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The cost of childhood atopic dermatitis in a multi-ethnic Asian population: a cost-of-illness study*

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Summary

Background Childhood atopic dermatitis can often have a negative impact on quality of life for affected children and their caregivers. The condition contributes to increased healthcare costs and can pose heavy economic burdens on healthcare systems and societies.
Objectives The objective of this study is to provide a comprehensive estimate of the economic burden of childhood atopic dermatitis in a Singaporean sample and to investigate associated factors.
Methods This cross-sectional cost-of-illness study applied a societal perspective. Data was collected between December 2016 and December 2017 in Singapore. Caregivers to children below 16 years of age with a physician-confirmed diagnosis of atopic dermatitis were recruited and sociodemographics, clinical characteristics, health service utilization data and time spent on caregiving were collected from all eligible participants.
Results The average annual cost per child with atopic dermatitis was estimated at U.S. dollars (USD) 7943 (mild USD 6651, moderate USD 7935 and severe USD 14 335) in 2017 prices. The major cost was for informal caregiving (46% of the total cost) followed by out-of-pocket expenses (37%). Healthcare utilization contributed to 17% of the total cost of which 43% was for medications.
Conclusions Childhood atopic dermatitis imposes substantial costs with a large proportion arising from informal caregiving and out-of-pocket expenses. The costs related to atopic dermatitis are also strongly related to disease severity. This information is important for policy makers and other health planners when considering how to better support affected families.

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Conflicts of interest
None to declare.

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What's already known about the topic?

- Childhood atopic dermatitis is a costly disease for society. However, comprehensive cost estimations are lacking.
- Previous cost studies are old, based on small sample sizes or are healthcare-setting specific.

What does this study add?

- This study comprises a health economic evaluation assessing different levels of care and includes various categories of costs.

- The result showed that informal caregiving was the most prominent cost for children with atopic dermatitis.

Atopic dermatitis (AD), or eczema, is a common chronic inflammatory dermatosis characterized by recurring exacerbations of red, dry and itchy skin.[1] International estimates from a 2009 study showed a global prevalence of 0·9% to 22·5% for children aged 6–7 years; and between 0·2% and 24·6% for children aged 13–14 years.[2] The prevalence of childhood AD in Singapore has remained high but stable over time, with a prevalence of 17·9% to 22·7% in a 2002 study compared with 20·6% in the year 2018.[3,4]

AD often affects every-day life as it commonly requires regular treatments to repair the skin barrier (e.g. moisturizers), avoidance of environmental triggers and topical anti-inflammatory management (topical corticosteroids or calcineurin inhibitors) to control the inflammation.[1,5] The condition reduces health-related quality of life for children and their parents.[6–9] Children often experience severe itching leading to subsequent sleep disturbances affecting both them and their caregivers.[7,8]

AD can have a negative effect on the child's psychosocial life because of their physical appearance and inability to take part in social activities such as swimming.[6,10] They are also often ostracized, bullied and isolated from their peers.[6,10] Childhood AD places substantial economic burden on families and societies as well,[11,12] with cost estimates varying between countries, study designs, included cost components and disease severity.[6,11,13] In the Asia Pacific region, the economic burden of childhood AD is higher in high- and middle-income countries such as Australia, South Korea and Singapore [range U.S. dollars (USD) 1000–6000 per patient per year] compared with lower-income countries (range USD 199–743 annually).[14] Previous studies have estimated the healthcare costs of AD in Singapore at USD 4753 annually per child, with USD 1097 being costs for healthcare visits and treatments.[15,16] However, these costs are speculative estimates as there have been no prior comprehensive cost assessments at a national level. International figures for childhood AD present varying annual cost estimates per child ranging between USD 71 and USD 4389 in Europe and the U.S.A.[12,13,17–19] It should, however, be noted that studies include different cost components and study populations when estimating the costs and thereby preventing direct comparisons.

Healthcare in Singapore comprises a government-run public healthcare system and a private healthcare sector. Healthcare is financed through a combination of direct government subsidies, compulsory savings, national healthcare insurance, cost sharing and optional private insurance. The proportion of direct government subsidies is dependent on the socioeconomic status of patients.

