Pediatr Allergy Immunol 2009: 20: 72–80
DOI: 10.1111/j.1399-3038.2008.00739.x



PEDIATRIC ALLERGY AND IMMUNOLOGY

# A multi-center survey of childhood asthma in Turkey – I: The cost and its determinants

Beyhun NE, Soyer ÖU, Kuyucu S, Sapan N, Altıntaş DU, Yüksel H, Anlar FY, Orhan F, Cevit Ö, Çokuğras H, Boz AB, Yazıcıoğlu M, Tanaç R, Şekerel BE. A multi-center survey of childhood asthma in Turkey – I: The cost and its determinants.
Pediatr Allergy Immunol 2009: 20: 72–80.


Successful management of childhood asthma requires a thorough idea of the economic impact of asthma and its determinants, as policy makers and physicians inevitably influence the outcome. The aim of this study was to define the cost of childhood asthma in Turkey and its determinants. In April 2006, a multi-center, national study was performed where data regarding cost and control levels were collected. Asthmatic children (6–18 yr) with at least a 1-yr follow-up seen during a 1-month period with scheduled or unscheduled visits were included. The survey included a questionnaire-guided interview and retrospective evaluation of files. Cost and its determinants during the last year were analyzed. A total of 618 children from 12 asthma centers were surveyed. The total annual cost of childhood asthma was US$1597.4 ± 236.2 and there was a significant variation in costs between study centers ($p < 0.05$). Frequent physician visits [odds ratio (95% confidence intervals)] [2.3 (1.6–3.4)], hospitalization [1.9 (1.1–3.3)], asthma severity [1.6 (1.1–2.8)], and school absenteeism due to asthma [1.5 (1.1–2.1)] were major predictors of total annual costs ($p < 0.05$ for each). The comparable cost of asthma among Turkish children with that reported in developed countries suggests that interventions to decrease the economic burden of pediatric asthma should focus on the cost-effectiveness of anti-allergic household measures and on improving the control levels of asthma.

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Key words: asthma; childhood; control; cost; risk factor

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Accepted 13 February 2008

Asthma is a disease prevalent throughout the world, with variable expression within and between countries, and is one of the most common chronic diseases of childhood (1). In recent decades, the prevalence of asthma has shown a steady increase, together with its social and economic impact. Pediatric asthma accounts for a large proportion of childhood hospitalizations, physician visits, absenteeism from school and parental absenteeism from work (1, 2). Efforts made to improve asthma management have included a variety of activities such as national educational interventions for patients and physicians, development and distribution of guidelines, specialist nurse interventions, and extensive audio-visual informational activities. Successful management also requires a perception of the economic impact and its determinants, as the background and expectations of policy makers and physicians inevitably influence the outcome (1). The knowledge of the cost of asthma is especially valuable in documenting the burden of the disease and in developing strategies for management and health economics.

Turkey is situated between Europe and Asia within the Balkan and Middle East regions and has a prevalence of current asthma symptoms among adults and children comparable with that of European countries, but a low rate of diagnosis and treatment of asthma (3–6). Even though childhood asthma is believed to cause a significant economic burden on families, health

insurance companies, and the government in Turkey, data on asthma costs are limited. Studies deal with single centers and show that annual direct and indirect costs are nearly US$1000 per patient. Determinants of asthma cost included disease severity, current use of preventive drugs, and unscheduled healthcare use (7).

Recently, a study was conducted by Turkey's pediatric asthma centers to define the cost and control levels of childhood asthma and their determinants. Our observations on the economic impact and its determinants form the basis of the present report.

## Material and methods

In a nationwide multi-center setting, using a cross-sectional and retrospective study design, we aimed to investigate the cost of childhood asthma and its determinants through face-to-face interviews based on a structured questionnaire and through a retrospective review of patient files.

### Selection of study centers and subjects

The study was performed in pediatric asthma outpatient clinics of the medical faculties of Turkey, where a file recording system was available for outpatients. Pediatric Allergy and Asthma Unit, Faculty of Medicine, Hacettepe University served as the coordinating institute of the study and invited other study centers to participate after announcement of the study protocol, with the aim to include one study center from each city in which an allergy-asthma outpatient clinic exists. While all clinics serve as referral centers for their specific regions, patients may also be admitted upon request; thus they function both as primary and tertiary healthcare services.

The study was performed in April 2006 at all study centers concurrently, and all asthmatic children aged 6 to 18 yr with scheduled or unscheduled visits were invited to participate. In order to arrive at cost data, only patients with at least 1-yr follow-up were included. No other sampling frame was used except age and follow-up duration.

All patients had a history of recurrent wheezing and dyspnea and had been diagnosed as asthmatic. All were documented to have reversible airway obstruction either clinically and/or with pulmonary function tests. Severity of asthma was assessed by physicians of the clinic, and atopy was defined as at least one positive skin prick test (3 mm greater wheal from negative control in the presence of flare reaction) to a panel of common aeroallergens, in the presence of positive and negative controls.

