

*Original article***Patient perspectives on the management of atopic dermatitis**

Torsten Zuberbier, MD,^a Seth J. Orlow, MD, PhD,^b Amy S. Paller, MD,^c Alain Taïeb, MD,^d Roger Allen, MBChB, FRCP,^e José M. Hernanz-Hermosa, MD, PhD,^f Jorge Ocampo-Candiani, MD,^g Margaret Cox,^h Joanne Langeraar,ⁱ and Jan C. Simon, MD^j

Berlin and Leipzig, Germany, New York, NY, Chicago, Ill, Bordeaux, France, Nottingham and London, United Kingdom, Madrid, Spain, Monterrey, Mexico, and San Rafael, Calif

Background: Atopic dermatitis (AD) is increasingly common, with a point prevalence of more than 30% in some countries, and is characterized by visible skin lesions and intense itching. **Objective:** The International Study of Life with Atopic Eczema (ISOLATE) is the first large-scale study to assess the effect of AD on the lives of patients and society, how patients and caregivers manage the condition, and how well patients and caregivers currently believe that AD is controlled. **Methods:** Two thousand two patients (>13 years) and caregivers of children (2-13 years) with moderate-to-severe AD randomly selected from 8 countries underwent standardized telephone interviews using questions developed in collaboration with national eczema patient groups and physicians. **Results:** During each year, patients spend, on average, 1 of 3 days in flare. The majority of patients receive prescription topical corticosteroids to treat flares; however, 49% of respondents are concerned about using these agents.

On average, patients and caregivers delay initiating treatment for 7 days after onset of a flare. Only 24% of patients and caregivers feel confident they can manage AD flares adequately. Seventy-five percent of caregivers and patients feel that being able to effectively control AD would be the single most important improvement to their or their child's quality of life. The avoidable secondary economic cost of AD is estimated at €2 billion per year across the European Union. **Conclusion:** ISOLATE highlights the need to improve patients' control of AD to reduce the significant effect this condition has on the patient and society. **Clinical implications:** ISOLATE shows that patients with AD are untreated for half the time they are in flare, and thus there is an urgent need for physicians to ensure that the patients are educated and confident in using medication as prescribed to gain disease control. (J Allergy Clin Immunol ■■■■;■■■: ■■■-■■■.)

Key words: Flare, patient management, atopic dermatitis, atopic eczema, International Study of Life with Atopic Eczema

From ^athe Department of Dermatology and Allergy, Allergy Centre Charité, Charité-Universitätsmedizin Berlin; ^bthe New York University School of Medicine, New York; ^cthe Departments of Dermatology and Pediatrics, Northwestern University's Feinberg School of Medicine, Chicago; ^dCHU de Bordeaux, Bordeaux; ^eQueens Medical Centre, Nottingham; ^fHospital General Universitario Gregorio Marañón, Madrid; ^gHospital Universitario, Universidad Autónoma de Nuevo León, Monterrey; ^hthe National Eczema Society, London; ⁱthe National Eczema Association for Science and Education, San Rafael; and ^jthe Department of Dermatology, Venerology and Allergology, Universitätsklinikum Leipzig.

This study was supported by an unrestricted educational grant from Novartis Pharma AG.

Disclosure of potential conflict of interest: T. Zuberbier has consultant arrangements with and is on the speakers' bureau for Novartis. S. Orlow has consultant arrangements with and is on the speakers' bureau for Novartis and Astellas. A. Paller has speaker and consultant arrangements with Novartis. A. Taïeb has consultant arrangements with and has received a travel grant from Novartis. R. Allen is on the speakers' bureau for Novartis. J. Ocampo-Candiani has received a travel grant from Novartis. M. Cox works for the National Eczema Society, which works closely with the pharmaceutical industry. J. Langeraar works for the National Eczema Association for Science and Education, which has received financial support from Astellas and Novartis. J. Simon has consultant arrangements with and is on the speakers' bureau for Novartis.

Received for publication September 28, 2005; revised January 24, 2006; accepted for publication February 1, 2006.

Reprint requests: Torsten Zuberbier, MD, Department of Dermatology and Allergy, Allergy Centre Charité, Schumannstrasse 20-21, D-10117 Berlin, Germany. E-mail: torsten.zuberbier@charite.de.

