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ARTICLE



Disease burden and treatment history among adults with atopic dermatitis receiving systemic therapy: baseline characteristics of participants on the EUROSTAD prospective observational study

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ABSTRACT

Background: Insights into the real-world treatment paradigm and long-term burden of atopic dermatitis (AD) are needed to inform clinical and health policy decisions.

Methods: The prospective, observational EUROSTAD study enrolled adults with moderate-to-severe AD starting or switching systemic therapy (51 sites in 10 European countries). We report the baseline characteristics, treatment patterns, and outcomes of these patients using descriptive statistics.

Results: A 12-month enrollment period of EUROSTAD was completed and 308 patients were enrolled: average age 37 years, AD duration 25 years, 43% were female. Most patients reported use of systemic therapy (93%) and ≥ 1 atopic comorbidity (82%). Mean [standard deviation] disease severity/burden measures were high: Investigator's Global Assessment (3.1 [0.8]), Eczema Area and Severity Index (16.2 [10.9]), Peak Pruritus Numerical Rating Scale (5.5 [2.5]), sleep impairment Visual Analog Scale (49.8 [31.6]) scores, and time lost from work (4.1 [13.7] days/year) or usual activities (16.8 [38.7] days/year). Most patients showed borderline or clinical levels of anxiety (59%) and/or depression (63%) using the Hospital Anxiety and Depression Scale.

Conclusions: Adults with moderate-to-severe AD starting/switching systemic treatment enrolled in EUROSTAD have a high burden of longstanding disease despite continuous use of topical drugs, emollients, and systemic therapies.

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Atopic dermatitis; systemic therapy; patient-reported outcomes; quality of life

Introduction


Atopic dermatitis (AD) is a chronic, systemic, type 2 inflammatory skin disease primarily characterized by eczema, intense, persistent pruritus, and atopic and non-atopic comorbidities such as anxiety and depression (1–3). The pathogenesis of AD involves immunological dysregulation and skin barrier dysfunction (4–6), including T-cell expansion and increased expression of the T helper type 2 cell cytokines interleukin (IL)-4 and IL-13 (7–10), possibly in part by the activation of type 2 innate lymphoid cells in the presence of low E-cadherin expression (11).

The prevalence of AD in adults ranges from 2% to 7% worldwide, with the highest rates in Europe (4%) and the USA

(5%–7%) (12,13). Clinical presentation is marked by cutaneous inflammation and intense pruritus often associated with chronic sleep disturbance and profound effects on daily functioning, quality of life (QoL), social interactions and psycho-social health (14–19). AD onset most often occurs during early childhood and remains a long-term condition for most patients (20,21), bearing substantial burden and risk of comorbid type 2 inflammatory diseases such as asthma and allergic rhinitis (22).

Patients with moderate-to-severe AD often have an inadequate response to topical treatments or are unable to taper to doses of topical corticosteroids or topical calcineurin inhibitors suitable for long-term use, and may receive long-term treatment with systemic therapy, though systemic treatment options have been historically

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limited (23,24). Long-term, real-world outcomes regarding the effectiveness and safety of systemic therapy for adults with AD have not been well characterized, thus showing a need to better understand the clinical course and outcomes of patients as well as the real-world treatment patterns related to AD management with systemic therapy. This paucity of data led us to design the European Prospective Observational Study in Patients Eligible for Systemic Therapy for Atopic Dermatitis (EUROSTAD), assessing real-world treatment practice patterns and patient outcomes related to the treatment of AD with systemic therapy in Europe. In the current manuscript we report the baseline demographic and clinical characteristics of patients participating in EUROSTAD, including medical and treatment history, disease severity, patient-reported outcomes (PROs), and healthcare resource utilization, in order to characterize the disease burden of patients with AD requiring systemic therapy.

Methods

EUROSTAD is an ongoing prospective observational study of patients treated for moderate-to-severe AD in Europe. The primary objectives of the EUROSTAD study are to characterize the demographics and medical histories of patients with AD who have received systemic therapy (excluding systemic antimicrobials or antihistamines) and to describe the overall systemic AD therapy paradigm and landscape. Secondary objectives include assessment of disease activity, symptoms, and the QoL of patients who have received systemic therapy for AD, and the long-term real-world effectiveness and safety of systemic AD therapy.

