ORIGINAL ARTICLE

Atopic eczema: burden of disease and individual suffering – results from a large EU study in adults

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Abstract

Background Atopic eczema (AE, atopic dermatitis) is one of the most common non-communicable inflammatory skin diseases affecting 1–5% of the adult population in Europe with marked impairment in quality of life. In spite of great progress in understanding the pathophysiology of disturbed skin barrier and immune deviation, AE still represents a problem in daily clinical practice. Furthermore, the true impact of AE on individual suffering is often not recognized.

Objectives With a large European study, we wanted to provide insights into the actual suffering and individual burden of disease in adult patients with AE.

Methods A total of 1189 adult patients (18–87 years, 56% female) with moderate to severe AE were recruited in nine European countries by dermatologists or allergists together with the help of patient organizations. A computer-assisted telephone interview was performed by experienced interviewers between October 2017 and March 2018. The following instruments were used to assess severity or measure quality of life: Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), Hospital Anxiety and Depression Scale (HADS-D) and a newly developed Atopic Eczema Score of Emotional Consequences (AESEC). Patients were also asked to self-assess the severity of their disease.

Results Despite current treatment, 45% of participants still had actual moderate to very severe AE in POEM. Due to their skin disease, 57% missed at least 1 day of work in the preceding year. DLQI showed moderate to extremely large impairment in 55%. According to HADS-D, 10% scored on or above the threshold of eight points with signs of depressive symptoms. Assessed with AESEC, 57% were emotionally burdened with feelings such as 'trying to hide the eczema', 'feeling guilty about eczema', having 'problems with intimacy' and more. Of persons actually suffering from severe AE, 88% stated that their AE at least partly compromised their ability to face life.

Conclusions This real-life study shows that adults with a moderate to severe form of AE are suffering more than what would be deemed acceptable. There is a need for increased awareness of this problem among healthcare professionals, policymakers and the general public to support research in the development of new and more effective treatments and provide access to better and affordable health care for affected patients.

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Conflicts of interest

None declared.

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Introduction

Atopic eczema (atopic dermatitis, eczema) is one of the most common non-communicable inflammatory skin diseases worldwide.[1–10] The disease itself is not new, and descriptions can be found in ancient medical literature[11,12] with Emperor Octavianus Augustus probably being the first documented atopic individual in history. The term 'Eczema' was coined by Aetius from Amida in the 6th century AD describing the boiling of a fluid in a kettle – a visionary description of the dermatopathological equivalent in spongiosis.[1,2] After first

dermatologic descriptions in the 19th century, it became a clear-cut entity in the 20th century,[11,12] especially when its prevalence started to increase in the last decades of the 20th century.[5,6]

Today, one can safely state that 10–20% of children – this is a moderate estimate – are suffering from atopic eczema. While the disease for a long time was regarded as a 'children disease', it has become clear that more and more adults are affected with an estimated prevalence of 3–5 per cent in the general population.[13–15]

Contrary to allergic bronchial asthma and allergic rhinoconjunctivitis ('hay fever'), the aetiopathogenesis of atopic eczema is still not well established. Three dimensions seem to play a major role, namely the

1 Epithelial barrier dysfunction, most notably shown in the filaggrin mutation leading to increased transepidermal water loss.[16]
2 The deviated immune response towards Th2-dominant responses with increased immunoglobulin E production and distinct inflammatory events leading to allergic reactions against a multitude of environmental allergens from the air or from foods.[4,17–20]
3 The psycho-neurogenic inflammation as the basis of the often intractable itch being the major subjective symptom of the disease.[21,22]

The disease goes along with a remarkable economic burden both for the affected individual and for society and with marked impairment in quality of life.[23–28]

A study measuring quality of life in children with AE showed that those with generalized eczema had an impaired quality of life score similar to children affected with cystic fibrosis, severe renal disease or cerebral palsy, while more localized forms showed similar scores to rheumatoid arthritis or diabetes.[29]

Furthermore, there are deficits in quality of health care for the affected persons and their families.[26,30–34] The actual degree of individual suffering in the single patient has so far not received adequate attention in scientific literature. In addition, studies focusing on patients' self-help have shown a high unmet need with the call for more patient support groups[35] as well as reliable online health information.[36] This is emphasized by the findings of Corcimaru *et al.*[36] that the vast majority of individual atopic eczema websites, blogs and forums currently are inconsistent with guidelines of professional dermatological societies, which can be dramatically misleading for affected patients. Patient–physician dialogues in atopic eczema as well require scientific assessments given the fact that doctors today typically misjudge and underestimate the needs of their patients with atopic eczema.[35,37]

Therefore, the aim of this large study performed in nine countries of the European Union was to assess the magnitude of individual suffering and the real-life burden of disease in adult patients with rather severe forms of atopic eczema. With these data, patient organizations should be supported in their advocacy efforts with health policymakers and payers. They also should be used in education of healthcare providers in order to improve the patient–physician dialogue.