0091-6749/\$32.00

© 2006 American Academy of Allergy, Asthma and Immunology

doi:10.1016/j.jaci.2006.02.031

Atopic dermatitis (AD), also known as atopic eczema, is a chronic relapsing skin condition characterized by intense itching, dry skin, and inflammation. Around 50% of cases are diagnosed by the age of 1 year,¹ with at least one third of patients having persistent disease throughout adulthood.^{2,3} It is one of the most common skin diseases worldwide, and in some countries it has a point prevalence of 30% or higher.^{4,5}

Despite its frequency, AD is often perceived by the medical community and by wider society as a minor dermatologic condition,⁶ with patients having to endure symptoms over time. However, studies in selected groups of adult patients have shown that AD has a greater effect on quality of life than other common skin diseases, such as psoriasis.⁷ AD also has a greater negative effect on the mental health of patients compared with other chronic conditions, such as diabetes and hypertension.⁸ In children the negative effect of AD can extend to a patient's family and affect the care of other unaffected siblings.⁹

Because of the genetically determined pathophysiology,¹⁰ there is no complete cure for AD, and therefore management currently focuses on avoidance of triggers, skin hydration, and reduction of skin inflammation.¹¹ Reactive use of topical corticosteroids to treat the

Abbreviations used

AD: Atopic dermatitis
 ISOLATE: International Study of Life with Atopic Eczema
 PIQoL-AD: Parent's Index of Quality of Life–Atopic Dermatitis
 QoLIAD: Quality of Life Index for Atopic Dermatitis

inflammation, in conjunction with emollients to treat dry skin, has formed the cornerstone of disease management.¹¹ Treatment with topical corticosteroids offers rapid and effective relief of AD symptoms in most patients. However, there are safety concerns associated with their long-term use, primarily cutaneous adverse events¹² (eg, skin atrophy), as well as possible systemic side effects.¹³ There is also some evidence to suggest that patients worry about using topical corticosteroids, which can lead to noncompliance.¹⁴

The recent introduction of a new class of nonsteroid immunomodulators, the topical calcineurin inhibitors, is intended to complement existing treatment options in patients with AD and overcome some of the drawbacks of topical corticosteroid therapy.³

The distressing nature of this condition can have serious implications for patients with AD, families, and caregivers. Concern over treatment side effects leading to noncompliance might also lead to reduced disease control and increased morbidity and burden of disease. However, there is a lack of comprehensive, large-scale, current research into how patients actually perceive and manage their condition and how well they believe their symptoms are controlled.

The International Study of Life with Atopic Eczema (ISOLATE) is the first large-scale study initiated to rigorously address the following questions: (1) How does AD currently affect the lives of patients and caregivers? (2) Does the effect of AD vary with age, sex, and severity of disease? (3) How do patients and caregivers currently manage the condition? (4) How well do patients believe that their AD is controlled?

METHODS

The study was conducted in 8 countries between July and September 2004 (see Table E1 in the Online Repository at www.jacionline.org). Patients (>13 years) and caregivers (of children 2–13 years old) with moderate to severe AD as defined by their treating physician underwent in-depth telephone interviews apart from those in the United States and the United Kingdom, where interviews were conducted face to face to enable the EQ-5D¹⁵ questionnaire to be administered. The results of the EQ-5D will be reported separately.

A minimum of 150 patients per country was recruited to enable analysis of results on a local basis. The results were weighted according to the prevalence of AD for each country to ensure that each country was fairly represented within the total pool (see Table E1 in the Online Repository at www.jacionline.org).

An independent UK-based survey company, NOP World Health, conducted the interviews and analyzed the results. Patients were contacted through their treating physician, who had been randomly selected from published registers representative of the geographic

spread of the population in the relevant country. The majority of the physicians were office- or hospital-based dermatologists (55%) and pediatricians (39%), whereas a minority were primary care physicians (7%). To reflect everyday clinical practice, the physicians were each asked to recruit 5 patients with moderate-to-severe AD based on and reflecting the proportions of their typical workload. The treating physician also obtained the consent of the patient or caregiver to participate in the study. Patients were then contacted by NOP World Health.

