

MS MAJA OLSSON (Orcid ID : 0000-0003-2228-5134)  
DR LYNETTE WEE (Orcid ID : 0000-0002-5395-0734)  
DR STEVEN THNG (Orcid ID : 0000-0002-5980-5319)  
PROFESSOR JOSIP CAR (Orcid ID : 0000-0001-8969-371X)

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

M. Olsson,<sup>1,2</sup> R. Bajpai,<sup>1,3</sup> L.W.Y. Wee,<sup>4</sup> Y.W. Yew,<sup>5,6</sup> M.J.A. Koh,<sup>4</sup> S. Thng,<sup>5,6</sup> J. Car<sup>1,7</sup> and K. Järbrink<sup>1</sup>

<sup>1</sup>Centre for Population Health Sciences (CePHaS), Lee Kong Chian School of Medicine, Nanyang Technological University, Clinical Sciences Building, 11 Mandalay Road, Singapore 308232, Singapore

<sup>2</sup>Queensland University of Technology, Brisbane, Australia

<sup>3</sup>Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire, UK ST55BG

<sup>4</sup>Dermatology Service, KK Women's and Children's Hospital, Singapore

<sup>5</sup>National Skin Centre, 1 Mandalay Road, Singapore 308205

<sup>6</sup>Skin Research Institute of Singapore, Singapore

<sup>7</sup>Global eHealth Unit, Department of Primary Care and Public Health, School of Public Health, Imperial College London, 3rd floor Reynolds Building, St Dunstan's Road, London W6 8RP, UK

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**Correspondence to:** Associate Professor Josip Car

**E-mail:** josip.car@ntu.edu.sg

**Running title:** Cost of childhood atopic dermatitis

### **What is 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 healthcare setting specific.

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### 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.

### ABSTRACT

**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 physician-confirmed diagnosis of atopic dermatitis were recruited and socio-demographics, clinical characteristics, health service utilisation 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 US\$7,943 (mild US\$6,651, moderate US\$7,935 and severe US\$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 utilisation 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 cost for atopic dermatitis is also strongly related to disease severity. This information is important for policymakers and other health planners when considering how to better support affected families.

## BACKGROUND

Atopic dermatitis (AD), or eczema is a common chronic inflammatory dermatosis characterised 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 to 20.6% in year 2018 (3, 4). AD often affects every day life as it commonly requires regular treatments to repair the skin barrier (e.g. moisturisers), 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 (HRQoL) for children and their parents (6-9). Children often suffer from 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 ostracised, 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 developed countries such as Australia, South Korea and Singapore (range US\$1,000 to US\$6,000 per patient per year) compared to less developed countries (range US\$199 to US\$743 annually) (14). Previous studies have estimated the healthcare costs of AD in Singapore at US\$4,753 annually per child, with US\$1,097 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 presents varying annual cost-estimates per child ranging between US\$71 and US\$4,389 in Europe and the United States (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 of 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 socio-economic 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 socio-demographics as well as the severity of AD.

## **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 authorised representative (LAR) who could give consent to enrol in the study and patients with a non-physician asserted diagnosis of AD were excluded to participate in the study.

## **Instrumentation and costing valuation for cost-consequences of childhood AD**

A modified version of the Client Service Receipt Inventory (CSRI) captured caregiver-reported retrospective data imposed by childhood AD on healthcare service utilisation, 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 United States dollars (USD) using purchasing power parity rates from the World Bank's international database (23). No discounting was applied since the study only assessed annual costs.

Conservative assumptions were made throughout the study so as not to overestimate the burden of AD, e.g. 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 utilisation comprised healthcare services from different levels of care (e.g. primary care, hospital care etc.) 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 hospitals 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 pre-set activities- personal care, preparing special meals due to dietary restrictions and providing emotional support. Time spent on personal care and specially-prepared homemade food, without noted duration, was assumed to be 5 minutes and 30 minutes per session, respectively. Informal caregiving was valued as an opportunity cost where one hour 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 by 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, e.g. moisturising creams, hygiene products, laundry costs due to the child's AD. Moisturisers are included as part of family expenses as these are pharmacy retail items and not subsidised 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 AD**

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 global assessment (PGA) (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 SG\$10 was given to participants as appreciation for their time.

