

The costs of atopy and asthma in children: Assessment of direct costs and their determinants in a birth cohort

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The aim of this study was to estimate costs accrued by the health care of children with asthma in comparison to children with atopic eczema and seasonal rhinitis and to investigate cost determinants. From the multicenter cohort study (MAS-90), we selected children with an asthma, atopic eczema and/or seasonal rhinitis diagnosis during the first 8 years of life, and overall 8-year health care utilization was estimated retrospectively by reviewing medical records. Asthma treatment ($n = 76$) incurs an average cost of US\$ 627 per year, 44% due to hospital stays. Atopic eczema treatment ($n = 91$) cost on average US\$ 219 and seasonal rhinitis ($n = 69$) US\$ 57 per year. In asthma and atopic eczema, costs increase significantly with disease severity. Allergy diagnostics use accounts for only 1% of total costs. Costs for asthma and atopic eczema treatment are highest in those years when topical steroids are used for the first time, but decrease with every further year of steroid use. A remarkable 25% of asthmatic children with severe symptoms were not treated according to national guidelines, so that most steroid treatment was initiated during the first hospital stay. In the case of asthma, total direct costs increased until the 3rd year of the disease, and then decreased with further years of diagnosis, while steroid use continued to increase. These results indicate a 'learning effect' in the treatment of asthma and atopic eczema for each patient as well as considerable cost-saving potential by preventing severe asthma. Moreover, the importance of considering cost-driving factors and using cohort or longitudinal designs in cost-of-illness approaches is emphasized.

Stefan Weinmann^{1,3}, Panagiotis Kamtsiuris², Klaus-Dirk Henke³, Magnus Wickman⁴, Asa Jenner⁵ and Ulrich Wahn¹

¹Department of Pediatric Pneumology and Immunology, Children's Hospital, Berlin, Germany,

²Robert-Koch-Institute for Infective and Non-communicable Diseases, Berlin, Germany,

³Department of Public Finances, Technical University, Berlin, Germany, ⁴Department of Environmental Health, Stockholm County Council, Sweden,

⁵Pharmacia Diagnostics AB, Uppsala, Sweden

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Stefan Weinmann, Department of Pediatric Pneumology and Immunology, University Children's Hospital, Charité – Campus Virchow, Augustenburger Platz 1, D-13353 Berlin, Germany
Tel.: + 49-30-450-66187
Fax: + 49-30-450-66943
E-mail: Stefan.Weinmann@gmx.de

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In order to establish primary and secondary preventive measures, considerable effort in recent years has gone into the early identification of children with a high risk for development of atopic diseases (1). The increasing prevalence of asthma in children (2) makes it a major public health problem, not only in industrialized countries. To evaluate the economic impact of asthma and other atopic diseases on national populations, several cost-of-illness studies have been conducted (3, 4). The majority of these studies use 1-year aggregate data from health statistics, or, within a 'bottom-up' design, retrospective

health care utilization data with a maximum time horizon of 1 year.

Asthma, atopic eczema and seasonal rhinitis are chronic conditions with considerable correlation to atopy status in children (5–7), therefore it is of interest to compare the resources used for these three diseases over time. In the case of asthma, it is well known that a subgroup of severely ill patients with low steroid use is responsible for a large portion of health care costs (8).

The aim of this study was to assess the financial cost of health care for children with asthma, atopic eczema and rhinitis over a period

of 8 years and, for asthma and atopic eczema, in correlation with disease severity, treatment regimen and disease duration.

Subjects and methods

Subjects

A total of 210 children who had developed asthma, atopic eczema and/or seasonal rhinitis symptoms during the first 8 years of life were retrospectively selected from the Berlin part of the MAS-90 (Multicenter Atopy Study) cohort (9). Thus, all children born in Berlin who regularly came to MAS follow-up visits until the 8th year of life were selected. Children enrolled in MAS-90, an epidemiological study undertaken to evaluate the predictive value of various clinical and immunological parameters and early environmental factors for the development of atopic diseases in childhood, were all born in 1990. A wide array of parameters in relation to atopic disease such as socio-economic and family risk factors, wheezing episodes, sneeze attacks, and quantitative assessment of severity using the SCORAD score were assessed every year.