Patients and caregivers were initially screened, and any patients not experiencing a flare of AD within the last 6 months were excluded from the survey. A flare was defined as a sudden worsening of symptoms requiring a physician consultation or application of prescription medication.

A nonstandard questionnaire consisting of 40 single and multipart questions for patients older than 13 years and 37 single and multipart questions for caregivers looking after children aged 2 to 13 years was developed in collaboration with all the potential stakeholders in the treatment of AD (ie, national eczema patient groups, practicing physicians, and medical experts from the 8 countries involved in the study). The questions were divided into sections focusing on the extent and severity of AD signs and symptoms, including flare characteristics, the significance of the flare to the individual patient or caregiver, the effect of the AD flare on daily life (eg, school or work and social life) and relationships, and the management of the flare, including attitudes to current treatment options and level of support from physicians and patient groups. In addition, one section concentrated on the effect of AD on patient and caregiver health-related quality of life by using either the 25-item Quality of Life Index for Atopic Dermatitis (QoLIAD)¹⁶ for patients older than 13 years or the 28-item Parent's Index of Quality of Life–Atopic Dermatitis (PIQoL-AD)¹⁷ for caregivers of patients aged 2 to 13 years. The full ISOLATE questionnaires can be viewed in the Online Repository (see Figs E1 and E2 at www.jacionline.org). Descriptive statistics were used to describe the sample. In addition, a *P* value of .05 or less was used as the criterion for statistical significance to enable analysis of the results across different age, sex, and disease severity groups.

A data analysis of the effect of AD on patient productivity across the European Union was carried out by using the methodology outlined in Table I^{18–20} to quantify the socioeconomic burden of the condition.

ISOLATE generated a large pool of data, and the results relating to overall disease effect and management are reported here. The authors intend to publish data from specific subanalyses in relevant medical journals.

RESULTS

Patient characteristics

A total of 2002 patients and caregivers from 8 countries took part in ISOLATE (see Table E1 in the Online Repository at www.jacionline.org). Sixty percent of the respondents were patients (>13 years), and 40% were caregivers looking after children (2–13 years). Table II shows that the distribution of patients by age, sex, and disease characteristics is similar to that of other published AD surveys.²¹ The proportion of patients with moderate-to-severe AD is also in line with the caseload of the treating physicians who nominated the patients to take part in the study (68.5% with moderate AD and 31.5% with severe AD).

The total sample was balanced in terms of marital status (patients >16 years) and employment status (patients >14

TABLE I. AD and the burden of disease*

Source of lost productivity†	Working hours in which performance was affected or lost because of absence (per year/per employee)	Total loss of working hours in EU15 per year	Lost productivity per year in EU15#
9.6% work time affected during flares	75.79‡	36,201,145.66	804,027,445
2.7 days lost per year because of work absence	20.89§	66,520,748.96¶	1,477,425,834
Total			2,281,453,279

Number of employees with moderate-to-severe AD in EU15 was calculated as follows: number of persons employed in EU15 (178,895,200) (Eurobusiness 2004) × prevalence of AD (1.78% based on UK data for adults older than 18 years, diagnosed/undiagnosed/treated and untreated). This result assumes 15% of performance is affected, and this is a conservative estimate (eg, work impairment in chronic hand dermatitis is 17.1%).¹⁸ The estimate of lost productivity per year is based on a human capital approach. Assuming diminishing marginal productivity, a profit-maximizing firm would employ additional labor until the marginal revenue product of the last unit of employment equals the employment costs faced by the firm, where the latter is the gross wage, including additional costs of employment, such as the employer's contribution to national insurance and superannuation.^{19,20} Seventy-five percent of opportunity costs are direct costs, and 25% are social contributions of employers.

*Costs do not include effects on labor market equilibrium, costs of forgone leisure time, and costs of household-productivity loss.

†Percentage time performance affected at work and days lost from work caused by AD per year based on results for greater than 18 years age groups Q13 and Q14 of the ISOLATE study.

‡Number of work days in flare per year (102) × average working hours per day (7.74) × work time affected during flares (9.6%).

