Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology 2007;**36**:977–985
doi:10.1093/ije/dym090

COHORT PROFILE

Cohort Profile: The Leicester Respiratory Cohorts

Claudia E Kuehni,[1]* Adrian M Brooke,[2] Marie-Pierre F Strippoli,[1] Ben D Spycher,[1] Anthony Davis[3] and Michael Silverman[2]

Accepted 2 April 2007

How did the study come about?

Asthma and other wheezing disorders are the most common chronic health problems in childhood and place a large burden on children, their families and society.[1] Prevalence is highest in infancy or early childhood and the aetiology is complex, with a strong influence of intrauterine and early life exposures. Clinical presentation, response to treatment and prognosis differ by age and the natural history is highly variable. It has been questioned whether asthma, especially in young children, should be regarded as one disease with a single underlying aetiology but a wide range of severity,[2] or as a syndrome comprising several separate conditions.[3,4] Furthermore, respiratory illness in early life is associated with adult respiratory disease and diminished lung function.[5,6] Despite this, most epidemiological studies of asthma before the 1990s had focused on schoolchildren and adults, and there were sparse population-based data on infants and preschool children.

The Leicester respiratory cohort studies were set up to fill this gap. The first Leicester cohort was established in 1990 by Hamish Simpson (with David Luyt and Adrian Brooke as principal fellows) as a community-based sample of 1650 children born between 1985 and 1990. This study provided the first data on prevalence[7–9] and subsequently on natural history of preschool wheeze in Europe.[10–12] The large age-spread of the Leicester 1990 cohort permitted an overview of the prevalence and characteristics of wheeze in preschool children, but complicated studying the natural history. This cohort was relatively small and did not include ethnic minority groups.

Therefore, Michael Silverman and Claudia Kuehni recruited a second cohort in 1998, consisting of 8700 children born between 1993 and 1997. A stratified sampling design was used to recruit 5400 children aged 1, and 3300 children aged 2–4 years. Of these, 6100 were white and 2600 were south Asians.

[1] Swiss Paediatric Respiratory Research Group, Department of Social and Preventive Medicine, University of Berne, Berne, CH-3012, Switzerland.

[2] The Leicester Children's Asthma Centre, Division of Child Health, Department of Infection, Immunity & Inflammation, University of Leicester, Leicester, LE2 7LX, UK.

[3] Specialist Community Child Health Services, Leicester City PCT, Bridge Park Plaza, Thurmaston, Leicester, LE4 8PQ, UK

* Corresponding author. E-mail: kuehni@ispm.unibe.ch

How is it funded?

The direct costs of the cohort studies (salaries, consumables and equipment) came from short-term project funding from bodies such as Asthma UK, The Wellcome Trust, the Swiss National Science Foundation, R&D Directorates of NHS Trusts, Children's Research Fund, Medisearch (Leicester), BUPA Foundation and many others. Infrastructure is provided by the Universities of Leicester, UK and Berne, Switzerland, where the data centre is located. Leicester City Council is a partner in research into air pollution. Studies are approved by the local Research Ethics Committee.

What does it cover?

The broad purpose of the Leicester cohorts is to study the childhood epidemiology of wheezing disorders and other common respiratory problems such as chronic cough, chronic rhinitis and habitual snoring.

Four major aims of the study were: (i) to estimate the prevalence of these respiratory disorders in young children and to determine whether secular trends in asthma and wheeze described for adults and schoolchildren were also evident for preschool children; (ii) to study the contribution of potential risk factors on incidence and persistence of wheeze and other respiratory disorders taking into account different age-exposure windows; (iii) to study wheezing disorders in children of south Asian origin, the predominant British ethnic minority and (iv) to study the natural history of wheeze and chronic cough and to determine how many disease phenotypes exist within the 'asthma' spectrum in childhood.

The results of these studies have implications for public health, giving detailed population-based information on respiratory disorders in children, on health care utilization and on treatment, and should lead to preventive interventions. For clinical purposes, research from the Leicester cohorts should provide diagnostic algorithms to predict prognosis and facilitate the management of children suffering from wheeze or chronic cough.