Patients and methods

Patients

For this cross-sectional non-interventional study, a total of 1189 adult patients (between 20 and 87 years) suffering from atopic eczema were recruited in 9 countries of the European Union, namely France (n = 180), Spain (n = 180), Italy (n = 180), United Kingdom (n = 180), Germany (n = 180), Netherlands (n = 150), Denmark (n = 50), Sweden (n = 37) and Czech Republic (n = 52).

Patients were recruited by experienced physicians (dermatologists, allergists) together with the help of patient organizations to volunteer for the study. Inclusion criteria were the dermatological diagnosis of atopic eczema, age over 18 years and indication for systemic immunomodulatory treatment defined as suffering from moderate to severe atopic eczema. Exclusion criteria comprised language or other barriers to follow questions and give answers in a telephone interview.

The study was done as a telephone interview (20–30 min) using standardized questions. A pretest in 100 patients in five countries had been done earlier to show the feasibility of the methods. The questions were asked in a computer-assisted telephone interview (CATI) with experienced interviewers. In all countries, local ethical committees had approved the study prior to beginning.

All questionnaire instruments had been validated, and they were used in the language of the country; also the translation had been validated for the specific language. The telephone interviewer read the questions to the participants slowly and verbatim in order to minimize interviewer bias. The interviewing was done between October 2017 and March 2018.

Instruments

The following instruments measuring patients' quality of life or burden of disease were used:

Dermatology life quality index (DLQI) The DLQI[38] comprises 10 questions scoring from 0 to 30 points: 0–1 = 'no effect on patients' life', 2–5 = 'small effect on patients' life', 6–10 = 'moderate effect on patients life', 11–20 = 'Very large effect on patients life' and 21–30 = 'Extremely large effect on patients' life'.[39] An example of a DLQI question is 'over the last week, how embarrassed or self conscious have you been because of your skin?' or 'over the last week, has your skin prevented you from working or studying?'.

Hospital anxiety and depression scale (HADS-D) The Hospital Anxiety and Depression Scale (HADS-D)[40] comprises seven

questions scoring from 0 to 21 points: 0–7 = 'Normal', 8–10 = 'Borderline' and 11–21 = 'Abnormal'. The HADS-D focuses on the occurrence of depressive symptoms and is measured with 7 questions, as, for example, 'I can laugh and see the funny life things', 'I feel as if I am slowed down' or 'I have lost interest in my appearance'. Questions can be answered with 'not at all' (0), 'sometimes' (1), 'very often' (2) and 'nearly all time' (3).

Patient-oriented eczema measure (POEM) The Patient-Oriented Eczema Measure[41] comprises seven questions scoring from 0 to 28 points: 0–2 = 'Clear or almost clear', 3–7 'Mild AE', 8–16 = 'Moderate AE', 17–24 = 'Severe AE' and 25–28 = 'Very severe AE'. The questions relate to experiences made in the week prior to the interview. It contains questions such as 'over the last week, on how many days has your skin been flaking off because of your eczema?' or 'over the last week, on how many days your skin been itchy because of your eczema?' or 'over the last week, on how many days has your skin been bleeding because of your eczema?'. Possible answers were evaluated as 'no days' = 0, '1–2 days' = 1, '3–4 days' = 2, '5–6 days' = 3 and 'every day' = 4 points. The added numbers result in the overall score.

