

REVIEW

Epidemiological aspects of paediatric asthma

J. Hess and J. C. de Jongste

Department of Paediatrics, Division of Paediatric Respiratory Medicine, Sophia Children's Hospital, Erasmus Medical Centre, Rotterdam, The Netherlands

Introduction

Hospital admissions for asthma in childhood started to rise strikingly in the 1960s in various, western cultured, countries [1]. Young children showed a continuing increase in hospital admissions for asthma in the 1980s [2, 3]. Besides the possibility of an increase in prevalence and (or) severity of asthma and changes in health care policies, correct diagnosis and appropriate therapy were questioned. The unfavourable trends occurred in a period of improved therapeutic possibilities for asthma when prophylactic drugs and more efficient bronchodilators were introduced. Consensus guidelines on the diagnosis and management of asthma have since been developed and updated, nationally and internationally. Important changes in treatment followed the changing concept of asthma, from a 'spastic' to an 'inflammatory' disease. The guidelines emphasize the importance of early recognition and preventive therapy directed to diminish the inflammatory processes in the airways. Defining asthma in children is still difficult and rather arbitrary in the very young [4].

Increased prevalences of asthma have been reported, but also questioned, as they may have been influenced by diagnostic practice [5]. The awareness of failing ambulatory care could have favoured asthma labelling in wheezy children to improve treatment.

Increased hospital admissions may also reflect increased severity of asthma [2]. This, however, has not yet been established. There are indications that increased prevalence may be due to mild asthma [6]. On the other hand, increased use of anti-inflammatory therapy may mask an increase in severity [6,7]. Mortality from asthma is rare in childhood; moreover, it seems not to occur primarily in severe asthmatic children [8], and is, therefore, a poor parameter in the epidemiology of asthma in children.

We examined trends in asthma in the Netherlands, against the background of other airways diseases with asthma-like symptoms, in the period 1980–1999 [9]. We evaluated national morbidity (Dutch Centre for Health Care Information, IMS Health) and mortality (Central Bureau of Statistics) data, according to the codes of the international classification of diseases (ICD). The Dutch data sources and the ICD codes of the respiratory diseases studied are described in detail elsewhere [9].

Furthermore, we studied asthma in the age group 0–4 years in more detail [10–12]. Respiratory symptoms often appeared to be transient in infants [13]. Nevertheless, most childhood asthma begins in infancy and children aged 0–4 years appear to be especially at risk for hospital admissions and readmissions for asthma [3,14].

In this review, we summarize our findings and describe epidemiological aspects of paediatric asthma in the Netherlands and the relation to data from other countries.

On asthma diagnosis

One of the difficulties in studies on (trends in) asthma is the lack of consistent diagnostic criteria. In childhood, distinction between asthma and 'wheezy bronchitis' is difficult. Especially at a young age, differentiation from other (viral induced) respiratory diseases, such as bronchiolitis, is problematic. Several wheezing phenotypes exist [15]. What wheezing will continue to manifest as asthma? In addition, there might be a relationship between respiratory syncytial virus bronchiolitis and asthma [16], and between pneumonia and asthma [17], but the nature is not clear. Does asthma predispose for these infections, or does asthma occur as a result? Monitoring trends not only for asthma but also for these diseases will add to a clearer picture of the respiratory burden in childhood.

In the past, the Netherlands has held an exceptional status by viewing asthma along with chronic bronchitis and emphysema as part of a disease entity named chronic non-specific lung disease (CNSLD). For long, the Dutch equivalent umbrella term CARA (chronische aspecifieke respiratoire aandoeningen) was used as diagnostic label, rather than making a distinction between asthma and COPD (chronic obstructive pulmonary disease) as was done in other countries [18]. The CARA-label was also applied to children. For example, the ratio of the label CARA to the label asthma was 1.50, 1.45, and 0.84 in age group 0–4, 5–11, and 12–19 years, respectively, for consultations by general practitioners (GPs) in 1993, although consultations with the label 'bronchitis' (not specified as acute or chronic) had a higher prevalence under the age of 11 [9]. For specialist consultations, these ratios were 0.93, 0.56, and 0.41, respectively, 'bronchitis' playing only a minor role [9]. These data likely reflect the difficult distinction between wheezy disorders at younger age, especially in general practice. The pattern of treatment for CARA and asthma was remarkably similar, mainly bronchodilators and anti-inflammatory drugs. Prescrip-

Correspondence: Professor J. C. de Jongste, Department of Paediatric Respiratory Medicine, Sophia Children's Hospital, Dr Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands.
E-mail: j.c.dejongste@erasmusmc.nl

tions by GPs for 'bronchitis' were mainly for antibiotics. However, in 1992 a consensus meeting of a Central Advisory Committee on Childhood Asthma was held and the use of CARA as diagnostic term was discouraged [19]. CARA categorized as 'chronic obstructive airway disease not classified elsewhere' is included in the ICD codes for COPD.

