


## REVIEW ARTICLE

**Burden of atopic dermatitis in Asia**

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**ABSTRACT**

**Atopic dermatitis is a chronic, inflammatory skin disease characterized by intense pruritus and eczematous lesions. It is considered one of the most common chronic conditions, with an estimated global prevalence of nearly 230 million. As in the rest of the world, prevalence of atopic dermatitis has been increasing in Asian countries over the last few decades. This increased prevalence in Asian countries has been attributed to factors such as rapid urbanization, increasingly Westernized lifestyles, and improved standards of living and education. As a result, it is important to understand the increasing burden of disease in Asian countries and the differences between the countries in terms of epidemiology, diagnostic criteria, management, quality of life and economic burden.**

**Key words:** Asia, atopic dermatitis, eczema, epidemiology, quality of life.

**INTRODUCTION**

Atopic dermatitis (AD) is a chronic, relapsing–remitting, inflammatory skin disease characterized by the development of intense pruritus and eczematous lesions.<sup>1</sup> AD most frequently develops in childhood, progressing from acute lesions on the face and dorsal aspects of the limbs in infancy, to lesions that affect the face, neck and flexures in older children.<sup>2</sup> For approximately 80% of children with AD, it will persist into adulthood, most often presenting as lichenified lesions that affect the flexures, head and neck.<sup>2,3</sup>

Once believed to be primarily allergic, AD is now considered a multifactorial disease that results from a combination of immune dysregulation, genetic susceptibility, environmental factors and impaired barrier function.<sup>1,4</sup> The burden associated with chronic and incurable skin diseases such as AD is significant and can encompass psychological, social and financial costs<sup>5–7</sup> and systemic comorbidities.<sup>8</sup>

Psychological comorbidities can include an increased incidence of psychiatric disorders and anxiety in adults and increased psychological disturbance, excess dependency and clinginess, fearfulness and behavioral problems in children.<sup>9</sup> AD can also have a significant social impact, resulting in altered family interaction, stigmatization from peers and negative effects on interpersonal relationships.<sup>9</sup> Because AD often affects children younger than 12 years, it also has a significant

impact on family quality of life (QoL) because of factors such as sleep deprivation, financial costs and lifestyle changes.<sup>5</sup> The economic costs associated with AD are significant, encompassing direct costs, such as medical visits and treatment costs, and indirect costs, including decreased productivity and time lost from work.<sup>5,9,10</sup>

With an estimated global prevalence of nearly 230 million, AD is considered one of the most common chronic conditions.<sup>1,11</sup> The prevalence of AD is also increasing in much of the world, including large parts of Asia.<sup>10,12,13</sup> For example, in Taiwan, the lifetime prevalence of AD in patients aged 12–15 years increased from 2.4% to 4.0% between 1996 and 2001, per an International Study of Asthma and Allergies in Childhood (ISAAC)-based report.<sup>13</sup> A separate report identified an increasing prevalence of atopic symptoms (i.e. asthma, rhinitis and AD) over a 7-year period (1994–2001) in a similar population (adolescents aged 13–14 years in Taipei, Taiwan).<sup>14</sup> Comparable increases in lifetime prevalence of AD in similarly aged patients have also been observed in China (aged 13–14 years), Japan (aged 7–15 years) and South Korea (aged 12–15 years).<sup>13</sup> This is most often attributed to changing socioeconomic and environmental factors, including rapid urbanization, adoption of a Westernized lifestyle, and improved standards of living and education.<sup>10,15,16</sup> Although the burden of AD in Western cultures has been reviewed extensively, information is limited regarding the impact of AD in the wider Asia region. In this

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review, we discuss the burden of AD in Asia based on a search of the published work covering areas such as epidemiology, diagnostic criteria, management, QoL and economic burden.

## AD EPIDEMIOLOGY IN ASIA

The most comprehensive global data available regarding the epidemiology of AD are from ISAAC, which is a large collaborative research project to investigate the prevalence of asthma, rhinitis and AD.<sup>17</sup> The most recently completed third phase of ISAAC was conducted between 2001 and 2002 and included a survey of 1.2 million school children from 98 countries. Results from the survey indicated that the global prevalence of AD in children aged 6–7 years is 7.9% (7.7% boys, 8.2% girls) and in children aged 13–14 years is 7.3% (6.2% boys, 8.3% girls).<sup>17</sup> Among 6–7-year-olds and 13–14-year-olds, 1.0% and 1.2% had severe AD, respectively, suggesting that approximately 15% of patients with AD had severe disease.<sup>18</sup> Interestingly, in the Asia–Pacific region, overall prevalence was 10.1% (10.2% boys, 10.0% girls) for children between the ages of 6 and 7 years; however, unlike in the overall global population, the rates in children aged 13–14 years are comparatively lower at 5.3% (4.7% boys, 5.9% girls).<sup>17,18</sup> Severe AD in the Asia–Pacific region was noted in 1.2% of 6–7-year-olds and 0.7% of 13–14-year-olds, suggesting that approximately 12% of patients with AD had severe disease.<sup>18</sup> Taken together, most pediatric patients (~88%) in the Asia–Pacific region have either mild or moderate AD.