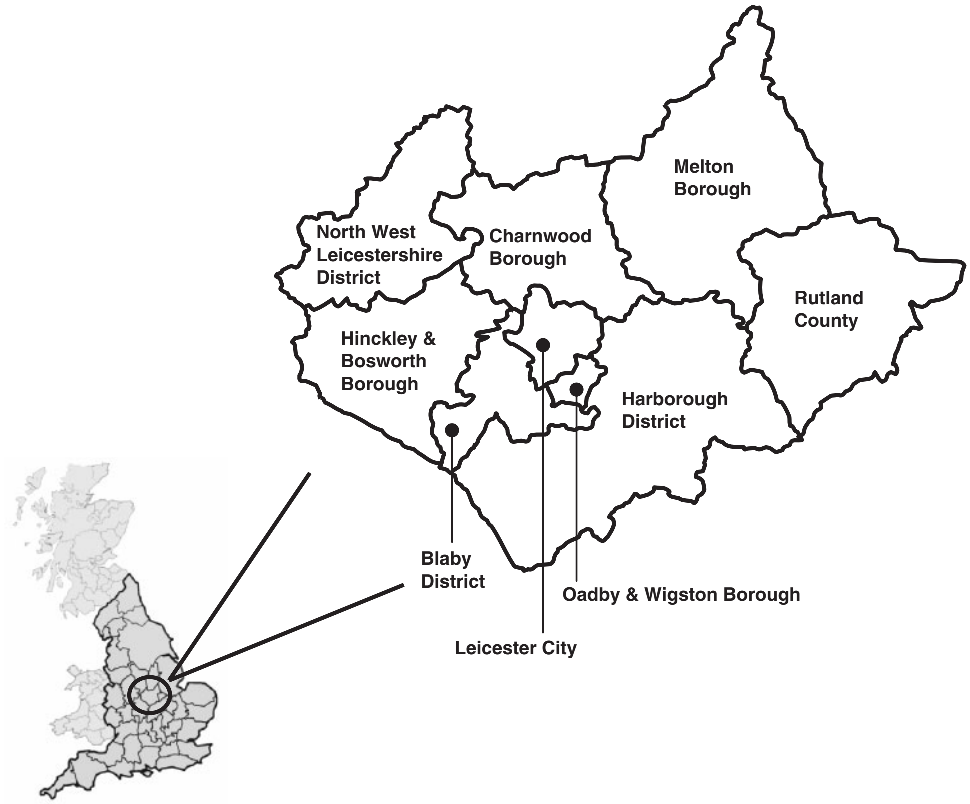

Figure 1 Geographical situation of the counties of Leicestershire and Rutland

Who is in the sample?

Both Leicester cohorts are stratified random samples from the Leicestershire Health Authority Child Health Database, a constantly updated database with perinatal demographic and health-related information for all children resident in the Leicestershire Health area. This region in the East Midlands of England covers the government local authority areas of Leicester City Council, Leicestershire County Council and Rutland County Council (Figure 1) with about 924 000 inhabitants (Census 2001). Over 106 000 of these were of south Asian ethnicity, accounting for 3.7% of the population of Leicestershire county and 29.9% of Leicester city.[13] The region has a mix of people from urban and rural neighbourhoods, long-established and immigrant, wealthy and poor, typical of England as a whole. The only hospital with a paediatric department in the region is located in Leicester city. Annual means of daily maximum and minimum temperatures in the English Midlands are 13 and 5.5°C, respectively and annual precipitation is about 800 mm.

Eligibility criteria for children taking part in the cohort studies were: registered in the Leicestershire Health Authority Child Health Database, complete birth records, born and living in Leicestershire and aged between 0 and 4 years at recruitment (1–4 years for 1998 cohort). In total 46 160 children fulfilled these criteria in 1998. Of these 30 771 (66.7%) were white (British or European) and 6194 (13.4%) were south Asian by self-assigned maternal ethnicity in the birth record. The remaining children were of other or unknown ethnicity.

The Leicester cohorts consist of stratified random samples of fixed sizes drawn from among all eligible children in 1990 and 1998, respectively. In total 1650 children were sampled in 1990 and 8700 in 1998. Table 1 summarizes the sample sizes for each age and ethnic group in both cohorts. In 1998 a large proportion of all preschool children in Leicestershire was recruited for the study (55.7% and 81.0%, respectively of white and south Asian 1-year olds, and 8.4% and 29.1% of white and south Asian 2–4-year olds, respectively). Amongst south Asian mothers (Table 2), 609 (23.4%) were born in the UK, 666 (25.6%) in East Africa and 1146 (44.1%) in the Indian subcontinent (902 from India, 137 from Bangladesh and 107 from Pakistan). The largest ethnic subgroup (874) were Gujarati-speakers born in India (398), Africa (289) or the UK (164). The second important subgroup were Punjabi-speaking families (207), born mainly in the UK (94) or in India (105).

How often have they been followed-up? What is attrition like?

Baseline routine data and recurrent updates were available for all children (100%) of the cohorts from the Leicestershire Health Authority Child Health Database. A first detailed postal questionnaire was sent to parents at the time of recruitment, in 1990 and 1998, respectively. Since then, the families received similar questionnaires every few years, adapted to the age of the children. Questionnaire surveys were carried out in 1990, 1992–94, 1998 and 2003 (addressed to the young people

Table 1 Summary of children recruited in the two cohorts, by age and ethnicity

		Age (completed years)					
Cohort	**Ethnicity**	0	1	2	3	4	**Total**
1990	White	330	330	330	330	330	1650
1998(a)	White	–	650	650	650	650	2600
	South Asian	–	450	450	450	450	1800
1998(b)	White	–	3500	–	–	–	3500
	South Asian	–	800	–	–	–	800
Proportion recruited of eligible children living in the area ($n = 46160$) in 1998 (only 1998 cohorts)							
	White	–	55.7% (4150/7457)	8.4% (650/7756)	8.6% (650/7563)	8.1% (650/7995)	
	South Asian	–	81.0% (1250/1548)	28.0% (450/1607)	30.3% (450/1484)	28.9% (450/1555)	

1998(a): These 4400 children were primarily recruited to assess secular trend since 1990 and perform cross-sectional analyses in different age groups. Respiratory questions were identical to those used in 1990.

1998(b): Additional 4300 children aged 1 year, to study natural history in more detail.