Self-assessment of severity

Furthermore, participants were asked the question 'would you describe your Atopic eczema/dermatitis as clear, almost clear, mild, moderate or severe?'. The answers were stated accordingly.[39,42]

Atopic eczema score of emotional consequences (AESEC) The Atopic Eczema Score of Emotional Consequences (AESEC)[43] was developed for the study on the basis of a review of available instruments and through intense contacts in direct interviews and social media asking individuals with atopic eczema about the emotional consequences in their experience. Validation was performed by testing in 103 individuals. The first collection of 119 very personal items was analysed for possible overlaps and finally reduced to 37 items; these were subjected to the testing of internal consistency and reliability with a Cronbach's $\alpha = 0.938$ and a low inter-item correlation with Spearman's $P = 0.22$. More detailed data have been published recently.[43] The final questionnaire contains 28 items (both positive and negative items to avoid a negative bias) which are answered from 0 to 3 and reflect the very personal feelings, suffering and the emotional consequences due to atopic eczema. The maximal score is 84 points.

Educational status

The educational status was evaluated by the highest level of completed education. Higher education was defined by reaching at least high school graduation.

Data statistics and analyses

Data were analysed using IBM SPSS Statistics (version 14-46, IBM Corporation, Armonk, NY, USA). The global significance level (α-error) was set as 0.05.

Results

Patient characteristics

A total of 1189 patients with atopic eczema were included (56% female). The average time of interview was 25 min. Most participants reported to have a higher school education (89%). The age distribution was 18–29 years: 13%, 30–39 years: 30%, 40–49 years: 35% and 50 years and older: 22%.

The mean age was 41.9 years. The light-sensitive skin types were 40% 'light skinned' (Celtic/Nordic), 42% intermediate, 15% Mediterranean and 3% dark.

Regarding the residential area, 25% were living in rural environments, 39% in a medium-size city, 26% in a big city suburb and 10% living in a big city inner-city. The household size was 1 person 14%, 2 persons 47% and 3 or more persons 39%.

The first diagnosis of atopic eczema was done by a general practitioner in 43%, a dermatologist in 41%, an allergist in 2%, a paediatrician in 11% and others in 3%. Twenty-four percent were members of a patient support group, 9% used such services without being member, 27 % had social media contact to other people affected, 3% had other contacts, and 47% were in no connection to support groups.

The following systemic immunomodulating therapies had been prescribed: glucocorticosteroids 57%, cyclosporine A 28%, azathioprine 15%, methotrexate 25%, mycophenolate mofetil 11% and UV therapy in 68%.

Concomitant diseases

Seventy-nine percent were suffering from other atopic diseases (airway allergy to pollen 44%, airway allergy to house dust mite 31%, airway allergy to animals 29%) as well as food allergy 28% or drug intolerance 7%. The general health status – beyond the skin – was felt as good/very good in 75%, as fair in 20% and as bad/very bad in 4%. Ten percent of the patients were suffering from other chronic diseases such as joint diseases 19%, metabolic diseases 15%, cardiovascular problems 14%, other skin diseases 12%, eye diseases 8%, thyroid diseases 8%, autoimmune/chronic diseases 7% and nervous disorders 5%.

Patient-oriented eczema measure (POEM)

According to POEM, 45% of patients were currently suffering from a moderate to severe skin condition while 38% noted mild and 16% currently/almost clear skin (Fig. 1). From the results of the POEM, most notably, the questions 'how many days had your skin been itchy?' (88% positive) and 'on how many days your skin has felt dry or rough' (86% positive) were of actual

relevance. The POEM score corresponded well with the severity self-assessment of the patients. Table 1 shows the characteristics of patients as stratified by POEM.

Dermatology life quality index (DLQI)

Altogether, 55% of patients reported to suffer from moderate to extremely large effects of atopic eczema on health-related quality of life. Itching, painful and stinging sensation of the skin occurred in three out of four patients. More than half of all patients (58%) reported to be embarrassed about their skin within the last 7 days, and 61% indicated AE to influence the choice of clothing. Overall mean of the DLQI was 7.2.

The burden on patients' life increased with increasing self-assessed AE severity.

Only 1% of patients with an 'almost clear or mild' self-assessed AE stated an extremely large negative effect in their quality of life in comparison with that. Two percent of the moderate and 18% of the severe AE patients reported an extremely large effect.

Skin disease-specific DLQI also increased with disease severity according to POEM score. Very and extremely large loss in quality of life ranged from 1% of patients with a clear or nearly clear AE to 67% of patients with a very severe actual form of AE. Mean DLQI increased from 2.8 to 13.9 when considering patients with clear/almost clear vs. severe/very severe eczema, respectively. When put in relation to the respective overall means, the POEM-stratified means showed an increase throughout AE severity.

