

The Burden of Atopic Dermatitis: Impact on the Patient, Family, and Society

Christie L. Carroll, M.D.,* Rajesh Balkrishnan, Ph.D.,*‡ Steven R. Feldman, M.D., Ph.D.,*†
Alan B. Fleischer Jr., M.D.,* and Janeen C. Manuel, Ph.D.*†

*Departments of *Dermatology and †Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, North Carolina, and ‡Ohio State University College of Pharmacy and School of Public Health, Columbus, Ohio*

Abstract: Atopic dermatitis is a common disease of increasing prevalence. Affected individuals must cope with a significant psychosocial burden, in addition to dealing with the medical aspects of the disease. Furthermore, because this is primarily a disease of childhood, family members, especially parents, are also affected by the condition. Individuals and family members are burdened with time-consuming treatment regimens for the disease, as well as dietary and household changes. The financial impact of atopic dermatitis on families can also be great. Moreover, the cost to society is significant, with estimates ranging from less than \$100 to more than \$2000 per patient per year. It is estimated that the direct cost of atopic dermatitis in the United States alone is almost \$1 billion per year. Reducing the onus of this disease must take into account the full breadth of its burden. Targeting parents and caregivers with education and psychosocial support can decrease family and personal burden, which in turn may decrease the cost of treating the condition because of better medical, psychosocial, and family outcomes.

DIAGNOSIS OF ATOPIC DERMATITIS

Atopic dermatitis (AD) is a common skin disease that places a large burden on patients, their families, and society. It is characterized as a chronic inflammatory disease that most commonly begins in childhood. The three stages of AD generally acknowledged are (i) the acute stage, where the skin is red and scaly and/or has small vesicles that rupture and weep from scratching; (ii) the subacute stage, where the skin has mild scaling and mild lichenification; and (iii) the chronic stage, where

there is prominent scaling with distinct lichenification. In all three stages, excoriations are often present (1). In addition, there is a chance of increased colonization with *Staphylococcus aureus* in the AD population, and superinfection often occurs (2).

Firm criteria to define the disease were first created by Hanifin and Rajka in 1980 (3), and included almost 30 signs, symptoms, and laboratory abnormalities. More recently, the United Kingdom Working Party developed a more straightforward criteria consisting of one major criterion: the presence of an itchy skin condition in

Address correspondence to Janeen Manuel, Ph.D., Departments of Dermatology and Public Health Sciences, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA, or e-mail: jmanuel@wfubmc.edu.

the last 12 months, and five other factors, at least three of which must be present for a diagnosis (4–6). These minor criteria include onset before 2 years of age, a history of flexural involvement, a history of dry skin, a personal history of other atopic diseases (or, for children under 4 years, a history of atopic disease in a first degree relative), and current visible flexural dermatitis. The newer criteria have simplified the diagnosis of AD. However, in clinical practice, diagnosis is more likely made based on a physician's global impression than on strict, well-defined criteria.

PREVALENCE OF ATOPIC DERMATITIS

Atopic dermatitis affects between 5% and 20% of all children (see Table 1) (7,8). These figures are based on multiple studies with different methodologies and populations. Furthermore, the results of studies in different racial, ethnic, or age groups may not be generalized. In Singapore, a large study ($n = 12,323$; ages 7 to 16) using questionnaires and examination by a trained nurse found a prevalence of 21% in a primarily Asian population (9). The prevalence in Northern European children was found to be 15.6% in a cross-sectional questionnaire study by Shultz et al (10). The questionnaire used in that study was investigator generated; 105 patients with the diagnosis of AD and 100 outpatients with other diagnoses were examined for AD using the Hanifin/Rajka criteria. A score of greater than 50 points was set, giving 88% sensitivity and 89% specificity for the presence of AD. However, using the United Kingdom Working Party diagnostic criteria, a subject could be

diagnosed at the 30-point level in this questionnaire. Therefore, the prevalence may have actually been underestimated in this sample.

Laughter et al (8) found a prevalence of 17% in a questionnaire-based study of Oregon schoolchildren. This questionnaire was based on Schultz et al's (10) previous study (with some modifications), and was validated in the clinic by a dermatologist by diagnosis. The diagnostic point value was raised to 80 to increase the specificity of diagnosis, creating an even more conservative prevalence estimate of 7%. The conflicting results of these studies highlight the difficulty of determining prevalence of a disease with population-based questionnaire studies.