Table 2 Characteristics of children of south Asian ethnicity recruited in 1998, by maternal country of birth, main household language and religion

	Main language and religion									Other	Total
	Gujarati		Punjabi	Bengali	Katchi	Urdu		English			
Maternal country of birth	Hindu	Muslim	Sikh	Muslim	Muslim	Muslim	Hindu	Muslim	Sikh		
UK	79	85	94	3	4	10	37	29	47	221	609
Africa	199	90	5		61	12	31	24	5	239	666
India	290	108	105		10	10	13	10	22	334	902
Bangladesh	2	1		48				2		84	137
Pakistan	5	8	1	1	7	24				61	107
Other/missing	6	1	2		2		2	1		165	179
Total	581	293	207	52	84	56	83	66	74	1104	2600

Table 3 Summary of surveys conducted with the Leicester cohorts

			Participating cohorts		
Year	**Type of survey/Instruments**	**Sample addressed**	1990	1998(a)	1998(b)
1990	Postal questionnaire	All children	x		
1992–94	•Postal questionnaire •Interviews •Measurements	All children who reported wheeze or cough in 1990; random sample of asymptomatics	x		
1998	Postal questionnaire	All children	x	x	x
1999	Postal questionnaire	All children who responded in 1998			x
2001	Postal questionnaire	All children		x	x
2003	Postal questionnaire	All children	x	x	x
2005-ongoing	•Postal questionnaire •Interviews •Measurements	All children who responded in 1998 and in at least one other survey		x	x
2006-ongoing	Postal questionnaire	All children who had not come to the lab in 2005–06		x	x

themselves) for the 1990 cohort, and in 1998, 1999, 2001, 2003 and 2006 for the 1998 cohort (Table 3).

Both cohorts underwent physiological measurements at early school age, when they were old enough to comply (Table 3). A nested sample of the 1990 cohort was studied in 1992–94 targeting all children for whom parents had reported wheeze ever ($n = 222$) or chronic cough ($n = 226$) in the first survey, and a nested sample of asymptomatic children ($n = 347$). The lab measurements for the 1998 cohort are ongoing. All children whose parents had completed the first survey in 1998 and at least one follow-up survey ($n = 5180$) are being invited for lab measurements, beginning with the oldest children. Currently about 500 children have finished their tests.

Response rates to questionnaire surveys in 1990 cohort were good, with 1422/1650 (86.2%) responding to the initial survey, 79.1% replying in 1998 and 57.3% in 2003. Figure 2a shows that a significant proportion of those who had not replied in the first survey answered one of the follow-up questionnaires, so that in total, 94.4% had replied at least once. Participation in laboratory measurements in 1992–94 was 65.3%, 57.5% and