§Average working hours per day (7.74) × days lost per year because of work absence (2.7).

||Number of employees with moderate-to-severe AD in EU15 (3,184,334.56) × working hours performance affected or lost because of AD (75.79) × estimate amount performance is affected (15%).

¶Number of employees with moderate-to-severe AD in EU15 (3,184,334.56) × working hours performance affected or lost because of AD (20.89).

#Total loss of working hours in EU15 per year × €22.21 per hour.

TABLE II. Patient and disease characteristics

	Total (n = 2002)	Age			Sex		Severity of disease	
		2-13 y (n = 779)	14-17 y (n = 125)	≥18 y (n = 1098)	Male (n = 660)	Female (n = 1342)	Moderate (n = 1371)	Severe (n = 631)
Patient characteristics								
Percentage of patients								
By age, sex, and disease severity	—	39	6	55	33	67	68	32
Female sex (%)	67	61	60	72	—	—	67	67
Married or living with partner (%; base >16 y)	52	—	—	52	45	55	51	54
Employed (%; base >14 y)	61	—	16	60	62	61	64	56
Disease characteristics								
Mean percentage of body affected by last flare	19	23	15	17	17	20	13	33
Percentage of patients with face and neck involvement	41	43	34	40	36	43	37	50

years) of the patients (Table II). However, a significantly higher percentage of male patients (>16 years) were single (46%) compared with the average for the total sample (38%, $P < .05$).

The effect of AD on patients and caregivers

Disease characteristics. Fifty percent of the total sample had been given diagnoses in the first 3 years of life, and 24% were given diagnoses after the age of 18 years. Sixty-eight percent of the total sample had been given diagnoses of moderate AD, and 32% were given diagnoses of severe AD. The most commonly affected part of the body in patients during AD flares was the face and neck area, regardless of age, sex, or severity of disease. Disease characteristics are summarized in Table II. AD had been severe enough to warrant admission to

the hospital at some point in their life in 9% of patients overall.

On average, patients experienced 9 flares per year, lasting 15 days each time (Table III). In total, patients spent 136 days per year in AD flare. Patients with severe disease experienced significantly more frequent (11.1 per year) and longer (17.3 days) flares than the total sample ($P < .05$), resulting in more than 192 days spent in flare each year on average. Those with severe disease also took significantly longer to clear (9.6 days) compared with the average for the total sample (8.2 days, $P < .05$).

Effect of the AD flare on patient and caregiver lifestyle. The AD flare disturbs the sleep of patients for an average of 7.3 nights during a flare (67 nights per year, Table III). Patients with severe disease have significantly more nights' sleep affected (14.6 nights per flare, equivalent to

TABLE III. Effect of AD

	Total (n = 2002)	Age			Sex		Severity of disease	
		2-13 y (n = 779)	14-17 y (n = 125)	≥18 y (n = 1098)	Male (n = 660)	Female (n = 1342)	Moderate (n = 1371)	Severe (n = 631)
No. of flares per year	9.2	8.7	7.5	9.6	10.4	8.6	8.3	11.1
Total duration of flare, d	14.8	14	15.4	15.2	13.2	15.5	13.6	17.3
No. of days per year in AD flare	136.2	121.8	115.5	145.9	137.3	133.3	112.9	192.0
No. of nights sleep affected during a flare	7.3	5.0	11.7	8.4	7.9	7.0	4.0	14.6
No. of times woken up at night during a flare	1.8	1.8	2.0	1.8	1.8	1.9	1.5	2.5
Percentage of patients								
Avoiding at least 1 everyday activity	86	86	83	87	83	88	84	90
School-work life affected	32	30	46	34	35	31	27	45
Home life affected	33	34	27	33	34	32	27	44
Social life affected	33	27	26	38	37	31	28	44
Percentage of time at work-school performance affected during flare	9	7	10	10	9	9	6	15
No. of days absent from school-work because of a flare	2.5	2.0	3.5	2.7	2.9	2.4	1.3	5.3

162 nights per year) compared with the total sample ($P < .05$).