Table 1 General characteristics of participants stratified by Patient-Oriented Eczema Measure (POEM) score [clear/mid vs. moderate/(very) severe]

	Total (n = 1189) [n (%)]	AE severity according to POEM score	
		Clear/mild (n = 648) [n (%)]	Moderate/(very) severe (n = 541) [n (%)]
Total	1189 (100)	648 (55)	541 (45)
Men	519 (44)	332 (51)	187 (35)
Women	670 (56)	316 (49)	354 (65)
18–29 years old	153 (13)	57 (9)	96 (18)
30–39 years old	357 (30)	206 (32)	151 (28)
40–49 years old	421 (35)	253 (39)	168 (31)
50 years and older	258 (22)	132 (20)	126 (23)
Higher education†	1011 (85)	566 (87)	442 (82)
Lower education	178 (15)	82 (13)	99 (18)
Mean DLQI	7.24 ± SD 5.500	4.52 ± SD 3.631	10.51 ± SD 5.582
MEAN HADS-D	2.67 ± SD 3.230	1.79 ± SD 2.438	3.73 ± SD 3.712
HADS-D score 0–7	1064 (90)	612 (94)	452 (84)
HADS-D score 8–21	125 (10)	36 (6)	89 (16)

†At least 10 years of school education.
AE, atopic eczema; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; POEM, Patient Oriented Eczema Measure.

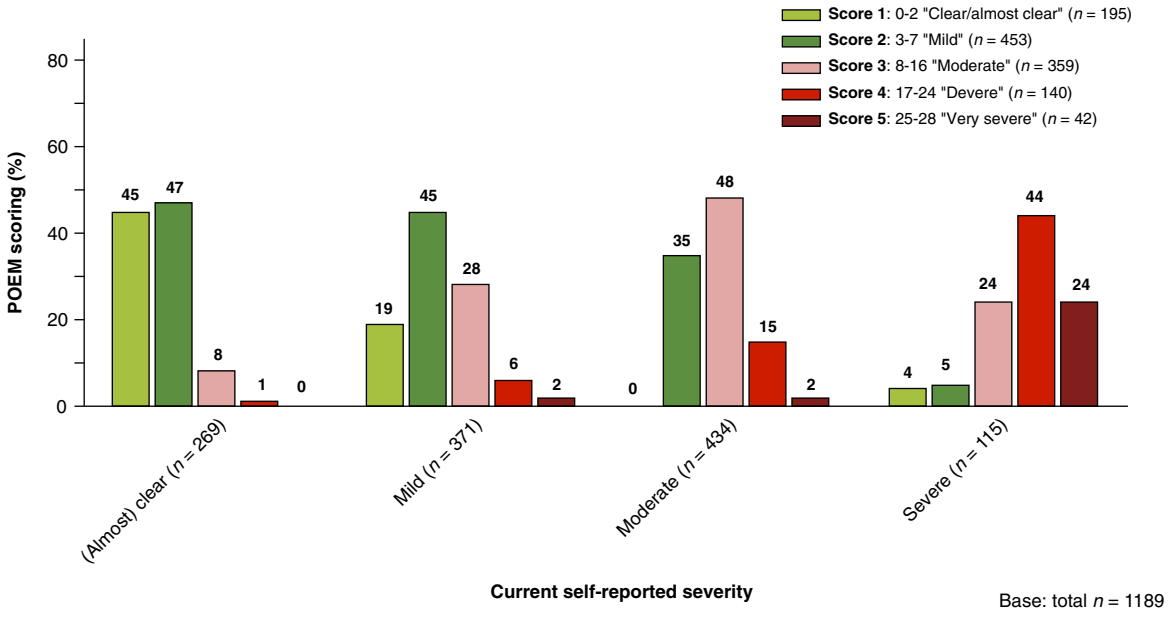


Figure 1 Patient-Oriented Eczema Measure (POEM) vs. self-assessment of disease severity.

Hospital anxiety and depression scale (HADS-D)

Ten percent of all participants showed an increased tendency for depression according to the HADS-D (Borderline/abnormal; Score 8–21). A clinical interference (Score 11–21) could be observed in 3% of participants. In single items, 58% stated to 'feel slowed down' and 36% stated to 'feel unhappy at least sometimes'. The mean HADS-D Score was 2.67. Stratified by self-assessed AE severity, 99% of clear patients were normal regarding HADS-D. Considering patients with a severe self-assessed AE, 16% showed a score indicating a depression. In 14%, a borderline score suggested at least depressive symptoms (Fig. 2). The presence of a depressive tendency correlated with the current POEM score. Depressive tendency reached from 1% in patients with no or almost no symptoms to 21% in patients with severe skin conditions. Mean HADS-D Score increased from 1.4 in patients with 'clear or almost clear' to 4.7 in patients with 'severe or very severe' POEM score.