When broken down by country, higher prevalence (>10%) was seen in children between 6 and 7 years of age in Thailand, Malaysia and South Korea, whereas lower prevalence (<5%) was seen in Hong Kong, Pakistan, Indonesia, India, Syria, Iran, Oman and Vietnam.<sup>18</sup> While Japan was not included in ISAAC, a study conducted in Japanese patients by the Japanese Ministry of Health, Labor and Welfare during a similar timeframe (2000–2002) found that prevalence of AD in children aged 6–7 years was 11.8%.<sup>19</sup> In ISAAC, for children between 13 and 14 years of age, higher prevalence (>10%) was seen in Pakistan whereas lower prevalence (<5%) was seen in Taiwan, India, Hong Kong, Vietnam, Indonesia, Syria, Iran and China (Fig. 1).<sup>18,19</sup> In the study in Japan, prevalence was 10.6% in a similar age group (12–13 years old).<sup>19</sup>

Several recent studies conducted within Asia have reported national epidemiology data, some of which are in line with the results seen in the ISAAC study and some that differ significantly. For example, a cross-sectional survey published in 2011 of 4003 children in South Korea, which used the South Korean-translated modified version of the ISAAC questionnaire, found a weighted 12-month prevalence of AD of 17.9% for children aged 6–7 years and 11.2% for children aged 13–14 years; these values were considerably higher than those found in the ISAAC study from 2000.<sup>18,20</sup> The results of the recently published Korea National Health and Nutrition Examination Survey (KHANES), which was a cross-sectional survey of data from 2008 to 2011 of 8947 children (≤18 years), reported a prevalence of AD of 13.5%, ranging from 7.94% (15 years) to 19.8% (5 years) in different age groups.<sup>21</sup> In general, the prevalence was higher in younger children, in those

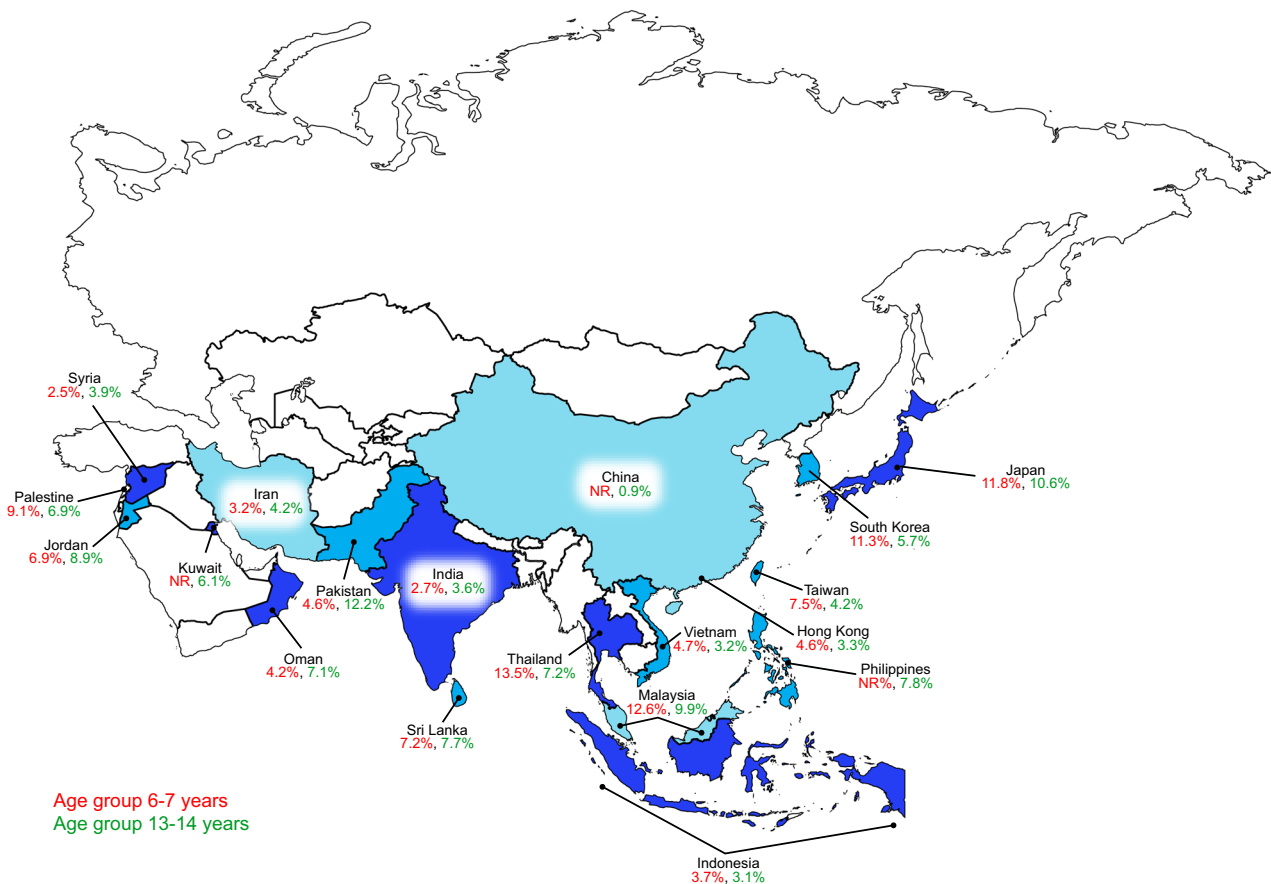
with higher household incomes and for those living in urban areas. However, there is an increasing trend in prevalence of AD in children over time. A cross-sectional survey in South Korea that compared prevalence of AD in 40 429 children from 1995 with that of 42 202 children from 2000 found that lifetime prevalence increased from 15.3% to 17.0% in children aged 6–12 years and from 7.2% to 9.5% in children aged 12–15 years.<sup>22</sup>