### Questionnaire and interviews

In the first part of the study, a questionnaire was completed by trained physicians of the outpatient clinics by a face-to-face interview, followed by the second part of the trial which involved retrospective analysis of the patients' files. In order to standardize the interview, a single physician in each center performed the interviews. To ensure consistency of the data, the interviewers received specific training for the project and were briefed about the cost of asthma by the study coordinators. All interviews with children were conducted in the presence of their parents, who supplied information that the patient was unable to provide.

The questionnaire was a slightly modified version of a previously used questionnaire and elicited data regarding parent and patient demographics, asthma in family members, comorbid diseases, treatments, follow-up duration, age of onset, atopy, and presence of indoor smoke (7). Following the demographic questions, they were queried regarding treatments received during the last year either for asthma or comorbid diseases, including other medical tools (i.e. nebulizer, peak flow meter, influenza vaccination, and immunotherapy) and ambulance usage. Thereafter, patients/caregivers were questioned regarding their educational background, smoking habits, loss of work-days because of their child's asthma, use of complementary/alternative medicine, and anti-allergic household measures for their child's asthma. The duration of the questionnaire interview was approximately 15–20 min.

The second part of the study was a retrospective analysis of files to document the severity of asthma as perceived by physicians, allergies, lung functions, treatments and the direct costs incurred at the clinic during scheduled/unscheduled visits and emergency/hospital admissions. The cost data were collected from the official and computerized registry of the accounts of related universities. Severity of the disease was clarified by the physicians of the outpatient clinics who followed their patients up according to Global Initiative for Asthma (GINA) guidelines (8).

### Analyses and management of data

The cost data were derived from the expenditures of the last 1-yr period (current costs) prior to the outpatient clinic admission when the patient was included in the study. All the costs mentioned

herein were those incurred because of asthma within the last 1-yr prior to the interview. All expenditures of the last year were examined and costs not related to asthma were excluded. Unfortunately, collection of the data concerning direct costs was limited to the clinics involved because of the unavailability of the cost data of other health services. In order to estimate the yearly cost, unavailable data were imputed as the mean of the available data (deterministic imputation method). For instance, if there were no data for the cost of any emergency visit in clinics other than study centers, then the mean of available emergency visit costs of the same patient were used as the cost of that missing visit. If there was no available emergency visit to study centers of the patient, then the mean cost of emergency visits of whole asthmatics who had any emergency visit cost during last one year prior to the study were imputed for the missing cost. This procedure was implemented for data on missing costs of hospitalization, outpatient and emergency visits to clinics other than study centers.

In Turkey, the cost of drugs is afforded by the Ministry of Health if the patient has any health insurance. Each patient who has any kind of health insurance has an official drug card on which prescriptions are recorded. By using these drug cards, the names of the drugs and the number of boxes for each drug prescribed for asthma during last 1 yr period were obtained. The drugs consumed by patients who did not have any health insurance were determined from self-report of parents (only 10 patients, 1.6% of the subjects). The unit costs of the drugs were obtained from the official registry of the Ministry of Health. Total drug costs of each patient were calculated by multiplying the number of boxes prescribed and the mean annual cost of that drug during the study period which was obtained from the Ministry of Health. This procedure was implemented for each of the drugs that were determined to be prescribed and summation of all drug costs was assigned as total drug cost of each patient.

The costs were allocated as direct or indirect costs. Direct costs were further categorized as direct medical costs and direct non-medical costs. Direct medical costs included costs of outpatient clinic visits including the cost of asthma control plans, emergency visits, hospitalizations, drugs (medication costs apart from hospital), medical devices (nebulizers, peak flow meters, chambers, volumatic, etc.), influenza vaccines, immunotherapy and medical care provided by nurses at home. Cost of medications consumed during hospitalization was covered by hospitalization costs. Direct non-medical costs were transportation for medical care and accommodation, anti-allergic household measures (special basement, air filters, special vacuum cleaners, anti-allergic bed covers, anti-allergic beds) and complementary/alternative treatment costs. Indirect costs, which included lost work productivity, lost full work-days of parents and loss of other productivities, were not assigned a monetary value because in Turkey incomes fluctuate every day and civil servants do not forfeit their daily income for missed work-days. Another reason for not assigning a monetary value to lost productivity of the parents is due to the lack of standardized unit monetary value of a single lost work-day. Monetary costs are expressed in US dollars, using the mean annual exchange rate of the Central Bank of Turkey from April 2005 to April 2006.