While AD can persist into adulthood (and, on occasion, have adult onset), adult disease is much less common than childhood disease. Although estimates vary, a 60% clearing of AD at adulthood is a reasonable estimate (11). Determining a precise prevalence of AD in adults is difficult, as many people have different forms of dermatitis (e.g., nummular and xerotic dermatitis) that may be within the spectrum of atopic disease. However, Muto et al (12) presented a questionnaire-based study (using the United Kingdom Working Party criteria) of over 10,000 Japanese adults seen for health checkups in Japan and found a lifetime prevalence of 3%. Their subjects were predominately male (75%), and the study was conducted in an urban area, both of which may bias results. Additionally, this study relied on distant memories of childhood diseases, creating a significant recall bias. Sugiura et al (13) found a prevalence of 11% in Japanese teenagers aged 16 to 18 in a study that

TABLE 1. Overview of Atopic Dermatitis Prevalence Studies

Study author	Publ. year	Population studied	Method	Sample size	Prevalence
Muto et al (12)	2003	Japanese adults visiting govt. medical center	Questionnaire	10,762	3.3% lifetime
Werner et al (66)	2002	School entrants in Hanover, Germany	Skin examination	4351	10.5% (incidence)
Tay et al (9)	2002	Singapore schoolchildren, aged 7, 12, and 16 years	Questionnaire and skin examination	12,323	20.8% 1 year
Inanir et al (67)	2002	Turkish schoolchildren	Skin examination	785	6.75% 1 year
Heinrich et al (68)	2002	German schoolchildren aged 5 to 14 (three cohort studies)	Questionnaire	7632	10.3 to 11.5% lifetime
Laughter et al (8)	2000	Oregon schoolchildren aged 5 to 9 years	Questionnaire	1465	17.2% lifetime
Schultz-Larsen (10)	1996	Schoolchildren from Northern European cities age 7 years	Questionnaire	2655	15.6% lifetime
Kay et al (69)	1994	Children aged 3 to 11 years in an English general practice	Interview/survey	1104	19.5% lifetime

included an examination and diagnosis based on the Hanifin and Rajka criteria. Prevalence of atopic dermatitis decreased with age; however, the rate was significantly higher than the 3% presented by Muto et al (12).

Recent epidemiological studies report a trend toward an increasing prevalence of AD in children (14,15). Possible reasons for this have been hypothesized to include: increased industrialization and pollution and changes in the home environment (including improved insulation, synthetic fabrics and bed linen, and wall-to-wall carpeting) (16,17). These environmental changes may contribute qualitatively or quantitatively to antigen exposures, which can trigger the disease. In addition, societal changes, such as generally better socioeconomic conditions and smaller family sizes, mean that children are being exposed to fewer infections in early life, which may result in an increased expression of AD (18).

TREATMENT OF ATOPIC DERMATITIS

AD treatment is targeted at both the disease and its symptoms. Patients are generally advised to keep their skin moisturized with the liberal use of emollients and home vaporizers. In addition, many patients are prescribed antihistamines because of their antipruritic effects in an effort to decrease the itch-scratch cycle. Finally, oral antibiotics are prescribed in addition to standard topical AD treatments if the skin becomes superinfected.

Originally, treatments for AD were primarily topical corticosteroid agents, which are often accompanied by side effects with the long-term use required to control a chronic disease. This situation has changed dramatically with the advent of topical calcineurin inhibitors such as tacrolimus and pimecrolimus. Although more expensive than topical corticosteroids, these medications can be used with great success in AD and have minimal side effects with continuous use for up to 3 years (19,20). In addition, the AD relapse rate with tacrolimus has been reported as lower than with the use of high potency topical steroids (21).

In cases of severe AD, additional treatment may be needed to control the disease. Systemic immunosuppression by cyclosporine, methotrexate, or azathioprine may be used with success (22). These medications are not without side effects, however, and must be used cautiously, especially in children. Another option for the treatment of severe disease is phototherapy (23). This might include simply encouraging patients to increase their sun exposure (contrary to dermatologist recommendations for most people). However, phototherapy may also entail formal UV-B or psoralen plus ultraviolet A (PUVA) treatment sessions. These treatments can be

more expensive than topical therapies, but in some cases are the only means of gaining remission.

IMPACT OF ATOPIC DERMATITIS ON THE PATIENT

Health care professionals frequently discount AD, despite its high prevalence, regarding it as a minor skin problem that will resolve with time (24). Those who realize the seriousness and chronicity of AD are often unaware of the full extent to which the disease affects patients. Individuals with AD are affected both by the condition itself and by the stigma associated with its visibility (25).

