 yrs		6.5
25–34 yrs		79.1
≥35 yrs		14.4
Maternal smoking during pregnancy^d	3926	17.8
Indoor smoking(≥ 1 × per week) at child's age 1 yr	3815	27.7
Birthweight	3914	
<2500 g		3.4
2500–4000 g		78.7
≥4000 g		17.9
Premature (< 37 weeks' gestation)	3930	4.8
Breastfeeding duration	3896	
0 weeks		17.9
1–12 weeks		38.4
≥12 weeks		43.7

^aNorth: provinces Groningen, Friesland, Drenthe; Central: Utrecht, Gelderland; West: Rotterdam and surrounding municipalities.

^bParental allergy defined as 'asthma ever and/or current house dust mite allergy and/or pet allergy and/or hay fever'.

^cParental education level: Low, primary school, lower vocational training or lower secondary education; intermediate, intermediate vocational education or intermediate/higher secondary education; high, higher vocational education or university degree.

^dMother smoked during at least the first 4 weeks of pregnancy.

Table 2 Participants still in the study and questionnaires completed per wave of data collection

Age child	Participants still in the study ^a (=questionnaires sent out)	Participants still in the study ^a % of baseline population ^b	Questionnaires completed	Questionnaires completed % of questionnaires sent out	Questionnaires completed % of baseline population ^b
	<i>n</i>		<i>n</i>		
Prenatal	4146	100	4108	99.9	99.9
3 months	3963	100	3934	99.3	99.3
1 year	3963	100	3746	94.5	94.5
2 years	3910	98.7	3740	95.7	94.4
3 years	3884	98.0	3694	95.1	93.2
4 years	3842	96.9	3563	92.7	89.9
5 years	3745	94.5	3518	93.9	88.7
6 years	3723	93.9	3472	93.3	87.6
7 years	3661	92.4	3374	92.2	85.1
8 years	3649	92.1	3270	89.6	82.5
11 years					
parents	3541	89.4	2660	75.1	67.1
children	3541	89.4	2651	74.9	66.9

^aParticipants were considered to be 'in the study' as long as they were not excluded (lost to follow-up) from the study population. Exclusion took place if participants themselves indicated that they were no longer able or willing to participate; when they moved and could not be traced; and when they failed to complete 2 or more subsequent questionnaires.

^b4146 pregnant women gave informed consent to participate; the number of children at baseline was 3963.

Home visits and clinical examinations were conducted at the child's ages of 3 months, 1 year, 4 years, 8 years and 12 years to collect house dust samples, blood samples and to take anthropometric and lung function measurements. These data collections were conducted in sub-groups of the total population. Clinical examination at the age of 16 years, including genomic characterization, is currently being prepared.

The baseline study population consisted of 3963 children, and 92% of them were still in the study 8 years later. When it was decided to extend the study with a new wave of data collection at the age of 11 years, families who had not responded to the last three questionnaires (ages 6, 7 and 8 years) or who had not responded to the last two questionnaires and had not participated in the clinical examination at age 8 years ($n=69$) were excluded from further follow-up. The remaining 3541 families were invited to participate in the further follow-up of the PIAMA study. Table 2 shows how many participants were still in the study and how many questionnaires were returned at each wave of data collection.

For the objective measurements 765, 1808, 3518 and 3202 children were invited at the age of 1 year, 4 years, 8 years and 12 years, respectively. Between 97% (at age 1 year) and 47% (at age 12 years) of those invited were willing to participate. However, not all children who participated in the clinical examinations were able and willing to give a blood sample

and/or perform the lung function measurements, so that the number of successful measurements of some markers was lower than the total number of participants.

Loss-to-follow-up

Loss-to-follow-up and non-response to individual questionnaires were very low during the first 8 years of the study, but increased when parents and children were invited for a new wave of data collection 3 years after they had completed the study period that they had originally agreed to. Among the families who did not complete the questionnaires administered at the child's age of 11 years, low parental education, parental smoking, maternal allergy and breastfeeding for less than 12 weeks were more prevalent than among the families who did participate again when the child was 11 years old (see Table 3).