### Statistical analysis

Statistical analyses were performed by the study coordinators, but evaluated by the study council. Kolmogorov–Smirnov test was performed in order to test normal distribution of costs. The statistical relations between sociodemographic factors, variables related to asthma-like disease severity and direct costs were tested with Mann–Whitney U-test and Kruskal–Wallis test. Binary logistic regression was used to determine the risks increasing direct costs. In order to apply logistic regression, direct costs were divided into two according to the median value in order to convert the continuous variable into a dichotomous variable. The 95% confidence interval (CI) was chosen to flag the significance. Variables that were associated with the outcomes in the univariate analysis at a p-value of less than 0.25 were examined in the multivariate logistic regression models. A forward likelihood ratio (LR) modeling strategy was used. The size of the effect of each of the risk factors was measured using the odds ratios (ORs) and 95% CIs. Confidence intervals of binomial distributions were assessed with normal approximation method. Statistical analysis was performed using the SPSS 11.5 package program (SPSS Inc., Chicago, IL, USA).

### Ethical issues

The designated respondents were assured of the voluntary nature of the survey and the confidentiality of all responses, and all parents provided written informed consent. Verbal and written

consents of children above 10 years of age were also obtained. Hacettepe University Medical Faculty Ethics Committee approved the study design and questionnaire.

## Results

### Characteristics

All the 12 centers invited to join the study accepted to participate, and a total of 618 physician-diagnosed asthmatic children with at least a 1-yr follow-up were included during the study period of April 2006. Of the asthmatics invited into the study, as reported by the study centers, over 80% agreed to participate; the remaining cited lack of time as their major reason for refusal. Less than 5% of questionnaires with non-reproducible replies were excluded from the statistical analysis, and this group had comparable characteristics with the whole group in terms of demographics and clinical characteristics (data not shown). Some characteristics of the study population are summarized in Table 1.

Mean (±SEM) ages during the study and at asthma diagnosis were 10.6 ± 0.1 yr (median = 10) and 5.6 ± 0.1 yr (median = 5), respectively, and mean follow-up duration of patients by study center was 3.9 ± 0.1 yr (median = 3). Of the families, 87.1% declared a monthly income of less than US$1470, which was approximately equal to total annual costs per patient. Of the subjects, 71.6% were atopic and 53.6% and 34.5% were allergic to house-dust mites and grass pollen, respectively. The most prominent comorbid disease was allergic rhinoconjunctivitis (35.9%).

Table 1. Characteristics of the study population

| | n | % | 95% CI |
|---|---|---|---|
| Gender (male) | 356 | 57.6 | 53.7–61.5 |
| Age | | | |
| 6–11 | 388 | 64.3 | 60.5–68.1 |
| ≥12 | 215 | 35.7 | 31.8–39.4 |
| Asthma severity | | | |
| Mild intermittent | 328 | 53.8 | 49.8–57.7 |
| Mild persistent | 194 | 31.8 | 28.1–35.5 |
| Moderate persistent | 78 | 12.8 | 10.1–15.4 |
| Severe persistent | 10 | 1.6 | 0.63–2.65 |
| Unscheduled healthcare resource use | 273 | 44.2 | 40.2–48.0 |
| Comorbid diseases | | | |
| Allergic rhinoconjunctivitis | 222 | 35.9 | 32.1–39.7 |
| Chronic sinusitis | 54 | 8.7 | 6.5–10.9 |
| Atopic dermatitis | 40 | 6.5 | 4.5–8.4 |
| Gastroesophageal reflux | 29 | 4.7 | 3.0–6.3 |
| Atopy | 438 | 71.6 | 68.0–75.1 |
| House dust-mite | 331 | 53.6 | 49.6–57.4 |
| Grass pollen | 213 | 34.5 | 30.7–38.2 |
| Mother's asthma | 55 | 8.9 | 6.6–11.1 |
| Father's asthma | 38 | 6.1 | 4.2–8.0 |
| Place of residence (urban) | 387 | 62.6 | 58.8–66.4 |
| No health insurance | 10 | 1.6 | 0.6–2.6 |
| Family income (US$ per month) | | | |
| <1500 | 533 | 87.1 | 84.4–89.7 |
| 1500–3000 | 71 | 11.6 | 9.0–14.1 |
| >3000 | 8 | 1.3 | 0.4–2.2 |

### Burden of asthma

Patients had been admitted 7.7 ± 0.2 times (median = 5) to any healthcare center because of asthma within the last year, and the numbers of scheduled and unscheduled visits during the last year were 5.3 ± 0.1 (median = 4) and 2.4 ± 0.2 (median = 0), respectively. Of the subjects, 44.2% had at least one unscheduled physician visit because of asthma during the previous year. Of the patients, 29.9% gave current (year prior to study) emergency visit history. Ever and current hospitalization were 47.4% and 13.6%, respectively. The mean numbers of current hospitalization and use of emergency service were 0.2 ± 0.04 and 0.7 ± 0.06, respectively, for the study group. According to GINA guidelines, 14.4% of the subjects had moderate to severe asthma.

Of the subjects, 37.4% were vaccinated for influenza during the last year and 16.3% were on immunotherapy. Of the families, 42.1% used anti-asthmatic household measures (24.6% anti-allergic pillow and puff; 13.4% special basement; 12.9% anti-allergic bed; 12.5% special vacuum cleaners). Of the patients, 34.8% who were not atopic to house-dust mites tried anti-allergic measures at home. Of the patients, 16.8% reported purchase of medical devices (nebulizers, peak flow meter, etc.) during the last year.