Design and participants

EUROSTAD was designed to include approximately 500 patients across 51 sites in 10 European countries. To ensure that a sufficient number of patients were recruited, patients were continuously enrolled over a 12-month period, with the patients' enrollment visit being considered the baseline. This was to be followed by a 60-month active participation period that includes follow-up visits every 3 or 4 months, quarterly or weekly collection of PROs for the first 18 months and then monthly or semiannually thereafter, and additional visits as needed to manage AD symptoms or treatment side effects.

The enrollment phase of the EUROSTAD study has been completed. Eligible participants were adults aged ≥ 18 years with AD who were eligible to receive systemic therapy such as methotrexate, mycophenolate, cyclosporine A, azathioprine, or systemic corticosteroids for a duration ≥ 1 month. Patients must have initiated a new systemic AD therapy or switched to a different systemic AD therapy on Day 1 or within 30 days prior to enrollment. Patients could not be clinical trial participants for AD treatments or have received investigational systemic AD therapy 6 months prior to the screening visit and could not have any skin comorbidities that would interfere with EUROSTAD study assessments. Eligible participants had to provide informed consent and be willing to participate in regular follow-up visits and to respond to requests for long-term information within the required timeframe.

Study outcomes

The main outcomes of interest focused on the clinical, humanistic, and economic burden of AD as well as patterns and impact

of systemic AD treatment. Primary outcomes included patient demographic and clinical characteristics, medical and treatment history (reported *via* a case record form), systemic AD treatment patterns, PROs related to AD disease activity and treatment, and indirect, costs including healthcare resource utilization (HRU) and impact on work productivity and activities of daily living. Systemic AD treatment use was captured by the number of systemic therapies received. Clinical and PROs related to AD severity and symptoms were captured using the Investigator's Global Assessment (IGA), the Eczema Area and Severity Index (EASI), the Patient-Oriented Eczema Measure (POEM), the Peak Pruritus Numerical Rating Scale (NRS), the Hospital Anxiety and Depression Scale (HADS), and the 100-mm Visual Analog Scale for sleep quality (VAS sleep).

With scores ranging from 0 to 4, the modified IGA scale used for the EUROSTAD study assesses overall disease severity at a given timepoint on a 5-point severity scale ranging from clear (No inflammatory signs of AD) to severe disease (Severe erythema and severe papulation/infiltration) (25). EASI assesses disease extent in 4 body regions (head and neck, torso, arms, and legs), evaluating severity of clinical signs (erythema, induration/papulation, excoriation, and lichenification) on a 4-point scale and takes into consideration the affected body surface area. EASI scores range from 0 to 72, with higher scores indicating more severe disease (26). POEM assesses the frequency of 7 AD symptoms (itching, soreness or pain; redness of the skin, bleeding, weeping or oozing of the skin; dryness or roughness of the skin; flaking of the skin; cracking of the skin; tightness of the skin; and impact of AD on sleep on a scale of 0–28) (27). Peak Pruritus NRS measures the intensity of worst itch in the previous 24 h on a scale of 0–10; higher scores indicate more severe pruritus (28,29).

Overall QoL was measured using the 5-dimension, 3-level EuroQol questionnaire (EQ-5D-3L) and the Dermatology Life Quality Index (DLQI). The EQ-5D is a standardized instrument for measuring QoL, with 1 question for each of 5 dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression (30). The DLQI includes 10 questions about the effect of AD on patients' QoL during the previous week, with ratings on a scale of 0–3 (31).

Atopic comorbidities were captured using the 5-item Asthma Control Questionnaire (ACQ-5) (32,33), the Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) (34), the global score ranges from 0 to 6 for both. The HADS and the 100-mm VAS sleep were used to measure QoL. The HADS assesses symptoms of anxiety and depression with 7 questions for each on a 0–3 scale (35). The following severity bands were used to categorize VAS sleep impairment: none or mild impairment (0 to <40 mm), moderate (40 to <70 mm), severe (70 to <90 mm), and very severe (≥ 90) (36,37). HRU in the past 12 months was measured by the number of healthcare provider office visits, emergency department visits, hospitalizations, and monthly medication costs to the patient (EUR). Impact on work productivity and activities of daily living were assessed according to time lost from work and days off from usual activities, related or unrelated to AD flares, in the 12 months prior to enrollment.

Statistical analysis

The Enrollment and Safety populations included patients who completed the Enrollment Visit (Visit 1). Demographic and clinical characteristics were summarized using descriptive statistics and measures of central tendency. No imputation of missing data was performed. All statistical analyses were performed using SAS version 9.2 or higher (SAS Institute, Cary, NC, USA).

Table 1. Baseline demographics and clinical characteristics.