### **Statistical analyses**

This study reported means with standard deviation (SD) for continuous variables, and frequencies with corresponding proportions for categorical variables. Skewed variables were presented as median and range (min–max). Normality of continuous variables was assessed by Kolmogorov-Smirnov and Shapiro-Wilk test. Costs by AD severity (mild, moderate, and severe) were compared using Kruskal-Wallis H-test, and categorical variables were compared using Chi-square 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, socio-demographics and severity of AD were analysed by univariable and multivariable generalised 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 (SE). The goodness-of-fit was assessed by two different statistics, the deviance and the Pearson  $\chi^2$  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, USA). Two-tailed p-value less than 0.05 was considered statistically significant.

## **RESULTS**

### **Sample characteristics**

Out of 735 eligible caregivers, 176 declined to participate in the study due to various reasons e.g. time constraints, language (English) deficiency, or if the caregiver not being the LAR of the child. A total of 559 caregivers and children with AD were recruited for the study (Table 1).

The average age was 6.6 ( $\pm 4.6$ ) years with a mean AD duration of 3.5 ( $\pm 3.6$ ) years. Most children were of Chinese ethnicity (72.5%), followed by Malay (16.0%), Indian (5.9%) and “other” (5.6%) ethnicities. This racial distribution fairly reflects the racial distribution of Singapore in general (31). Approximately half of the responding caregivers were university graduates (49.2%), followed by post-secondary 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 of families lived in government flats (77%), which is not necessarily related to socioeconomic status (31, 33), while 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 the 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 (25.5%), and severe (12.5%) AD.

### **AD related healthcare service utilisation**

The mean total cost for healthcare service utilisation across all degrees of AD severity was US\$1,349 per child per year (Table 2). The cost for medications accounted for 42.6% (US\$574) of the total cost for healthcare utilisation, followed by specialist outpatient services accounting at 30.6% (US\$413), while 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%) (Supplementary Table 1). Topical- and oral steroids accounted for the highest cost, due to its widespread use, estimated at US\$252 (43.9% of the total cost for medications); followed by calcineurin inhibitors at an average cost of US\$150 (26%) per patient per annum.

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

The severity of AD significantly impacted the total healthcare cost with mild AD at US\$1,062, moderate AD at US\$1,217 and severe AD at US\$3,035 ( $p < 0.001$ ) per child per annum. Thus, the cost for severe AD is almost two and a half times the cost compared to moderate AD, and three times the cost compared to mild AD.

### **Informal caregiving**

As many as 91.6% of the caregivers reported spending an average of 10.3 hours of time each week providing informal caregiving due to their child's AD (Table 3). Most caregivers reported that the largest proportion of time was spent on providing personal care for the child e.g. application of moisturisers (87.7%, estimated cost US\$1,625 per patient per annum) and preparation of specially-made foods due to diet restrictions (51.1%, estimated at US\$600 per patient per annum), as well as to accompany and to provide emotional support (42.3%, estimated cost US\$1,217 per patient per annum) to the child. The average total cost for informal caregiving amounted to US\$3,659 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 (estimated to cost US\$3,244 per patient per year), 10.8 (US\$3,801 per patient per year) and 15.2 (US\$5,395 per patient per year) hours ( $p= 0.019$ ) respectively per week, hence establishing that the cost of informal care in severe AD is 1.4 to 1.7 times more than mild and moderate disease.