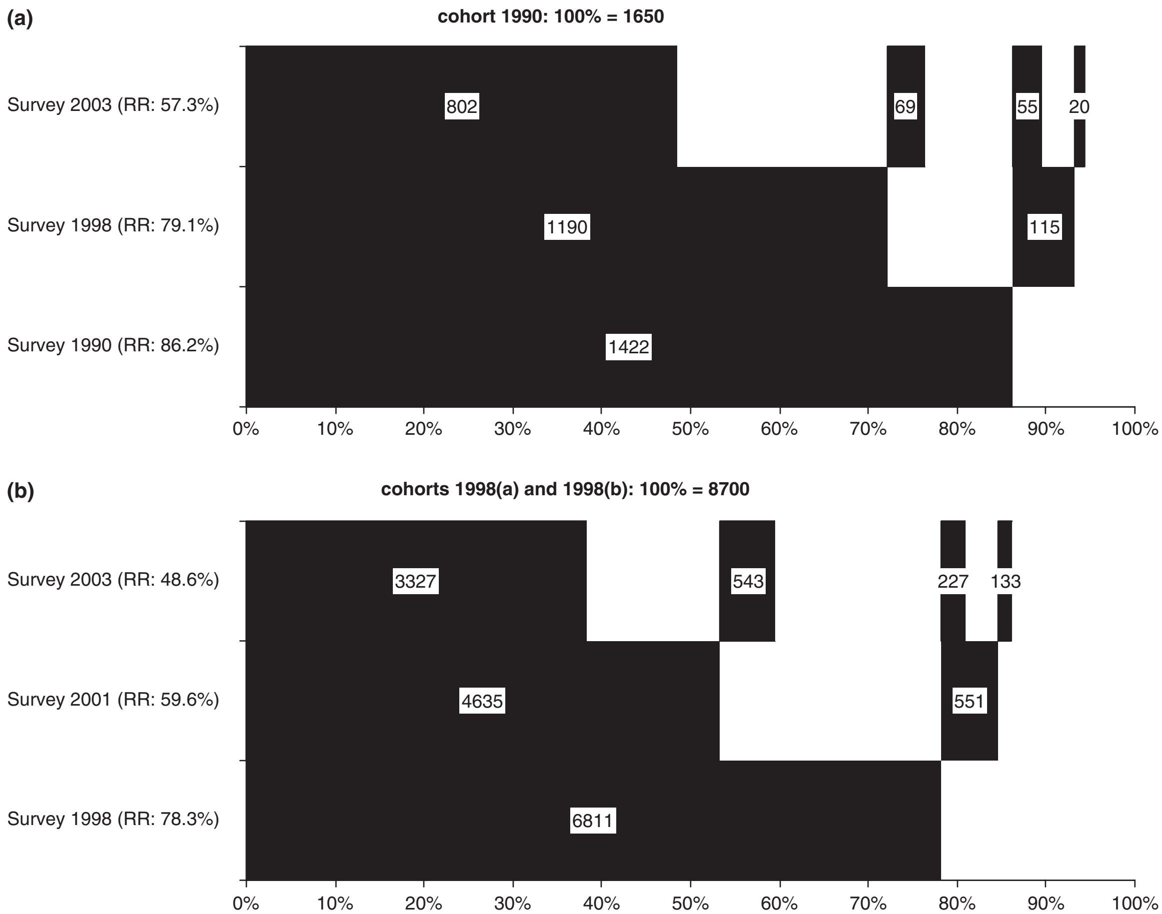

Figure 2 Patterns of response to the first three surveys in (a) the 1990 cohort and (b) the 1998 cohort. The black bar in the lowest layer represents response to the initial survey as a percentage of the total cohort. The two black bars of the next layer show response to this follow-up as a percentage of respondents and non-respondents to the initial survey, respectively. In the top layer, response to the next follow-up is given for each of the four patterns of response to the first two surveys. Figures in the black bars represent numbers of respondents. Overall response rates (RR) are also reported for each survey

61.4% for children with wheeze, chronic cough and no symptoms, respectively.

Follow-up rates in the 1998 cohort were lower, with 78.3%, 59.6% and 48.6% responding in 1998, 2001 and 2003, respectively, and with 86.2% replying at least once (Figure 2b). The 2006 survey is still ongoing. The main reason for attrition was the mobility of these families. Within 4 years (April 1997 to April 2001), the Leicestershire Health Authority Child Health Database had been notified of address changes in 1933/4400 [cohort 1998(a)] (44%) families, with 1265 moving once, 438 moving twice and 230 moving more than twice in this period.[14] With increasing age, notification of address changes in the database became increasingly incomplete. Subjects participating in more than one survey tended to be of higher social class and of white ethnicity, but had a lower frequency and severity of symptoms than children participating only once.

The entire 1990 and 1998 cohorts of 1650 and 8700 children respectively, are representative, for the population of preschool children in Leicestershire and Rutland, being randomly sampled. Baseline routine data are available for all of them. However, there were some systematic differences between respondents and non-respondents to specific surveys. For instance, respondents to the first questionnaire in 1998 had a higher socioeconomic status than non-respondents (in whites 44.5% of respondents and 24.8% of non-respondents were in the least deprived tertile of the Townsend score; in south Asians these proportions were 17.5% and 12.2%, respectively) and a higher maternal age at birth (mean age in whites: 28.9 vs 25.9 years; south Asians: 28.1 vs 27.6 years).

What has been measured?

Information was available for both cohorts from routine databases, questionnaires and physiological examinations (Table 4).

Routine data were available from the Leicestershire Health Authority Child Health Database for all children, whether or not they had responded to the questionnaires. This included demographic and ethnic information from maternity records and birth notification, perinatal data and data on growth, immunizations and other health-related events during childhood. The complete postcodes (7-digits) for all addresses at which the child had ever lived allowed area-based deprivation

Table 4 Summary of what has been measured

Questions	Initial survey 1990 cohort	Surveys since 1998, all cohorts
Symptoms	• Wheeze ever and age at onset; frequency and duration of wheeze attacks in previous 12 months; triggers of wheeze (colds, exercise, food, drinks, grass, dust, animals); shortness of breath; seasonal and diurnal pattern	• Wheeze ever and age at onset; frequency and duration of wheeze attacks in previous 12 months; triggers of wheeze (colds, exercise, food, drinks, grass, dust, animals); shortness of breath; interference with sleep; speech limitation due to wheeze
	• Cough with colds, and apart from colds; interference with sleep	• Cough with colds, apart from colds; interference with sleep; triggers of cough (exercise, food, drinks, pollen, house dust, animals)
	• Doctor-diagnosed asthma or bronchitis	• Doctor-diagnosed asthma or bronchitis
	• History of pneumonia, whooping cough, bronchiolitis, other chest infections, eczema, croup, ear infections	• History of pneumonia, whooping cough, bronchiolitis, other chest infections, eczema, croup, ear infections
		• Frequency of colds or flu in previous 12 months; chronic rhinitis or snoring in previous 12 months; interference of these symptoms with daily activities and sleep
Treatment and healthcare use	• Asthma-related hospitalization	• Asthma-related hospitalization; asthma-related GP visits
	• Asthma-related treatment	• Detailed questions on asthma treatment
		• Use of complementary or alternative treatment
Environment	• Attendance at day care, nursery or play school	• Attendance at day care, nursery or play school
	• Contact with animals	• Contact with animals
	• Exposure to tobacco smoke at home; maternal smoking during pregnancy	• Exposure to tobacco smoke at home; maternal smoking during pregnancy
	• Family history of wheeze, asthma, bronchitis, hayfever, eczema	• Family history of wheeze, asthma, bronchitis, hayfever, eczema
		• Duration of breastfeeding
	• Fuel used for heating and for cooking	• Fuel used for heating and for cooking
	• Number of rooms; number of children and adults in household; sharing bedroom	• Number of rooms; number of children and adults in household
	• Parental education and employment status	• Parental education
Special themes		• Understanding of the term 'wheeze'
		• Physical activities
Measurements	**1990 cohort at age 4–8 years**	**1998 cohort at age 7–11 years**
Measurements (laboratory-based)[a]	• Growth (weight, height)	• Growth (weight, height)
		• Blood pressure
	• Clinical status	
	• Noisy breathing, cough, nasal discharge, skin rash and eczema	
	• Skin prick tests (cat dander, dog dander, *Dermatophagoides pteronyssinus*, mixed grass pollens, histamine and negative controls)	• Skin prick tests (cat dander, dog dander, *Dermatophagoides pteronyssinus*, mixed grass pollens, histamine and negative controls)
	• Spirometry	• Pre- and post-bronchodilator spirometry
	• Methacholine bronchial challenge (PC_{20} - tc-PO_2)[b]	• Methacholine bronchial challenge (PC_{20} – FEV_1)[c]
		• Exhaled NO
	• Peak flow and symptom diary during two weeks	
	• Overnight cough monitoring	
		• Blood or buccal smear for genetic analyses
		• Serum aliquots for IgE and other measurements