Trends in the Netherlands between 1980 and 1999 [9]

Because of the coding practices by IMS Health in the 1980s, we performed trend analyses on consultation and prescription rates for asthma and COPD combined in children aged 0–19 years. We analysed trends on hospital admissions and mortality for asthma, COPD, acute bronchi(oli)tis, and pneumonia and influenza in children aged 0–14 years.

Consultations and prescriptions

First consultations showed stable rates, except for an increase in age group 0–4 years in specialist practice. Rates of repeat consultations increased in age groups 0–4 years and 5–11 years for both GPs and specialists, and also in age group 12–19 years for specialists. Prescription rates of pulmonary medication increased. The ratios of prescription rate to consultation rate for the anti-inflammatory drugs increased significantly in all three age groups. The prevalence of consultations and prescriptions was negatively associated with age. Figure 1 presents the rates of first and repeat consultations for asthma in 1999 by age and doctor's category.

Hospital admissions

Hospital admissions for asthma showed an increase in age group 0–4 years, and a decrease in age groups 5–9 years and 10–14 years. These trends occurred primarily in the 1980s. Notably, admissions for acute bronchi(oli)tis increased also in age group 0–4 years. A marked decrease in paediatric admissions for COPD occurred after 1993, that was mirrored by an increasing trend for asthma in children over 4, albeit smaller. Hospital admissions for pneumonia and influenza

fluctuated in all three age groups, without significant trends. Figure 2 shows the respective admission rates.

Mortality

No trends were found in the mortality from asthma and COPD. In the 20-year study period, an average of 1.65 deaths per year occurred in age group 0–4 years in a population of nearly one million children, and of 1 death per year in age group 5–14 years in a population of nearly two millions. The figures for COPD were similar. Mortality from acute bronchi(oli)tis and from pneumonia and influenza decreased in age group 0–4 years, at which age death rates were highest.

Interpretation of trends

Improved asthma management

Trends in prescriptions were in line with the asthma guidelines, especially the increased prescriptions for anti-inflammatory drugs. Along with the increase in repeat consultations, which may reflect more frequent follow-up visits for review of treatment, particularly with respect to inhaled steroids in children, these data suggest better asthma management. The hospital admissions trends in age group 10–14 years and to a lesser extent in age group 5–9 years fit with better asthma management, but the increased hospitalization in age group 0–4 years is a conflicting finding. In other countries, reductions in hospitalization for asthma have been linked with increases in prophylactic treatment [20–22]. The changes in children under the age of 5 years were also not clear-cut [20]. In a study from Norway, age group 0–3 years showed an increase in first admissions for asthma, but a decrease in readmissions, possibly due to increasing use of anti-inflammatory treatment and better management. Increasing prevalence of childhood asthma was suggested, however [22]. Only recently attempts were made to enhance the therapeutic efficacy of the inhaler devices for treatment in young children [23]. The levelling off of the admissions for asthma in age group 0–4 years in the 1990s with the concurrent decrease in admissions for COPD may indicate improvement in management in this age group as well.

Increased asthma prevalence and severity

Consultation rates may also reflect need for care, and the increase in consultations and prescriptions may point to increased prevalence and severity of asthma. This is supported by the finding that the percentage of primary school-children with asthmatic symptoms and doctor diagnosed asthma increased in the Netherlands [24]. An increased prevalence of asthma would be in line with findings from other countries [5]. In this respect, the increasing hospital admissions in age group 0–4 years may be an early reflection of an increase in prevalence. Furthermore, an increase in first consultations with specialists was observed in age group 0–4 years. In the Netherlands, patients being referred to the specialist by their GP is a common practice. A shift in medical care is not in line with the Dutch guidelines for asthma in children, whereas an increase in severity would be in line with the increase in hospital admissions for asthma in this age