Accordingly, people with AD tend to report lower health-related quality of life and greater psychological distress than the general population, and those with some other medical conditions (26–30). For example, Kiebert et al (26) examined the quality of life of 318 patients with AD aged 4 to 70 years using the SF-36, a general health-related quality of life measure. Patients over 16 years of age had significantly lower scores on the vitality, social functioning, and mental health subscales than the general population. In addition, study participants had statistically significant lower mental health scores than patients with diabetes or hypertension, and significantly lower social functioning scores than those with hypertension. Further, when Kiebert et al (26) compared individuals with AD to those with psoriasis, another common skin disorder long acknowledged to affect quality of life, patients with AD had significantly lower role-physical, vitality, social functioning, role-emotional, and mental health subscale scores. Of note, this study was conducted in a clinic population, which may have skewed the results by over-representing those with more severe disease and worsened quality of life.

Linnert et al (28) also found that adults with AD reported lower quality of life [using the Dermatology Life Quality Index (DLQI)] than controls. This small study also found higher levels of anxiety among persons with AD than healthy controls. Anxiety in people with AD is of particular concern, as stress has been found to trigger the itch-scratch cycle, potentially setting off AD flare-ups (31).

Adults and children with AD are also at risk for psychosocial difficulties. Anderson's study of 559 adults with self-reported AD noted that 47% of subjects reported feeling frustrated with their disease often or always, 39% were often or always embarrassed by their appearance, and 35% were often or always angry about their appearance (30). Previous studies have also found that adults with AD often report being overprotected and

undisciplined as children, and experience an increased incidence of psychiatric disorders as adults (32,33).

Moreover, numerous researchers have found a relationship between childhood AD and psychosocial difficulties in children. Children with AD often have behavioral problems such as increased dependency, fearfulness, and sleep difficulties (34). These behavioral problems can affect social development, as well as interfere with intellectual development. Peer and teacher relations may be affected by AD because of fear of infection, the child's physical appearance, or limitations on sports participation (35).

The effect of AD on sleep, primarily related to nighttime itching and scratching, is often significant. Yosipovitch et al (36) reported that the sensation of itch was more frequently reported at night; 84% of the 100 AD patients completing the study reported difficulty falling asleep, with 79% reported being awakened by pruritus. Furthermore, a recent study of 28 subjects (14 with AD, 14 controls) using wrist actigraphy to measure sleep disturbance found that individuals with AD slept more poorly, with more waking episodes and increased activity than healthy controls (37). Reid et al (38) suggested that children with AD lose an average of 2 hours of sleep per night secondary to the condition. Sleep loss during the night can lead to increased daytime drowsiness, and may result in school problems, as can oral antihistamines prescribed to control the condition and physical discomfort from pruritus.

In summary, AD is often associated with significant morbidity in the patient. Pruritus can affect both sleep and mood, and affected individuals often must modify several aspects of their lives because of treatment regimens and associated lifestyle changes. Individuals with AD are also at risk for psychosocial difficulties that may have long-lasting consequences, potentially affecting career choices and personal relationships.

FAMILY IMPACT OF ATOPIC DERMATITIS

Because AD most commonly affects children, parents and other family members are often involved in caregiving. This can greatly impact family dynamics as well as family life in general. Research has revealed that families of children with AD often report lower quality of life than families of healthy children (27,35). Not surprisingly, the family impact of the disease has been positively correlated with AD severity, with more severe cases associated with increased family disruption (39).

Parents have reported both high stress levels associated with treating and taking care of the child with AD, and feelings of helplessness regarding the child's symptoms. Mothers of children with AD are more likely to

show their affection in terms of a hygienic ritual, which in turn changes the relationship dynamics between the mother and the child to more of a nurse-child relationship (40). In addition, the burden of caring for the child with AD can negatively affect spousal relationships and interfere with giving adequate attention to siblings (27). An Australian study reported that taking care of a child with moderate or severe AD was more stressful than caring for a child with insulin-dependent diabetes (41).

A recent qualitative investigation into the family impact of childhood AD found several areas where AD impacts the family. An analysis of data from focus groups with parents of children with AD aged 12 years and below was conducted (Manuel et al 2003, unpublished data). Nine major areas of AD family impact were determined, including sleep issues, time management, lifestyle changes, treatment issues, social impact, school and daycare, family activities, financial stresses, and personal strain. Other studies have presented data, and several investigators are beginning to build conceptual models of family impact based upon these data (Manuel et al, in preparation) (35,42,43).