A total of 158 parents (75.2%) gave written consent, and data of 145 children (69%) could be collected and evaluated. The other 13 children were without any data because of treating physician's death or refusal to cooperate, or families having moved away, and were not included into the cost evaluation. Regarding histories of the three atopic diseases with symptoms for at least 1 year during the first 8 years of life, a total of 76 children suffered from asthma (52.4% of 145), 91 from atopic eczema (62.8% of 145) and 69 from seasonal rhinitis (46.5% of 145). Of all the children, only 52.4% (76/145) had symptoms of one atopic disease (18.6% only asthma, 25.5% only atopic eczema, 8.3% only seasonal rhinitis), 32.4% (47/145) of all children had symptoms of two atopic diseases, and 15.2% (22/145) had symptoms of all three atopic diseases.

Methods

Asthma was defined yearly by the presence of at least four reported wheezing episodes during the last 12 months (ISAAC questionnaire) (2), and/or a pediatrician's diagnosis of bronchial asthma or status asthmaticus. Atopic eczema was defined by a pediatrician's diagnosis of atopic eczema and/or by a positive response to the combination of all of the following questions covering the 12-month period and answered by parents: 'Did your child have dry skin?', 'Was there frequent or

permanent scratching?' and 'Did your child have itchy pustules?'. Seasonal rhinitis was defined by the presence of persistent sneeze attacks for at least 2 months and/or a pediatrician's diagnosis of atopic or seasonal rhinitis.

For each year of life, children with asthma or atopic eczema symptoms were additionally classified retrospectively according to severity of disease, treatment, and disease duration. Asthma severity was assessed by evaluating parents' answers to annual ISAAC questionnaires. Mild asthma was classified as 1–3 wheezing episodes over 12 months, moderate asthma as 4–12 episodes, and severe asthma as more than 12 annual wheezing episodes. Atopic eczema severity was assessed according to SCORAD (10). A score of 1–25 was classified as mild disease, from 26 to 50 moderate, and above 50 as severe.

Asthma and atopic eczema treatments were classified for each year according to the highest class of pharmaceutical medication. At least one prescription characteristic for a higher treatment level resulted in classification of the patient in that level for the year. In the case of asthma, children were classified according to having been prescribed no anti-asthmatic medication (0), only β_2 -agonist and/or ipratropium bromide (A), cromoglycate with or without β_2 -agonist/ipratropium bromide (B), or inhaled corticosteroids with or without cromoglycate/ β_2 -agonist/ipratropium bromide (C). Children with atopic eczema were classified according to having received no dermatological medication (0), only emollients (A), or topical steroid medication with or without other substances (B).

Data collection and resource use

Only expenditure related directly to asthma, atopic eczema and seasonal rhinitis medical care and rehabilitation was evaluated (direct costs) (6). In Germany, rehabilitation treatment refers to treatment units run by a physician, mostly under favorable climatic conditions, and often with an emphasis on mother–child convalescence, reimbursed by the health insurance agency to improve the disease course. Health care utilization and resource use was assessed from the third party's perspective (health insurance organization).

Utilization data was collected directly by retrospective chart reviews in the offices of all physicians involved in children's treatment. The parents provided physicians' names. Data entries were standardized by a trained physician investigator. The following items were assessed: use of inpatient services (hospitalization and

rehabilitation clinic stays), physician visits (general practitioners and specialists), physician telephone contacts, hospital outpatient services (emergency room and special outpatient clinics), outpatient drugs, appliances and devices, and atopy related diagnostics (e.g. serologic diagnostics, lung function, skin tests, X-ray). Each health care contact was classified individually by the investigator as asthma, rhinitis and/or eczema related. In most cases (91%) whole utilization data for the first 8 years of life were available. Years with incomplete data were classified as missing.