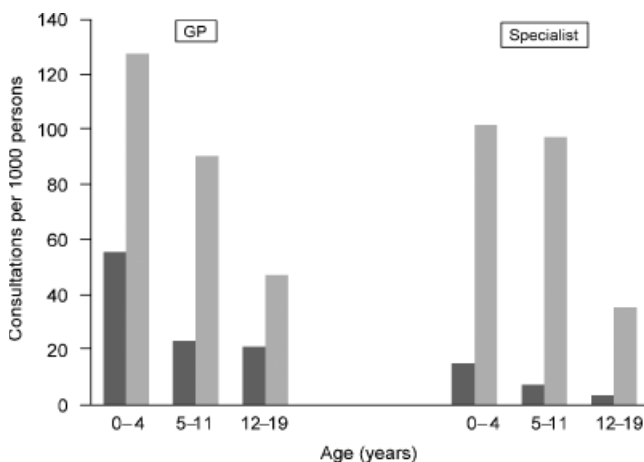


Fig. 1. Number of consultations for asthma per 1000 persons by doctor's category and age group in the Netherlands in 1999. Asthma: international classification of diseases (ICD)-10 code J45. ■, first consultations; □, repeat consultations.

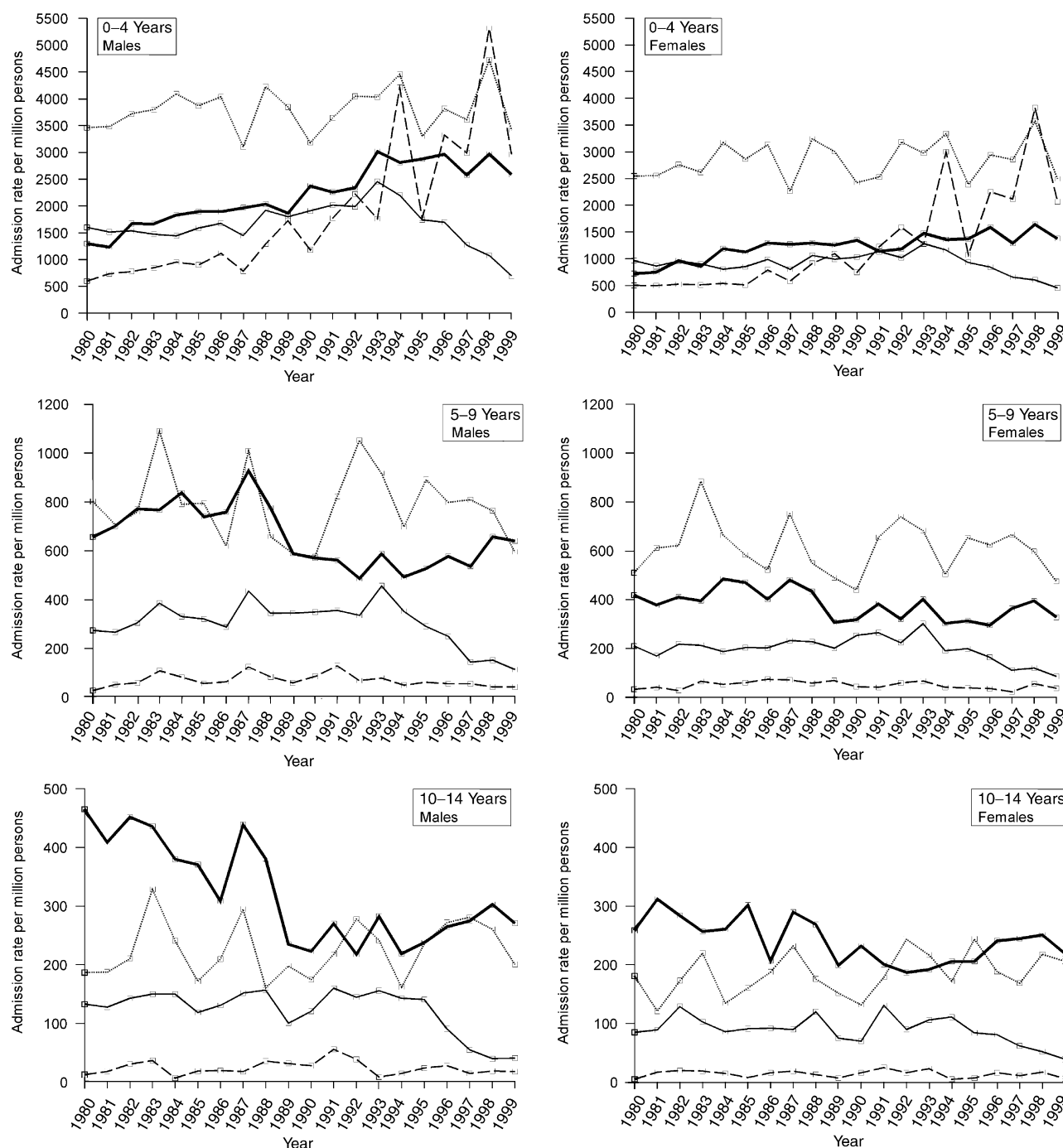


Fig. 2. Hospital admission rates per million persons for asthma (ICD-9 code 493), chronic obstructive pulmonary disease (COPD) (ICD-9 codes 490–492, 496), acute bronchi(ol)itis (ICD-9 code 466), and pneumonia and influenza (ICD-9 codes 480–487), in males (left panels) and females (right panels) in age groups 0–4 years (upper panels), 5–9 years (middle panels), and 10–14 years (lower panels) in the Netherlands, 1980–1999. —, asthma; —, COPD; ----, acute bronchi(ol)itis; pneumonia/influenza.

group. An increase in severity has also been suggested for the United States [25]. Data on severity have not been unambiguous. In questionnaire surveys from the United Kingdom, indicators for severity of asthma did not point to an increase, but increased severity may have been masked by better management [6, 7].

The increase in hospital admissions had no impact on mortality. Although most asthma deaths in childhood appear to occur at ages over 10 years [8, 26, 27] and in mild

asthmatics [8, 27], deaths in under 4-year-olds might occur in more severe cases [27]. It is unlikely that an increase has been masked in view of the observed decrease in mortality from acute bronchi(ol)itis and from pneumonia and influenza in age group 0–4 years. Hence the risk of dying from asthma seemed to have decreased [4]. However, among children in the United States, mortality showed an increase between 1980 and 1998 especially in black children, possibly due to unfavourable patterns of care [26].

Interacting factors

Factors that could have contributed to the observed trends are shifts in diagnostic labelling and changes in health care policies, in which age is a parameter to take into account.

Diagnostic labelling