On average, 86% of patients avoid at least one type of everyday activity while in flare (eg, bathing; wearing shorts, skirts, or T-shirts; and swimming; Table III). The flare also has an effect on the work-school, home, and social lives of, on average, 33% of patients, increasing to 44% of patients with severe disease ($P < .05$, Table III).

The AD flare also negatively affects overall patient school-work performance and productivity (Table III). On average, patients take 2.5 days off school or work per year because of AD, and a further 9% of the time, their concentration is affected at school or work while in flare. Patients with severe disease take significantly more days (5.3 days) off work or school per year because of AD, and their concentration is affected for an average of 15% of the time while in flare compared with the total sample ($P < .05$).

An analysis of the effect of AD on adult patient performance at work and occupational absence shows that the social cost of lost productivity across the European Union amounts to more than €2 billion per year (Table I).

Emotional effect of AD. On average, 55% of patients are either always or sometimes worried about the next flare of AD. Significantly more caregivers looking after younger children (62%) and those with severe disease (65%) are worried about the next flare compared with the total sample ($P < .05$).

ISOLATE demonstrates how the stigma of the AD flare can affect patients' self-esteem, mood, self-confidence, and ability to establish and manage relationships (Table IV). On average, 43% of patients are fairly or very concerned about being seen in public during a flare. This is significantly more common in adult patients (>18 years; 53%) and those with severe disease (51%) compared with the total sample ($P < .05$). The AD flare has either some or a huge effect on the self-confidence of 36% of patients, increasing to 46% of those with severe disease

($P < .05$) and 52% of those aged 18 to 35 years ($P < .05$). Likewise, on average, 51% of patients are either always or sometimes unhappy-depressed, and of these, 37% feel frustrated, 34% feel irritated-annoyed, 30% feel sad-upset, and 27% feel helpless during a flare.

Twenty-seven percent of patients have experienced bullying because of their AD, and this is significantly worse in children (8-17 years; 39%) and those with severe disease (33%, $P < .05$). Adult patients also feel discriminated against because of their AD in 11% of cases, and 14% believe that their career progression has been hindered.

On average, 30% of patients and caregivers believe that either their or their child's AD has an effect on other members of their family-household, increasing to 38% for the 2- to 7-year age group and 40% in those patients with severe disease ($P < .05$). On average, 21% of adult patients with AD (>18 years) have experienced difficulty in forming relationships. A significantly greater percentage of male patients (30%) and those with severe AD (30%) have experienced difficulty in forming relationships compared with the average for the total sample ($P < .05$). This might relate to the finding that a significantly higher percentage of male patients (>16 years) were single (46%) compared with the average for the total sample (38%, $P < .05$), as shown in Table II. In established relationships 12% of adult patients (>18 years) have, on average, experienced problems with their partner caused by AD.

The majority of the patients and caregivers (75%) believe that their treating physician is either very or fairly sympathetic to either their or their child's AD. The same high percentage of patients and caregivers regard the factual information provided by their doctor about the condition as satisfactory (77%). However, 74% of patients and caregivers state that their physician has never discussed the emotional effect that AD has had on their lives.

TABLE IV. Emotional aspects of AD

	Total (n = 2002)	Age			Sex		Severity of disease	
		2-13 y (n = 779)	14-17 y (n = 125)	≥18 y (n = 1098)	Male (n = 660)	Female (n = 1342)	Moderate (n = 1371)	Severe (n = 631)
Emotional aspects of AD								
Percentage of patients during an AD flare								
Fairly or very concerned about being seen in public	43	29	50	53	38	46	40	51
With effect on self-confidence	36	24	36	45	31	39	32	46
Unhappy or depressed	51	52	52	51	49	53	48	59
Percentage of patients who have been teased or bullied because of AD at some time during their life	27	25	39	28	23	29	24	33
Effect of AD on relationships								
Percentage of patients								
Where AD has an effect on other household members	30	37	25	26	33	29	26	40
Who find it difficult to form relationships with a partner (base = adults)	21	–	–	21	30	18	17	30
Who have experienced relationship problems with an existing partner (base = adults)	12	–	–	12	16	10	8	21
Who always or sometimes felt awkward about a partner touching or seeing their body during a flare (base = adults)	42	–	–	42	40	43	39	50

In contrast to professional support, 84% of the patients and caregivers were not aware of the existence of an AD patient group, 12% were aware but have not contacted any groups, and only 2% were in contact and receiving support from an AD patient group.