Cost estimates

Disease-related expenditures were estimated using market prices, or by multiplying the units of resource use by the respective charges. All costs were valued in constant 1996 German marks (DM) and converted to US\$ using gross domestic product purchasing power parities, as published by the Organization for Economic Cooperation and Development for 1996 (exchange rate US\$ 1 = DM 1.80). Medication prices were based on the 1996 fixed prescription prices. Diagnostic costs were assessed according to the 1996 official German schedule of physician's fees. One doctor visit received the 1996 unit cost of US\$ 45 for general practitioners, and US\$ 51 for specialists. A telephone contact cost US\$ 5. The number of inpatient hospital days was multiplied by US\$ 482, the 1996 average price per hospital day of all pediatric departments in Berlin. Inpatient medication costs are included in the hospital inpatient cost component. The average daily charge for rehabilitation clinics in Germany was US\$ 139. The unit price for one hospital outpatient contact was US\$ 111.

Cost evaluation

Costs were evaluated for each year and for each disease separately whether or not children had two or more atopic diseases at the same time. Drugs prescribed for more than one atopic disease were not considered. Thus, double counts could be avoided. Costs were expressed as costs per disease-year and represent the total annual disease specific health care costs in years with symptoms.

Statistical analysis

Statistical analysis was performed in MS-ACCESS and SPSS 8.0. Results were calculated as mean values. *t*-Tests and Wilcoxon rank sum tests were used to compare costs according to

disease severity and treatment, and 95% confidence intervals (95% CI) were calculated. A sensitivity analysis was performed using a low-prize and a high-prize scenario.

Results

The socio-economic and family characteristics of the study group are described in Table 1. Sex distribution, age of mother, nationality, family status and mother's education are comparable to the whole MAS cohort. The frequency of atopic diseases in the families and family risk was increased compared to the MAS population, which was already a high-risk group. This could be expected because positive family history is an important risk factor for atopic diseases, although most children developing atopic diseases will not be identified at birth by family history (7).

Of the children with asthma, 57.8% (44/76) already had symptoms in the first 2 years of life, and 53.8% (49/91) of children with atopic eczema already had eczema symptoms in the first 2 years.

Table 1. Socio-economic and family characteristics of the study group (n = 145 children with asthma, atopic eczema and/or rhinitis) in comparison with the MAS cohort (9)

	Frequency	%	% in MAS n = 1314
Gender			
Female	69	47.6	47.9
Age of mother			
<25	20	13.8	15.3
25–30	66	45.5	48.8
31–35	39	26.9	24.9
36–40	18	12.4	10.1
>40	2	1.4	0.9
Family status			
Unmarried	11	7.7	9.9
Married	130	91.6	88.8
Divorced	1	0.7	1.3
Nationality			
German	136	93.8	94.0
Mother's school education			
Basic	37	25.5	29.7
Secondary School	42	32.3	32.3
High School	29	22.3	22.3
University degree	22	16.9	19.9
Atopic disease, mother	63	43.4	35.8
Atopic disease, father	53	36.8	29.9
Atopic disease, sibling	25	37.9	25.9
Atopic family risk*			
1 relative	53	36	33.9
2 relatives	39	26.9	19.7
3 or more relatives	3	2.1	1.0

*Atopic family risk defined as occurrence of at least one atopic disease (asthma, atopic eczema or rhinitis) within the family.

Average treatment costs

Medical treatment of asthma between 1990 and 1998 was almost three times as expensive as atopic eczema treatment and 11 times as expensive as seasonal rhinitis treatment (Table 2). For asthma, hospital inpatient treatment was the

Table 2. Costs per disease year (in US\$) and cost components for asthma (n = 76), atopic eczema (n = 91) and seasonal rhinitis (n = 69); CI = 95% confidence interval