(continued)

Table 4 Continued

Routine data	**All children from all cohorts**
(*Source:* Leicester Health Authority Child Health Database otherwise noted)	• Birth notification and perinatal details: gender; date of birth; number of older siblings; gestational age; birth weight • Demographic and socio-economic information: mother's occupation, ethnicity, religion, country of birth and language; father's occupation at time of child's birth • Health visitor records: complete information on growth (height, weight, head circumference at 1, 8, 18, 38 months); complete records of childhood immunizations (type of vaccine, dose, date); routine development tests • Townsend score (1991 census data) • Proximity to roads and modelled exposure to air pollutants based on postcode (Indic–Airviro dispersion model Version 2.2, Swedish Meteorological and Hydrological Institute, Norrköping, Sweden) • All home addresses since the child was born

[a]Measurements of 1990 cohort were described elsewhere [10,11].

[b]Using a 20% decrease in transcutaneous oxygen tension (tc-PO_2) to assess response.

[c]Using a 20% decrease in FEV_1 to assess response.

measures (Townsend score) and exposure to air pollutants and road traffic to be calculated.[14]

The baseline questionnaire for the 1990 survey was developed *de novo*, including questions derived from the American Thoracic Society (ATS) childhood questionnaire[15] and other validated questionnaires adapted for preschool children.[16,17] Exactly the same questions were applied in 1998 to 2600 white and 1800 south Asian children [cohort 1998(a)] to assess secular trends.

The questionnaire for the 4300 additional 1-year olds recruited in 1998 [cohort 1998(b)] was slightly modified. Some questions were adapted or added to allow a better phenotype description of children with wheeze and cough. We also included those questions from the International Study of Asthma and Allergies in Childhood (ISAAC) which could be applied to infants and young children.[18] The initial questionnaires for cohorts 1998(a) and (b) were used with little variation in all subsequent surveys. They define wheezing as 'breathing that makes a high-pitched whistling or squeaking sound from the chest, not the throat.' Additional questions on symptoms and exposures were introduced at follow-up surveys according to the age of the children. Repeatability of both the 1990 and the 1998 questionnaires was good.[7,19,20]

What has been found? Key findings and publications

Prevalence, impact and secular trends of respiratory symptoms in preschool children

A major aim of the Leicester cohorts was to provide data on prevalence, risk factors and secular trends of wheeze in preschool children. In 1990, 11% of 1–5-year olds had doctor-diagnosed asthma, 16% had wheezed and 13% reported attacks in the past 12 months.[7,8] These were the first population-based prevalence data for preschool wheeze in the UK and Europe. When we repeated the survey 8 years later (1998) the prevalence of wheeze and asthma had doubled.[21] The fact that all wheezing disorders increased (including viral wheeze, a non-atopic condition occurring only with respiratory infections) suggested that factors unrelated to atopy were probably implicated in the changing epidemiology of wheeze. An economic analysis showed that in 1998–99, 1–5-year olds with wheeze cost the health service a total of £53 million, representing 0.15% of total NHS expenditure.[1] This is a large sum for one single disorder in a 5-year age-band and highlights the need to find effective prevention strategies at the population level.

Risk factors for wheezing disorders

Exposure to locally generated PM_{10}, a traffic-related air pollutant, was associated with increased prevalence of chronic cough and with increased incidence of wheeze and cough in young children.[14] This was independent of many confounders and dose-related.

Linking incidence data on wheeze with independently collected vaccination records from the NHS, a carefully conducted longitudinal analysis contradicted earlier claims that vaccination might increase the risk of childhood asthma, especially of the late onset classical asthma phenotype and suggested that it might even be protective. Reverse causation is unlikely to have explained the protective effect against late-onset asthma.[22,23] The secular trends shown for preschool wheeze were therefore not explained by changing immunization rates.[24]

Respiratory disorders in south Asian families

Another main aim of the 1998 cohort was to investigate asthma in children of south Asian ethnicity. Asthma is less common in children living in India compared with the UK.[25] Data from south Asian children living in the UK are scarce and contradictory, suggesting a lower prevalence of wheeze but a higher hospitalization rate compared with whites.[26] We found in mothers of the 1998 cohort, that south Asian women who migrated to the UK at the age of 5 years or older had a lower risk of asthma than those born in the UK or who migrated before age 5. This strongly supports the hypothesis that early life environmental factors influence the risk of adult asthma.[27] In infants, crude and adjusted prevalence of wheeze was lower in south Asian compared with whites. Conversely, in toddlers south Asians were at greater risk than whites of developing multiple-trigger wheeze (the classical asthma phenotype), after adjustment for socio-economic, environmental and family factors.[28] Consistent with this, food-related wheeze, a clinically significant marker of severe disease and long-term symptom persistence, was more common in south Asians.[29] Together with the relative under-treatment of south Asian children with inhaled corticosteroids[30] these findings might explain the discrepancy in published data. The ethnic studies are currently being taken further by comparing physiological characteristics and genetic associations in south Asian and white wheezers in ongoing lab studies.