Atopic eczema score of emotional consequences (AESEC)

In the AESEC, there was a mean value of 32.2 in the score from 0 to 84 maximum. Fifty-seven percent of the patients had a moderate to large emotional consequences Score. In detail, 43% scored with 1 (small emotional consequences), 26.9% scored with 2 (moderate emotional consequences), 21.2% scored with 3 (large emotional consequences), and 8.8% scored with 4 (very large emotional consequences) (Fig. 3).

In detailed questions, 72% of participants stated 'I envy people with normal skin', 57% said that 'itching drives me crazy', 50% said 'I feel sad about having eczema', 51% of patients answered 'I try to hide my eczema', and 75% reported about 'problems with intimacy'.

In a final attempt to assess the whole of individual burden, patients were asked 'When thinking about your life with atopic eczema, have there been moments when the disease compromised your ability to face life?'. Of the person actually suffering from severe eczema, 88% stated that their eczema at least partly compromised their ability to face life. The longer the duration of the disease was, the more severe and the stronger the answers were (Fig. 4).

Correlation between POEM, DLQI, HADS-D and AESEC

When the various questionnaires were correlated, there was a moderate correlation with quality of life measured by DLQI, HADS-D 7 and POEM. A particular good correlation was found in the group of patients who assessed themselves as suffering from severe eczema: there was a direct correlation to the emotional impact as measured in AESEC (Fig. 5).

Work absenteeism

Over half of the respondents at least had missed 1 day at work due to AE in the preceding year, 31% missed 1–5 days, and one quarter had been missing more than 6 days.

Additional costs

Extra out-of-pocket spending on everyday necessities was common and with an average amount of ca 900 Euro per year.[44]

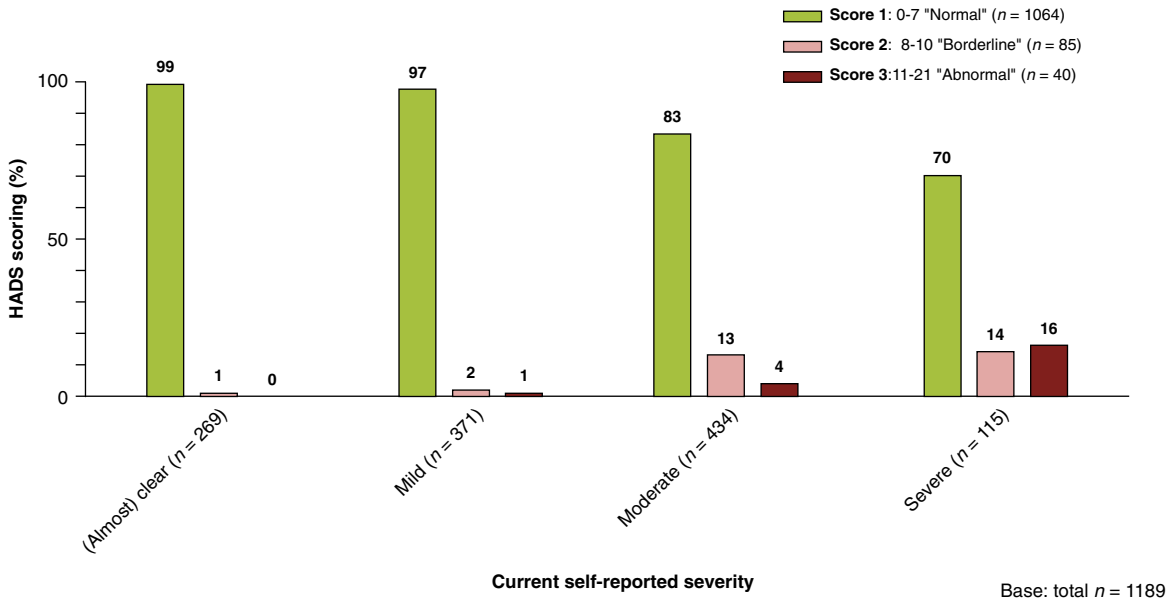


Figure 2 Hospital Anxiety and Depression Scale (HADS-D) and self-reported severity of eczema.