Asthma and COPD The trends in hospital admissions for asthma and COPD in the 1990s suggest a diagnostic transfer from COPD to asthma in children of all age groups. This is plausible after a consensus meeting, discouraging the use of CARA as a diagnostic label [19]. This does not need to imply better management in children with asthma, as asthma and CARA had a similar treatment pattern, suggesting that asthma treatment reached a broad spectrum of possibly asthmatic children in the Netherlands. An 'asthma' label in favour of a 'bronchitis' label may reduce antibiotic therapy and improve asthma treatment [28]. However, we found a stable prescription rate of antibiotics, while the prescription rate of anti-inflammatory drugs increased, suggestive of increased prevalence/severity of asthma rather than a shift in labelling.

Asthma and acute bronchi(oli)tis The striking increase in hospital admissions for acute bronchi(oli)tis in age group 0–4 years between 1980 and 1999 in the Netherlands is an interesting observation. This increase was mainly due to increased admissions for acute bronchiolitis in children under the age of 1 year. In the United States, hospitalization rates for bronchiolitis in infants increased substantially between 1980 and 1996, not explained by prematurity or underlying lung disease [29]. Respiratory syncytial virus (RSV) infection is the commonest cause of acute bronchiolitis. It is questioned whether RSV respiratory morbidity is a marker or a cause for the development of wheezing illness including asthma. Only a minority of the children with RSV infection need hospitalization, and the observed increased rates are especially worrying if the hypothesis is true that RSV infection promotes the development of asthma and allergy in children [30]. On the other hand, more infants may be predisposed to develop severe RSV infection. Further research should clarify this issue [16]. Unlike the decrease in hospitalization for pneumonia found in the United States [26], admissions for pneumonia and influenza remained stable in the Netherlands. The increase in hospital admissions for asthma as well as for acute bronchi(oli)tis in age group 0–4 years, while admissions for pneumonia and influenza remained stable, indicates increased respiratory morbidity in young children.

Health care policies

In the Netherlands, a policy discouraging hospital referral was in force along with an actual reduction in the number of hospital beds in the 1980s. A steady decline occurred in admissions overall, but the respiratory diseases showed contrasting trends, especially asthma in age group 0–4 years [31].