Missing of data due to loss-to-follow-up or non-response to individual questionnaires or questions was not completely at random ('MCAR'), but strongly associated with participants' characteristics collected in the early years of the study. This enabled us to use multiple imputation in order to avoid bias that might result from complete case analysis and to make efficient use of the available data.

Table 3 Characteristics of children/families that completed the child or the parent questionnaire at the child's age of 11 years, and of those who did not complete these questionnaires

Characteristic	Child or parent questionnaire completed at age 11	
	Yes ^c n = 2749 %	No ^c n = 1214 %
Sex		
Male	50.7	54.5
Female	49.3	45.6
Region^a		
North	32.0	29.0
Central	41.5	36.6
West	26.5	34.4
Urbanization (addresses per km²)		
<500	14.8	13.0
500–1000	17.9	18.6
1000–1500	23.4	20.9
1500–2500	31.1	29.9
≥2500	12.9	17.6
Home country of parents		
Dutch (both parents)	92.8	89.1
Western, non-Dutch (at least 1 parent)	4.3	5.5
Non-Western (at least 1 parent)	2.9	5.5
Older siblings present	50.1	51.9
Maternal allergy^b	28.7	36.9
Paternal allergy^b	30.4	31.6
Maternal education^c		
Low	19.9	32.8
Intermediate	41.7	41.3
High	38.5	25.9
Paternal education^c		
Low	22.9	33.6
Intermediate	33.4	37.2
High	43.7	29.2
Maternal age (at birth of child)		
<25 yrs	4.6	10.9
25–34 yrs	79.1	79.0
≥35 yrs	16.3	10.1
Maternal smoking during pregnancy^d	15.5	23.2
Indoor smoking (≥ 1 x per week) at child's age 1 yr	25.4	33.8
Birth weight		
<2500 g	3.3	3.6
2500–4000 g	77.8	80.6
≥4000 g	18.9	15.8
Premature (<37 weeks' gestation)	4.9	4.6
Breast feeding duration		
0 weeks	16.5	21.0
1–12 weeks	35.8	44.4
≥12 weeks	47.7	34.5

^aNorth: provinces Groningen, Friesland, Drenthe; Central: Utrecht, Gelderland; West: Rotterdam and surrounding municipalities.

^bParental allergy defined as 'asthma ever and/or current house dust mite allergy and/or pet allergy and/or hay fever'.

^cParental education level: Low, primary school, lower vocational training or lower secondary education; intermediate, intermediate vocational education or intermediate/higher secondary education; high, higher vocational education or university degree.

^dMother smoked during at least the first 4 weeks of pregnancy.

^eDifferences between the 2 groups were statistically significant for all characteristics shown except for the presence of older siblings, paternal allergy and prematurity.

Table 4 Topics covered by the PIAMA questionnaires

Topic	Data on:
Demographic, parental and family characteristics	Region, urbanization, area code, parental ethnicity, parental age, maternal weight and height (pre-pregnancy and at child's age 1 year), parental education, parental occupational status, parental weight, height, waist and hip circumference (at child's age 8), siblings, family (parents and siblings) history of asthma and allergy
Pregnancy	Maternal intake of food (major food groups), supplements and medication, active and passive smoking, exposure to pets
Birth and infancy	Birthweight, gestational age, home or hospital delivery, caesarean section, infant feeding, introduction of solids, daycare attendance
Growth and development	Weight and height (annually, measured by professional or parents and reported by the parents), waist and hip circumference (at age 8 only, measured by the parents), stages of puberty (at ages 11 and 14)
Environmental exposures, indoor and outdoor	Housing characteristics (incl. mould and dampness, carpeting, gas cooking), passive and active (at ages 11 and 14) smoking, pets, traffic
Lifestyle exposures	Food and drinks (incl. alcohol at ages 11 and 14) consumption, physical activity, sedentary behaviour, sleep duration and quality (at ages 11 and 14)
Health	Asthma, eczema, rhinitis, allergy, respiratory and other infections; at ages 11 and 14 also headaches/migraine, musculoskeletal complaints, indicators of mental well-being
Health care and medication use	Vaccinations, GP visits, hospitalization, tonsillectomy, use of medication (incl. antibiotics, asthma and allergy medication)
Education	School results at the end of primary education, type of secondary education and results

What has been measured?