Characteristic	Patients (N = 308)
Age, years	37.2 (13.8)
Mean (SD)	36 (18–81)
Median (range)	
Sex, female, n (%)	133 (43.2)
Mean (SD)	
Body mass index, kg/m ²	24.7 (4.9)
Mean (SD)	24.3 (15.6–61.5)
Median (range)	
Duration of AD, years	
Mean (SD)	25.4 (15.6)
Median (range)	24.5 (0–72)
Age at AD onset, years	
Mean (SD)	11.8 (16.8)
Median (range)	3.0 (0–70)
Country, n (%)	308 (100)
Belgium	14 (5)
Czech Republic	12 (4)
Denmark	21 (7)
France	50 (16)
Greece	25 (8)
Italy	93 (30)
The Netherlands	38 (12)
Spain	17 (6)
Sweden	6 (2)
United Kingdom	32 (10)

AD: atopic dermatitis; SD: standard deviation.

EUROSTAD is being conducted in accordance with the principles defined by the 18th World Medical Association General Assembly Declaration of Helsinki and all subsequent amendments. The EUROSTAD protocol was reviewed and approved by institutional review boards before patient recruitment. All patients provided written informed consent before any EUROSTAD procedures began.

Results

Patients

During the planned enrollment period 360 patients were able to be screened, of whom 308 (86%) were eligible and enrolled in EUROSTAD. Among the reasons for ineligibility, the most frequent were patient refusal to participate in the EUROSTAD study (28%), patient refusal of systemic therapy (12%), and other (51%; further detail not provided).

Demographic and clinical characteristics

The mean age of EUROSTAD participants was 37 years; 43% were female (Table 1). At baseline, patients reported having AD for an average of 25 years, with a median age of onset of 3 years, and the majority (82%) reported ≥ 1 atopic comorbidity, suggesting a longstanding disease burden throughout most of their lives. Asthma, allergic rhinitis (AR), and allergic conjunctivitis (AC) were the most common atopic comorbidities reported at baseline and were concurrent with other atopic conditions to varying degrees (Figure 1; Supplementary Table S1).

Baseline use of systemic AD therapies

Nearly all patients (92.9%) were either on or just started a systemic AD therapy at baseline. Among those patients, 55% started systemic AD therapy prior to EUROSTAD study commencement, and 50% started a systemic AD therapy on

Day 1 (5% of whom had been on a different systemic therapy prior to EUROSTAD study start). Participants reported an average of 21 years between AD onset and first use of systemic therapy (Table 2). The most frequent reason for starting a systemic treatment was lack of efficacy with previous therapy (88.4%), though most patients (81.8%) were still using a topical drug or emollient. Cyclosporine was the most frequently used systemic therapy (39.2%), followed by methotrexate (23.1%), and dupilumab (19.6%).

Clinical and patient-reported burden of AD

Substantial disease severity was evident among patients enrolled in EUROSTAD based on the IGA (mean 3.1, standard deviation [SD] 0.8) and EASI (mean 16.2, SD 10.9; Table 3), despite the use of systemic treatments by most patients. The distribution of IGA scores was generally similar across systemic therapy groups. Mean EASI scores appeared to vary between systemic therapy groups, ranging from 14.9 to 19.2, though group-wise comparisons were not performed. The burden of the most common atopic comorbidities, asthma (53.6%) and AR (63.3%) (Supplementary Table S1), was expectedly high according to the ACQ-5 and MiniRQLQ (Supplementary Figure S1).

Further clinical and humanistic burden of AD was notable from patient-reported symptoms and QoL measures (Table 4; Figure 2). 'Peak itch' according to the Peak Pruritus NRS was high, with mean and median scores of 5.5 and 6.0 out of a maximum of 10 (Table 4, Figure 2(d)). More than half of patients (62%) reported sleep impairment (≥ 40 mm on sleep VAS; Figure 2(b)); sleep VAS scores increased with higher Peak Pruritus NRS scores, suggesting a relationship between peak itch and sleep impairment ($R = 0.40$, $p < .0001$; Supplementary Figure S2). Anxiety and depression were common among patients with AD based on the HADS, where 59% and 63% of patients were scored with 'borderline' or 'abnormal' levels of anxiety and depression, respectively (Table 4, Figure 2(c)). More than half of patients also reported 'very' or 'extremely' large impairment of overall health-related QoL (56.3%) according to the DLQI (Figure 2(a)); similarly, patients reported the most problems with pain/discomfort and anxiety/depression on the EQ-5D-3L (Supplementary Figure S3). On the POEM, 87% of patients reported that their AD had 'moderate', 'severe', or 'very severe' effects (Figure 2(e)).