In the Netherlands, length of stay in hospital for asthma decreased substantially, from about 14 days in 1980 to about 7 days in 1990, and 5–6 days in 1998. The average length of stay was thus remarkably higher than in other countries [2, 20, 22, 32, 33], where it varied from 5 days or lower in the 1980s [2, 20, 22, 32] to 2–3 days in the 1990s [20, 22].

However, in one study more than 80% of the hospitalizations in children aged 2–14 years were shorter than 24 h [33], drawing attention to the possibility of differences in management of acute asthma in hospitals, or differences in coding practices of the admission, i.e. between day care and ward admissions. In the Netherlands, day care admissions for asthma were negligible in the 1980s, but started to rise in the late 1990s. It is, therefore, not plausible that a shift to day care was a contributory factor for the observed trends in admissions for asthma in the study period, but it is a factor to take into account in future analyses.

The decline in length of stay was independent of age. Therefore, it does not explain differences in admission trends. Readmissions for asthma in childhood appear to occur mainly under the age of 5 [3, 14]. In age group 0–4 years, we found no difference in severity of episode between first admission and readmission [12]. The 0–1-year olds had a higher readmission rate compared to the 2–4-year olds. We found no indication for a lower threshold for admission, rather the reverse [12]. Clinical data indicated a similar practice regarding hospitalization and readmissions for young asthmatic patients. Also in the United Kingdom, routine case notes provided no evidence for a threshold reduction to explain increased hospital admissions [2]. A study from the United States explained stable hospital admission rates for asthma in childhood by an increase in admission threshold, using oxygen saturation as objective parameter [25]. The relation between trends in severity of asthma and admission for asthma needs further clarification.

Apart from prevalence and severity, social factors can play a role in asthma morbidity and mortality. Ethnicity rather than deprivation seems to be a risk factor for hospitalization, which may be due to undertreatment with inhaled steroids rather than to a higher prevalence of asthma [26, 34]. Differences in access to and utilization of health care may also play a role in the asthma mortality trends in the United States [26]. In the Netherlands, data on ethnicity in asthma morbidity and mortality were not available. It is unlikely that the Dutch health insurance system accounts for socio-economic differences in asthma health care utilization [35]. Importantly, access to GP consultations and prescription drug consumption is covered by public insurance, which is compulsorily associated with lower socio-economic status.

Asthma in the young

The health care utilization was highest and increasing in the age group 0–4 years. The increase in hospital admissions for asthma, as well as for acute bronchi(oli)tis, is cause for concern. From the United Kingdom an increase in respiratory morbidity in preschool children was also reported [36]. Young children are at risk for inadequate treatment, and diagnosing asthma appropriately remains essential to ensure effective management [37].

There are still no markers that can be used in routine clinical practice to recognize preschool wheezing children who are at risk for asthma [4], and clinical history and evaluation are still the cornerstones for diagnosis. At ages 0–4 years, we found an inverse association between the number of referrals by GPs to the hospital's outpatient department and age in

children with possible asthma [10]. Also, younger age was a risk factor for exacerbations [11] and hospital readmissions [12] because of asthma. Besides variables from history taking (trigger factors, damp housing), total immunoglobulin E production and sensitization to inhalant allergens proved to be risk factors for exacerbations and hospital (re)admissions [11, 12]. In the 0–1-year-olds, the highest risk of readmission was within the first months after discharge [12]. In general, younger children have shorter intervals between admissions [3]. In older children, inhaled anti-inflammatory therapy was suggestive of a protective effect on the risk for hospitalization and emergency room visits [38]. Application of inhaled steroids in wheezy young children is more controversial for fear of systemic adverse effects and inappropriate asthma diagnosis. In persistent asthma, preschool children may safely benefit from conventional dosages and careful evaluation [39]. The high rates of disease presentation in the very young indicate areas for further research and improvement of management.

Concluding remarks

The Dutch data pointed to a change in diagnostic labelling, likely due to disuse of the Dutch CARA label, improvement in asthma management, as well as a true increase in prevalence and severity of asthma, particularly in the age group 0–4 years.