Table 4 shows the main topics that have been addressed in the questionnaires and Table 5 shows the most important materials and measurements that were obtained during home visits and clinical examinations. Details of the data available from the PIAMA cohort can also be found at <http://www.birthcohorts.net/> and <http://www.enrieco.dk/Default.asp>. The ENRIECO website also includes the numbers available for many of the measures.

Apart from the serum markers of primary interest, shown in Table 5, a number of other markers have been measured in serum that remained. These include vitamin D, CRP, erythrocyte fatty acids, visfatin, leptin, IL1RL1-a and helicobacter antibodies.

What has the study found? Key findings and publications

The main focus of the study has been on asthma and allergy. With respect to the first of the original research questions, the PIAMA study found that early intervention with mite-impermeable mattress covers

did not result in a substantial reduction in mite allergen exposure. It only temporarily reduced the risk of asthma symptoms and did not reduce the risk of hayfever, eczema or allergic sensitization to house dust mite up to the age of 8 years.⁸ These results indicate that there is no reason to advise parents of high risk children to use mite-impermeable mattress covers on the child's bed as the only intervention, in order to prevent the development of asthma and allergy.

With respect to the second research question, we observed that several lifestyle and environmental factors early in life played a role in the development of asthma. For example, we reported an almost 2-fold increased risk of asthma at the age of 8 years in children who were born after caesarean section as compared with vaginal delivery, in particular in children with allergic parents.⁹ We observed a protective effect of breastfeeding for more than 16 weeks on the risk to develop asthma during childhood up to the age of 8 years for children of allergic as well as children of non-allergic mothers.¹⁰ Overweight at 6–7 years was shown to be a risk factor for asthma and bronchial hyper-responsiveness (BHR) at the age of 8 years. Children who had a high body mass index (BMI)

Table 5 Sub-groups invited for clinical examination and materials and measurements collected at different ages^a

Child's age	Sub group ^b	Material: measurements
Prenatal	IS	Dust samples: allergens (house dust mite, cat, dog), endotoxin, beta-glucans, EPS
3 months	Intensive follow up	Dust samples: allergens (house dust mite, cat, dog), endotoxin, beta-glucans, EPS
	Intensive follow up	Breast milk samples: fatty acids
1 year	IS	Dust samples: allergens (house dust mite, cat, dog), endotoxin, beta-glucans, EPS
	IS	Serum: IgE (specific and total)
4 years	Intensive follow up	Dust samples: allergens (house dust mite, cat, dog)
	Intensive follow up	Weight, height
	Intensive follow up	Serum: IgE (specific and total)
	Intensive follow up	DNA
	Intensive follow up	Airways: peak flow, Rint
	Intensive follow up	Exhaled NO
8 years	All	Weight, height, waist and hip circumference
	All	Serum: IgE (specific and total)
	All	DNA
	Intensive follow up	Dust samples: allergens (house dust mite, cat, dog)
	Intensive follow up	Skin prick test
	Intensive follow up	Plasma: cholesterol (total, HDL), HbA1c
	Intensive follow up	Airways: Rint, spirometry, BHR
	Intensive follow up	Exhaled NO
12 years	All	Weight, height, waist and hip circumference
	All	Blood pressure
	All	Serum: IgE (specific and total)
	All	Serum: cholesterol (total, HDL), HbA1c
	All	Airways: spirometry
	All	Exhaled NO

^aIS, Intervention Study participants; EPS, extracellular polysaccharides; Rint, interrupter resistance measurement; BHR, bronchial hyper-responsiveness; NO, Nitric Oxide.