A major stress-causing factor that most families deal with is sleeplessness as a result of itching in a child with AD (27,35,41,44). Sleep deprivation can affect all family members, including siblings. Long et al (44) found that 60% of a sample of parents of children with AD rated loss of sleep as a significant problem. Other researchers have noted that parents can lose up to 1 to 2 hours of sleep per night while dealing with AD symptoms; loss that can translate into poor work functioning and decreased coping skills at work and at home (38).

Additional factors that add to the burden of caring for a child with AD are the financial costs of treatment, time missed from work for physician appointments, and lack of understanding and social support from friends and family members (44-46). Many AD families are advised to make lifestyle changes, including restricting or modifying diets; using special soaps and detergents; wearing clothing or using linens of all natural fibers; only; adding dust mite protectors; and removing carpets (47). These lifestyle changes take time to complete and are often a strain to the family's budget. In addition, treatment for AD can be a very time-consuming process for the parents or caregivers, and affects the amount of time they have for other family members and themselves. Estimates by Su et al (41) suggested that 2 to 3 hours per day are spent caring for a child with AD, depending on disease severity.

The effects of AD on the family can be extensive and pervasive. Unfortunately, because AD is not life-threatening, families often do not receive potentially useful educational or psychosocial support, which can

result in further stress and frustration. A perceived lack of support from medical professionals can lead to decreased trust in the medical system, which in turn may result in decreased adherence to treatment and suboptimal medical, psychosocial, and economic outcomes.

COST OF ATOPIC DERMATITIS

When estimating the cost of any disease, there are many factors that must be considered. Direct costs estimates usually are based on medicare or HMO reimbursement data and claims information. Indirect costs include time lost from work, over-the-counter treatments, and therapies that are not covered by insurance, such as allergy testing and alternative medicine. These costs must be considered along with the incidence and prevalence of disease in the population being studied. Further, the range of severity of the disease must be weighed in, as patients with severe disease will often incur greater costs.

Estimates of the direct costs of AD vary because of the health care management systems employed by the different countries researched, the variability of cost components included in the study, and the severity of the disease population examined. Verboom et al's (48) review, however, found that the health care costs of AD ranged from \$71 to \$2559 per patient per year.

Lapidus et al (49) studied emergency room visits and ambulatory care billing records of an urban hospital and extrapolated the direct costs to the United States to be \$364 million annually. However, this study, published in 1993, was thought to underestimate the true cost of AD because it calculated only ER and physician visits.

Su et al (41) presented results from an Australian study that divided the direct costs of AD into severity groups. Costs calculated included medication, dressings, and medical visits, but excluded indirect expenses related to lifestyle changes such as dust mite covers, nonirritating clothing, or nontraditional AD treatments. The calculated costs were \$216 per patient per year for mild disease, \$535 per year per patient for moderate disease, and \$821 per year per patient for severe disease.¹ This estimate is again conservative because of the noted exclusions.

Emerson et al (50) presented an all-inclusive (direct and indirect) cost estimate for preschool children in 2001 in the United Kingdom. Their estimate of \$130²

per child per year was based on national health care system data (prescription and visits), as well as surveys of families for over-the-counter medications, transportation to medical visits, cost estimates for lifestyle changes, alternative treatments or out-of-pocket specialist visits, and income loss. This estimate included children with AD of all severities.

In a systematic review of third party claims data, Ellis et al (51) presented the estimated direct cost of AD and eczemas in the United States as \$900 million. In this analysis, claims from a managed care payer and state Medicaid program were used, with AD diagnoses based on International Classification of Diseases (ICD-9-CM) codes. Claims were reviewed by a panel, and comorbidities were classified as most likely related to AD and possibly related to AD. The cost quoted included all AD claims for visits, prescription drugs, and "likely" AD-related comorbidities. The estimate, however, did not include any indirect costs related to over-the-counter medications or lifestyle changes.

Fivenson et al (52) presented an estimate of direct and indirect costs of AD to be \$609 per patient annually, using a patient survey to estimate indirect costs (including time lost from work) and managed care claims data to estimate the direct costs. Of importance, the direct medical costs were found to be only 27% of the total, suggesting the significant underestimation that occurs if only direct costs were used to estimate the AD financial burden. Additionally, as discussed in an editorial by Ellis (53), there may be fewer severely affected patients in Fivenson's study sample, which would lead to lower cost estimates (52).