Increases in the prevalence of asthma were reported and questioned, by various countries, particularly the United Kingdom, Australia, New Zealand [5] and the United States [26]. The International Study of Asthma and Allergy in Childhood (ISAAC), which showed substantial geographical differences in the prevalence of asthma symptoms and diagnosed asthma, aims to gain new insights in the causes of asthma and to assess validated trends in prevalence [40]. Unfortunately, the Netherlands was not among the early participants of ISAAC.

Compared to data from other countries, the Dutch hospital admission rates were low, even when asthma and COPD were taken together, and the duration of stay was longer. Nevertheless, age and gender patterns were similar, as was readmission rate in age group 0–4 years, and the trends pointed in the same direction [1, 3, 12, 22, 26, 32]. Summarizing, hospitalization increased in young children and declined in older children, except for the increase in black children in the United States [26].

In the Netherlands, as in other countries, the trends in hospital admissions occurred primarily in the 1980s and levelled off in the 1990s. Childhood asthma deaths are rare and trends appear to be stable or decreasing. Ambulatory care utilization increased and its role in asthma morbidity trends needs further clarification. Some studies suggest that the increase in prevalence of asthma may have come to an end [41, 42]. Continuing epidemiological evaluation of asthma and asthma-like diseases is indicated to confirm trends and explore outcomes in the health care of asthmatic children.

References

- Mitchell EA. International trends in hospital admission rates for asthma. *Arch Dis Child* 1985; 60:376–8.
- Anderson HR. Increase in hospital admissions for childhood asthma: trends in referral, severity, and readmissions from 1970 to 1985 in a health region of the United Kingdom. *Thorax* 1989; 44:614–9.
- To T, Dick P, Feldman W, Hernandez R. A cohort study on childhood asthma admissions and readmissions. *Pediatrics* 1996; 98:191–5.
- Warner JO, Naspitz CK, Cropp GJA. Third international pediatric consensus statement on the management of childhood asthma. *Pediatr Pulmonol* 1998; 25:1–17.
- Magnus P, Jaakkola JJK. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. *Br Med J* 1997; 314:1795–9.
- Ng Man Kwong G, Proctor A, Billings C et al. Increasing prevalence of asthma diagnosis and symptoms in children is confined to mild symptoms. *Thorax* 2001; 56:312–4.
- Anderson HR, Butland BK, Strachan DP. Trends in prevalence and severity of childhood asthma. *Br Med J* 1994; 308:1600–4.
- Robertson CF, Rubinfeld AR, Bowes G. Pediatric asthma deaths in Victoria: the mild are at risk. *Pediatr Pulmonol* 1992; 13:95–100.
- Hess J.. Epidemiology of asthma in the Netherlands with special reference to childhood. Thesis, Rotterdam, 2003, ISBN 90-9016524-X.
- Wever-Hess J, Kouwenberg JM, Duiverman EJ, Hermans J, Wever AMJ. Prognostic characteristics of asthma diagnosis in early childhood in clinical practice. *Acta Paediatr* 1999; 88:827–34.
- Wever-Hess J, Kouwenberg JM, Duiverman EJ, Hermans J, Wever AMJ. Risk factors for exacerbations and hospital admissions in asthma of early childhood. *Pediatr Pulmonol* 2000; 29:250–6.
- Wever-Hess J, Hermans J, Kouwenberg JM, Duiverman EJ, Wever AMJ. Hospital admissions and readmissions for asthma in the age group 0–4 years. *Pediatr Pulmonol* 2001; 31:30–6.
- Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Group Health Medical Associates Asthma and wheezing in the first six years of life. *N Engl J Med* 1995; 332:133–8.
- Mitchell EA, Bland JM, Thompson JMD. Risk factors for readmission to hospital for asthma in childhood. *Thorax* 1994; 49:33–6.
- Silverman M, Wilson N. Wheezing phenotypes in childhood [editorial]. *Thorax* 1997; 52:936–7.
- Wennergren G, Kristjánsson S. Relationship between respiratory syncytial virus bronchiolitis and future obstructive airway diseases. *Eur Respir J* 2001; 18:1044–58.
- Clark CE, Coote JM, Silver DAT, Halpin DMG. Asthma after childhood pneumonia: six year follow up study. *Br Med J* 2000; 320:1514–6.
- Sluiter HJ, Koëter GH, de Monchy JGR, Postma DS, de Vries K, Orie NGM. The Dutch Hypothesis (chronic non-specific lung disease) revisited. *Eur Respir J* 1991; 4:479–89.
- Kerrebijn KF. Consensus on asthma in children (English summary). *Ned Tijdschr Geneesk* 1993; 137:1239–46.
- Wennergren G, Kristjánsson S, Strannegård I-L. Decrease in hospitalization for treatment of childhood asthma with increased use of antiinflammatory treatment, despite an increase in the prevalence of asthma. *J Allergy Clin Immunol* 1996; 97:742–8.
- Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA* 1997; 277:887–91.
- Jónasson G, Carlsen K-H, Lødrup Carlsen KC, Mowinkel P, Leegaard J, Halvorsen KS. Trends in hospital admissions for childhood asthma in Oslo, Norway, 1980–95. *Allergy* 2000; 55:232–9.
- Janssens HM, Heijnen EMEW, de Jong VM et al. Aerosol delivery from spacers in wheezy infants: a daily life study. *Eur Respir J* 2000; 16:850–6.