The primary aim of this study is to provide a comprehensive estimate of the economic burden of childhood AD by assessing healthcare costs, costs for informal caregiving and other financial expenses for the family. We also aim to investigate associations between costs and sociodemographics as well as the severity of AD.

Patients and methods

Study design and participants

This cross-sectional cost-of-illness study explored the cost of childhood AD from a societal perspective. Children below 16 years of age with a physician-confirmed diagnosis of AD were recruited from two public healthcare service providers in Singapore – an outpatient dermatology clinic in a tertiary paediatric hospital (KK Women's & Children's Hospital) and a speciality centre for skin diseases (National Skin Centre). Data were collected from all eligible children and caregivers who consented to take part in the study between December 2016 and December 2017. Children with no legally authorized representative who could give consent to enrol in the study and patients with a nonphysician-asserted diagnosis of AD were excluded from participation in the study.

Instrumentation and costing valuation for cost-consequences

A modified version of the Client Service Receipt Inventory captured caregiver-reported retrospective data imposed by childhood AD on healthcare service utilization, medications, informal caregiving, out-of-pocket expenses and cost for transportation to healthcare visits.[20,21] The total societal cost was calculated as the sum of all costs. Costs were reported in Singapore dollars (SGD) and attributed to the cost year of 2017, with prices adjusted by the Singapore consumer price index (healthcare component) for the same year when appropriate.[22] Singapore dollars were converted into USD using purchasing power parity rates from the World Bank's international database.[23] No discounting was applied as the study only assessed annual costs.

Conservative assumptions were made throughout the study so as not to overestimate the burden of AD, for example when valuing costs, and in the process of entering the data when information was inadequate or incomplete.

Healthcare service costs and cost for medications

Costs for healthcare service utilization comprised healthcare services from different levels of care (e.g. primary care, hospital care) related to the child's AD. The numbers of healthcare visits were linked to unit costs for specified services obtained from collaborating hospitals and other sources.[24] Medication usage (including food supplements and complementary

medicines) was reported by the caregiver stating medication/type of medication and dosage/frequency. Unit costs for medications were retrieved from one of the collaborating hospital's pharmacy and the average cost per category was calculated for each medication.

Transportation to attend healthcare visits was included as a healthcare cost. The calculation for transportation was made assuming a return trip for each visit, and based on unit costs for public transport, taxi or use of private vehicles.[25–27] For inpatient hospital admissions, transportation calculations were made with the assumption that parents visited their child every second day. The annual cost of transportation was derived from the number of visits multiplied by the unit costs for the reported mode of transportation.

Informal caregiving

Informal caregiving included care that parents provided in caring for the child's AD based on preset activities – personal care, preparing special meals because of dietary restrictions and providing emotional support. Time spent on personal care and specially prepared homemade food, without noted duration, was assumed to be 5 min and 30 min per session, respectively. Informal caregiving was valued as an opportunity cost where 1 h of caregiver leisure time lost was assumed to be equivalent to 35% of the average per hour gross salary.[28,29] The annual cost for informal caregiving hours was calculated from the average hours of support given per week multiplied by the number of weeks in a year.

Family expenses

Out-of-pocket expenses for the family included cost for services or products used or purchased, such as moisturizing creams, hygiene products and laundry costs because of the child's AD. Moisturizers are included as part of family expenses as these are pharmacy retail items and not subsidized by the healthcare system. Costs for family expenses were reported as a weekly cost per item and converted into an annual cost. For items with a one-time cost, such as a humidifier, water filter and vacuum cleaner, the costs were converted to a yearly cost based on the arbitrarily assumed service life of the item.