While these estimates of the cost of AD to society vary, in sum they indicate that the economic burden of this disease is considerable. Moreover, the lack of inclusion of indirect costs in most of these estimates indicates that the cost of AD is even greater than reported. A comparison of AD to other common skin diseases such as psoriasis, in which the direct costs were recently estimated by Javitz et al (54) as \$650 million, demonstrates the magnitude of the financial burden of this condition. Cost-effective treatments for AD are needed to decrease its financial impact on the patient and society.

REDUCING THE BURDEN OF ATOPIC DERMATITIS

This disease causes a significant burden in terms of cost to society, and in addition, has a great impact on the family, including psychological, social, and financial. The potential for psychosocial difficulties makes it clear that individuals dealing with AD and their families need more than just the physical treatment of symptoms.

¹ Rough estimate – converted from Australian dollars to US dollars on 6/2/03.

² Rough estimate – converted from UK pounds to US dollars on 6/2/03.

Because constant scratching can maintain or aggravate skin inflammation, educational and psychosocial support for patients and their families in addition to medical treatment of AD may improve the long-term physical outcomes.

Support programs for adults with AD have shown promise in reducing AD symptoms. For instance, a 1995 randomized controlled trial compared the effectiveness of a dermatologic educational program, autogenic (relaxation) training, cognitive behavioral training, and a combination of dermatologic education and cognitive behavioral training versus standard care for patients with AD (55). Assessments 1 year after the completion of the program demonstrated that the psychological training groups had significantly greater improvements in AD severity than the dermatological education group alone or the standard care group. However, adults with AD have presumably been dealing with symptoms for years, and often have significant knowledge about their condition. Psychological support alone may therefore be enough to decrease severity levels in adults. Parents of children with AD, however, often need both information on AD and psychological support. Encouraging patients and parents to join a support and patient advocacy group like the National Eczema Association may serve this purpose.

While educational programs for families of children with AD have been scarce, existing programs have provided preliminary evidence that both parent education and psychosocial support are helpful in reducing AD-related stress, increasing confidence in managing AD, and decreasing AD severity (56–59). For example, in a pilot study of parents of children with AD, McSkimming et al (59) found less anxiety, helplessness, and loneliness in 11 parents who attended a support group.

In one of the few controlled studies of the effects of parent AD education, Broberg et al (56) compared a group of parents of children with AD who received a 2-hour educational session led by a nurse ($n = 22$) with a control group of parents who received routine information from a physician during the office visit ($n = 20$). The educational group received general information about AD and about different treatments and factors known to exacerbate the condition. After 2 months, children of parents receiving the educational intervention had decreased AD severity as measured by type, intensity, and distribution of the skin lesions. These studies provide some preliminary evidence that educational or psychosocial programs are useful for parents of children with AD.

The most comprehensive educational program for parents of children with AD to date was recently developed in Germany. The Berlin Education Program (57,58) was conducted to improve parents' AD manage-

ment skills, the course of the disease, and the family's quality of life. A multidisciplinary team of physicians, psychologists, and nutritionists instructed parents on issues related to AD in six 2-hour group sessions. Ninety-three parents participated in the groups, and 111 parents served as wait-list controls. This study found a positive effect on the families' quality of life and coping. In addition, parents attending the program had increased satisfaction with medical treatment and better treatment management skills (such as the proper use of emollients, antiseptics, and topical corticosteroids). These families also had a significant reduction in treatment costs.

Further studies to develop these educational programs and to prove efficacy in decreasing the burden of AD are necessary. This type of program may be as important as, and potentially more cost effective than, developing new medical treatments for the disease. Decreasing the severity can decrease the costs related to medications, physician visits, and personal expenses because of time lost from work and over-the-counter treatments.

In addition, specialist care for individuals with AD may also be useful in decreasing the family impact of the condition. A recent study determined that an episode of specialist care (i.e., the dermatologist) was associated with decreased family impact (45). This study also determined that the visit to the specialist led to decreased out-of-pocket nonmedical care expenses.

Furthermore, the simple acknowledgment of the potential effects on the family by health care workers can improve the physician–patient relationship and therefore the trust in the physician. With improved physician–patient (parent) relationships, adherence to treatment protocols can be improved as well (60). Increased adherence will in turn improve treatment outcomes, which has implications for patient and societal costs associated with the disease.