The epidemiological data available in India vary, with a prevalence rate of 0.55% reported in a study conducted in eastern India compared with an incidence of 29.9% reported by a study conducted in northern India.<sup>23</sup> Meanwhile, data gathered from the ISAAC study indicated a relatively low prevalence of 2.7% in 6–7-year-old children and 3.6% in 13–14-year-old children (Fig. 1).<sup>18</sup> The number of population-based studies regarding the epidemiology of AD in India are few, and significant regional differences are likely because of climate. For example, northern India experiences more severe and longer winters than southern India.<sup>23,24</sup> However, it does seem that AD prevalence has been increasing in India in recent decades. For example, a study conducted in 1972 in Bihar, India, showed an incidence of AD of 0.38% among outpatients; however, a study conducted in Bihar in 2012 revealed a prevalence of AD of 7.21%.<sup>25</sup> Considering the trend of increasing prevalence of AD, the current rate of AD is likely higher.

In contrast to the extremely low prevalence reported in the ISAAC phase 3 study, epidemiological analyses conducted in China suggest that the prevalence in China is much higher. A descriptive cross-sectional study conducted in eight different districts in Shanghai in 2010 that included 10 436 children found a prevalence of AD of 8.3%.<sup>26</sup> In addition, results of an epidemiological study conducted in 2013 and 2014 in 12 metropolises throughout China and including 13 998 children 1–7 years of age showed a prevalence of 12.94% (ranging 9.00–24.69% between metropolises).<sup>27</sup> Similar to other countries, there has been a trend of increasing prevalence of AD in China, with one study that compared ISAAC phase 1 data and ISAAC phase 3 data in children in Guangzhou City showing that the prevalence of AD in children aged 13–14 years increased from 1.7% in 1994–1995 to 3.0% in 2001.<sup>13,28</sup>

In the Philippines, prevalence of any history of AD in children aged 13–14 years ranged 7.1–8.4% in the ISAAC surveys.<sup>29</sup> In a recent survey from 2007 to 2011 of 14 363 dermatology patients in outpatient clinics, the rate was relatively lower, with 3.4% diagnosed with AD.<sup>30</sup> Of the survey participants, 89% were newly diagnosed and only 11% were previously diagnosed with AD.<sup>30</sup>

In Taiwan, a claims database analysis from 2007 to 2011 of 997 729 subjects of all ages showed the overall 8-year prevalence of AD to be 6.7%.<sup>31</sup> A higher prevalence was identified in children, adolescents and adults younger than 20 years (9.6%); however, the highest prevalence was identified in infants younger than 1 year (22.4%).<sup>31</sup> Based on the report using ISAAC data (which include 42 919 adolescents from the 1995–1996 survey and 10 215 adolescents from the 2001 survey), AD prevalence increased from 2.4% in 1995–1996 to 4.0% in 2001 among those aged 12–15 years.<sup>13,32</sup>



**Figure 1.** Prevalence based on current AD symptoms in select countries included in the ISAAC phase 3 study and Japan.<sup>a,18,19</sup> <sup>a</sup>Japan data from study of 48 072 children throughout Japan from 2000 to 2002.<sup>19</sup> <sup>b</sup>Age group 12–13 years. AD, atopic dermatitis; NR, not reported.

The prevalence of AD in Japan is reported to be relatively high in infants and young children (12.8% in infants aged 4 months, 9.8% in infants aged 1.5 years and 13.2% in children aged 3 years), with prevalence reducing significantly in adults as they age (9.4% in adults in their 20s, 8.3% in adults in their 30s, 4.8% in adults in their 40s, and 2.5% in adults in their 50s and 60s).<sup>33</sup> It has also been reported that age distribution has changed significantly over time: in 1967, 73.9% of those with AD were children, and in 1996, 23.4% of those with AD were children.<sup>19</sup> Based on a study of children from 1985 to 1997, it seemed that prevalence in children also increased over time, with a lifetime prevalence of those aged 7–15 years increasing from 15.0% in 1985 to 24.1% in 1993 and leveling off thereafter.<sup>34</sup>

An observation common to the majority of epidemiological analyses conducted in Asian countries is that prevalence of AD is increasing significantly.<sup>10,13,24–26,35</sup> There is almost unanimous agreement that this increasing prevalence can be largely attributed to environmental and socioeconomic factors, including rapid urbanization, increased family income, improved parental education, adoption of a more Westernized lifestyle, increased exposure to allergens, frequent bathing and use of

soap, change of diet and clothing choice.<sup>10,15,35</sup> In addition, increases in some areas may be partially attributable to improved accuracy of diagnosis.<sup>35</sup> Much of the available information on epidemiology in Asia is limited by the age of the data and may underestimate current rates of AD.