Analysis of QoLIAD and PIQoL-AD single-item responses. The analysis of the ISOLATE QoLIAD and PIQoL-AD single-item response data confirms the negative effect of AD on patients and caregivers. The QoLIAD and PIQoL-AD responses are presented in Table V.

The main effect of AD on the lives of adult patients stems from embarrassment and not wanting to be seen in public, as well as being restricted in the choice of clothes the patient can wear and the unrelenting nature of the condition itself. For caregivers, major factors are concerns over what their child can wear (71%), worry about the way their child looks (63%), feelings of being out of control (52%), and also anxiety about what the future will hold (46%). In addition to concerns about the effect of the condition, 64% of caregivers are also worried about the side effects of the treatment their child receives for their AD.

Patient and caregiver management of the AD flare

Sixty-five percent of the overall sample use topical corticosteroids prescribed by their physician to treat the AD flare. In 54% of cases, topical corticosteroids are used as the main means of treating the flare. Although prescribed emollients are used by 27% of patients overall, only 4% use them as the main means of treating flares. Pimecrolimus was used by 25% of respondents overall and in 18% of cases as the main medication used to control

TABLE V. QoLIAD and PIQoL-AD responses

	Total (%)	Patients with severe AD (%)
QoLIAD parameter: Adults		
I worry about my appearance.	73	82
I don't want people to see my skin.	63	71
I get embarrassed when I am with people I don't know very well.	47	56
I can't wear the clothes I want to wear.	47	60
There is no release from it.	46	61
I am embarrassed about my appearance.	44	54
PIQoL-AD parameter: Caregivers		
I have to be careful what he or she wears.	71	76
I worry about possible side effects of his or her treatment.	64	71
I worry about the way he or she looks.	63	70
I feel that I have no control over his or her eczema.	52	61
I worry about his or her future.	46	57

Base = All patients: responses greater than 40% patients or caregivers affected.

the AD flare. Tacrolimus was used by 9% of respondents overall and in 6% of cases as the main medication used to treat the AD flare.

Limitations of pharmacologic treatment. Despite their widespread prescription, topical corticosteroids are a concern for 49% of respondents overall and 56% of caregivers of young children ($P < .05$). A further 18% of

TABLE VI. Patient perception of topical AD treatment side effects

Side effect	Patients-caregivers concerned about side effect (%)	Patients-caregivers experiencing side effect (%)
Skin thinning	28	15
Treatment resistance	18	11
Skin bleaching	17	14
Burning sensation	15	20
Rebound symptoms	15	12

Base = all respondents (n = 2002).

the sample expressed concerns over oral medication, 7% over herbal treatments (eg, Chinese remedies), and 6% over topical steroid-free drugs, and 37% of the sample had no concerns about any of the specified treatment options. Of those respondents who expressed concern about the use of topical corticosteroid treatment, 89% of the caregivers and 83% of the patients (>13 years) were either very or fairly concerned regarding their use. Table VI outlines the side effects of topical AD treatments that patients had either experienced or over which they expressed concerns.

Compliance with pharmacologic treatment. Fifty-eight percent of the sample restrict their use of topical corticosteroids to particular sites, 39% use them less frequently or for shorter time periods than prescribed, and 66% use topical corticosteroids as a last resort. On average, patients endured the symptoms of AD without initiating specific treatment 47% of the time they were in flare (7 days per flare, Fig 1). This level of noncompliance is independent of disease severity.

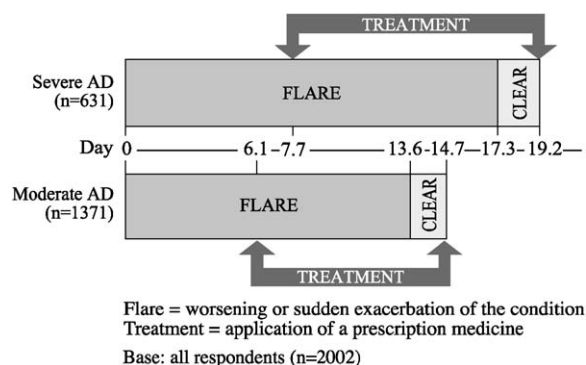
AD disease control

The majority of patients with AD (77%) and caregivers (74%) do not feel fully confident managing the condition without direction from the physician. This was not just restricted to patients with severe disease but was also a common theme in those with moderate disease and across all age and sex groupings. Seventy-five percent of the survey sample stated that being able to effectively control their AD would be the single most important improvement to their quality of life.