### **Out-of-pocket expenses**

Most caregivers (92.2%) reported out-of-pocket expenses to treat their child's AD at an average of US\$2,935 per child per year (Table 2). Moisturisers accounted for the highest out-of-pocket expenses at US\$1,084 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 US\$648 (purchased by 78.6% of participants) per child per annum. Analysing out-of-pocket expenses by AD severity revealed significant differences between mild AD (US\$2,344), moderate AD (US\$2,908) and severe AD (US\$5,906) ( $p<0.001$ ). Out-of-pocket expenses for severe AD were 2 times the cost of a mild or moderate AD.

### **Total financial cost**

The average cost for the total sample including all cost categories amounted to US\$7,943 per child per year (Table 2). Stratified by severity, the cost for a child with mild AD was estimated at US\$6,651, for moderate AD US\$7,935, and US\$14,335 for severe AD ( $p<0.001$ ) per patient per annum. The total cost for a child with severe AD was greater than two times the cost for a child with mild or moderate condition. An 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 multivariable generalised linear model are presented in Table 4. The multivariable analysis identified significant factors associated with increasing cost as being of Malay ethnicity (coef.: 0.31, SE: 0.12,  $p=0.010$ ) or “other ethnicity” (coef.: 0.42, SE: 0.15,  $p=0.005$ ) compared with the Chinese ethnic group; having a longer duration (years) of AD (coef.: 0.07, SE: 0.02,  $p<0.001$ ), and moderate (coef.: 0.28, SE: 0.11,  $p=0.007$ ) or severe (coef.: 0.94, SE: 0.16,  $p<0.001$ ) AD. The age of the child was also statistically associated with the total cost (coef.: -0.07, SE: 0.09,  $p<0.001$ ). Goodness-of-fit statistics showed that the model was of moderate fit overall. The mean adjusted total societal costs ( $\pm$ SE) per year was US\$6,602  $\pm$  US\$404 for mild AD, US\$8,336  $\pm$  US\$686 for moderate AD, and US\$14,684  $\pm$  US\$2,081 for severe AD.

## Discussion

The average total annual cost per child with AD was conservatively estimated at US\$7,943 in our study which is substantially higher when compared to estimates from other countries e.g. the United States US\$3,288 and Italy US\$1,540 (17, 19). Findings from our study also show that the larger proportion of the overall costs for childhood AD were attributed to informal caregiving and out-of-pocket expenses rather than actual healthcare costs, strongly suggesting that the cost of caring for a child with AD goes far beyond the expenditures on actual healthcare. These findings add new insights as 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 since some diseases, such as childhood AD, are associated with rather substantial time costs due to 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 impact healthcare economic policies.

In accordance to 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 policymakers to address since 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 cost of outpatient treatment of AD,

especially for moderate to severe conditions and that efficiency gains can be made by improved outpatient management. A better disease management of AD on an outpatient level could also minimise costly inpatient care. Recommendations from a governmental level should consider healthcare subsidies for affected families, better provision of support to informal caregivers and to use national healthcare insurances to pay for outpatient costs. We also suggest that AD should be included in the chronic disease management program (CDMP) 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 to 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 AD patients and their caregivers to improve compliance and outcomes. In addition, we also found significant differences in total cost due to ethnicity with Malay origin having a lower total cost. This may be due to socio-economic differences impacting healthcare seeking behaviour and out-of-pocket expenses, or even genetic heritage related to degree of severity. These findings were unexpected and not at focus when designing the study but calls out for 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 prioritisation as it addresses cost-driving components (39, 40).

### **Limitations**

Limitations of the study include the self-reporting of healthcare utilisation, 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 since a conservative approach was applied to not overestimate the costs. There is also likelihood that the surveyed patients attended the clinic due to an exacerbation and were potentially more severely affected by their AD compared to 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 convenient sampling approach may have excluded non-healthcare seeking caregivers of children with AD introducing a selection bias since this subgroup of patients were not represented in the study.