Mean work-day loss of parents per patient was 2.5 ± 0.2. Mean school-day loss per patient was 5.7 ± 0.3 and in 74.6% of the patients at least one school-day because of asthma during the last 1 year prior to the study.

### Direct costs

Data for over 85% of individual cost items were available, as most health services due to asthma were received from the study centers (data not shown). Annual cost and its components are summarized in Table 2.

Total annual cost per patient was US$1597.4 ± 236.2 (median = 752.9), and 48.6% and 51.4% of direct costs were medical and non-medical costs, respectively. Total annual cost per patient varied between US$5 and 71,762. Mean out-of-pocket payment per patient was

Table 2. Annual costs and their components (US$)

| Components | Costs | | | |
|---|---|---|---|---|
| | Mean ± s.e.m. | 95% CI | Median | %* |
| Medical | 775.7 ± 60.4 | 657.0–894.3 | 509.4 | 48.6 |
| Outpatient | 322.3 ± 16.6 | 289.6–354.9 | 210 | 20.3 |
| Emergency | 28.3 ± 4.9 | 18.6–38.1 | 0 | 1.7 |
| Hospitalization | 93.8 ± 52.0 | −8.3–196.0 | 0 | 5.9 |
| Drug | 274.8 ± 15.9 | 243.5–306.1 | 122.6 | 17.4 |
| Medical device† | 9.1 ± 1.0 | 6.9–11.2 | 0 | 0.5 |
| Influenza vaccination | 5.1 ± 0.4 | 4.2–6.0 | 0 | 0.3 |
| Immunotherapy | 34.6 ± 3.1 | 28.4–40.8 | 0 | 2.1 |
| Home nurse care | 7.3 ± 5.1 | −2.6–17.4 | 0 | 0.4 |
| Non-medical | 821.7 ± 229.1 | 371.7–1271.7 | 102.2 | 51.4 |
| Anti-allergic household measures | 710.3 ± 228.5 | 261.5–1159.2 | 0 | 44.6 |
| Complementary/alternative therapy | 36.0 ± 4.7 | 26.6–45.4 | 0 | 2.2 |
| Transportation | 70.1 ± 5.1 | 60.0–80.2 | 22.0 | 4.3 |
| Accommodation | 5.1 ± 2.4 | 0.3–9.9 | 0 | 0.3 |

*% of total costs
†Nebulizer, peak flow meter, chamber, etc.

US$844.3 ± 222.0 (median = 121.7). Of the total annual costs, 52.8% was afforded by families directly from out-of-pocket payments. Anti-allergic household measures were the dominant component (44.6%) of total costs. Of the total costs, 20.3% and 17.4% were outpatient and drug costs, respectively. Variation in total annual costs per patient as derived from the 12 study centers in comparison with the mean of the whole study group is shown in Fig. 1. Total annual costs per patient in Mersin, Bursa and Adana were above the mean of the whole group.

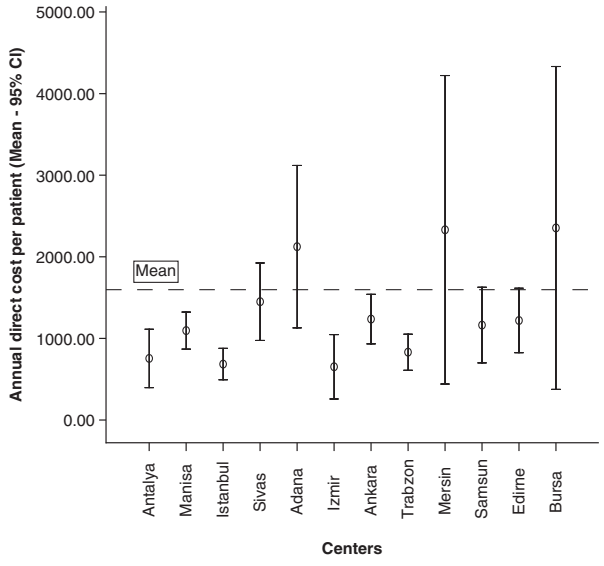


*Fig. 1.* Variation of annual direct cost per patient between centers.

Similarly, total annual non-medical costs were higher in Mersin and Bursa (data not shown).

According to univariate analysis, total annual costs of each patient with moderate to severe asthma were significantly higher than that of mild asthmatics ($p < 0.001$). As with disease severity, having any unscheduled physician visit was found to significantly increase total ($p < 0.001$), medical ($p < 0.001$) and non-medical costs ($p < 0.05$) per patient. Patients having any unscheduled physician visit had threefold higher total annual costs (mean = US$2548.5 ± 527.0) compared with patients with no unscheduled visit (mean = US$844.8 ± 42.5). There was also a weak but statistically significant and positive correlation between number of unscheduled physician visits because of asthma and total annual costs ($r_s = 0.33$, $p < 0.001$), total medical costs ($r_s = 0.34$, $p < 0.001$) and total non-medical costs ($r_s = 0.17$, $p < 0.001$).