## DIAGNOSTIC CRITERIA

The diagnostic criteria used to identify AD differ between countries and across studies, which can account for variability in reported data, particularly epidemiology. The most commonly used criteria include the UK Working Party diagnostic criteria<sup>36–38</sup> and the diagnostic criteria identified by Hanifin and Rajka.<sup>39</sup> However, familiarity with these criteria is inconsistent between countries within Asia. For example, a survey of 255 dermatologists from Southeast Asia indicated considerable variation in familiarity with these criteria, with all respondents in Indonesia being familiar with the UK Working Party diagnostic criteria, whereas the respondents in Malaysia, Singapore and Thailand were more likely to be familiar with the Hanifin and Rajka diagnostic criteria.<sup>40</sup> Meanwhile, less than half of all

respondents in the Philippines and Vietnam were familiar with either the UK Working Party or the Hanifin and Rajka criteria.<sup>40</sup> In a clinical profile study published in 2016 that included several sites in the Philippines,<sup>30</sup> the diagnostic criteria included the Hanifin and Rajka, UK Working Party, Schultz-Larsen, Diepgen, Kang and Tian, and ISAAC sets.<sup>41</sup> As a result, the diagnosis of AD in this study did not rely on a single specific set of diagnostic criteria. However, the most commonly used criteria were those of Hanifin and Rajka.<sup>30</sup> Meanwhile, in northern India, Hanifin and Rajka and the UK Working Party diagnostic criteria were compared in a hospital setting; results showed that the Hanifin and Rajka criteria were more accurate in identifying AD.<sup>42</sup>

A few dermatological or AD-specific associations from Asian countries have published guidelines outlining alternative diagnostic criteria. The criteria developed by the Japanese Dermatological Association (JDA) are based on Hanifin and Rajka criteria but differ in two primary ways. First, the personal or family history of atopic diseases is included as a diagnostic aid in the JDA criteria rather than a basic feature of the disease. Second, the 23 minor features characteristic of AD have been removed in the JDA criteria because of variation in frequency.<sup>43</sup> Meanwhile, the Korean Atopic Dermatitis Association Atopic Dermatitis Criteria Group has proposed that novel diagnostic criteria – the Reliable Estimation of Atopic Dermatitis of Childhood (REACH) – be adopted as a means to detect major and minor groups of AD for epidemiological surveys.<sup>21</sup> Major groups of AD were those which manifested with eczematous skin lesions on the antecubital or popliteal fossa while minor groups were those who manifested with eczematous skin lesions on other locations except the antecubital or popliteal fossa.<sup>21</sup>

Chinese diagnostic criteria specific for adult/adolescent AD have been proposed because adult-onset AD is common within the Chinese population.<sup>44</sup> The criteria require a patient to have symmetrical eczema for more than 6 months and one or more of the following: a personal or family history of atopic disease, elevated serum immunoglobulin (Ig)E levels, positive allergen-specific IgE or eosinophilia.<sup>44</sup>

In Thailand, an analysis in children found that the three major criteria identified in the Hanifin and Rajka criteria (pruritus, typical distribution, chronic relapsing course) were very common in Thai children.<sup>45</sup> Extensor dermatitis was identified frequently but can also be common in non-atopic individuals, whereas the frequency of perifollicular accentuation was similar to that of other Asian populations.<sup>45</sup> Aggravating factors, such as smoking and having pets in the house, are considered less relevant in Thailand because the houses are well-ventilated.<sup>45</sup>

Because of the lack of universality in diagnostic criteria among Asian countries, comparing clinical and epidemiological data between countries can be difficult. It is recommended that clinicians make use of established and validated diagnostic criteria where possible.

## MANAGEMENT

A number of countries in Asia have published guidelines regarding the treatment of AD.<sup>25,33,46–48</sup> The majority follows a

similar treatment paradigm to that of Western countries, with basic therapy focusing on the use of moisturizers or emollients to improve skin hydration and anti-inflammatory therapy focusing on topical corticosteroids (TCS) as the mainstay of treatment, with topical calcineurin inhibitors (TCI) recommended for use when TCS are not appropriate.<sup>49–51</sup> Individual countries have incorporated specific alterations to the standard treatment regimen. For example, in Taiwan, the effectiveness of wet-wrap therapy may be limited because of the humid climate of the country.<sup>46</sup> Treatment in Taiwan and other countries may also be influenced by steroid phobia among patients.<sup>52</sup> In India, it is suggested that in warmer months, patients be kept cool using air conditioning or fans (when air conditioning is not feasible). It is also suggested that ear piercing be delayed in children until they are at least 8 years old.<sup>25</sup> In Japan, one of the available TCI, pimecrolimus, is not available under Japanese health insurance, which likely limits its use. However, the immunosuppressant cyclosporin was added to Japanese health insurance in 2008, prompting its inclusion in the treatment guidelines for adult patients with severe and recalcitrant AD.<sup>43</sup> Although cyclosporin is often not approved for treatment of AD in Asian countries, such as in Taiwan, it is often recommended for refractory AD.<sup>46</sup> In India, cyclosporin has been used, but the country does not have standard guidelines for practitioners to follow regarding its use, and therapy is often individualized according to the knowledge of the physician and the comfort level of the patient.<sup>53</sup> Biologic treatments, namely dupilumab, are also not widely available in Asian countries: dupilumab approval (as of 2018) was given in Japan, South Korea and Taiwan for treatment of moderate to severe AD.<sup>54–56</sup>