Economic burden of AD

The indirect cost of time lost from work or usual activities was the greatest economic burden reported by EUROSTAD participants at baseline, with AD flares contributing to a greater burden. Among participants, 290 (out of 308 total) provided their employment status, with 57% employed full time and 11% employed part time (data not shown). Among patients currently employed, patients took an average of 4.1 (SD 13.7) sick leave days per year due to their AD, with some missing as many as 30 days for AD but not specifically for flares, and as many as 140 days due to AD flares specifically. Nearly one-third of patients reported that their AD hindered their educational attainment (31%) and/or their professional career decisions (27%) 'a lot' or 'very much'. In the past 12 months, on average, patients lost 16.8 (SD 38.7) days for non-work activities due to their AD (11.4 days due to AD flares, and 5.5 days due to AD but not related to flares; Table 5). Overall, there were few

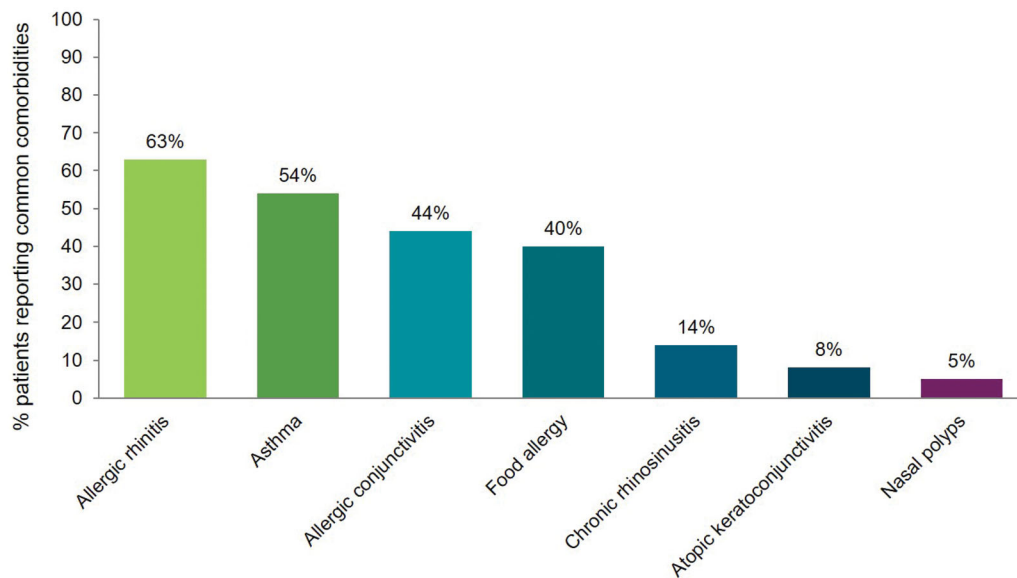


Figure 1. Prevalence of atopic comorbidities among EUROSTAD participants for all reported atopic/allergic comorbidities.

Table 2. Baseline AD treatment history.

Characteristic	Patients (N = 308)
Systemic AD therapy (<i>n</i> ≥ 5% patients), <i>n</i> (%)	286 (92.9)
Cyclosporine	112 (39.2)
Methotrexate	66 (23.1)
Dupilumab	56 (19.6)
Corticosteroids ^a	51 (17.8)
Azathioprine	16 (5.6)
Topical drugs and emollients (<i>n</i> ≥ 5% patients), <i>n</i> (%)	252 (81.8)
Topical corticosteroids	203 (65.9)
Emollients	121 (39.3)
Topical calcineurin inhibitors	74 (24.0)
Ultraviolet light therapy, <i>n</i> (%)	5 (1.6)
Time from AD onset to first systemic therapy, years	
Mean (SD)	21.1 (15.1)
Median (range)	20.0 (0–72)
Reasons for first systemic AD therapy initiation, <i>n</i> (%) ^b	302 (98)
Lack of efficacy with previous therapy	267 (88.4)
Systemic treatment used for induction	26 (9.6)
Patient unable to taper topical corticosteroids	19 (6.3)
High impact on work/daily activities	16 (5.2)
Side effects with previous therapy	13 (4.3)
Low compliance with previous therapy	6 (2.0)

AD: atopic dermatitis; SD: standard deviation. Patients were prescribed systemic therapy for AD within 30 days prior to enrollment or during the enrollment visit, therefore some patients were not on the systemic treatment at the baseline.