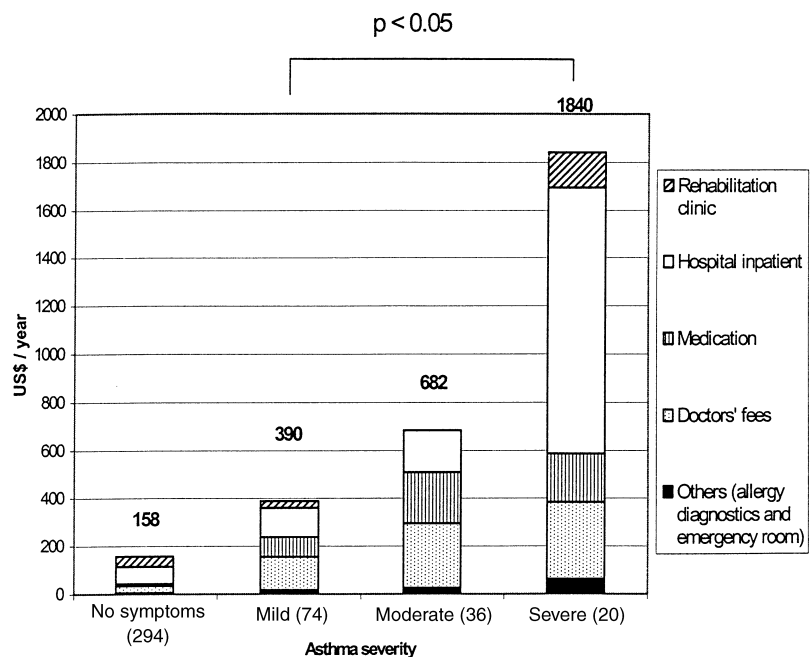
	Costs (US\$)	CI	% of total
Asthma			
Total	627	157–1918	100.0
Rehabilitation clinic	34	0–81	5.6
Hospital	265	0–552	43.5
Emergency Room	17	8–24	2.8
Diagnostics	7	4–10	1.1
Medication	121	82–159	19.9
Doctors' fees	183	121–216	30.0
Atopic eczema			
Total	219	129–309	100.0
Rehabilitation clinic	67	0–135	30.4
Hospital	29	0–69	13.4
Emergency Room	7	2–13	3.3
Diagnostics	2	1–3	1.0
Medication	37	26–49	17.1
Doctors' fees	76	61–92	34.9
Seasonal rhinitis			
Total	57	15–204	100.0
Rehabilitation clinic	8	0–32	14.0
Emergency Room	1	0–18	1.8
Diagnostics	11	4–21	19.3
Medication	3	0–14	5.3
Doctors' fees	34	27–45	59.6

biggest cost component, whereas doctors' costs were highest for atopic eczema and seasonal rhinitis. In terms of cost distribution, 20% of children with asthma incurred 76% of the total health care costs, whereas 20% of children with atopic eczema incurred 85% of the total costs.

Costs and disease severity

Asthma and atopic eczema treatment costs increased with the severity of symptoms. Direct costs evaluated for 424 disease years in 76 children with asthma are shown in Fig. 1. Because well-treated asthmatics can be asymptomatic for a year while consuming resources, years without symptoms after the first asthma diagnosis were evaluated too. Treatment of severe asthma was disproportionately expensive (US\$ 1840, 95% CI 0–4017) with inpatient hospital costs of US\$ 1108 (0–3272) as the highest cost component (60.2% of total costs), followed by physicians' fees of US\$ 320 (195–445, 17.4% of the total) and medication costs of US\$ 203 (96–311, 11.0% of the total). The cost increase between mild and moderate asthma was mainly caused by doctor visits (US\$ 138, 108–167 in mild compared to US\$ 213, 186–350, in moderate asthma) and an increase in prescriptions (medication costs of US\$ 82, 30–143, compared to US\$ 213, 113–313, respectively). However, inpatient treatment costs were mostly responsible for the cost increase between moderate and severe asthma (US\$ 174,

Fig. 1. Annual treatment costs (in US\$) for childhood asthma in relation to disease severity irrespective of mode of treatment or disease duration. All years when asthma was first diagnosed and all years after the first asthma diagnosis were taken into account whenever occurring during the first 8 years of life. Numbers in brackets (*) indicate the number of years evaluated.



0–405 in moderate asthma compared to US\$ 1108, in severe asthma), while costs for physician fees and medication remained stable.