An Asia-Pacific consensus guideline for the management of AD has also recently been published, which included Australia, Hong Kong, India, Indonesia, Malaysia, the Philippines, Singapore and Taiwan.<sup>48</sup> The guideline highlighted that there are wide variations in skin types, socioeconomic conditions, climates and access to therapies within and between countries in the Asia-Pacific region, necessitating region-specific guidelines.<sup>48</sup> The treatment paradigm outlined within the guideline was similar to that of Western countries but discussed the limited effectiveness of wet-wrap therapy in humid environments and highlighted that at least among southeast Asian countries (Indonesia, Malaysia, Philippines, Singapore, Thailand, Vietnam) use of phototherapy is limited; outside of Singapore, 71–97% of dermatologists do not use it.<sup>40,48</sup>

The management practices of AD in Indonesia, Malaysia, the Philippines, Singapore, Thailand and Vietnam were investigated in a study that involved the survey of 255 dermatologists from those countries.<sup>40</sup> The results indicated that all or almost all respondents in the Philippines (98%) and Thailand (100%) always use emollients and that the majority of respondents in Indonesia (79%), Malaysia (97%) and Singapore (89%) sometimes or always use moisturizers for the clearance phase of treatment, whereas 77% of respondents in Vietnam use moisturizers sometimes or infrequently.<sup>40</sup> In the Philippines in particular, management options available at first consultation could be one or a combination of emollients, TCS, TCI, topical antibiotics, oral steroids, oral antihistamines, oral immunosuppressants, oral



antibiotics or phototherapy. Based on a study in three outpatient clinics in the Philippines, patients were most commonly treated with emollients (86%) and corticosteroids (67%).<sup>30</sup>

The majority of respondents in all six countries in the survey of dermatologists (91–100%) used TCS in infants and children with mild to moderate AD, although a number of respondents in the Philippines (17–19%) and Vietnam (11–25%) indicated that TCS were only used in infants and children in cases of severe AD.<sup>40</sup> Some areas of Asia have limited access to TCI; a large proportion of the respondents in Malaysia (45%) and Vietnam (33%) indicated that TCI were not available to them.<sup>40</sup> Because of a lack of availability, the majority of respondents in Indonesia (76%), Malaysia (88%) and Vietnam (91%) reported never using TCI.<sup>40</sup> In contrast, TCI were used by the majority of respondents in Singapore (86%) and Thailand (90%).<sup>40</sup>

Although Asian countries tend to manage AD similar to Western countries, there can be large variation in management patterns even between Asian countries. This seems to be largely a result of environmental factors and accessibility to certain treatments.

## QUALITY OF LIFE

Available data regarding the impact of AD on QoL in Asian countries are limited. The results of a multi-country survey conducted in 12 countries in the Asia-Pacific region – Hong Kong, South Korea, Singapore, Taiwan, China, Malaysia, Thailand, India, Indonesia, the Philippines and Vietnam – found that, overall, AD had a large impact on QoL, with poorer QoL identified in patients with severe disease.<sup>57</sup> QoL of children was found to have a significant impact on the QoL of the family.<sup>57</sup> The wealth of countries also played a role in the QoL of patients with AD: greater impact on QoL was observed in low-income countries than in high-income countries.<sup>57</sup>

Some nuances have been observed in the QoL of specific Asian countries. In a study conducted in Japan, patients with AD had significantly higher Skindex-16 scores than patients with isolated lesions in all three domains (symptoms, emotions and functioning) and the global scale (higher scores reflect worse QoL).<sup>58</sup> Unsurprisingly, patients with severe disease exhibited significantly worse QoL than patients with mild or moderate disease.<sup>58</sup> In addition, longitudinal analysis showed that patient QoL was associated with patient perception of their skin condition: scores improved in patients who believed their AD had improved, and scores worsened in patients who reported that their AD had worsened.<sup>58</sup> A patient survey of Japanese patients found that health-related QoL was significantly reduced in patients with AD compared with non-AD-matched controls in mental, physical and overall health domains, though no significant difference was observed between patients with moderate/severe AD and patients with mild AD.<sup>59</sup> Patients with AD also reported higher rates of depression, anxiety and sleep disorders than controls as well as higher rates of work impairment and impaired activity.<sup>59</sup> In addition, the longitudinal, prospective, observational disease registry study (ADDRESS-J) which focuses on Japanese adult patients with moderate to severe AD found that worse Patient-