Scoring procedure:

Each question was rated in accordance to the below:

Negative Items:		**Positive Items:**	
Applies fully	= 3	Applies fully	= 0
Somewhat applies	= 2	Somewhat applies	= 1
Rather not	= 1	Rather not	= 2
Does not apply at all	= 0	Does not apply at all	= 3
No anser/D.K.	= 0	No answer/D.K.	= 0

Meaning of score:

0 - 27	= No/small impact on life
28 - 39	= Moderate impact on life
40 - 52	= Large impact on life
53 - 84	= Very large impact on life

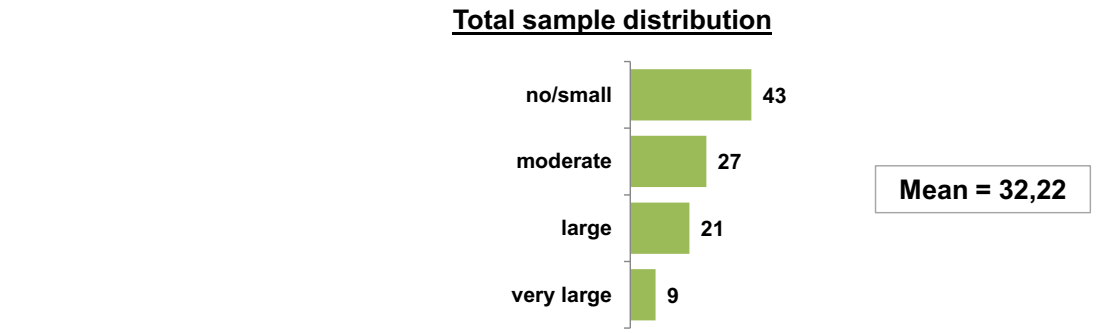
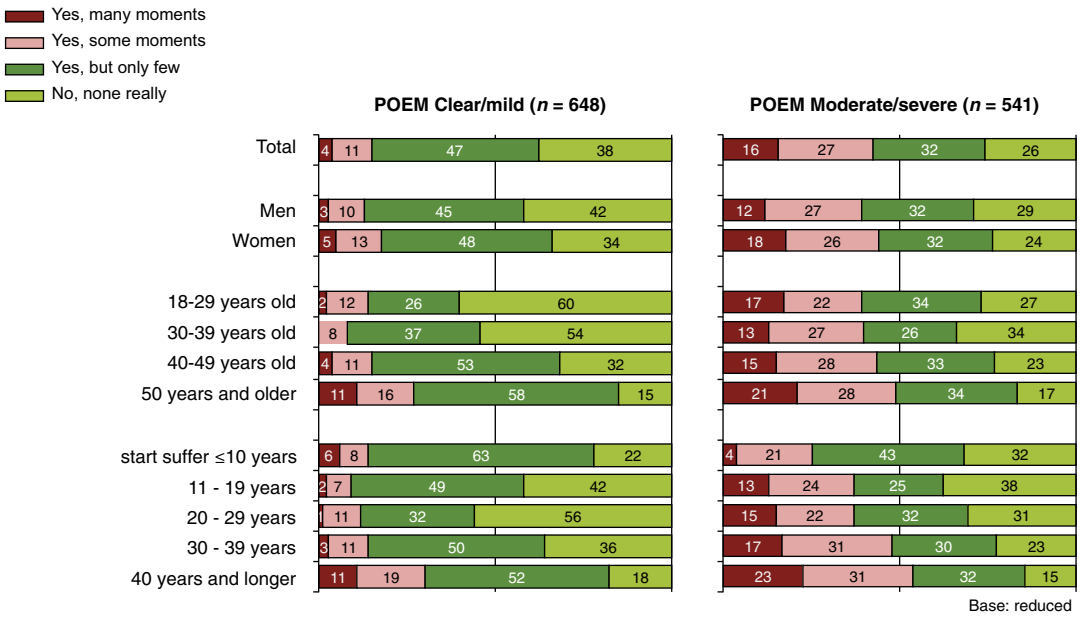


Figure 3 AESEC (Atopic Eczema Score of Emotional Consequences) in adult patients with AE. 57% showed increased emotional burden (from 43). In the figure the distribution of different severity grades is given as % of total (n = 1189).