Diagnosis and treatment of wheeze in the community

The Leicester studies reported repeatedly on management of wheeze in preschool children in the community, describing predictors of diagnosis and treatment.[8,9,30] A large proportion (19%) of preschool children used asthma inhalers, but that treatment was insufficiently adjusted to asthma phenotype and severity, with relative under-treatment of severe wheeze, especially in girls and south Asian children, but apparent over-treatment of mild episodic wheeze and chronic cough. This underlines the need for development and implementation of phenotype-specific treatment guidelines.[30]

Natural history and clinical phenotypes of wheeze and chronic cough in childhood

The fourth main aim of the Leicester cohorts relates to understanding natural history and phenotypes in childhood asthma. Follow-up of the 1990 cohort showed that less than half of the children who wheezed during preschool years continued to do so at early school age, but that those who did displayed many features consistent with classical asthma in schoolchildren.[10] Although some children with chronic cough displayed many features typical of asthma, few proceeded to develop wheeze 2–4 years later.[11,12] Several studies describing the natural history of preschool wheeze and chronic cough with varying methodological approaches are currently underway. We are developing a statistical approach for identifying disease phenotypes using latent variable analysis. These models can accommodate mixed categorical and continuous data, conditional question structures and missing data and are therefore an attractive tool for identifying disease phenotypes using data from epidemiological or clinical cohorts. Using this approach in a feasibility study on the 1990 cohort, we found evidence for the existence of three phenotypes of wheeze, and two phenotypes of chronic cough, confirming and partly reconciling existing classifications.[31,32] The method will be extended and replicated on the 1998 cohort. Serum levels of mannan-binding lectin (MBL) were significantly higher in more severe childhood wheezers, defined by treatment step, suggesting a disease-modifying effect of MBL or a differential effect in distinct asthma phenotypes.[33]

Methodological issues

The short-term repeatability of our preschool questionnaire was excellent[19,20] and parental recall of preschool symptoms at school-age was good.[34] In contrast, we showed that misunderstanding of the term ‘wheeze’ in parent-completed questionnaire surveys can bias estimates of prevalence of wheeze, leading to an underestimate in children from south Asian and deprived family backgrounds.[35] Questionnaire surveys should therefore incorporate both a definition of wheeze and measures of parents’ understanding of the term. Parental recall of traffic-related air pollution, an environmental exposure which had received much publicity in the context of respiratory disorders, differed according to the respiratory health of the children. We calculated that reporting bias could explain some or even all the association between reported exposure to road traffic and disease.[36] Only objective exposure measures should be used in future surveys.

What are the main strengths and weaknesses?

The Leicester respiratory cohorts are the largest community-based cohort studies focusing purely on childhood respiratory disease in the UK. In contrast to other UK cohorts which aim to report on many health outcomes, the Leicester cohorts include a comprehensive range of questions relating to upper and lower respiratory symptoms at each survey, allowing us to distinguish different phenotypes within the syndrome of ‘wheezing disease’ or asthma with greater confidence and resolution. The 1998 cohort provides an excellent data source for studying ethnic differences in wheezing illness, and is in fact the largest population-based database on respiratory disorders in British south Asian children. We took care to obtain the most reliable reporting of the main symptom by providing an operational definition of ‘wheezing’ and including questions on parental understanding of the term in the questionnaire. We also paid attention to other methodological aspects, assessing repeatability of the questionnaires and estimating the influence of different biases on our results. We collected prospective information on many potential confounders to study aetiological mechanisms. A wide range of independently collected data from the Leicestershire Health Authority Child Health Database complements data from questionnaires. Finally, the study comprises two separate cohorts from the same general population that vary considerably with respect to years of birth and age-spread of their respective members. This allows us to study cohort effects and gives us the opportunity to perform both cross-sectional and longitudinal analyses in different age groups. Within respective age and ethnicity strata, the cohorts are representative because they were sampled randomly from the entire local population. Routine data is available for the entire cohort and can thus be used for weighting adjustments to account for systematic differences between respondents and non-respondents to postal questionnaires.

Weaknesses include the considerable attrition rate in later surveys especially of the 1998 cohort because of difficulties in obtaining valid addresses. Respiratory outcomes were mainly assessed by questionnaire. Although a majority of the families received the first questionnaire when the child was aged 1 year, a proportion of children in both cohorts were aged 2–4 at the time of the first questionnaire. These children are being excluded in analyses relating to natural history of respiratory outcomes. Due to financial constraints, we have performed objective measurements only on one occasion at early school age. Some exposures (such as pets, diet or parental smoking) were not assessed objectively, but only by questionnaire. Prospectively collected objective data were, however, available on growth, immunizations and exposure to air pollution. For genetic studies, our data may need to be pooled with those from other cohort studies[37,38] to increase statistical power.