Oriented Eczema Measure (POEM) and worse pruritus numerical rating scale (NRS) scores correlated with worse QoL (per the Dermatology Life Quality Index [DLQI]).<sup>60</sup>

A cross-sectional survey to investigate the QoL of infants and children in Singapore also showed that AD has a significant impact on QoL.<sup>61</sup> Patients with severe AD exhibited significantly worse QoL than those with mild or moderate AD ( $P = 0.005$ ).<sup>61</sup> Differences by sex were also identified: QoL was worse in boys aged 4 years or less and in girls aged 5 years or more, the latter due to having a greater social impact.<sup>61</sup> QoL was also significantly affected in children with AD in Malaysia.<sup>62</sup> The results of a survey of 110 children indicated that itchiness, sleep loss, embarrassment and treatment difficulty were the most significantly affected QoL variables.<sup>62</sup> Unfortunately, studies are lacking to examine potential differences in the correlation between severity of AD and QoL among Asian countries/ethnicities. At least in the population of patients with psoriasis, QoL is higher in Japanese patients despite their having more severe psoriasis than seen in other Asian ethnicities.<sup>63</sup>

Several studies have been conducted to look at the effect of AD on the psychological component of QoL specifically. A survey of 8208 Taiwanese patients with AD indicated that patients with AD had a higher incidence of major depression, any depressive disorder and anxiety disorders than age- and sex-matched controls.<sup>64</sup> A cross-sectional study conducted in Singapore identified that 18% of patients with AD exhibited symptoms of anxiety, and 5% could be considered cases of depression, suggesting that AD is associated with a significant impact on psychological well-being.<sup>65</sup> Disease that was more severe also correlated with greater psychological burden.<sup>65</sup>

The impact of AD on family QoL was specifically investigated in a questionnaire-based study of South Korean families of children with AD and showed that in families of children with more severe AD the probability of a low family QoL was 6.6-times more than in families of children with less severe disease.<sup>66</sup> Families of girls with AD also had lower QoL than families of boys with AD, which may be indicative of sex differences in perception by both the child and the parents.<sup>66</sup> Thus, the QoL burden of AD extends beyond individuals affected by the disease.

## ECONOMIC BURDEN

To understand the economic burden that AD poses in Asia, it is important to first be aware of the varied medical reimbursement systems used in different Asian countries. For the most part, many Asian countries, including South Korea, Thailand and Taiwan, pay for health care primarily through government-funded or subsidized basic universal health care, although many also include a smaller private insurance sector (Table 1).<sup>67–81</sup> Others may have a mixture of public and private health-care systems, such as in India or Malaysia. There are some notable nuances among Asian countries when it comes to paying for AD treatment. For example, in India, insurance plans typically do not cover the cost of AD treatment, leaving the costs to be borne solely by the patient, subsequently impacting adherence to treatment.<sup>82</sup>

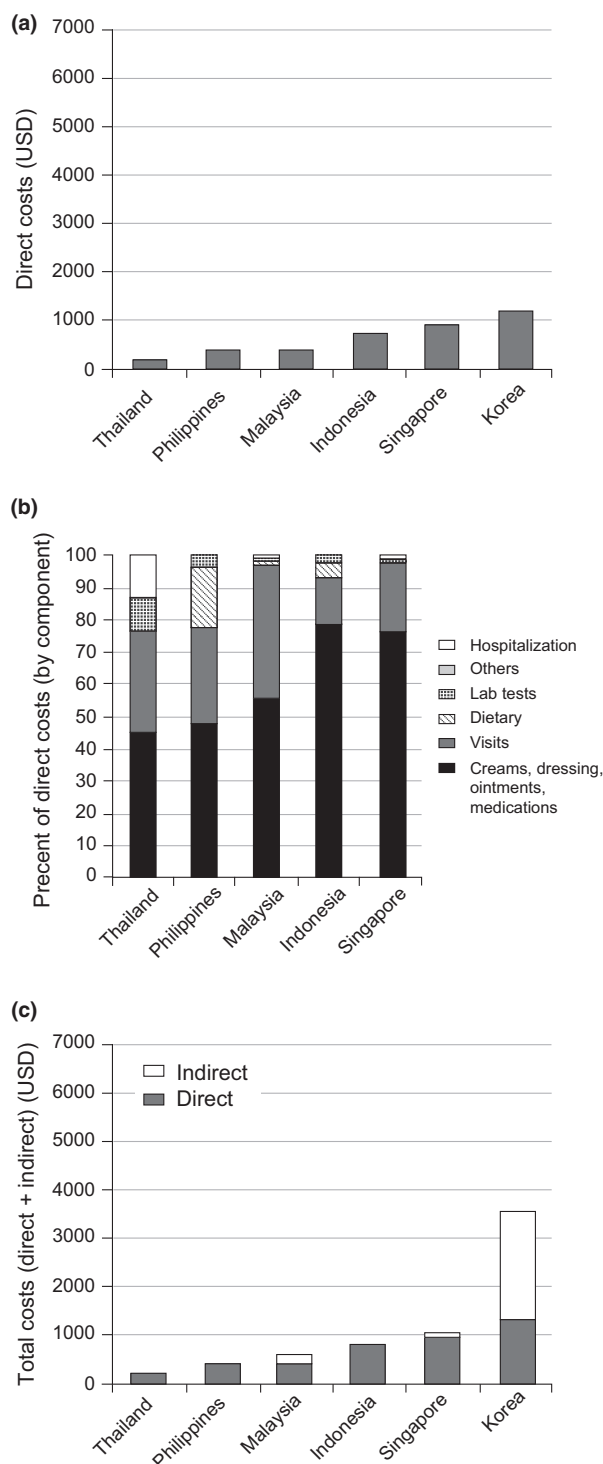
**Table 1.** Medical reimbursement systems in Asian countries