### **Conclusion**

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

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**Table 1. Socio-demographic and clinical profile of children with atopic dermatitis**

<b>Characteristics (N = 559)</b>	<b>Mean ± SD / n</b>	<b>%</b>
Age in years	6.6 ± 4.6	-
Diagnose duration in years (n = 550)	3.5 ± 3.6	-
Gender		
Female	277	49.5
Male	282	50.5
Ethnic group (n = 557)		
Chinese	404	72.5
Malay	89	16.0
Indian	33	5.9
Other	31	5.6
Severity (n = 513)*		
Mild	316	61.6
Moderate	133	25.9
Severe	64	12.5
Responder's relation		
Mother	398	71.2
Father	158	28.3
Other	3	0.5
Responder's qualification		
Secondary school or lower	103	18.4
Post-secondary or polytechnic	181	32.4
University	275	49.2
Responder's employment status		
Employed	452	80.9
Unemployed	107	19.1
Accommodation type (n = 557)		
1-3 bedroom HDB-flat	68	12.2
4-5 bedroom HDB-flat	361	64.8
Condominium/landed property	128	23.0

\* Clinician assessed severity was based on PGA score

**Table 2. Annual average costs (US\$) for healthcare, informal caregiving and out-of-pocket expenses for children with atopic dermatitis**