Assessment of severity level of atopic dermatitis

Severity of the child's AD was assessed by the treating physician and retrieved from medical records. Physicians at both study sites ascertained the severity of AD by using the modified Physician's Global Assessment.[30]

Ethical considerations

This study was approved by the Institutional Review Board of the National Healthcare Group (NHG-DSRB: 2015/01228) and Nanyang Technological University, Singapore (NTU IRB: IRB-2016-10-059-01). Caregivers and children received verbal and written information about the purpose of the study and that participation was voluntary before giving consent to participate. A token incentive of SGD 10 was given to participants as appreciation for their time.

Statistical analyses

This study reported means (± SD) for continuous variables, and frequencies with corresponding proportions for categorical variables. Skewed variables were presented as median and range (minimum–maximum). Normality of continuous variables was assessed by Kolmogorov–Smirnov and Shapiro–Wilk test. Costs by AD severity (mild, moderate and severe) were compared using the Kruskal–Wallis *H*-test, and categorical variables were compared using chi-squared or Fisher's exact test. Spearman's rank correlation was used to assess the relationship between cost and continuous predictors such as disease duration and age. Relationships between total cost, sociodemographics and severity of AD were analysed by univariable and multivariable generalized linear model (GLM). As the total cost was strictly positive and heavily skewed to the right, we used 'gamma family with' and 'log link function' to avoid any retransformation bias. The modified Park test was used to select the appropriate family within the GLM approach. Predictors are reported as log coefficients with corresponding standard errors (SEs). The goodness-of-fit was assessed by two different statistics, the deviance and the Pearson χ^2-statistic. The mean predicted total cost by AD severity was also estimated. In cases of missing or incorrect data (e.g. unrealistic values), the participant was excluded from further analysis for that specific variable. All statistical analyses were performed using Stata statistical software version 14·2 (StataCorp LLC, College Station, Texas, U.S.A.). Two-tailed *P*-values less than 0·05 was considered statistically significant.

Results

Participant characteristics

Out of 735 eligible caregivers, 176 declined to participate in the study for various reasons such as time constraints, language (English) deficiency or if the caregiver was not the legally authorized representative of the child. A total of 559 caregivers and children with AD were recruited for the study (Table 1).

The average (± SD) age was 6·6 (± 4·6) years with a mean AD duration of 3·5 (± 3·6) years. Most children were of Chinese ethnicity (72·5%), followed by Malay (16·0%), Indian (5·9%) and 'other' (5·6%) ethnicities. This ethnic distribution fairly reflects the ethnic distribution of Singapore in general.[31] Approximately half of the responding caregivers were university graduates (49·2%), followed by postsecondary or polytechnic (32·4%) and secondary school and lower (18·4%) qualifications. This generally reflects the educational levels of the similarly aged population in the country.[32] The majority

Table 1 Sociodemographic and clinical profile of children with atopic dermatitis (N = 559)[a]

Characteristics	Value
Age, years: mean ± SD	6·6 ± 4·6
Diagnose duration in years (n = 550), mean ± SD	3·5 ± 3·6
Sex, n (%)	
Female	277 (49·6)
Male	282 (50·4)
Ethnic group (n = 557), n (%)	
Chinese	404 (72·5)
Malay	89 (16·0)
Indian	33 (5·9)
Other	31 (5·6)
Severity (n = 513),[b] n (%)	
Mild	316 (61·6)
Moderate	133 (25·9)
Severe	64 (12·5)
Responder's relation, n (%)	
Mother	398 (71·2)
Father	158 (28·3)
Other	3 (0·5)
Responder's qualifications, n (%)	
Secondary school or lower	103 (18·4)
Postsecondary or polytechnic	181 (32·4)
University	275 (49·2)
Responder's employment status, n (%)	
Employed	452 (80·9)
Unemployed	107 (19·1)
Accommodation type (n = 557), n (%)	
1–3-bedroom HDB-flat	68 (12·2)
4–5-bedroom HDB-flat	361 (64·8)
Condominium/landed property	128 (23·0)

HDB, Housing and Development Board. [a]N = 559 unless otherwise indicated. [b]clinician-assessed severity was based on the Physician's Global Assessment score.

of families lived in government flats (77%), which is not necessarily related to socioeconomic status.[31,33] and 23% lived in condominiums or landed properties. This distribution is also reflective of the general population as it has been estimated that approximately 80% of citizens and permanent residents resides in public housing in Singapore.[33] Clinician-assessed severity of AD could only be retrieved for 513 participants and therefore, 46 participants were excluded from the analysis by severity. Most of the children had mild AD (61·6%), followed by moderate (25·9%) and severe (12·5%) AD.