Country	Type of health-care system
Thailand	Universal national health care
Japan	Universal national health care
Malaysia	Two-tier government-funded public sector and private sector
South Korea	Universal national health care
Singapore	Government and individual funded
Taiwan	Universal national health care
Sri Lanka	Universal national health care and a private sector
Vietnam	Government-funded health care and a private sector
Hong Kong	Universal public health care and a private sector
Pakistan	Private sector (70%) with public sector (30%)
Indonesia	Universal national health care and a private sector
India	Mixed public and private health system
Philippines	Mixed public and private health system
China	Universal national health care and a private sector

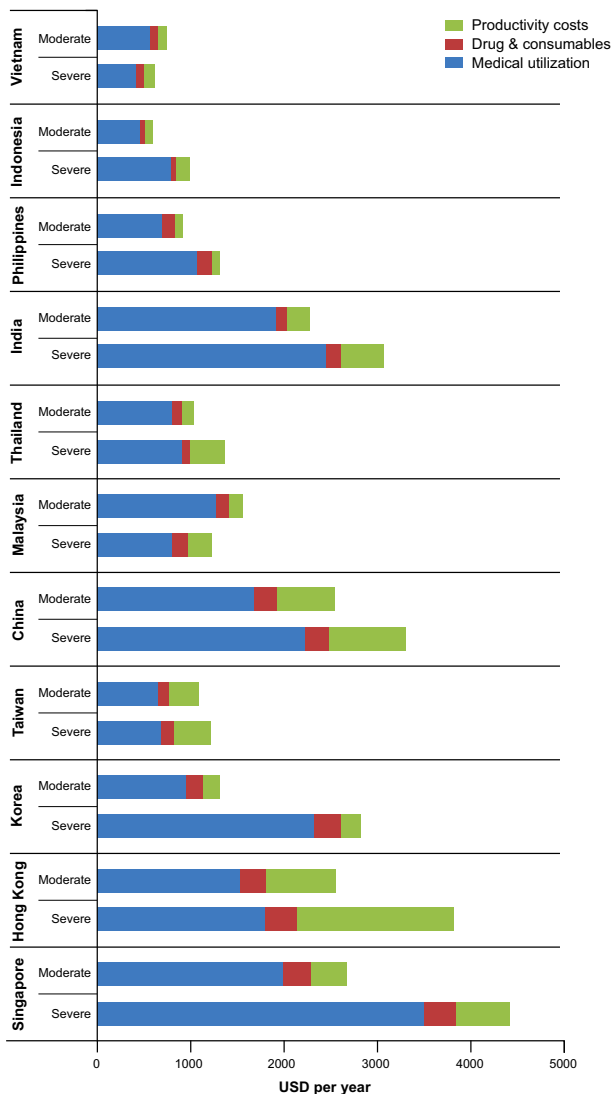
Atopic dermatitis is usually associated with significant economic burden, a fact well documented in Western medical published work; however, this is often not investigated in Asian countries. In general, economic cost can be divided into direct costs (which include medical visits and the costs of medical tests, procedures and medications) and indirect costs (which include loss of earning for patients or caregivers, productivity loss and transportation costs).<sup>10,83</sup>

Two studies that considered the economic burden in the wider Asia-Pacific region were identified.<sup>10,84</sup> In one study, a published work review was conducted to estimate the economic burden of pediatric AD patients in the Asia-Pacific region and showed that the annual direct cost of AD ranged from \$US199 in Thailand to approximately \$US1250 in South Korea (Fig. 2a).<sup>10</sup> Creams, dressing, ointments and medications constituted the biggest portion of direct costs (Fig. 2b).<sup>10</sup> Meanwhile, indirect costs ranged from \$US8 in the Philippines to \$US2268 in South Korea (Fig. 2c).<sup>10</sup> In general, total costs were higher in South Korea and Singapore (\$US1000–6000) than in the Philippines, Indonesia and Malaysia (\$US199–743).<sup>10</sup>