Atopic eczema treatment costs according to disease severity evaluated for 234 disease years in 91 children are shown in Fig. 2. The main reason for the cost increase between moderate and severe disease were rehabilitation clinic stays (US\$ 454, 95% CI 0–1467, 49.8% of total costs in severe disease, compared to US\$ 69, 73–212, 16.6% of total costs in moderate disease). However, physician costs were also substantially higher (US\$ 245, 106–382, 26.8% of total costs in severe, vs. US\$ 141, 78–205, 33.8% of total costs in moderate disease). In the case of atopic eczema, hospital inpatient costs were incurred only during years with moderate symptoms, but not with mild or severe symptoms.

Costs and treatment

Both in asthma and atopic eczema direct costs increased with the level of medication, an indicator

of treatment intensity (Fig. 3). For years when asthma was treated with inhaled steroids (US\$ 2090, CI 327–3854), the highest cost component was hospital inpatient treatment (55.3% of total costs). In those years, medication (22.2%) cost more than physicians (16.5%), whereas in years with cromoglycate as maximum therapy (total costs of US\$ 689, 419–960), physicians' costs (45.0%) were higher than medication costs (28.0%) and rehabilitation costs (11.2%). An unexpected result was the high hospital inpatient costs in years without any anti-asthmatic medication (51.2% of total costs). In the evaluation of costs according to treatment, children were not differentiated according to having, or not, a diagnosis in that year. Further evaluation revealed that hospital inpatient costs in the group of children treated with steroids were highest in the 1st year of steroid treatment (68.6% of the 1st year total costs) and decreased for further steroid treatment in absolute and relative terms (27.4% of total costs in the 2nd year of treatment, and 25.1% of total costs in the 3rd or more years of treatment).

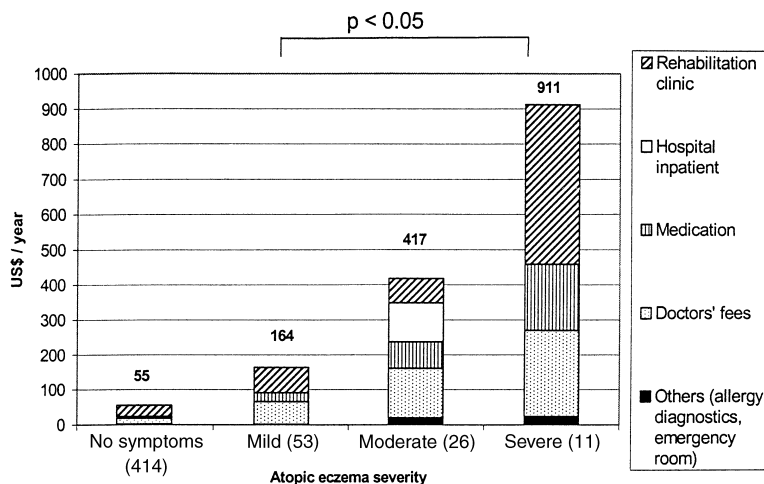


Fig. 2. Annual treatment costs (in US\$) for childhood atopic eczema in relation to disease severity irrespective of mode of treatment or disease duration. All years when atopic eczema was first diagnosed and all years after the first atopic eczema diagnosis were taken into account whenever occurring during the first 7 years of life. Numbers in brackets (*) indicate the number of years evaluated.

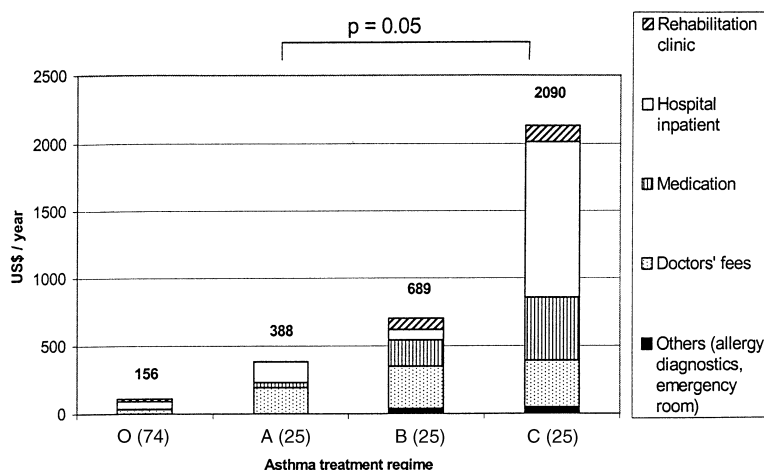


Fig. 3. Annual treatment costs (in US\$) for childhood asthma according to treatment regimen. All years when asthma was first diagnosed and all years after the first asthma diagnosis were taken into account whenever occurring during the first 8 years of life. Numbers in brackets (*) indicate the number of disease years evaluated.