Atopic dermatitis-related healthcare service utilization

The mean total cost for healthcare service utilization across all degrees of AD severity was USD 1349 per child per year (see Table 2 and Table S1 in the Supporting Information for a more detailed version of this table). The cost for medications accounted for 42·6% (USD 574) of the total cost for healthcare utilization, followed by specialist outpatient services accounting at 30·6% (USD 413), and the remaining 26·8% comprised inpatient, accident and emergency, general practitioner and polyclinic, and other care, as well as transportation to healthcare visits. The most frequently used medications were topical and oral steroids (used by 57·7%) followed by antihistamines (25·0%) and combination creams (15·0%) (Table S2; see Supporting Information). Topical and oral steroids accounted for the highest cost because of their widespread use, estimated at USD 252 (43·9% of the total cost for medications); followed by calcineurin inhibitors at an average cost of USD 150 (26%) per patient per annum.

Fewer than 5% of the participants required inpatient treatment for AD, accounting for an average cost of USD 164 per patient annually. Nearly all participants (99%) had incurred costs for transportation for healthcare visits, amounting to USD 94 per patient per year.

The severity of AD had a significant impact on the total healthcare cost with mild AD at USD 1062, moderate AD at USD 1217 and severe AD at USD 3035 ($P < 0·001$) per child per annum (Table S1; see Supporting Information). Thus, the cost for severe AD is almost two and a half times the cost compared with moderate AD, and three times the cost compared with mild AD.

Informal caregiving

As many as 91·6% of the caregivers reported spending an average of 10·3 h of time each week providing informal caregiving because of their child's AD (Table 3). Most caregivers reported that the largest proportion of time was spent on providing personal care for the child, for example, application of moisturizers (87·7%, estimated cost USD 1625 per patient per annum) and preparation of specially made food because of diet restrictions (51·1%, estimated at USD 600 per patient per annum), as well as to accompany the child and provide them with emotional support (42·3%, estimated cost USD 1217 per patient per annum). The average total cost for informal caregiving amounted to USD 3659 per child per year (Table 2).

Analysing informal caregiving by severity showed that parents caring for children with mild, moderate and severe AD spent an average of 9·2 h (estimated to cost USD 3244 per patient per year), 10·8 h (USD 3801 per patient per year) and 15·2 h (USD 5395 per patient per year) ($P = 0·019$), respectively per week, hence establishing that the cost of informal care in severe AD is 1·4 to 1·7 times more than in mild and moderate disease (Table S1; see Supporting Information).

Out-of-pocket expenses

Most caregivers (92·2%) reported out-of-pocket expenses to treat their child's AD at an average of USD 2935 per child per year (Table 2). Moisturizers accounted for the highest out-of-pocket expenses at USD 1084 per child per year (purchased by 90·3% of participants). Spending on hygiene products accounted for the second most costly out-of-pocket cost at USD 648 (purchased by 78·6% of participants) per child per annum. Analysing out-of-pocket expenses by AD severity

Table 2 Annual average costs (in U.S. dollars) for healthcare, informal caregiving and out-of-pocket expenses for children with atopic dermatitis (see Table S1 in the Supporting Information for a more detailed version that includes data by atopic dermatitis severity)