^aCorticosteroids include betamethasone, methylprednisolone, triamcinolone.

^bMultiple reasons for initiating systemic therapy were permitted.

emergency room visits or hospital admissions due to AD. However, patients had an average of 8.8 (SD 9.7) physician office visits for AD in the past year, with 5.7 due to AD flares and 3.1 for AD-related visits that were not specifically attributed to management of a flare (Table 5).

Discussion

Adults with moderate-to-severe AD enrolled in the EUROSTAD prospective observational study had a high burden of long-standing disease with a history of inadequate response to traditional therapeutic options. Participants had not been using systemic AD therapies for a long time relative to their disease duration, considering the mean age of onset and the time from AD onset to the first

use of a systemic therapy for AD. This may suggest a general under-treatment of adults with AD, an area which may benefit from education of healthcare professionals dealing with AD in providing optimal treatment pathways and more proactive management strategies that evaluate clinical- and patient-reported outcomes and account for the recent addition of new systemic therapy options. Many participants experienced the added burden of comorbid type-2 inflammatory diseases, with 54% of participants having asthma and 62% experiencing allergic rhinitis at enrollment. This reflects the comorbidity burden of patients with AD requiring a multidisciplinary approach for the treatment of AD.

Despite receiving systemic treatments (participants must have started or switched to another systemic treatment within 30 days prior to enrollment, or at Day 1), most of the EUROSTAD participants had moderate-to-severe AD based on their baseline EASI and IGA scores (25,38). One reason for patients switching or starting a new systemic therapy for AD may be the lack of availability and/or experience with systemic treatment options, which may be related to the benefit-risk profiles of systemic therapies that have been used to treat AD but were not developed for AD specifically.

Patients visited their physician approximately every other month for AD flares, on average, but did not generally require emergency or hospital care. Time lost from work due to AD flares was moderate, but patients reported losing nearly 2 weeks per year from non-work-related activities due to flares. While there is not much reported about the effects of AD on lost work productivity, the 4.1 days/year of work lost reported here aligns with other studies that have reported a loss of 2.6–11.6 days/year (39–42). Clinical levels of anxiety and depression were common, as was sleep impairment, which appeared to be related to the severity of pruritus. These findings were consistent with patient-reported impairment of overall QoL.

Regarding the frequency of measurement of outcome measures, the TREATment of ATopic eczema (TREAT) Registry Taskforce published a consensus on how and when to measure their previously reported domain items for research registries for patients with atopic eczema. TREAT recommended an initial follow-up frequency of 4 weeks following treatment initiation,

Table 3. Baseline disease activity overall and by most common systemic AD treatment use.

	Overall N = 308	Cyclosporine (n = 112)	Methotrexate (n = 66)	Corticosteroids ^a (n = 51)	Dupilumab (n = 56)	Azathioprine (n = 16)
EASI score						
Mean (SD)	16.2 (10.9)	16.8 (11.4)	16.2 (11.9)	15.8 (9.8)	14.9 (9.6)	19.2 (10.1)
Median (range)	14.6 (0–55.3)	15.0 (0–55.3)	15.0 (0–52.8)	14.8 (1.2–40.5)	12.6 (0.3–38.3)	19.3 (2.7–35.7)
IGA score						
Mean (SD)	3.1 (0.8)	3.0 (0.8)	3.2 (0.9)	3.2 (0.6)	3.0 (0.9)	3.1 (0.5)
Median (range)	3.0 (0–4.0)	3.0 (0–4.0)	3.0 (0–4.0)	3.0 (2.0–4.0)	3.0 (0–4.0)	3.0 (2.0–4.0)
IGA score, n (%)						
0 – Clear	2 (0.8)	1 (1.0)	1 (1.8)	0	1 (1.8)	0
1 – Almost clear	8 (3.0)	2 (2.1)	3 (5.5)	0	2 (3.6)	0
2 – Mild	29 (10.9)	15 (15.6)	1 (1.8)	4 (9.3)	10 (18.2)	1 (6.3)
3 – Moderate	143 (53.8)	55 (57.3)	28 (50.9)	26 (60.5)	24 (43.6)	12 (75.0)
4 – Severe	84 (31.6)	23 (24.0)	22 (40.0)	13 (30.2)	18 (32.7)	3 (18.8)

AD: atopic dermatitis; EASI: Eczema Area and Severity Index; IGA: Investigator's Global Assessment; SD: standard deviation. Patients were prescribed systemic therapy for AD within 30 days prior to enrollment, or during the enrollment visit.