*Direct medical costs*. According to univariate analysis, patients with any unscheduled physician visit because of asthma had significantly higher total annual medical costs (mean = US$1096.8 ± 131.1) compared with patients with no unscheduled physician visits (mean = US$521.5 ± 23.1) ($p < 0.001$). The patients with at least a single hospitalization had almost threefold higher medical costs (mean = US$1819.2 ± 401.9) than patients with no hospitalization (mean = US$611.5 ± 23.6) ($p < 0.001$). In patients with moderate or severe asthma, the annual medical costs increased approximately twofold compared with that in subjects with mild asthma ($p < 0.001$). Cost per single hospitalization and emergency visit did not differ significantly according to disease severity ($p > 0.05$).

*Direct non-medical costs*. Total annual direct non-medical costs per patient were US$821.7 ± 229.1 (median = 102.2). Anti-allergic household measures accounted for 86.4% of non-medical costs.

Any unscheduled physician visit because of asthma significantly increased total non-medical costs ($p < 0.05$) and expenses due to anti-allergic household measures ($p < 0.05$), compared with patients with no unscheduled visit. Similarly, patients who were hospitalized within the last year had significantly higher annual non-medical costs ($p < 0.001$) and expenses because of anti-allergic household measures ($p < 0.05$), compared with patients with no current hospitalization. Patients who visited the emergency room during the last year had significantly higher

annual non-medical costs compared with those with no emergency visit ($p < 0.05$). Disease severity was not found to affect total annual non-medical costs ($p > 0.05$) or expenses because of anti-allergic household measures ($p > 0.05$).

### Risk analysis

Determinants of costs were analyzed with multivariate logistic regression and are shown in Table 3. Frequent physician visits [OR (95%CI)] [2.3 (1.6–3.4)] and hospitalization because of asthma [1.9 (1.1–3.3)] were the dominant factors increasing total annual costs per patient. They were also the most prominent risk factors that increased medical and non-medical costs.

Moderate to severe asthma (GINA) was found to significantly increase total annual costs [1.6 (1.1–2.8)] and direct medical costs [1.8 (1.1–3.1)] per patient. School absenteeism because of asthma was determined to be a risk factor that increased total direct costs per patient [1.5 (1.1–2.1)]. Anti-allergic household measures was a risk factor that increased direct medical costs [1.4 (1.1–2.1)] per patient.

## Discussion

This multi-center study is the first nationwide cost of childhood asthma study in Turkey, and was based on data collected from 618 asthmatic children admitted to 12 different pediatric asthma outpatient clinics. We showed that the total annual direct cost of pediatric asthma is almost US$1600 per patient and 52.8% of total annual costs were afforded directly from out-of-pocket payments by families. The majority of the yearly cost can be attributed to anti-allergic household measures (44.6%), and this accounts for more than the total monthly income of 87.1% of families in the study group. Furthermore, any hospitalization causes an approximately twofold increase in yearly total cost (US$2911.1 ± 1596.8).

Table 3. Risk factors to increase annual total, medical and non-medical costs

| | Total direct cost, OR (95% CI) | Medical direct cost, OR (95% CI) | Non-medical direct cost, OR (95% CI) |
|---|---|---|---|
| Frequent physician visit (≥4 visits per year) | | | |
| No | 1 (Ref) | | |
| Yes | 2.3 (1.6–3.4) | 2.9 (2.0–4.2) | 1.8 (1.1–2.9) |
| Hospitalization | | | |
| No | 1 (Ref) | | |
| Yes | 1.9 (1.1–3.3) | 1.8 (1.1–3.2) | 1.8 (1.3–2.6) |
| Disease severity | | | |
| Mild | 1 (Ref) | | |
| Moderate to severe | 1.6 (1.1–2.8) | 1.8 (1.1–3.1) | – |
| School absenteeism | | | |
| No | 1 (Ref) | | |
| Yes | 1.5 (1.1–2.1) | – | – |
| Anti-allergic household measures | | | |
| No | | 1 (Ref) | |
| Yes | – | 1.4 (1.1–2.1) | – |

According to the Global Burden of Asthma Report, the prevalence of asthma was between 1% and 18% (1). Particularly, in western countries such as the UK, USA, and Australia, the prevalence of childhood asthma approaches 20%, whereas in Asian countries it varies between 1.5% and 6.2% (10). Asthma prevalence in school children in Turkey is 7.0% (4). As one of the most common chronic diseases in childhood, asthma causes an important economic burden for families, the health system and the community, and awareness of its magnitude and determinants is critical in the development of management strategies. The economic evaluation of the disease can provide insights into how healthcare resources are distributed and can lay the basis for further policy decisions.