Treatment costs for children with atopic eczema (Fig. 4) were highest in years with steroid treatment (US\$ 444, CI 161–727). Moreover, the proportion of hospital costs was highest in years when steroid medication was applied (25.5% of total costs). The biggest cost component in those years was physicians' costs (47.1% of total costs, compared to 23.0% of total costs in years when only emollients were applied). Rehabilitation stays occurred only in years without steroid treatment (with costs of US\$ 144, 0–319, making up 41.5% of annual costs in years with treatment A). Further evaluation revealed a cost reduction with further steroid treatment (US\$ 589, 0–1208, of total costs in the 1st year of treatment, compared to US\$ 376, 211–541, of total costs in the 2nd year of steroid treatment, and US\$ 239, 76–403, in subsequent years of treatment), whereas treatment costs with non-steroid medication in the 3rd or more years with this regimen were

higher than in the 2nd year (US\$ 373, 30–716, compared to US\$ 259, 0–526, in the 2nd year).

Costs and disease duration in children with asthma

Total asthma treatment costs increased until the 3rd year of asthma diagnosis from US\$ 328 (167–469, $n = 69$) in the 1st year to US\$ 925 (0–4558, $n = 17$) in the 3rd year. Then costs began to decrease in further symptomatic years and made up only US\$ 465 (213–718, $n = 14$) after the 6th year, whereas medication costs increased, constituting more than 75% of total costs after the 6th year of disease. Costs in the 3rd year were dominated by the hospital inpatient component (69.2% of total costs), but no further hospital stays took place following the 5th year after diagnosis. Physicians' costs developed parallel to the course of total costs. A comparison to the applied treatment regimens over time (Fig. 5)

Fig. 4. Annual treatment costs (in US\$) for childhood atopic eczema according to treatment regimen. All years when atopic eczema was first diagnosed and all years after the first atopic eczema diagnosis were taken into account whenever occurring during the first 7 years of life. Numbers in brackets (*) indicate the number of disease years evaluated.

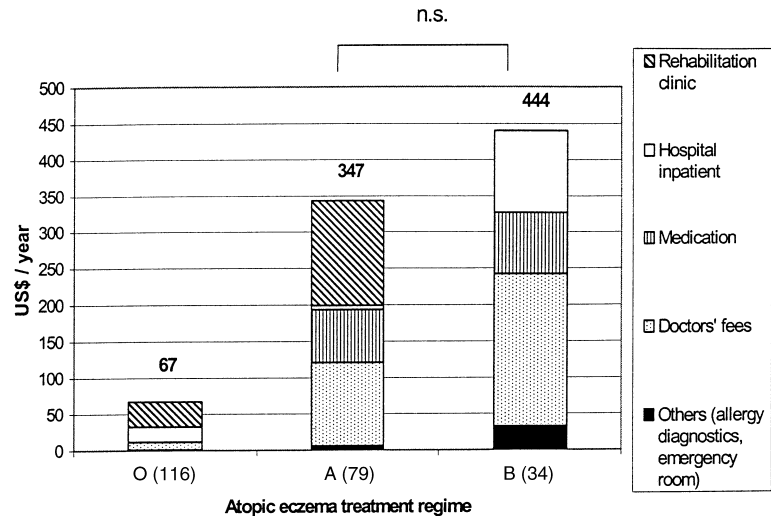
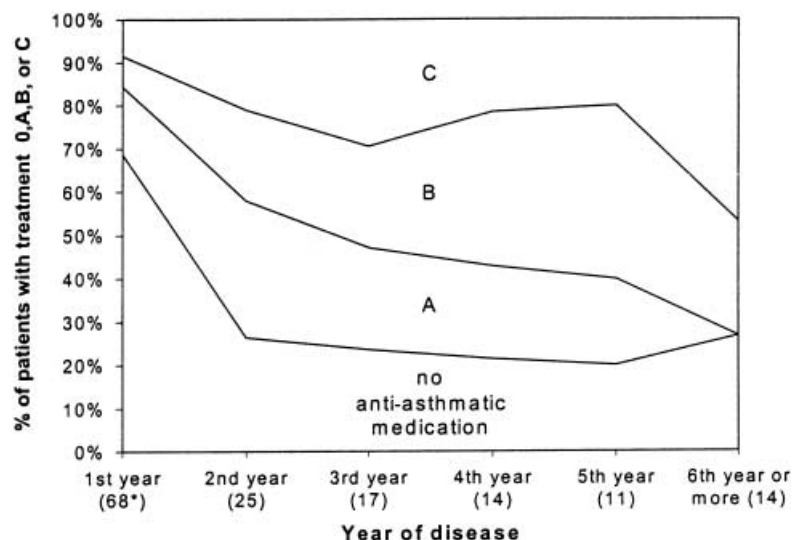