	Participants, total (n = 513)		
Type of healthcare utilization	% users	Mean ± SD	Median (minimum–maximum)
Healthcare service utilization			
Inpatient care	4·7	163·6 ± 1239·8	0·0 (0·0–17 559·6)
Accident and emergency	6·6	20·2 ± 95·5	0·0 (0·0–1175·5)
Outpatient care – speciality services	100	412·8 ± 549·7	233·4 (185·7–9146·5)
General practitioner/polyclinic services	45·2	80·5 ± 149·1	0·0 (0·0–1241·9)
Other health services[a]	1·4	4·0 ± 48·0	0·0 (0·0–695·1)
Medication	77·8	574·0 ± 774·8	336·2 (0·0–4109·5)
Transportation	99	93·8 ± 127·2	56·2 (0·0–1506·8)
Total	100	1348·9 ± 1862·9	901·8 (185·7–20 090·4)
Informal care			
Personal care	87·7	1625·1 ± 2662·0	708·7 (0·0–29 764·9)
Accompanying to healthcare visits	36·6	194·8 ± 755·5	0·0 (0·0–9787·0)
Companionship and emotional support	42·3	1217·3 ± 3304·6	0·0 (0·0–46 592·0)
Specially prepared homemade food	51·1	599·9 ± 1840·2	0·0 (0·0–25 512·8)
Other additional housework activities	1·6	22·0 ± 257·5	0·0 (0·0–4960·8)
Total	91·6	3659·1 ± 5913·8	1594·6 (0·0–47 127·8)
Out-of-pocket expenses			
Moisturizing creams	90·3	1083·7 ± 1706·2	511·1 (0·0–17 717·2)
Hygiene products	78·6	647·8 ± 969·1	354·3 (0·0–10 630·3)
Extra laundry	22·2	169·3 ± 527·6	0·0 (0·0–4429·3)
Clothing and textiles	16·2	182·8 ± 715·1	0·0 (0·0–8858·6)
Humidifier	14·6	163·3 ± 975·9	0·0 (0·0–13 287·9)
Water filter	9·6	218·4 ± 2180·3	0·0 (0·0–44 293·0)
Special diet	11·7	282·9 ± 1220·4	0·0 (0·0–17 717·2)
Others	5·1	199·7 ± 2523·7	0·0 (0·0–53 151·6)
Total	92·2	2934·6 ± 6236·3	1328·8 (0·0–75 121·0)
Combined total		7942·6 ± 9595·4	4769·9 (190·8–79 381·3)

[a]'Other health services' comprise, for example, light therapy and visit to dietitian.

revealed significant differences between mild AD (USD 2344), moderate AD (USD 2908) and severe AD (USD 5906) ($P < 0·001$) (Table S1; see Supporting Information). Out-of-pocket expenses for severe AD were two times the cost for mild or moderate AD.

Total financial cost

The average cost for the total sample including all cost categories amounted to USD 7943 per child per year (Table 2). Stratified by severity, the cost for a child with mild AD was estimated at USD 6651, for moderate AD USD 7935 and USD 14 335 for severe AD ($P < 0·001$) per patient per annum (Table S1; see Supporting Information). The total cost for a child with severe AD was greater than two times the cost for a child with a mild or moderate condition. The increased cost for more severe AD was seen in all cost categories, especially for healthcare expenditure, but also for informal care and out-of-pocket expenses.

Multivariable regression analyses

Factors associated with the total cost for children with AD using a multivariable GLM are presented in Table 4. The multivariable analysis identified the significant factors associated with increasing cost as being of Malay ethnicity (coefficient ± SE: 0·31 ± 0·12, $P = 0·010$) or 'other ethnicity' (coefficient: 0·42 ± 0·15, $P = 0·005$) compared with the Chinese ethnic group; having a longer duration (years) of AD (coefficient: 0·06 ± 0·02, $P < 0·001$), and moderate (coefficient: 0·28 ± 0·10, $P = 0·007$) or severe (coefficient: 0·94 ± 0·16, $P < 0·001$) AD. The age of the child was also statistically associated with the total cost (coefficient: –0·07 ± 0·01, $P < 0·001$). Goodness-of-fit statistics showed that the model was of moderate fit overall. The mean adjusted total societal costs (± SE) per year was USD 6602 ± 404 for mild AD, USD 8336 ± 686 for moderate AD and USD 14 684 ± 2081 for severe AD.