When given the option of several treatment modalities, the majority of the patients (>13 years, 62%) and caregivers (74%) would prefer to apply a nonsteroid treatment as early as possible to either prevent a flare occurring or prevent a flare from getting worse.

DISCUSSION

The results of ISOLATE highlight AD as a condition that still has a significant physical and emotional effect on patients and caregivers despite the availability of effective treatment strategies and sources of patient support. Less than optimal disease control results in patients experiencing sleep deprivation, lack of concentration, and impaired

**FIG 1.** Flare management.

school-work productivity. The resulting stigma of AD can also affect the patient's self-esteem, mood, self-confidence, and ability to establish and manage relationships. More than one third of patients report that AD has eroded their self-confidence; a similar percentage of patients are concerned about being seen in public, and half of patients experience depression or unhappiness caused by their condition. The occurrence of the next flare occupies the thinking of more than half of patients and caregivers, even when in remission.

The study has also highlighted several groups in whom AD seems to have a particularly significant effect. For example, adult males with AD are more likely to find it difficult to form relationships and a greater proportion is single compared with adult females. The exact reason for this social isolation is not evident from this study and warrants further investigation to optimize management of this patient group. Although one might expect the effect of AD to be greater in patients with severe disease, it is also interesting to see how patients with moderate AD still experience significant morbidity and burden of disease.

However, it is not a lack of available efficient treatments but a disparity between the prescriber's intention and patient compliance that has led to patients experiencing untreated AD symptoms. The majority of patients and caregivers in the ISOLATE study used topical corticosteroid-based regimens to treat the AD flare. Although topical corticosteroids are usually effective, concern over their side effects has led to compliance issues and patients delaying or otherwise restricting the way in which they use them. For this reason, 39% of patients and caregivers used topical corticosteroids less frequently and for shorter periods than recommended by their doctor, and 66% used them only as a last resort. The fear of topical corticosteroid side effects might also, at least partly, explain why patients delay initiating treatment when the disease flares. These delaying tactics result in patients having untreated disease for half of the time they are in flare. It is therefore not surprising given this level of undertreatment and resultant residual disease that the most important improvement to the quality of life of three quarters of patients with AD would be to gain control over their condition.

ISOLATE also demonstrates the wider socioeconomic implications of the undertreatment of AD. Lost productivity caused by occupational absenteeism and the amount of time for which the AD flare affects patient performance while at work could amount to more than €2 billion per year across the EU (Table I).

The results of the ISOLATE study highlight AD as an undertreated disease that has a significant, yet mostly avoidable, negative effect on patients, their caregivers, and society. The cost to both the individual and society could be reduced if better treatment options were offered and convincingly explained by the physician.

The results of the ISOLATE study demonstrate the significant physical and emotional effect that AD currently has on patients and caregivers, despite the availability of effective treatment strategies. It also highlights the differences between prescriber intention and patient perception of current management options, resulting in undertreatment of this highly prevalent and distressing condition. These results demonstrate a significant and urgent need to improve the management of AD to help patients gain disease control. ISOLATE also outlines the significant and avoidable socioeconomic cost of AD to society in terms of lost productivity and effect on learning capacity in younger patients.

We thank Bernd W. M. Arents and Monique Zwaan, Vereniging voor Mensen met Constitutioneel Eczeem (VMCE), Nijkerk, The Netherlands; J. Diniz Almeida, Asociación de Familiares y Pacientes de Dermatitis Atópica (ADEA), Madrid, Spain; Professor Charles N. Ellis, University of Michigan Medical School, Ann Arbor, Mich; Professor Giampiero Girolomoni, University of Verona, Verona, Italy; Professor Dedee Murrell, St George Hospital, University of New South Wales, Sydney, NSW, Australia; Thomas Schwennesen, Deutscher Neurodermitis Bund, Hamburg, Germany; Anna Stanczyk-Przyluska, Association for Patients with Asthma and Allergy, Pomorska, Poland; and Professor Kristian Thestrup-Pedersen, Aarhus University Hospital, Aarhus, Denmark.