Fig. 5. Relative frequency of asthma medication treatment regimens according to disease duration. A: only β_2 -agonist and/or ipratropium bromide; B: cromoglycate with or without β_2 -agonist/ipratropium bromide; C: inhaled corticosteroids with or without cromoglycate/ β_2 -agonist/ipratropium bromide. Numbers in brackets (*) indicate the number of children evaluated.



shows that with disease progression anti-inflammatory medication (B and C) was increasingly applied (in 15% of cases in the 1st year compared to 70% of cases in the 6th year), whereas the proportion of children with only β_2 -agonist or no anti-asthmatic medication decreased. Steroid medication use increased from 10% of cases in the 1st year to 45% of cases after the 5th year. However, after the 2nd year a proportion of about 20% of children with symptoms remained without any anti-asthmatic medication.

Sensitivity analysis

Modification of key assumptions (hospital and rehabilitation clinic charges per day and physician's fees per visit) according to acceptable lower and higher values did not change the cost distribution significantly. As a rule, using 50% lower charge values, the proportion of hospital and rehabilitation inpatient costs decreased by only 10% in asthma and atopic eczema. Thus, with lower values, both cost components together made up 42% of total costs in asthma and 40% in eczema, compared to 49% in asthma and 44% in atopic eczema with our original values. Using 50% higher charge values, the proportion of inpatient costs and of medication costs both increased by 10%. Cost differences between severity and regime groups remained statistically significant.

Discussion

The pattern of health care spending for specific diseases gives information about an increasingly important part of the socio-economic impact of these diseases on society (11, 12). Economic outcomes can be compared with other outcomes like quality of life or clinical data, in order to establish priorities to improve health care (13). Recently, outpatient data as measures of asthma-related health care utilization have been identified as one of the most relevant areas of research (14). They permit the analysis of chronic disease management in longitudinal designs in a more realistic way than hospital-based data.

In this study, patient records in physicians' offices were the primary data source. Health care utilization could be assessed retrospectively over a period of 8 years. We estimate the annual expenditures for pediatric asthma care in Germany to amount to US\$ 627 per capita, in comparison with US\$ 219 spent on atopic eczema care. The originality of the study consists in the selection of children and the array of available parameters with which costs could be

correlated. Based on a birth cohort, selection resulted in a distribution of severity levels among the study group that is closer to the actual epidemiological situation than in most other studies. Selection bias towards more severe cases and therefore higher resource use is minimized when patient recruiting is not dependent on caregivers' judgements.