Q 22. When thinking about your life with atopic eczema, have there been moments when the disease compromised your ability to face life?

Figure 4 Ability to face life in patients with mild and severe atopic eczema [assessed with Patient-Oriented Eczema Measure (POEM)].

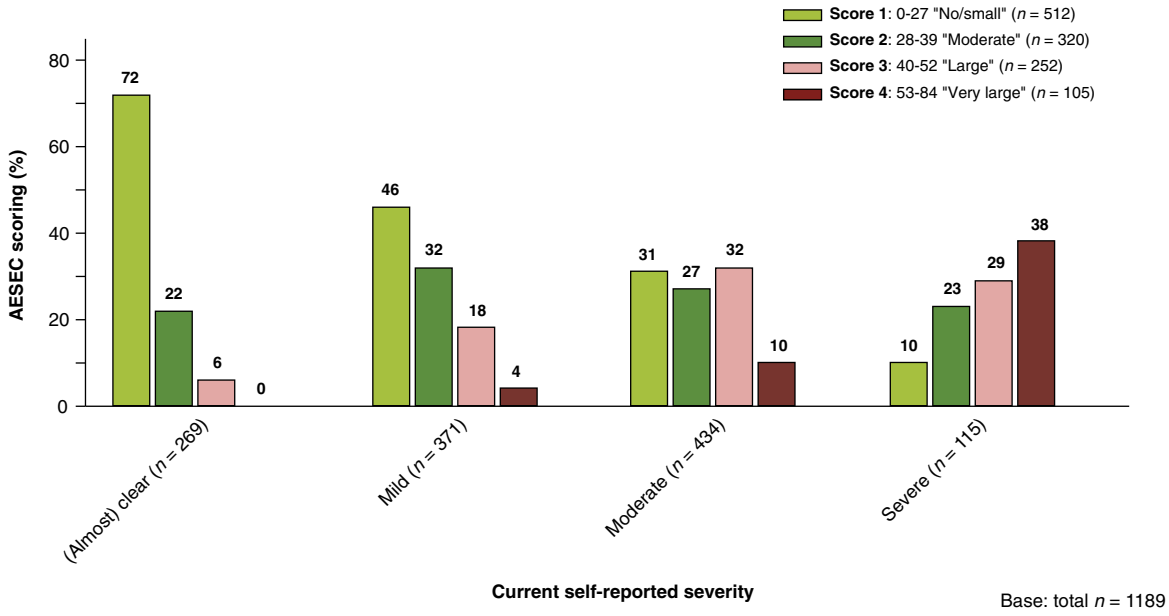


Figure 5 Atopic Eczema Score of Emotional Consequences (AESEC) correlation with self-assessment.

Patients' wishes and postulates

At the end of the interview, an open question was asked: 'What can you tell us about living with severe eczema that the general public and politicians need to know? What message to you have?' Patients answered expressing their most important ideas, and wishes are summarized in Table 2.

Table 2 Wishes of patients in the last open question of the survey

Wishes of patients	%
Better acceptance, understanding in general	22
Better financial support also from insurances	19
More research/studies/funds	18
Emotional, psychological burden recognized	18
Better education of public/increased awareness/attention	18
Avoid discrimination/not be regarded as disgusting	14
Better understanding from medical site/be taken seriously	8
New drugs, effective drugs	8
Consider holistic approach/not only symptom treatment	6
Physical burden	6
More support in general/also morally	5
More alternative medicine/natural remedies and cures	4
Better support of environment protection/labelling of groceries	4

Discussion

This large study performed in nine European countries showed that adult patients with atopic eczema, in spite of actual and 'adequate' treatment, are suffering to an extent which does not seem acceptable for today's standards. The study gives information on a large number and variety of patients suffering from atopic eczema in different European countries and with different severities of the skin lesions. It clearly shows a high degree of individual suffering and burden of disease with regard to everyday life and psychological and emotional well-being. Furthermore, considerable economic costs also represent a burden to the patient when he has to pay quite a lot out of pocket which will not be reimbursed by insurances or society.[44] The degrees of suffering were found to be correlated to the severity of actual symptoms but also to the history of their eczema.