REFERENCES

1. Leung DYM. Atopic dermatitis: immunology and treatment with immune modulators. *Clin Exp Immunol* 1997;107(suppl 1):25-30.
2. Herd RM, Tidman MJ, Prescott JR, Hunter JA. Prevalence of atopic eczema in the community: the Lothian Atopic Dermatitis study. *Br J Dermatol* 1996;135:18-9.
3. Ellis C, Luger T, on Behalf of the ICCAD II Faculty. International consensus conference in atopic dermatitis II (ICCAD II): clinical update and current treatment strategies. *Br J Dermatol* 2003;148(suppl 63):3-10.
4. Åberg N, Hesselmar B, Åberg B, Eriksson B. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995;25:815-9.
5. Peat JK, van den Berg RH, Green WF, Mellis CM, Leeder SR, et al. Changing prevalence of asthma in Australian children. *BMJ* 1994;308:1591-6.
6. Lapidus CS, Kerr PE. Social impact of atopic dermatitis. *Med Health R I* 2001;84:294-5.
7. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;19:210-6.
8. Kiebert G, Sorensen SV, Revicki D, Fagan SC, Doyle JJ, Cohen J, et al. Atopic dermatitis is associated with a decrement in health-related quality of life. *Int J Dermatol* 2002;41:151-8.
9. Finlay AY. Quality of life assessments in dermatology. *Semin Cutan Med Surg* 1998;17:291-6.
10. Lee YA, Wahn U, Kehrt R, Tarani L, Businco L, et al. A major susceptibility locus for atopic dermatitis maps to chromosome 3q21. *Nat Genet* 2000;26:470-3.
11. Darsow U, Lubbe J, Taieb A, Seidenari S, Wollenberg A, Calza AM, et al. Position paper on diagnosis and treatment of atopic dermatitis. *J Eur Acad Dermatol Venereol* 2005;19:286-95.
12. Schiffner R, Schiffner-Rohe J, Landthaler M, Stolz W. Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non-corticosteroids. *Pharmacoeconomics* 2003;21:159-79.
13. Ellison JA, Patel L, Ray DW, David TJ, Clayton PE. Hypothalamic-pituitary-adrenal function and glucocorticoid sensitivity in atopic dermatitis. *Pediatrics* 2000;105:794-9.
14. Charman CR, Morris AD, Williams HC. Topical corticosteroids phobia in patients with atopic eczema. *Br J Dermatol* 2000;142:931-6.
15. The EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
16. Whalley D, McKenna SP, Dewar AL, Erdman RA, Kohlmann T, Niero M, et al. A new instrument for assessing quality of life in atopic dermatitis: international development of the Quality of Life Index for Atopic Dermatitis (QoLIAD). *Br J Dermatol* 2004;150:274-83.
17. McKenna SP, Whalley D, Dewar AL, Ruud AM, Erdman AM, et al. International development of the Parent's Index of Quality of Life in Atopic Dermatitis (PIQoL-AD). *Qual Life Res* 2005;14:231-41.
18. Reilly MC, Lavin PT, Kahler KJ, Pariser DM. Validation of the dermatology life quality index and the work productivity and activity impairment—chronic hand dermatitis questionnaire in chronic hand dermatitis. *Am Acad Dermatol* 2003;48:128-30.
19. Rice DP. Estimating the cost of illness. *Am J Public Health* 1967;68:424-40.
20. Koopmanschap MA, Rutten FF. A practical guide for calculating indirect costs of disease. *Pharmacoeconomics* 1996;10:460-6.
21. Paller AS, McAllister RO, Doyle JJ, Jackson A. Perceptions of physicians and pediatric patients about atopic dermatitis, its impact, and its treatment. *Clin Pediatr* 2002;41:323-32.