For pediatric asthma, annual treatment costs in our study are almost identical with the Swiss figure of US\$ 640 (15), although the proportion from outpatient physician care was higher in our study (28% vs. 17.5% in the Swiss study). Financial costs of hospital care were comparable in both studies, indicating a similar waste of resources on tertiary disease control in both countries during the study period. Our cost estimates for pediatric asthma are considerably lower than in another German study (16). Taking into account the selection bias in the study of Schulenburg *et al.*, caused by an uncontrolled patient selection within physicians' outpatient offices and non-standardized severity scores based solely on physicians' assessment, our cost estimates are closer to the actual severity distribution. Compared to the 1992 data of a health care utilization study within a large health maintenance organization in the USA (17), our results were quite similar to the 'marginal' asthma treatment costs of US\$ 615 for pediatric asthma in this study. Taking the treated prevalence of 5% as population prevalence between 1 and 17 years of age in Germany, the medical treatment costs of pediatric asthma from the third party's perspective would amount to US\$ 220 million per year. Yet the actual asthma prevalence in Germany of about 10% in children would yield the more convincing number of US\$ 440 million per year, because in our study untreated asthma was also included in calculating the average per patient estimate.

Atopic eczema treatment costs for children were lower in our study than in a 1995 Australian estimate (18). The Australian study also involved selection of more severe cases by hospital-based patient recruiting. This, and the different health care systems with higher out-of-pocket costs compared to Germany, is responsible for the higher cost values in the Australian study. Therefore comparability of absolute cost-of-illness estimates between countries is extremely limited when study designs differ.

The costs of seasonal rhinitis treatment were low in our study, but there seems to be considerable under-diagnosis and under-treatment of seasonal rhinitis. There is only one Japanese study estimating the per patient cost of seasonal

rhinitis (19). In this study, 1994 indirect and direct costs together were estimated at US\$ 118 per patient, and were thus twice as high as in our study.

We identified a disproportionate increase in direct costs with severity, but also with treatment regimen in both asthma and atopic eczema. However, there was a strong tendency towards lower costs with disease progression while maintaining preventive steroid treatment in asthma. The finding that steroid treatment for asthma only began in most cases in the year of the first hospitalization, implies considerable cost-saving potential by earlier preventive treatment and earlier risk assessment (family history and immunodiagnostics use). The average annual costs for allergy diagnostics were only 1% of total costs. Consequent steroid treatment in atopic eczema resulted in decreasing costs with every further year of eczema manifestation, compared with the use of emollients alone. An interesting finding was asthma cost distribution according to disease duration, with a decrease of total and hospital costs and an increase in medication costs after the 3rd year. The use of anti-inflammatory medication also increased with disease duration. This suggests a 'learning effect' in asthma disease management for each individual patient. An unexpected result was the high proportion of asthmatic children without any anti-asthmatic medication treatment. In years following the first asthma diagnosis the proportion of inadequately treated children (about 20%) did not diminish significantly with time, suggesting considerable undertreatment in almost a quarter of patients.

Preventive measures and diagnostics are relevant for asthma, atopic eczema and seasonal rhinitis, thus it is interesting to compare the economic burden and influence of intervention strategies on all three diseases (13). Given the evidence of significantly lower health care costs of controlled vs. non-controlled asthma (20), and other findings that patients with asthma attacks had average expenditures 3.5 times higher than those without (21), disease management programs will lead to a more efficient use of increasingly limited health care resources (22).

There are some limitations of the study. First, estimates are the average of the expenditures between 1990 and 1998, and therefore represent treatment pathways over a time when preventive steroid treatment was gradually entering clinical practice. Second, treatment regimens were not classified according to the medication doses, but according to the presence of at least one prescription characteristic for the treatment level. This could have led to a bias towards higher

treatment levels, because an inhaled steroid could for example have been used only once in a year. However, a data check showed that it was rare for there to be only one or two prescriptions of the same treatment level within a year. Third, we were unable to identify out-of-pocket expenditures, which are considerable in the case of atopic eczema. A further limitation is the inability to use micro-costing techniques, especially for hospital resource consumption. However, when estimating costs from the perspective of the third party, fixed hospital charges during the study period were a satisfactory approximation of actual expenditures in Germany.

In conclusion, the present study gives a realistic estimate of health care costs for pediatric asthma and atopic eczema in Germany, and stresses the importance of including the severity, the treatment, the disease course and the disease duration for data calculation and interpretation.

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Conflict of interests: A.J. is an employee of Pharmacia Diagnostics AB.

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