Discussion

The average total annual cost per child with AD was conservatively estimated at USD 7943 in our study, which is substantially higher when compared with estimates from other countries for example the U.S.A. (USD 3288) and Italy (USD 1540).[17,19] Findings from our study also show that the larger proportion of the overall costs for childhood AD were attributed to informal caregiving (46% of total costs) and out-of-

Table 3 Time (h) spent on informal caregiving per week by atopic dermatitis severity

	Total (n = 513)		Hours per week						
			Mild (n = 316)		Moderate (n = 133)		Severe (n = 64)		P-value
Activity	Mean ± SD	Median (min–max)	Mean ± SD	Median (min–max)	Mean ± SD	Median (min–max)	Mean ± SD	Median (min–max)	
Personal care	4·6 ± 7·5	2·0 (0·0–84·0)	4·1 ± 6·8	2·0 (0·0–50·0)	4·9 ± 6·5	2·0 (0·0–42·0)	6·2 ± 11·6	3·0 (0·0–84·0)	0·202
Accompanying to healthcare visits[a]	0·6 ± 2·1	0·0 (0·0–27·6)	0·5 ± 1·9	0·0 (0·0–27·6)	0·8 ± 2·9	0·0 (0·0–27·0)	0·6 ± 1·2	0·0 (0·0–5·5)	0·026
Companionship and emotional support	3·4 ± 9·3	0·0 (0·0–112·0)	2·8 ± 7·5	0·0 (0·0–56·0)	3·6 ± 7·0	0·2 (0·0–56·0)	6·6 ± 17·6	0·0 (0·0–112·0)	0·040
Specially prepared homemade food	1·7 ± 5·2	0·0 (0·0–72·0)	1·8 ± 5·9	0·0 (0·0–72·0)	1·5 ± 4·0	0·0 (0·0–28·0)	1·7 ± 3·8	0·0 (0·0–21·0)	0·573
Other additional housework activities	0·1 ± 0·7	0·0 (0·0–14·0)	0·1 ± 0·8	0·0 (0·0–14·0)	0·1 ± 0·4	0·0 (0·0–3·5)	0·1 ± 0·9	0·0 (0·0–7·0)	0·741
Total	10·3 ± 16·7	4·5 (0·0–133·0)	9·2 ± 16·1	3·5 (0·0–133·0)	10·8 ± 13·2	5·9 (0·0–81·5)	15·2 ± 24·0	7·0 (0·0–126·0)	0·019

min, minimum; max, maximum. [a]n = 512 not 513.

pocket expenses (37%) rather than actual healthcare costs (17%), strongly suggesting that the cost of caring for a child with AD goes far beyond expenditures on actual health care. These findings add new insights about costs for informal caregiving that generally have not been comprehensively assessed in previous studies of childhood AD, highlighting the so far unknown socioeconomic burden of the condition. Previous health economic studies assessing costs for childhood AD included the cost for loss in productivity for parents but did not include costs for informal caregiving.[19,34] Including the cost of informal caregiving in cost-of-illness studies is crucial as some diseases, such as childhood AD, are associated with rather substantial time costs because of caregivers' involvement in their child's daily skin care.[35] The average time spent on informal caregiving for childhood AD is comparable with other chronic diseases such as caring for an elderly person with diabetes,[36] and should in consequence have an impact on healthcare economic policies.

In accordance with previous studies, we found that out-of-pocket expenses was the second highest cost factor in caring for childhood AD.[7,18] This again is important for policy makers to address as personal expenses, accelerated by the potentially long duration of disease can lead to financial strain for families, especially those with lower incomes.[37] Increased awareness about the condition's impact on the cost burden for affected families informs policy makers to divert resources for developing more efficient treatment options. The government also need to understand the substantial costs of outpatient treatment for AD, especially for moderate-to-severe conditions and that efficiency gains can be made by improved outpatient management. Better disease management of AD on an outpatient level could also minimize costly inpatient care. Recommendations at a governmental level should consider healthcare subsidies for affected families, better provision of support to informal caregivers and use of national healthcare insurances to pay for outpatient costs. We also suggest that AD should be included in the chronic disease management programme to acknowledge the burdens and subsequent costs that the condition imposes.