Although the number of hospitalizations is another measure of asthma severity and control, this information is lacking in most developing countries (1). During recent decades, through effective use of preventive (anti-inflammatory) drugs in persistent asthma, hospitalization rates seemed to have decreased due to adequate control of the disease (11). For instance, hospitalization rates for asthmatics in the United States declined from 16% to 8% between 1980 and 1994. The hospitalization rate was 22% in a study conducted in Brazil, Mexico, and Argentina (12). Apart from clinical studies, Korhonen et al. determined with a field study in Finland that 5.0% of asthmatics needed hospitalization (13). In our study group, the hospitalization rate was 13.6%. Along with the improved control levels, medication costs have emerged as one of the largest components of the direct cost of asthma. In line with the declining trend in hospitalizations, the proportion of hospitalization costs to total direct medical costs also declined, and in our study population, hospitalization costs were 5.9% of total direct costs. In Finland, the annual total cost of asthma increased eightfold if a child on regular medication was hospitalized (13). We found that, any hospitalization causes approximately a twofold increase in yearly total cost (US$2911.1 ± 1596.8).

In a comprehensive study, Van den Akker-van Marle et al. noted that annual cost of childhood asthma ranges between €142 to 1529 in EU countries (3). The cost of treating asthma per

patient was estimated to be €354 in Denmark based on estimations for the year 2000. In Finland, the mean annual direct medical cost per patient was €334 (1998 prices). The mean annual cost per patient was €741 (95% CI: 599–884) in Italy (14). Indirect cost of childhood asthma was demonstrated only in three studies. Schramm et al., Stevens et al. and Ungar et al. found that 36.0%, 18.0% and 12.0% of total costs were indirect costs, respectively (17–25). In Germany, Schramm et al. showed that the average annual cost of asthma per patient aged 6–17 yr was €2870 (2000 prices) which was higher than the costs we calculated for our study group; however they included the indirect costs (15). Ungar et al. showed that adjusted annual societal costs per patient in 1995 varied from Can$1,122 in children aged 4–14 years to Can$1,386 in children under 4 years of age in Canada (17).

In most EU countries, there is a lack of knowledge in the field of cost of childhood asthma and extrapolations have been done to estimate its cost. The direct cost of childhood asthma was available in the literature for only nine of 25 EU countries. Determination of costs in the other 16 countries was done via estimations. In some countries, extrapolation from cost of adult asthma was used. The cost of asthma per patient in the countries where no estimate was available was calculated as €613, which was approximately half of the total costs determined in our study group. Our study compared direct costs with those EU countries with available data, and we found that annual direct cost of asthma was approximately US$1600 and fell above the range of costs in the EU. Total cost of asthma in the EU was estimated to be €3011 million in 2004. Sensitivity analyses showed that this amount could vary between €2300 and 4500 million (3). As Van den Akker-van Marle et al. showed, there was a large variation in costs between countries in the EU, we also found that costs vary within the country. Large variations in asthma-related cost between different countries occur because of the differences in the treatment of the disease, unit cost values of expenditures at inpatient and outpatient care facilities, different estimation methods used in cost-of-illness studies and the items constituting the indirect costs (18). In a recent trial, mean annual direct medical costs of adult asthma were demonstrated to be US$1465.7 ± 111.8 per capita in Ankara, Turkey, suggesting a similar significant economical burden of asthma in adults compared with children (19).

Direct non-medical cost was 51.4% of total costs and higher than direct medical costs, and this result is in contrast to the findings of Schramm et al., Stevens et al. and Ungar et al. They all demonstrated that the direct medical costs were higher than non-medical costs (17–25). Another significant and unique result of our large multi-center study was that the main component of cost of childhood asthma was expenses due to anti-allergic household measures (special basement, air filter, etc.). Patients who were hospitalized or had any unscheduled physician visit because of asthma (uncontrolled asthma) had paid significantly higher costs for anti-allergic household measures. Schramm et al. also found that the major components of cost of childhood/adolescent asthma were related to household modifications, and reported the average cost of household modifications as €535 (15). The average cost of household measures was determined as US$710 for our study group and most of the out-of-pocket payments were due to these anti-allergic household measures. Many clinicians suggest avoiding allergens to control asthma in atopic patients but this is not the case in many aeroallergen-induced diseases. In a double-blind, placebo-controlled trial of mite allergen avoidance (with the use of allergen-impermeable covers), it was found to be clinically ineffective in adults with asthma (20). There is no progress in non-pharmacological treatment of asthma in recent years, with allergen avoidance measures, diet modifications and complementary medicines proving to be beneficial (21). Therefore, the rational consumption of sources due to childhood asthma is a critical point to achieve cost-effective control of the disease.

Countries can have specific circumstances and patterns of costs in childhood asthma. Local cultural features might play a role in cost patterns. Being atopic to house-dust mites can play a dominant role in considering household measures. Inappropriate resource use might increase the costs because 34.8% of the patients who did not have atopy to house-dust mites tried anti-allergic measures at home. Another possible reason for increases in the use of anti-allergic household measures may be the perception of asthma as a solely allergic disease, i.e. families believe their children's asthma will resolve if they can successfully control their exposure to allergens. This inaccurate perception may increase the use of anti-allergic household measures and hence the economic burden of asthma on families. High anti-allergic household measure costs lead to high out-of-pocket payments (52.8% of total costs) which brings heavy burden to family budgets, although most of patients have health insurance.