Type of health care utilisation	Total (n = 513)			AD severity*									P-value
	% users	Mean ± SD	Median (min - max)	Mild (n = 316)			Moderate (n = 133)			Severe (n = 64)			
				% users	Mean ± SD	Median (min - max)	% users	Mean ± SD	Median (min - max)	% users	Mean ± SD	Median (min - max)	
<b>Healthcare service utilisation</b>													
Inpatient care	4.7	163.6 ± 1239.8	0.0 (0.0 – 17559.6)	2.5	87.4 ± 1011.0	0.0 (0.0 - 17559.6)	3.8	48.1 ± 282.0	0.0 (0.0 - 2615.0)	17.2	779.4 ± 2602.3	0.0 (0.0 - 16196.8)	<0.001
A&E	6.6	20.2 ± 95.5	0.0 (0.0 – 1175.5)	3.8	8.1 ± 42.0	0.0 (0.0 - 391.8)	9.8	26.5 ± 89.2	0.0 (0.0 - 587.7)	14.1	67.3 ± 213.0	0.0 (0.0 - 1175.5)	<0.001
Outpatient care –speciality services	100	412.8 ± 549.7	233.4 (185.7 – 9146.5)	100	351.9 ± 227.0	233.4 (185.7 - 2185.7)	100	378.0 ± 295.5	233.4 (185.7 - 2891.0)	100	785.6 ± 1361.1	395.2 (233.4 - 9146.5)	<0.001
GP/ polyclinic services	45.2	80.5 ± 149.1	0.0 (0.0 – 1241.9)	42.4	69.8 ± 133.3	0.0 (0.0 - 1241.9)	45.9	77.6 ± 131.6	0.0 (0.0 - 800.7)	57.8	139.6 ± 226.6	80.1 (0.0 - 1240.2)	0.024
Other health services*	1.4	4.0 ± 48.0	0.0 (0.0 – 695.1)	0.6	0.2 ± 2.4	0.0 (0.0 - 30.7)	0.8	0.2 ± 2.7	0.0 (0.0 - 30.7)	6.3	30.7 ± 133.6	0.0 (0.0 - 695.1)	<0.001
Medication	77.8	574.0 ± 774.8	336.2 (0.0 – 4109.5)	73.1	466.7 ± 641.3	336.2 (0.0 – 4109.5)	81.2	596.9 ± 818.5	336.2 (0.0 - 3676.3)	93.8	1056.1 ± 1060.0	672.4 (0.0 - 3979.7)	<0.001
Transportation	99	93.8 ± 127.2	56.2 (0.0 – 1506.8)	99.1	78.9 ± 80.4	49.4 (0.0 - 647.4)	98.5	89.7 ± 101.3	58.8 (0.0 - 741.7)	100	176.1 ± 264.0	98.8 (5.1 - 1506.8)	<0.001
Total	100	1348.9 ± 1862.9	901.8 (185.7 – 20090.4)	100	1062.9 ± 1251.3	863.2 (185.7 - 18178.6)	100	1217.1 ± 1073.2	871.1 (219.8 - 5674.4)	100	3034.8 ± 3824.5	1470.3 (267.5 - 20090.4)	<0.001
<b>Informal care</b>													
Personal care	87.7	1625.1 ± 2662.0	708.7 (0.0 – 29764.9)	87.7	1457.9 ± 2406.3	708.7 (0.0 - 17717.2)	89.5	1741.0 ± 2309.9	708.7 (0.0 - 14882.5)	84.4	2210.3 ± 4116.2	1063.0 (0.0 - 29764.9)	0.202
Accompanying to healthcare visits	36.6	194.8 ± 755.5	0.0 (0.0 – 9787.0)	32.9	160.1 ± 667.5	0.0 (0.0 - 9787.0)	39.1	267.0 ± 1027.0	0.0 (0.0 - 9567.3)	50	216.0 ± 429.2	3.4 (0.0 - 1962.5)	0.027
Companionship and emotional support	42.3	1217.3 ± 3304.6	0.0 (0.0 – 46592.0)	38.6	974.2 ± 2657.7	0.0 (0.0 - 19843.3)	51.1	1257.1 ± 2493.7	59.1 (0.0 - 19843.3)	42.2	2335.2 ± 6231.7	0.0 (0.0 - 39686.5)	0.040
Specially prepared homemade food	51.1	599.9 ± 1840.2	0.0 (0.0 – 25512.8)	20.6	632.5 ± 2072.9	0.0 (0.0 - 25512.8)	19.5	524.9 ± 1425.6	0.0 (0.0 - 9921.6)	26.6	594.3 ± 1327.1	0.0 (0.0 - 7441.2)	0.573
Other additional housework activities	1.6	22.0 ± 257.5	0.0 (0.0 – 4960.8)	1.3	19.4 ± 282.5	0.0 (0.0 - 4960.8)	2.3	20.0 ± 144.1	0.0 (0.0 - 1240.2)	1.6	38.8 ± 310.1	0.0 (0.0 - 2480.4)	0.741
Total	91.6	3659.1 ± 5913.8	1594.6 (0.0 – 47127.8)	89.9	3244.0 ± 5687.6	1240.2 (0.0 - 47127.8)	94	3801.0 ± 4685.8	2090.6 (0.0 - 28879.1)	95.3	5394.6 ± 8515.1	2480.4 (0.0 - 44647.4)	0.019
<b>Out-of-pocket expenses</b>													
Moisturising creams	90.3	1083.7 ± 1706.2	511.1 (0.0 – 17717.2)	89.6	947.7 ± 1666.6	442.9 (0.0 - 17717.2)	94	1259.3 ± 1830.9	664.4 (0.0 - 11073.3)	85.9	1390.4 ± 1579.0	885.9 (0.0 - 6644.0)	0.009
Hygiene products	78.6	647.8 ± 969.1	354.3 (0.0 – 10630.3)	76.3	571.2 ± 816.7	302.8 (0.0 - 4429.3)	85	723.2 ± 971.2	442.9 (0.0 - 4429.3)	76.6	869.2 ± 1493.4	442.9 (0.0 - 10630.3)	0.027
Extra laundry	22.2	169.3 ± 527.6	0.0 (0.0 – 4429.3)	22.3	154.1 ± 537.8	0.0 (0.0 - 4429.3)	24.8	141.1 ± 391.1	0.0 (0.0 - 2214.7)	26.6	303.0 ± 689.0	0.0 (0.0 - 2657.6)	0.3227
Clothing and textiles	16.2	182.8 ± 715.1	0.0 (0.0 – 8858.6)	13.9	128.5 ± 588.7	0.0 (0.0 - 8858.6)	18	215.8 ± 800.4	0.0 (0.0 - 6644.0)	23.4	382.6 ± 1011.4	0.0 (0.0 - 4429.3)	0.090
Humidifier	14.6	163.3 ± 975.9	0.0 (0.0 – 13287.9)	13.9	150.7 ± 961.3	0.0 (0.0 - 13287.9)	15	121.5 ± 582.7	0.0 (0.0 - 4429.3)	17.2	312.6 ± 1543.0	0.0 (0.0 - 11073.3)	0.818