^b'Intensive follow up' covers all high risk children ($n=1245$) and a random selection of low risk children ($n=663$), total $n=1935$. 'All' covers all children except those that have moved outside the range of the study centres (incl. abroad) and children that lived in an institution.

early in life, but a normal BMI at 6–7 years, however, did not have an increased risk of asthma or BHR at 8 years.¹¹ Also, we reported that children of mothers with overweight before pregnancy had a higher risk to develop asthma, irrespective of the BMI of the child.¹² Maternal smoking during pregnancy is known to increase the child's risk of respiratory symptoms. One of the genetic studies conducted in the PIAMA cohort suggested that interaction of variants of 'asthma and COPD gene' *ADAM33* with *in utero* cigarette smoke exposure (but not with postnatal exposure) resulted in reduced lung function and the development of BHR.¹³

Early daycare attendance was found to be associated with an increase in airway symptoms until the age of 4 years followed by fewer symptoms between the ages of 4 and 8 years, but we observed no association with asthma symptoms, hyper-responsiveness or allergic

sensitization at the age of 8 years.¹⁴ Also the presence of pets in the household was not associated with asthma development. Children with a cat or dog at home at 3 months of age had a significantly lower prevalence of sensitization to inhalant allergens at age 8, but not of asthma.¹⁵

The PIAMA cohort has participated in the European FP6 and FP7 programmes on genetics of asthma and allergy. Here the first genome-wide association (GWA) study on asthma showed that several genes were related to asthma and some genes in the 17q regions specifically to early onset asthma.¹⁶ We extended the observations and demonstrated that *IL1RL1* polymorphisms that are associated with asthma in GWA studies were associated with serum *IL1RL1*-a levels, the transcript of this gene, with blood eosinophil numbers and with asthma in childhood.¹⁷

The PIAMA study has provided several new insights into the role of traffic-related air pollution in the development of asthma. Air pollution concentrations at the children's birth addresses, estimated by land-use regression models, were shown to be associated with incidence and prevalence of asthma during the first 8 years of life.¹⁸ It is known that exposure to ambient air pollution can exacerbate existing asthma, but our results provided evidence that air pollution exposure may also contribute to the pathogenesis of asthma in children. Variant alleles of *TLR2* and *TLR4* genes influenced the susceptibility to adverse effects of traffic-related air pollution on childhood asthma.¹⁹

Advanced statistical methods are applied to make optimal use of the longitudinal design of the study. Longitudinal latent class analysis was used to identify wheezing phenotypes based on the annual reports of wheezing from 0 to 8 years. Besides the commonly observed phenotypes 'early transient', 'late onset' and 'persistent', an 'intermediate onset wheeze' phenotype was identified, with onset of wheeze after 2 years of age, in line with similar observations in the ALSPAC study.²⁰ Prediction modelling was used to develop a clinical risk score to predict the risk of asthma at 7–8 years of age for pre-school children who present with asthma-like symptoms for the first time. In this population of children with asthma symptoms at pre-school age, the prevalence of asthma at 7–8 years was 11%. Eight clinical parameters independently predicted asthma at 7 to 8 years of age: male sex, post-term delivery, parental education, parental inhaled medication, wheezing frequency, wheeze/dyspnoea apart from colds, respiratory infections and eczema. In 72% of the cases, the model accurately discriminated between asthmatic and non-asthmatic children. A clinical risk score was developed (range 0–55 points). Symptomatic pre-school children with a score of less than 10 points had a 3% risk, whereas children with a score of 30 points or more had a 42% risk of asthma at 7–8 years.²¹ In addition, we demonstrated and quantified the added value of objective measures of lung function (Rint) and airway inflammation (FeNO) for predicting the development of asthma.²²

A list of all PIAMA publications, including those on health outcomes other than asthma and allergy, is available at <http://piama.iras.uu.nl/piama-project-pub.php>

Main strengths and limitations

Main strengths of the study are the high follow-up rate, the large number of repeated measurements up to the age of 15 years with annual questionnaires in the first 8 years, the large range of different exposures and health outcomes investigated combining data from questionnaires, objective measurements, genetic information and geographical exposure data linked to the participants' addresses.