Although use of alternative/complementary therapies is popular in Turkey and in our study population, the contribution of this type of cost per patient was low, at 2.2%. We have shown in a previous study that the major predictors for the use of alternative/complementary therapies are low asthma control, i.e. unmet expectations, and advice of relatives and friends (22).

As mentioned above, control of asthma was seen as the most important factor indicating the cost of childhood asthma. The mean annual cost per patient ranged from €379 (95% CI: 216–541) for well-controlled asthmatics to €1341 (95% CI: 978–1706) for poorly controlled cases (14). Sullivan et al. found that costs for uncontrolled patients were more than double those of uncontrolled patients (23). Similar to the reports of Accordini et al. and Sullivan et al., we found that the determinants of uncontrolled asthma, such as any unscheduled physician visit, frequent physician visits, and asthma severity, were major factors that increased annual direct costs per patient (14, 23). We also showed that the total direct cost of asthma was significantly higher for patients who had any unscheduled physician visit or frequent physician visits, and similar to other studies, asthma-related resource use was affected by disease severity (15, 24). Moderate to severe asthma was determined as a significant risk factor to increase total direct costs per patient [OR 1.6 (95% CI 1.1–2.8)]. Similar to disease severity, hospitalization was determined to be one of the most important risk factors that increased both medical and non-medical costs per patient. Sekerel et al. demonstrated that even though half of the patients had symptoms at least once per week, one-third was not receiving regular prophylactic treatment in Turkey, indicating under-treatment and inadequate control (25). According to the Asthma Insights and Reality (AIRET) study, it was determined that 72.7% of asthmatic children had persistent asthma and three quarters of children were experiencing daytime symptoms. Use of anti-inflammatory therapy every day including inhaled corticosteroids was low in patients with persistent disease (26).

There have been two main types of studies investigating the economic burden of asthma: population-based sampling frames which provide estimations for nations and entire regions, and studies like ours using clinical-based sampling frames (27). The clinical-based studies of cost of childhood asthma have more diagnostic certainty with respect to disease severity, which has a great impact on the cost of asthma (19). The results of this multi-center cost of illness study were based on costs occurred at university clinics because the management of childhood asthma is a problem in primary healthcare settings and state hospitals in Turkey. Costs of patients which were derived from the admittances to healthcare settings (primary health care and state hospitals) other than university clinics were imputed from the existing costs in university clinics. This may cause an overestimation of the costs. However, asthmatic children who are followed up by experienced university clinics rather than state hospitals and primary healthcare settings can be under more adequate control that decreases costs due to asthma. Therefore, these two contrasting issues may affect the estimation of the costs. Another limitation of this study is that the results could not be generalized to whole childhood asthmatic population in Turkey, as the data were collected in university clinics rather than patients screened out in random samples from the general population. As this multi-center study was based on official records and a questionnaire, the adherence of subjects to the recommended drugs could not be adequately identified, which is a common problem in questionnaire-oriented studies.

The current level of asthma control falls far behind the goals for long-term adequate management in GINA guidelines (28). Control of asthma is seen as the major factor to predict the costs. More global modelling of costs of childhood asthma, including country-specific factors, should be performed (29). Suggestions and measures of governments should be directed towards evidence-based interventions of childhood asthma including the avoidance of house dust mites to prevent families from irrationally using economic resources (30).

In conclusion, we demonstrated that pediatric asthma causes significant burden on families, and allergen-avoidance measures, uncontrolled disease, and disease severity are the major predictors of cost of pediatric asthma in Turkey. The annual cost of asthma is comparable with that reported in many European countries. Considering the limited financial resources of Turkey, measures to reduce the economic burden of asthma should be taken. In this regard, allergen-avoidance measures and uncontrolled asthma seem to be potential targets for future interventions.

## Contributors' list

- *N. E. Beyhun* participated in the development of the protocol and analytic framework of the study, had primary responsibility for data analysis, and prepared the manuscript with *B. E. Sekerel*.

- *O. Soyer* participated in the development of the protocol and analytic framework of the study, contributed to preparation of the manuscript, and had primary responsibility for patient screening in her study center.
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- *B. E. Sekerel* had primary responsibility for protocol development and outcome assessment, contributed to data analysis, and prepared the manuscript with *N. E. Beyhun*.