It has been suggested by many that quality of life (QOL) assessment tools be administered to patients as an outcome measure for treatment success. These measures, including the Dermatology Life Quality Index (DLQI), the Children's Dermatology Life Quality Index (CDLQI), the Dermatology-specific Quality of Life (DSQL) instrument, and the Parent's Index of Quality of Life in Atopic Dermatitis (PIQoL-AD), have often been used to assess outcomes in clinical trials, but are rarely used in clinical practice (61–65). Increased attention to the individual's quality of life by health care professionals would represent a significant step toward a more comprehensive treatment of AD.

Finally, information on the cost effectiveness of different treatment regimens for AD is greatly needed to decrease the economic impact of the disease on the patient, the family, and society (18). In one of the few

existing cost-effectiveness analyses of AD treatments, Ellis et al (53) found that topical tacrolimus ointment was similar in cost to treatment with high potency topical corticosteroids. Cost ratios for various steroid formulations ranged from \$5.85 per disease controlled day (DCD) to \$7.59 per DCD, and \$6.97 per DCD for tacrolimus (21). The cost-effectiveness of other new AD treatments, including educational programs for individuals and families dealing with the condition, are urgently needed to ensure that the treatment of the disease is managed optimally in a cost-effective manner.

CONCLUSIONS

AD is a common disease of increasing prevalence, and it can cause significant morbidity in the affected individual. The impact of this condition is extremely onerous for the family, and the societal economic burden is high. There is a need for cost-effectiveness studies of newer treatments that take into account the possibility of long-term remission. In addition, targeting parents and caregivers with education and psychosocial support may decrease family and personal burden. This in turn may decrease the cost of this condition to society through better medical, psychosocial, and family outcomes.

REFERENCES

- Raimer SS. Managing pediatric atopic dermatitis. *Clin Pediatr (Phila)* 2000;39:1–14.
- Hauser C, Wuethrich B, Matter L, et al. *Staphylococcus aureus* skin colonization in atopic dermatitis patients. *Dermatologica* 1985;170:35–39.
- Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980;92:44–47.
- Williams HC, Burney PG, Hay RJ, et al. The UK Working Party's diagnostic criteria for atopic dermatitis. I. Derivation of a minimum set of discriminators for atopic dermatitis. *Br J Dermatol* 1994;131:383–396.
- Williams HC, Burney PG, Pembroke AC, et al. The UK Working Party's diagnostic criteria for atopic dermatitis. III. Independent hospital validation. *Br J Dermatol* 1994;131:406–416.
- Williams HC, Burney PG, Strachan D, et al. The UK Working Party's diagnostic criteria for atopic dermatitis. II. Observer variation of clinical diagnosis and signs of atopic dermatitis. *Br J Dermatol* 1994;131:397–405.
- Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999;103:125–138.
- Laughter D, Istvan JA, Tofte SJ, et al. The prevalence of atopic dermatitis in Oregon schoolchildren. *J Am Acad Dermatol* 2000;43:649–655.
- Tay YK, Kong KH, Khoo L, et al. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore schoolchildren. *Br J Dermatol* 2002;146:101–106.
- Schultz LF, Diepgen T, Svensson A. The occurrence of atopic dermatitis in North Europe: an international questionnaire study. *J Am Acad Dermatol* 1996;34:760–764.
- Graham-Brown RA. Atopic dermatitis: predictions, expectations, and outcomes. *J Am Acad Dermatol* 2001;45:S61–S63.
- Muto T, Hsieh SD, Sakurai Y, et al. Prevalence of atopic dermatitis in Japanese adults. *Br J Dermatol* 2003;148:117–121.
- Sugiura H, Umemoto N, Deguchi H, et al. Prevalence of childhood and adolescent atopic dermatitis in a Japanese population: comparison with the disease frequency examined 20 years ago. *Acta Derm Venereol* 1998;78:293–294.
- Schafer T, Ring J. Epidemiology of allergic diseases. *Allergy* 1997;52:14–22.
- Schultz LF. Atopic dermatitis: an increasing problem. *Pediatr Allergy Immunol* 1996;7:51–53.
- McNally NJ, Williams HC, Phillips DR. Atopic eczema and the home environment. *Br J Dermatol* 2001;145:730–736.
- Williams HC. Epidemiology of atopic dermatitis. *Clin Exp Dermatol* 2000;25:522–529.
- Lamb SR, Rademaker M. Pharmacoeconomics of drug therapy for atopic dermatitis. *Expert Opin Pharmacother* 2002;3:249–255.
- Kang S, Lucky AW, Pariser D, et al. Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. *J Am Acad Dermatol* 2001;44:S58–S64.
- Kapp A, Papp K, Bingham A, et al. Long-term management of atopic dermatitis in infants with topical pimecrolimus, a nonsteroid antiinflammatory drug. *J Allergy Clin Immunol* 2002;110:277–284.
- Ellis CN, Drake LA, Prendergast MM, et al. Cost-effectiveness analysis of tacrolimus ointment versus high-potency topical corticosteroids in adults with moderate to severe atopic dermatitis. *J Am Acad Dermatol* 2003;48:553–563.
- Hanifin JM, Tofte SJ. Update on therapy of atopic dermatitis. *J Allergy Clin Immunol* 1999;104:S123–S125.
- Leung DY, Bieber T. Atopic dermatitis. *Lancet* 2003;361:151–160.
- Bridgman A. Management of atopic eczema in the community. *Health Visit* 1994;67:226–227.
- Finlay AY. Quality of life in atopic dermatitis. *J Am Acad Dermatol* 2001;45:S64–S66.
- Kiebert G, Sorensen SV, Revicki D, et al. Atopic dermatitis is associated with a decrement in health-related quality of life. *Int J Dermatol* 2002;41:151–158.
- Lapidus CS, Kerr PE. Social impact of atopic dermatitis. *Med Health R I* 2001;84:294–295.
- Linnert J, Jemec GB. An assessment of anxiety and dermatology life quality in patients with atopic dermatitis. *Br J Dermatol* 1999;140:268–272.
- Lundberg L, Johannesson M, Silverdahl M, et al. Health-related quality of life in patients with psoriasis and atopic dermatitis measured with SF-36, DLQI, and a subjective measure of disease activity. *Acta Derm Venereol* 2000;80:430–434.
- Anderson RT, Rajagopalan R. Effects of allergic dermatosis on health-related quality of life. *Curr Allergy Asthma Rep* 2001;1:309–315.
- Fleischer AB Jr. Atopic dermatitis. Perspectives on a manageable disease. *Postgrad Med* 1999;106:49–55.