The study's main limitation results directly from its main strength. Due to the large size of the study population which remained large throughout follow-up, financial resources fell short for performing clinical examinations in all children at all ages. Another limitation is the limited availability of detailed data on the prenatal period and of measurements, such as lung function, immediately after birth. At the start of the study, the 'Developmental Origins of Health and Disease' (DOHaD) hypothesis had only just started to gain attention in relation to the development of asthma and allergy, and prenatal recruitment was not yet common practice. Although we have collected information on relevant exposures during pregnancy, such as parental smoking habits and the presence of pets in the household, with today's knowledge we would have put even more emphasis on prenatal exposure information (for example on maternal weight gain during pregnancy, detailed dietary information, pregnancy complications, etc.).

Can I get hold of the data? Where can I find out more?

The PIAMA study group was or is involved in a number of European collaborative projects with other birth cohorts, including TRAPCA, AIRALLERG, ENRIECO, ESCAPE, GA²LEN, MeDALL and CHICOS.

Researchers interested in collaboration or further information are invited to contact the principal investigators via alet.wijga@rivm.nl. Information on the data available in the PIAMA study can also be found at <http://www.birthcohorts.net/bch2/?action=show&UserID=25> and <http://www.enrieco.dk/Default.asp>

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KEY MESSAGES

- Use of mite-impermeable mattress covers by high risk infants was associated with a decreased risk of asthma symptoms at age 2 years, but not at other ages up to the age of 8 years, and did not reduce the risk of hayfever, eczema and allergic sensitization up to the age of 8 years.
- Exposure to ambient air pollution can exacerbate existing asthma, but the PIAMA results provided evidence that air pollution exposure may also contribute to the development of asthma in children.
- Maternal pre-pregnancy overweight, delivery by caesarean section, formula feeding instead of breast-feeding and childhood overweight increased the risk of asthma, whereas early daycare attendance and presence of pets in the household were not associated with asthma development.
- The presence of asthma at 7–8 years of age for pre-school children who present with asthma-like symptoms for the first time could be predicted using eight readily available clinical parameters.