- 24 Van der Wal MF, Uitenbroek DG, Verhoeff AP. Increased proportion of elementary school pupils with asthmatic symptoms in the Netherlands, 1984/85-1994/95; a study of the literature (English summary). *Ned Tijdschr Geneesk* 2000; 144:1780-4.
- 25 Russo MJ, McConnochie KM, McBride JT, Szilagyi PG, Brooks AM, Roghmann KJ. Increase in admission threshold explains stable asthma hospitalization rates. *Pediatrics* 1999; 104:454-62.
- 26 Akinbami LJ, Schoendorf KC. Trends in childhood asthma: prevalence, health care utilization, and mortality. *Pediatrics* 2002; 110:315-22.
- 27 Jørgensen IM, Jensen VB, Bülow S, Dahm TL, Prah P, Juel K. Asthma mortality in the Danish child population: risk factors and causes of asthma death. *Pediatr Pulmonol* 2003; 36:142-7.
- 28 Wilson NM. Wheezy bronchitis revisited. *Arch Dis Child* 1989; 64:1194-9.
- 29 Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980-1996. *JAMA* 1999; 282:1440-6.
- 30 Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman B. Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7. *Am J Respir Crit Care Med* 2000; 161:1501-7.
- 31 Wever-Hess J, Wever AMJ, Yntema JL. Mortality and morbidity from respiratory diseases in childhood in the Netherlands, 1980-1987. *Eur Respir J* 1991; 4:429-33.
- 32 Skobeloff EM, Spivey WH, St Clair SS, Schoffstall JM. The influence of age and sex on asthma admissions. *JAMA* 1992; 268:3437-40.
- 33 Benito J, Lopez Bayon J, Montiano J, Sanchez J, Mintegui S, Vazquez C. Time trends in acute childhood asthma in Basque Country, Spain. *Pediatr Pulmonol* 1995; 20:184-8.
- 34 Giltthorpe MS, Lay-Yee R, Wilson RC, Walters S, Griffiths RK, Bedi R. Variations in hospitalization rates for asthma among Black and minority ethnic communities. *Respir Med* 1998; 92:642-8.
- 35 Bongers IMB, van der Meer JBW, van den Bos J, Mackenbach JP. Socio-economic differences in general practitioner and outpatient specialist care in the Netherlands: a matter of health insurance? *Soc Sci Med* 1997; 44:1161-8.
- 36 Kuehni CE, Davis A, Brooke AM, Silverman M. Are all wheezing disorders in very young (preschool) children increasing in prevalence? *Lancet* 2001; 357:1821-5.
- 37 Keeley DJ, Silverman M. Are we too ready to diagnose asthma in children. *Thorax* 1999; 54:625-8.
- 38 Adams RJ, Fuhlbrigge A, Finkelstein JA et al. Impact of inhaled antiinflammatory therapy on hospitalization and emergency department visits for children with asthma. *Pediatrics* 2001; 107:706-11.
- 39 Allen DB. Inhaled corticosteroid therapy for asthma in preschool children: growth issues. *Pediatrics* 2002; 109:373-80.
- 40 Janson C, Anto J, Burney P et al. On behalf of the European Community Respiratory Health Survey II. The European Community Respiratory Health Survey: what are the main results so far? *Eur Respir J* 2001; 18:598-611.
- 41 Ronchetti R, Villa MP, Barreto M et al. Is the increase in childhood asthma coming to an end? Findings from three surveys of schoolchildren in Rome, Italy. *Eur Respir J* 2001; 17:881-6.
- 42 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12:315-35.