Water filter	9.6	218.4 ± 2180.3	0.0 (0.0 – 44293.0)	7	73.3 ± 467.4	0.0 (0.0 - 6644.0)	14.3	223.5 ± 1583.7	0.0 (0.0 - 17717.2)	12.5	924.2 ± 5628.0	0.0 (0.0 - 44293.0)	0.040
Special diet	11.7	282.9 ± 1220.4	0.0 (0.0 – 17717.2)	11.1	269.0 ± 1276.1	0.0 (0.0 - 17717.2)	10.5	214.9 ± 957.1	0.0 (0.0 - 8858.6)	17.2	493.2 ± 1409.1	0.0 (0.0 - 8177.2)	0.291
Others	5.1	199.7 ± 2523.7	0.0 (0.0 – 53151.6)	5.1	65.9 ± 550.2	0.0 (0.0 - 8858.6)	3	16.3 ± 106.1	0.0 (0.0 - 1022.2)	9.4	1241.3 ± 6997.1	0.0 (0.0 - 53151.6)	0.143
Total	92.2	2934.6 ± 6236.3	1328.8 (0.0 – 75121.0)	90.1	2344.2 ± 4298.4	1063.0 (0.0 - 53560.5)	94.7	2907.9 ± 4927.3	1533.2 (0.0 - 46507.7)	93.8	5905.7 ± 12731.8	2274.3 (0.0 - 75121.0)	<0.001
<b>Combined total</b>		<b>7942.6 ±</b> <b>9595.4</b>	<b>4769.9 (190.8 –</b> <b>79381.3)</b>		<b>6651.1 ±</b> <b>7708.8</b>	<b>4240.8 (190.8 –</b> <b>59118.2)</b>		<b>7935.0 ±</b> <b>7956.3</b>	<b>5796.1 (364.6 –</b> <b>52670.8)</b>		<b>14335.1 ±</b> <b>16389.5</b>	<b>7881.9 (1144.0 –</b> <b>79381.3)</b>	<b>&lt;0.001</b>

\*\*Other health services” comprise e.g. light therapy and dietician

**Table 3. Time (hours) spent on informal caregiving per week by AD severity**

Activity	Total (n=513)		Hours per week						p-value
			Mild (n=316)		Moderate (n=133)		Severe (n=64)		
	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 *	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 & 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
<b>Total</b>	<b>10.3 ± 16.7</b>	<b>4.5 (0.0 – 133.0)</b>	<b>9.2 ± 16.1</b>	<b>3.5 (0.0 – 133.0)</b>	<b>10.8 ± 13.2</b>	<b>5.9 (0.0 – 81.5)</b>	<b>15.2 ± 24.0</b>	<b>7.0 (0.0 – 126.0)</b>	<b>0.019</b>

\* n=512

**Table 4. Factors associated with the annual total costs (healthcare, informal caregiving and out-of-pocket expenses in US\$) for children with atopic dermatitis using generalised linear model**

Variables	Univariable analysis			Multivariable analysis		
	Coeff.	SE	p-value	Coeff.	SE	p-value
Age of children (years)	-0.01	0.01	0.451	-0.07	0.01	<0.001
Gender						
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						
Post-secondary 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

Ref.: reference category; Coeff.: coefficient; SE: standard error