References

- 1 Brunekreef B, Smit J, de Jongste J *et al*. The prevention and incidence of asthma and mite allergy (PIAMA) birth cohort study: design and first results. *Pediatr Allergy Immuno*. 2002;**13**(Suppl 15):55–60.
- 2 Lakwijk N, van Strien RT, Doekes G, Brunekreef B, Gerritsen J. Validation of a screening questionnaire for atopy with serum IgE tests in a population of pregnant Dutch women. *Clin Exp Allergy* 1998;**28**:454–58.
- 3 Statistics Netherlands. Almost as many higher as lower educated Dutch. Web magazine, 15 April 2008. <http://www.cbs.nl/en-GB/menu/themas/onderwijs/publicaties/artikelen/archief/2008/2008-2436-wm.htm?Languageswitch=on> (15 July 2012, date last accessed).
- 4 Statistics Netherlands Statline. Geboorte; herkomstgroepering kind en leeftijd moeder. 28 June 2011. <http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37380B&EV&D1=0&D2=0-4&D3=0&D4=2&VW=T> (15 July 2012, date last accessed).
- 5 Statistics Netherlands Statline. Birth; age mother (on 31 December), birth order and fertility rates. 22 June 2012. <http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLNL&PA=37744ENG&D1=0&D2=0,36-42&D3=47&HD=120716-1351&LA=EN&HDR=T&STB=G1,G2> (15 July 2012, date last accessed).
- 6 Statistics Netherlands Statline. Bevallings, lengte en gewicht bij geboorte en borstvoeding [Delivery, length and weight at birth and breastfeeding]. <http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37302&D1=47&D2=1&HDR=T&STB=G1&VW=T> (15 July 2012, date last accessed).
- 7 Statistics Netherlands Statline. Bevallings, lengte en gewicht bij geboorte en borstvoeding [Delivery, length and weight at birth and breastfeeding]. <http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37302&D1=26-33&D2=1&HDR=T&STB=G1&VW=T> (15 July 2012, date last accessed).
- 8 Gehring U, de Jongste JC, Kerkhof M *et al*. The 8-year follow-up of the PIAMA intervention study assessing the effect of mite-impermeable mattress covers. *Allergy* 2012;**67**:248–56.
- 9 Roduit C, Scholtens S, de Jongste JC *et al*. Asthma at 8 years of age in children born by caesarean section. *Thorax* 2009;**64**:107–13.
- 10 Scholtens S, Wijga AH, Brunekreef B *et al*. Breast feeding, parental allergy and asthma in children followed for 8 years. The PIAMA birth cohort study. *Thorax* 2009;**64**:604–09.
- 11 Scholtens S, Wijga AH, Seidell JC *et al*. Overweight and changes in weight status during childhood in relation to asthma symptoms at 8 years of age. *J Allergy Clin Immunol* 2009;**123**:1312–18.
- 12 Scholtens S, Wijga AH, Brunekreef B *et al*. Maternal overweight before pregnancy and asthma in offspring followed for 8 years. *Int J Obes (Lond)* 2010;**34**:606–13.
- 13 Reijmerink NE, Kerkhof M, Koppelman GH *et al*. Smoke exposure interacts with ADAM33 polymorphisms in the development of lung function and hyperresponsiveness. *Allergy* 2009;**64**:898–904.
- 14 Caudri D, Wijga A, Scholtens S *et al*. Early daycare is associated with an increase in airway symptoms in early childhood but is no protection against asthma or atopy at 8 years. *Am J Respir Crit Care Med* 2009;**180**:491–98.
- 15 Kerkhof M, Wijga AH, Brunekreef B *et al*. Effects of pets on asthma development up to 8 years of age: the PIAMA study. *Allergy* 2009;**64**:1202–28.
- 16 Moffatt MF, Gut IG, Demenais F *et al*. GABRIEL Consortium. A large-scale, consortium-based genome-wide association study of asthma. *N Engl J Med* 2010;**363**:1211–21.
- 17 Savenije OE, Kerkhof M, Reijmerink NE *et al*. Interleukin-1 receptor-like 1 polymorphisms are associated with serum IL1RL1-a, eosinophils, and asthma in childhood. *J Allergy Clin Immunol* 2011;**127**:750–56.
- 18 Gehring U, Wijga AH, Brauer M *et al*. Traffic-related air pollution and the development of asthma and allergies during the first 8 years of life. *Am J Respir Crit Care Med* 2010;**181**:596–603.
- 19 Kerkhof M, Postma DS, Brunekreef B *et al*. Toll-like receptor 2 and 4 genes influence susceptibility to adverse effects of traffic-related air pollution on childhood asthma. *Thorax* 2010;**65**:690–97.
- 20 Savenije OE, Granell R, Caudri D *et al*. Comparison of childhood wheezing phenotypes in 2 birth cohorts: ALSPAC and PIAMA. *J Allergy Clin Immunol* 2011;**127**:1505–12.
- 21 Caudri D, Wijga A, Schipper CM *et al*. Predicting the long-term prognosis of children with symptoms suggestive of asthma at preschool age. *J Allergy Clin Immunol* 2009;**124**:903–10.
- 22 Caudri D, Wijga AH, Hoekstra MO *et al*. Prediction of asthma in symptomatic preschool children using exhaled nitric oxide, Rint and specific IgE. *Thorax* 2010;**65**:801–07.