32. Howlett S. Emotional dysfunction, child–family relationships and childhood atopic dermatitis. *Br J Dermatol* 1999;140:381–384.
33. Hughes JE, Barraclough BM, Hamblin LG, et al. Psychiatric symptoms in dermatology patients. *Br J Psychiatry* 1983;143:51–54.
34. Solomon CR, Gagnon C. Mother and child characteristics and involvement in dyads in which very young children have eczema. *J Dev Behav Pediatr* 1987;8:213–220.
35. Lawson V, Lewis-Jones MS, Finlay AY, et al. The family impact of childhood atopic dermatitis: the Dermatitis Family Impact Questionnaire. *Br J Dermatol* 1998;138:107–113.
36. Yosipovitch G, Goon AT, Wee J, et al. Itch characteristics in Chinese patients with atopic dermatitis using a new questionnaire for the assessment of pruritus. *Int J Dermatol* 2002;41:212–216.
37. Bender BG, Leung SB, Leung DY. Actigraphy assessment of sleep disturbance in patients with atopic dermatitis: an objective life quality measure. *J Allergy Clin Immunol* 2003;111:598–602.
38. Reid P, Lewis-Jones MS. Sleep difficulties and their management in preschoolers with atopic eczema. *Clin Exp Dermatol* 1995;20:38–41.
39. Balkrishnan R, Housman TS, Carroll C, et al. Disease severity and associated family impact in childhood atopic dermatitis. *Arch Dis Child* 2003;88:423–427.
40. Ring J, Palos E. Psychosomatic aspects of parent–child relations in atopic eczema in childhood. II. Child-rearing style, the family situation in a drawing test and structured interview. *Hautarzt* 1986;37:609–617.
41. Su JC, Kemp AS, Varigos GA, et al. Atopic eczema: its impact on the family and financial cost. *Arch Dis Child* 1997;76:159–162.
42. Chamlin S, Frieden I, Williams M, et al. The impact of atopic dermatitis on young American children and their families: a qualitative analysis. *Int Invest Dermatol (Abstract Book)* 2003;69:4–30–2003.
43. Friedman J, Reed S, Kahler K, et al. Parent’s perceptions of the quality of life impact of childhood atopic dermatitis disease states. 61st Annual Meeting. *Am Acad Dermatolgy* 2003 (Abstract Book) 2003;156:3–21.
44. Long CC, Funnell CM, Collard R, et al. What do members of the National Eczema Society really want? *Clin Exp Dermatol* 1993;18:516–522.
45. Balkrishnan R, Housman TS, Grummer S, et al. The family impact of atopic dermatitis in children: the role of the parent caregiver. *Pediatr Dermatol* 2003;20:5–10.
46. Lapidus CS. Role of social factors in atopic dermatitis: the US perspective. *J Am Acad Dermatol* 2001;45:S41–S43.
47. Lapidus CS, Honig PJ. Atopic dermatitis. *Pediatr Rev* 1994;15:327–332.
48. Verboom P, Hakkaart-Van L, Sturkenboom M, et al. The cost of atopic dermatitis in the Netherlands: an international comparison. *Br J Dermatol* 2002;147:716–724.
49. Lapidus CS, Schwarz DF, Honig PJ. Atopic dermatitis in children: who cares? Who pays? *J Am Acad Dermatol* 1993;28:699–703.
50. Emerson RM, Williams HC, Allen BR. What is the cost of atopic dermatitis in preschool children? *Br J Dermatol* 2001;144:514–522.
51. Ellis CN, Drake LA, Prendergast MM, et al. Cost of atopic dermatitis and eczema in the United States. *J Am Acad Dermatol* 2002;46:361–370.