In alignment with other studies, our study found that severe AD is associated with greater costs compared with mild and moderate AD.[18,38] With optimal treatment patients with moderate or even severe AD can improve significantly leading to a possible overall reduction in cost, emphasizing the need for proper education of patients with AD and their caregivers to improve compliance and outcomes. In addition, we also found significant differences in total cost because of ethnicity with Malay origin having a lower total cost. This may be because of socioeconomic differences that have an impact on healthcare-seeking behaviour and out-of-pocket expenses, or even genetic heritage related to degree of severity. These findings were unexpected and not a focus when designing the study but this requires further research. Using a cost-of-illness approach allows us to understand the distributive efficiency and equity aspects of the disease burden of AD by generating information for policy and prioritization as it addresses cost-driving components.[39,40]

Table 4 Factors associated with annual total costs (healthcare, informal caregiving and out-of-pocket expenses in U.S. dollars) for children with atopic dermatitis using a generalized linear model

	Univariable analysis			Multivariable analysis		
Variables	Coefficient	SE	P-value	Coefficient	SE	P-value
Age of children (years)	–0·01	0·01	0·451	–0·07	0·01	< 0·001
Sex						
Female	1 (Ref)			1 (Ref)		
Male	–0·04	0·11	0·707	–0·15	0·92	0·114
Ethnic group						
Chinese	1 (Ref)			1 (Ref)		
Malay	0·31	0·13	0·014	0·31	0·12	0·010
Indian	0·39	0·28	0·155	0·36	0·24	0·128
Others	0·75	0·29	0·009	0·42	0·15	0·005
Duration of disease (years)	0·03	0·02	0·055	0·06	0·02	< 0·001
AD severity						
Mild	1 (Ref)			1 (Ref)		
Moderate	0·18	0·11	0·104	0·28	0·10	0·007
Severe	0·77	0·16	<0·001	0·94	0·16	< 0·001
Responder's education						
Postsecondary or polytechnic	1 (Ref)			1 (Ref)		
Secondary school or lower	–0·09	0·15	0·562	–0·14	0·13	0·302
University	–0·17	0·13	0·195	–0·16	0·12	0·184
Responder's employment						
Unemployed	1 (Ref)			1 (Ref)		
Employed	–0·14	0·14	0·326	–0·36	0·12	0·754
Accommodation						
1–3-bedroom HDB	1 (Ref)			1 (Ref)		
4–5-bedroom HDB	–0·14	0·14	0·344	–0·10	0·11	0·380
Condominium/landed property	–0·18	0·20	0·366	–0·20	0·15	0·203

SE, standard error; Ref, reference category; HDB, Housing and Development Board.

Limitations of the study include the self-reporting of healthcare utilization, possibly introducing recall bias.[41] Furthermore, there was no control group (healthy children without AD) in the study to provide a comparison of the incremental disease burden. Several assumptions were made regarding the health economic study design for valuation of costs and data entry, which may have underestimated the real costs as a conservative approach was applied so as not to overestimate the costs. There is also a likelihood that the surveyed patients attended the clinic because of an exacerbation and were potentially more severely affected by their AD compared with children with AD cared for solely by primary care clinics. This may possibly reflect a higher cost and affect the overall result. Furthermore, as we used a cross-sectional study design our conclusions do not reveal more long-term costs. Lastly, our use of a convenience sampling approach may have excluded nonhealthcare-seeking caregivers of children with AD, introducing a selection bias as this subgroup of patients were not represented in the study.

In conclusion, childhood AD imposes substantial costs with a large proportion arising from informal caregiving and out-of-pocket expenses. The cost of AD is also strongly related to disease severity. This information is important for policy makers and other health planners when considering how to better support affected families.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Annual average costs (U.S. dollars) for healthcare, informal caregiving and out-of-pocket expenses for children with atopic dermatitis, total and by atopic dermatitis severity.

Table S2 Annual cost (U.S. dollars) for atopic dermatitis-related medications.

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