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

The Leicester cohort studies are conducted at the Division of Child Health at Leicester University in collaboration with the Leicester City Primary Care Trust, Specialist Community Child Health Services for Leicester, Leicestershire and Rutland, and the Department of Social and Preventive Medicine at the University of Berne, Switzerland. The Leicester cohorts' home-page holds detailed information on methodology and publications (http://www.leicestercohorts.org/index.htm). Researchers interested in collaborative work are invited to contact the principal investigators (Michael Silverman, ms70@le.ac.uk, or Claudia Kuehni, kuehni@ispm.unibe.ch).

Acknowledgements

We thank all families in Leicestershire for participating in the study. Funding sources are acknowledged above. CEK, BS and MPS were supported by grants from the Swiss National Science Foundation (numbers no 823B-046481, 3233-069348 and 3200-069349).

References

1 Stevens CA, Turner D, Kuehni CE, Couriel JM, Silverman M. The economic impact of preschool asthma and wheeze. *Eur Respir J* 2003;**21:**1000–6.

2 Williams H, McNicol KN. Prevalence, natural history, and relationship of wheezy bronchitis and asthma in children. An epidemiological study. *Br Med J* 1969;**4:**321–25.

3 Silverman M, Grigg J, Mc Kean M. Virus-induced wheeze in young children - A separate disease? In: Johnston S, Papadopoulos N (eds). *Respiratory Infections in Allergy and Asthma*. New York: Marcel Dekker, 2002. pp. 427–71.

4 Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. *N Engl J Med* 1995;**332:**133–38.

5 Barker DJ, Godfrey KM, Fall C, Osmond C, Winter PD, Shaheen SO. Relation of birth weight and childhood respiratory infection to adult lung function and death from chronic obstructive airways disease. *Br Med J* 1991;**303:**671–75.

6 Sears MR, Greene JM, Willan AR *et al*. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003;**349:**1414–22.

7 Luyt DK, Burton PR, Simpson H. Epidemiological study of wheeze, doctor diagnosed asthma, and cough in preschool children in Leicestershire. *Br Med J* 1993;**306:**1386–90.

8 Luyt DK, Burton P, Brooke AM, Simpson H. Wheeze in preschool children and its relation with doctor diagnosed asthma. *Arch Dis Child* 1994;**71:**24–30.

9 Luyt DK, Brooke AM, Lambert P, Burton P, Simpson H. Wheeze in preschool children: who is followed-up, who is treated and who is hospitalized? *Eur Respir J* 1995;**8:**1736–41.

10 Brooke AM, Lambert PC, Burton PR, Clarke C, Luyt DK, Simpson H. The natural history of respiratory symptoms in preschool children. *Am J Respir Crit Care Med* 1995;**152:**1872–78.

11 Brooke AM, Lambert PC, Burton PR, Clarke C, Luyt DK, Simpson H. Night cough in a population-based sample of children: characteristics, relation to symptoms and associations with measures of asthma severity. *Eur Respir J* 1996;**9:**65–71.

12 Brooke AM, Lambert PC, Burton PR, Clarke C, Luyt DK, Simpson H. Recurrent cough: Natural history and significance in infancy and early childhood. *Pediatr Pulmonol* 1998;**26:**256–61.

13 Ethnicity in Leicestershire: key results from the 2001 census. *Leicestershire County Council* 2004. Retrieved from: http://www.leics.gov.uk/ethnicity_in_leicestershire_web.pdf.

14 Pierse N, Rushton L, Harris RS, Kuehni CE, Silverman M, Grigg J. Locally-generated particulate pollution and respiratory symptoms in young children. *Thorax* 2006;**61:**216–20.

15 Ferris B. Epidemiological standardization project. *Am Rev Respir Dis* 1978;**118:**1–120.

16 Clifford RD, Radford M, Howell JB, Holgate ST. Prevalence of respiratory symptoms among 7 and 11 year old school children and association with asthma. *Arch Dis Child* 1989;**64:**1118–25.

17 Salome CM, Peat JK, Britton WJ, Woolcock AJ. Bronchial hyperresponsiveness in two populations of Australian schoolchildren. I. Relation to respiratory symptoms and diagnosed asthma. *Clin Allergy* 1987;**17:**271–81.

18 Asher MI, Keil U, Anderson HR *et al*. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8:**483–91.

19 Strippoli M-PF, Silverman M, Kuehni CE. Repeatability of a questionnaire on wheeze and asthma in preschool children. *Eur Respir J* 2006;**28 (Suppl 50):**270s.

20 Strippoli M-PF, Silverman M, Michel G, Kuehni CE. A parent-completed respiratory questionnaire for one-year olds: repeatability, *Arch Dis Child* 2007.

21 Kuehni CE, Davis A, Brooke AM, Silverman M. Are all wheezing disorders in very young (preschool) children increasing in prevalence? *Lancet* 2001;**357:**1821–25.

22 Spycher BD, Silverman M, Brooke AM, Zwahlen M, Kuehni CE. Is routine immunisation associated with a reduced incidence of childhood asthma? *Eur Respir J* 2006;**28 (Suppl 50):**836s.

23 Spycher BD, Brooke AM, Silverman M, Kuehni CE. Routine vaccination and childhood asthma: a population-based cohort study, Submitted for publication.