## References


1. Bousquet J, Bousquet PJ, Godard P, Daures JP. The public health implications of asthma. Bull WHO 2005: 83: 548–54.
2. Townsend M, Feeny DH, Guyatt GH, Furlong WJ, Seip AE, Dolovich J. Evaluation of the burden of illness for pediatric asthmatic patients and their parents. Ann Allergy 1991: 67: 403–8.
3. Van den Akker-van Marle ME, Bruil J, Detmar SB. Evaluation of cost of disease: assessing the burden to society of asthma in children in the European Union. Allergy 2005: 60: 140–9.
4. Saraclar Y, Kuyucu S, Tuncer A, Sekerel B, Sackesen C, Kocabas C. Prevalence of asthmatic phenotypes and bronchial hyperresponsiveness in Turkish schoolchildren: an International Study of Asthma and Allergies in Childhood (ISAAC) phase 2 study. Ann Allergy Asthma Immunol 2003: 91: 477–84.
5. Saraclar Y, Cetinkaya F, Tuncer A, et al. The prevalence of self-reported asthma and respiratory symptoms in Ankara, Turkey. Respir Med 1997: 91: 461–3.
6. Saraclar Y, Sekerel BE, Kalayci O, et al. Prevalence of asthma symptoms in school children in Ankara, Turkey. Respir Med 1998: 92: 203–7.
7. Beyhun NE, Cilingiroglu N, Sekerel BE. Cost of childhood asthma and its determinants in Ankara, Turkey. Turk J Pediatr 2007: 49: 179–88.
8. National Institutes of Health (National Heart Lung and Blood Institute). Global Initiative for Asthma; Global Strategy for Asthma Management and Prevention. Bethesda, MD: National Institutes of Health, 2002. Publication: 02-3659.
9. Chung F, Barnes N, Allen M, et al. Assessing the burden of respiratory in the UK. Respir Med 2002: 96: 963–75.
10. Singh M. The burden of asthma in children: an Asian perspective. Paediatr Respir Rev 2005: 6: 14–9.
11. Masoli M, Fabian D, Holt S, Beasley R Global Burden of Asthma Summary Report (available at: http://www.splf.org/s/thotlib/pub/lib/pdf/GINAsum.pdf; accessed 12 February 2005).
12. Fischer GB, Camargos PAG, Mocelin HT. The burden of asthma in children: a Latin American perspective. Paediatr Respir Rev 2005: 6: 8–13.
13. Korhonen K, Reijonen TM, Remes K, Malmström K, Klaukka T, Korppi M. Reasons for and costs of hospitalization for pediatric asthma: a prospective 1-year follow-up in a population-based setting. Pediatr Allergy Immunol 2001: 12: 331–8.
14. Accordini S, Bugiani M, Arossa W, et al. Poor control increases the economic cost of asthma. A multicentre population-based study. Int Arch Allergy Immunol 2006: 141: 189.
15. Schramm B, Ehlken B, Smala A, Quednau K, Berger K, Nowak D. Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study. Eur Respir J 2003: 21: 116–22.
16. 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.
17. Ungar WJ, Coyte PC. Prospective study of the patient-level cost of asthma care in children. Pediatr Pulmonol 2001: 32: 101–8.
18. Akobundu E, Ju J, Blatt L, Mullins CD. Cost-of-illness studies: a review of current methods. Pharmacoeconomics 2006: 24: 869–90.
19. Celik GE, Bavbek S, Pasaoglu G, et al. Direct medical costs of asthma in Ankara, Turkey. Respiration 2004: 71: 587–93.
20. Woodcock A, Forster L, Matthews E, et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. N Engl J Med 2003: 349: 225–36.
21. Warner JO. Non pharmacological management of asthma: little change in the evidence base over 5 yr. Pediatr Allergy Immunol 2007: 18: 91.
22. Orhan F, Sekerel BE, Kocabas CN, Sackesen C, Adalioglu G, Tuncer A. Complementary and alternative medicine in children with asthma. Ann Allergy Asthma Immunol 2003: 90: 511–5.
23. Sullivan SD, Rasouliyan L, Russo PA, et al. Extent, patterns, and burden of uncontrolled disease in severe or difficult-to-treat asthma. Allergy 2007: 62: 126–33.
24. Van Gasse E, Antonicelli L, Zhang Q, et al. Asthma-related resource use and cost by GINA classification of severity in three European countries. Respir Med 2006: 100: 140–7.
25. Sekerel BE, Saraclar Y, Ones U, et al. Childhood asthma perception in Turkey under real-life environment (CAPTURE) study. Pediatr Allergy Immunol 2001: 12: 266–73.
26. Sekerel BE, Gemicioglu B, Soriano JB. Asthma insights and reality in Turkey (AIRET) Study. Respir Med 2006: 100: 1850–4.
27. Stempel DA. Assessing the economic burden of asthma. J Allergy Clin Immunol 2003: 111: 1203–4.
28. Rabe KF, Adachi M, Lai CK, et al. Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. J Allergy Clin Immunol 2004: 114: 40–7.
29. Bousquet PJ, Daures JP. Modelization of cost assessment in childhood asthma is essential for policy makers. Allergy 2005: 60: 135–7.
30. Warner JO. Allergy – a public health issue: When should governments act? Pediatr Allergy Immunol 1999: 10: 1–2.