In spite of all these obvious facts, atopic eczema is often not taken seriously by many physicians, health officials and society.[1,2] Although the mortality and lethality is low – except for patients who committed suicide because of the intractable condition[45] – atopic eczema can ruin lives by impairing the quality of life and preventing normal development and fulfilling of life achievements.[27,28] The aspect of quality of life has been brought into dermatology not so long ago[38] and makes a major issue in the dynamics of skin diseases in general and atopic eczema in particular.[46,47] However, the general population as well as healthcare professionals are not yet aware of the impairment in quality of life and the massive suffering in everyday life of patients affected by atopic eczema.[48] These facts need to be added not only to the curricula of medical schools but especially to information provided for the interested public in favour of a general acceptance of atopic eczema

as potentially severe disease. This real burden comprises not only dysaesthesias with itch and pain sensations but also disfigurement, stigmatization, social isolation, restrictions in occupation as well as sport and leisure activities, problems in relationships with sexuality and finally direct and indirect financial costs some to be paid out of pocket by the patient himself.

In the following, the results of the various measurements will be discussed in detail:

In the HADS-D Score, there was only 3% who could be regarded as 'depressive'; this is an important finding in that the impairment in quality of life and the remarkable individual suffering is not a 'psychiatric' or a 'mental health' condition. It reflects the influence of the somatic disease 'eczema' upon psychological and emotional feelings. Atopic eczema is a classical 'psycho-somatic' disease, whereby one always should have in mind that this is not a one-way street: psycho-somatic and somato-psychic aspects go hand in hand in the clinical course of severe atopic eczema.[49]

In a study by Dalgard *et al.*, depression was found in 10% of patients.[50] In explaining the difference to our data, one reason might be that Dalgard *et al.* only studied outpatients with current skin disease without reporting about the severity. With regard to DLQI and POEM, our study participants seemed to suffer from more severe forms of atopic eczema than participants of other studies in the United States.[25]

One limitation of our study may be the fact that patients were recruited from nine different European countries and interviews were done in different languages leading to a possible interviewer, translation or cultural bias. The selection of participants cannot be regarded as representative for a population; that is why we resisted the temptation to compare results in-between various European countries. Occasional differences may be further analysed in the future.

Furthermore, a selection bias may be seen in the fact that 85% of the participants reported to have higher education. This high percentage is not representative for the total distribution in a population, although there is some evidence that 'atopics' may be more 'intelligent' or more 'sensitive' than non-atopic individuals.[1,2]

Selection of patients was done by experienced physicians on the basis of actual clinical disease and reflecting on the clinical course of atopic eczema over the life of the patients. Physicians tried to motivate more severely affected patients which was defined not so much by disease or symptom scores, but rather by the overall clinical conditions and the fact that they could not be treated satisfactorily by topical treatment alone but there was a need of a systemic immunomodulatory therapy with, for example, cyclosporine, methotrexate, mycophenolate, azathioprine or UV therapy. Since patients were not actually examined during the interview, the subjective assessment was done by POEM, a rather subjective measure compared to PO-SCORAD which would have needed some training for the patients.[7]

With regard to comorbidities, our patients were relatively healthy. In subanalyses, one could see that the answers to the skin-specific or eczema-specific questions were not influenced by simultaneously underlying other diseases.

The fact that almost 70% of our patients – in spite of being selected as 'severe cases needing systemic immunomodulatory therapy' – reported that they were 'satisfied' with the current treatment shows how rational, realistic and also modest these patients are: they feel 'adequately treated' when the doctor takes care and uses topical or systemic therapy although the direct effect of the treatment upon the manifold symptoms is by no means satisfactory.

Conclusions

In spite of adequate normal treatment including systemic immunosuppression, 45% of patients with atopic eczema still have moderate to severe eczema skin lesions. Fifty-five percent have a moderate to extremely large impairment in quality of life. An equal amount is suffering individually from emotional consequences affecting their life, their intimacy, their social contacts and their occupational, sport and leisure activities. Of all patients suffering from actual severe atopic eczema, 88% stated that this condition compromised their ability to face life. It is concluded that too many adult patients with moderate to severe form of atopic eczema in Europe are suffering considerably and more than acceptable.

There is a silver streak of hope on the horizon with the appearance of new targeted therapies with biologics such as monoclonal antibodies against relevant cytokines or receptors, for example the interleukin 4 receptor (dupilumab), interleukin 5 (mepolizumab), interleukin 13 (tralokinumab), interleukin 31 (nemolizumab) as well as new kinase inhibitors and others.[51–59] Finally, there is hope for new effective treatments for the severely affected patients with atopic eczema in the future.

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