52. Fivenson D, Arnold RJ, Kaniecki DJ, et al. The effect of atopic dermatitis on total burden of illness and quality of life on adults and children in a large managed care organization. *J Manag Care Pharm* 2002;8:333–342.
53. Ellis CN, Prendergast MM, Tokar M, et al. Quantifying costs associated with atopic dermatitis. *J Manag Care Pharm* 2003;9:278–279.
54. Javitz HS, Ward MM, Farber E, et al. The direct cost of care for psoriasis and psoriatic arthritis in the United States. *J Am Acad Dermatol* 2002;46:850–860.
55. Ehlers A, Stangier U, Gieler U. Treatment of atopic dermatitis: a comparison of psychological and dermatological approaches to relapse prevention. *J Consult Clin Psychol* 1995;63:624–635.
56. Broberg A, Kalimo K, Lindblad B, et al. Parental education in the treatment of childhood atopic eczema. *Acta Derm Venereol* 1990;70:495–499.
57. Staab D, von Rueden U, Kehrt R, et al. Evaluation of a parental training program for the management of childhood atopic dermatitis. *Pediatr Allergy Immunol* 2002;13:84–90.
58. Wenninger K, Kehrt R, von Ruden U, et al. Structured parent education in the management of childhood atopic dermatitis: the Berlin model. *Patient Educ Couns* 2000;40:253–261.
59. McSkimming J, Gleeson L, Sinclair M. A pilot study of a support group for parents of children with eczema. *Australas J Dermatol* 1984;25:8–11.
60. Ohya Y, Williams H, Steptoe A, et al. Psychosocial factors and adherence to treatment advice in childhood atopic dermatitis. *J Invest Dermatol* 2001;117:852–857.
61. Finlay AY, Khan GK. Dermatology life quality index (DLQI) – a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;19:210–216.
62. Lewis-Jones MS, Finlay AY. The children’s dermatology life quality index (CDLQI): initial validation and practical use. *Br J Dermatol* 1995;132:942–949.
63. Drake L, Prendergast M, Maher R, et al. The impact of tacrolimus ointment on health-related quality of life of adult and pediatric patients with atopic dermatitis. *J Am Acad Dermatol* 2001;44:S65–S72.
64. Lewis-Jones MS, Finlay AY, Dykes PJ. The infants’ dermatitis quality of life index. *Br J Dermatol* 2001;144:104–110.
65. Whalley D, Huels J, McKenna SP, et al. The benefit of pimecrolimus (Elidel, SDZ ASM 981) on parents’ quality of life in the treatment of pediatric atopic dermatitis. *Pediatrics* 2002;110:1133–1136.
66. Werner S, Buser K, Kapp A, et al. The incidence of atopic dermatitis in school entrants is associated with individual lifestyle factors but not with local environmental factors in Hannover, Germany. *Br J Dermatol* 2002;147:95–104.
67. Inanir I, Sahin MT, Gunduz K, et al. Prevalence of skin conditions in primary school children in Turkey: differences based on socioeconomic factors. *Pediatr Dermatol* 2002;19:307–311.
68. Heinrich J, Hoelscher B, Frye C, et al. Trends in prevalence of atopic diseases and allergic sensitization in children in Eastern Germany. *Eur Respir J* 2002;19:1040–1046.
69. Kay J, Gawkrödger DJ, Mortimer MJ, et al. The prevalence of childhood atopic eczema in a general population. *J Am Acad Dermatol* 1994;30:35–39.