24 Kuehni CE, Brooke AM, Davis A, Silverman M. Vaccinations as risk factors for wheezing disorders. *Lancet* 2001;**358:**1186.

25 Beasley R, Keil U, Von Mutius E, Pearce N. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998;**351:**1225–32.

26 Netuveli G, Hurwitz B, Levy M *et al*. Ethnic variations in UK asthma frequency, morbidity, and health-service use: a systematic review and meta-analysis. *Lancet* 2005;**365:**312–17.

27 Kuehni CE, Strippoli M-PF, Low N, Silverman M. Asthma in young south Asian women in the UK: the importance of early life. *Clin Exp Allergy* 2007;**37:**47–53.

28 Kuehni CE, Strippoli M-PF, Low N, Brooke AM, Silverman M. Wheeze and asthma prevalence and related health-service use in white and south Asian pre-school children in the UK. *Clin Exp Allergy*, Submitted for publication.

29 Kuehni CE, Strippoli M-PF, Silverman M. Food intolerance and wheezing in south Asian and white children: prevalence and clinical significance. *J Allergy Clin Immunol* 2006;**118:**528–30.

30 Chauliac ES, Silverman M, Zwahlen M, Strippoli M-PF, Brooke AM, Kuehni CE. The therapy of pre-school wheeze: appropriate and fair? *Pediatr Pulmonol* 2006;**41:**829–38.

31 Spycher BD, Silverman M, Minder C, Kuehni CE. Phenotype definition in childhood wheezing illness: a data-driven approach. *Eur Respir J* 2006;**28 (Suppl 50):**267s.

32 Spycher BD, Silverman M, Brooke AM, Minder C, Kuehni CE. A multidimensional data-driven approach to phenotype definition in childhood wheeze and cough, Submitted for publication.

33 Staley KG, Stover C, Strippoli M-PF, Spycher BD, Silverman M, Kuehni CE. Mannan-binding lectin in young children with asthma differs by level of severity. *J Allergy Clin Immunol* 2007;**119:**503–5.

34 Kuehni CE, Brooke AM, Silverman M. Prevalence of wheeze during childhood: Retrospective and prospective assessment. *Eur Respir J* 2000;**16:**81–85.

35 Michel G, Silverman M, Strippoli M-PF *et al*. Parental understanding of ''wheeze'' and its impact on asthma estimates. *Eur Respir J* 2006;**28:**1124–30.

36 Kuehni CE, Strippoli M-PF, Zwahlen M, Silverman M. Association between reported exposure to road traffic and respiratory symptoms in children: evidence of bias. *Int J Epidemiol* 2006;**35:**779–86.

37 Keil T, Kulig M, Simpson A *et al*. European birth cohort studies on asthma and atopic diseases: I. Comparison of study designs—a GALEN initiative. *Allergy* 2006;**61:**221–28.

38 Keil T, Kulig M, Simpson A *et al*. European birth cohort studies on asthma and atopic diseases: II. Comparison of outcomes and exposures—a GA2LEN initiative. *Allergy* 2006;**61:**1104–11.

Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology 2007;**36**:985–987
doi:10.1093/ije/dym132

Celebration: William Farr (1807–1883)—an appreciation on the 200th anniversary of his birth

DE Lilienfeld

Accepted 22 March 2007

If one were to ask a student in an introductory epidemiology course which Victorian epidemiologist most influenced the field's development, there's a good chance the student would say 'John Snow'. As that student begins collecting surveillance data as part of a doctoral thesis, the odds are good the student will not know who first developed the concept of surveillance. When the student begins analysing those data, there's a likelihood the data will be coded using the International Classification of Diseases (ICD), especially if the data concern more than one disease entity. Should the results indicate the need for public health action, the student might contact a local, state or federal public health agency to report the results and advocate for appropriate intervention. Yet, in each of these instances, the influential Victorian epidemiologist who pioneered in the area of the student's actions was William Farr (Figure 1).

Farr is relatively unappreciated by modern epidemiologists compared with his more feted peer, John Snow.[1–3] Yet, it was Farr who developed the first national vital statistics system and assured its use as a surveillance instrument. His efforts also facilitated the use of that system for the conduct of epidemiologic studies. Farr's endeavours to craft a disease nosology usable by vital statisticians and epidemiologists led to the creation of the ICD.[4] The structure of the ICD derives from Farr's 1860 proposal.[4] These concepts and ideas have become interwoven into the fabric of epidemiology, so much so that Farr's name is not necessarily mentioned as the innovator. Yet, without his many contributions, the face of epidemiology today would be markedly different.

A definitive biography of Farr and compilations of his writings provide ample opportunity for modern epidemiologists to learn about Farr.[4–8] In view of his considerable contributions to the discipline, it seems fitting to celebrate his 200th birthday with brief considerations of both his biography and his impact on our field.

Biography

William Farr (November 30, 1807 to April 14, 1883) was born in Kenley, Shropshire, England to poor parents.[9] When Farr was 2 years old, he moved to Dorrington. In Dorrington, he came under the influence of Joseph Pryce, the town's squire (http://en.wikipedia.org/wiki/William_Farr, accessed November 25, 2006).

Stanford University School of Medicine, Palo Alto, California, USA.
E-mail: lilienfeld@comcast.net