The second study that considered the economic burden in the wider Asia-Pacific region was a survey of 1028 respondents regarding household expenditure on pediatric AD conducted in 12 countries, including Hong Kong, South Korea, Singapore, Taiwan, China, Malaysia, Thailand, India, Indonesia, the Philippines, Vietnam and Australia (not discussed here).<sup>84</sup> When stratified by disease severity (moderate or severe), household expenditure ranged from \$US2722 in Singapore to \$US583 in Indonesia for those with moderate AD, and from \$US4488 in Singapore to \$US600 in Vietnam for those with severe AD (Fig. 3).<sup>84</sup> In general, severe AD was associated with higher costs, including in some wealthier countries.<sup>84</sup> Across all countries and all levels of disease severity, the bulk of expenditure was for health-care utilization, such as visits to general practitioners, specialists and hospitals.<sup>84</sup>



**Figure 2.** Economic burden of AD in Asia-Pacific countries, including (a) annual direct costs; (b) components of direct costs (data for components of direct costs in South Korea are not included because of insufficient details); and (c) annual total (direct and indirect costs). Adapted from Lee and Detzel<sup>10</sup> with permission from ©2015 S. Karger AG, Basel, Switzerland. AD, atopic dermatitis.



**Figure 3.** Mean annual expenditures and productivity cost of pediatric AD in Asian countries. Reproduced from Azmi and Goh<sup>84</sup> with permission. AD, atopic dermatitis.

Only a few studies were available that considered the cost of AD within Asian countries. The results of a recent cost analysis study conducted in South Korea estimated that the total direct costs associated with AD over a 3-month period were ₩541 280 (\$US1 = ₩1146).<sup>83</sup> Of this, ₩457 038 was associated with direct medical costs, encompassing consultation fees, costs of medical test and procedures, prescription fees, dispensing fees, medication storage fees and the cost of drugs.<sup>83</sup> A slightly higher cost was incurred by adults than by children, and by females compared with males.<sup>83</sup> The costs associated with AD also increased as disease severity increased. For example, costs were ₩282 850 for mild AD, ₩485 732 for moderate AD and ₩668 682 for severe AD.<sup>83</sup> Some patients spend a significant amount of money on

traditional folk medicine: one patient spent ₩192 000 on AD-related folk medicine over the 3-month period.<sup>83</sup> In another analysis, a questionnaire given to 196 South Korean children with AD identified an average direct medical cost of ₩596 3000 over a 1-year period.<sup>85</sup> Indirect time cost was estimated at ₩657 000 per year, with transportation expenses at ₩598 000 per year.<sup>85</sup>

In Thailand, a study involving the development of a cost-of-illness model to estimate the total direct costs of atopic diseases calculated an average yearly direct medical cost per patient of ฿5432 (\$US175).<sup>86</sup> Treatment costs constituted the largest portion of this burden, at ฿2228, followed by outpatient care at ฿1678.<sup>86</sup> Monitoring and laboratory tests were associated with a cost of ฿962; inpatient care had a cost of ฿564.<sup>86</sup> These relatively small costs compared with the cost in some other countries may in part be a result of climate differences: Thailand weather is generally warm with a high degree of humidity, possibly aiding in keeping the skin hydrated.<sup>86</sup>

Last, in the first study of its kind conducted in India, the costs associated with AD in an outpatient setting showed that mean total cost over a 6-month period (calculated as the sum of the mean caregiver cost, provider cost and indirect costs) was found to be ₹6235.<sup>82</sup> Caregiver cost constituted 50.2% of this cost, 73.7% of which was the cost of drugs and 25.6% was attributed to the cost of travel.<sup>82</sup> Provider costs constituted 18.1%, of which 66.1% was consultation cost, 21.0% was the cost of nursing and staff, and 12.9% was the cost of infrastructure.<sup>82</sup> Unsurprisingly, mean total cost significantly increased as disease severity increased ( $P = 0.0001$ ).<sup>82</sup> However, compared with other cost analysis studies, the total mean cost was not significantly different from that associated with diabetes mellitus or schizophrenia in India.<sup>82</sup> As the average 6-month household income at the time of the study was between ₹4000 and ₹6000, the cost of caring for AD constitutes a significant proportion of household earnings, although this may differ between rural and urban communities.<sup>82</sup> The study also showed that the cost of treatment in India is shouldered entirely by the patient or family, which is unlike many other countries where the state or insurance companies bear the cost of treatment.<sup>82</sup>

In general, data that examine the economic burden in Asian countries are limited, and more studies are needed in this area; however, available information suggests that AD is associated with significant economic cost. Additional difficulties in controlling these costs may arise because of disparate medical reimbursement systems in individual countries.

## CONCLUSIONS

The prevalence of AD in Asia, largely consisting of mild or moderate disease, is widely documented to be increasing, a development largely attributed to the changing environmental climate and socioeconomic shifts within Asia. A lack of agreement and education regarding diagnostic criteria has resulted in varied estimates of prevalence and likely impacts the quality of care received in some countries. In general, management practices are similar between Western and Asian countries,

with only a few differences in treatment guidelines associated with climate and cultural practices.

Atopic dermatitis is associated with a significant burden within Asian countries, with results of studies showing a significant impact on patient and family QoL and a high AD-associated economic burden. Low socioeconomic status, possibly resulting in poor follow up in outpatient clinics, poses a public health burden and, consequently, is detrimental to the management and control of this chronic condition. Ultimately, additional studies are needed to provide more details regarding the impact of AD within and between Asian countries.

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