^aCorticosteroids include betamethasone, methylprednisolone, and triamcinolone (systemic).

Table 4. Baseline AD symptoms and quality of life.

	Overall (N = 308)
DLQI score (scale, 0–30)	n = 272
Mean (SD)	11.8 (6.9)
Median (range)	11 (0–29)
POEM score (scale, 0–28)	n = 279
Mean (SD)	17.0 (7.2)
Median (range)	18 (0–28)
POEM score categories, n (%)	n = 279
Clear or almost clear	6 (2)
Mild	30 (11)
Moderate	84 (30)
Severe	112 (40)
Very severe	47 (17)
Peak Pruritus NRS score (scale, 0–10)	n = 290
Mean (SD)	5.5 (2.5)
Median (range)	6 (0–10)
HADS anxiety score (scale, 0–21)	n = 271
Mean (SD)	8.3 (3.7)
Median (range)	8 (0–19)
Score categories, n (%)	
Normal (0–7)	113 (41)
Borderline abnormal (8–10)	92 (33)
Abnormal (11–21)	72 (26)
HADS depression score (scale, 0–21)	n = 271
Mean (SD)	8.6 (4.7)
Median (range)	10 (0–21)
Score categories, n (%)	
Normal (0–7)	103 (37)
Borderline abnormal (8–10)	50 (18)
Abnormal (11–21)	124 (45)
VAS sleep score (scale, 0–100)	n = 272
Mean (SD)	49.8 (31.6)
Median (range)	52.5 (0–100)
EQ-5D-3L VAS score (scale, 0–100)	n = 270
Mean (SD)	65.9 (21.4)
Median (range)	70 (0–100)

AD: atopic dermatitis; DLQI: Dermatology Life Quality Index; EQ-5D-3L: 5-dimension, 3-level EuroQoL questionnaire; HADS: Hospital Anxiety and Depression Scale; NRS: Numerical Rating Scale; POEM: Patient-Oriented Eczema Measure; SD: standard deviation; VAS: Visual Analog Scale.

then every 3 months when on treatment and 6 months when off treatment. In EUROSTAD, which started before the TREAT consensus was published, Peak Pruritus NRS were collected weekly, however, other measures were collected every 3 months, without the initial 4-weekly follow-ups (43).

The demographic and clinical characteristics of EUROSTAD participants were generally aligned with those in BIODAY,

another prospective multicenter registry (44,45). Compared with BIODAY, EUROSTAD participants had slightly lower baseline EASI scores. 18% of EUROSTAD participants were already taking dupilumab at enrollment, whereas use of cyclosporine and azathioprine was much higher in BIODAY participants (44,45).

The high clinical and patient-reported burden of AD in this population despite prevalent use of topical drugs/emollients and systemic therapies is consistent with recent studies of the burden of moderate-to-severe AD in adults (7,19,46,47). Eckert et al. reported a higher prevalence of anxiety, depression, sleep impairment, QoL, and work productivity among European adults with AD compared with their peers without AD, particularly among those with inadequately controlled disease (17). Girolomoni et al. reported similarly high clinical and humanistic burden of moderate-to-severe AD on adults in Europe and Canada, particularly for those with inadequate response to historical systemic immunosuppressive therapies (such as cyclosporine), due to lack of efficacy, intolerance, or contraindication (46).

Zuberbier et al. projected a high negative impact of allergic diseases as a whole, including those of the skin and airway, on work productivity, and associated indirect and direct costs to both patients and employers in Europe (47). The authors modeled the annual cost of absenteeism to be EUR 528 per patient/employee per year, yielding total annual costs of EUR 55–151 billion in the EU. Citing the unmet treatment needs for allergic conditions where only 10% of patients are optimally controlled, the authors projected potential annual savings of EUR 50–142 billion by managing untreated patients according to guideline-approved therapies. Applying a similar assumption of 3 lost days/year to that observed in EUROSTAD (2.6 days/year; 4.1 days/year among patients currently employed), one may assume a comparable annual cost of absenteeism for patients in the EUROSTAD study. Our findings of persistent, active disease with prevalent comorbidities are also analogous to those of psoriasis patient registries in Europe (48–52).

The observations of patients enrolled in the EUROSTAD study should be considered in light of certain strengths and limitations. EUROSTAD is an ongoing, prospective, real-world research environment capturing disease burden and care patterns. As this report only includes cross-sectional baseline characteristics, PROs, and treatment use, it will be important to observe the longitudinal safety and effectiveness of systemic treatments and

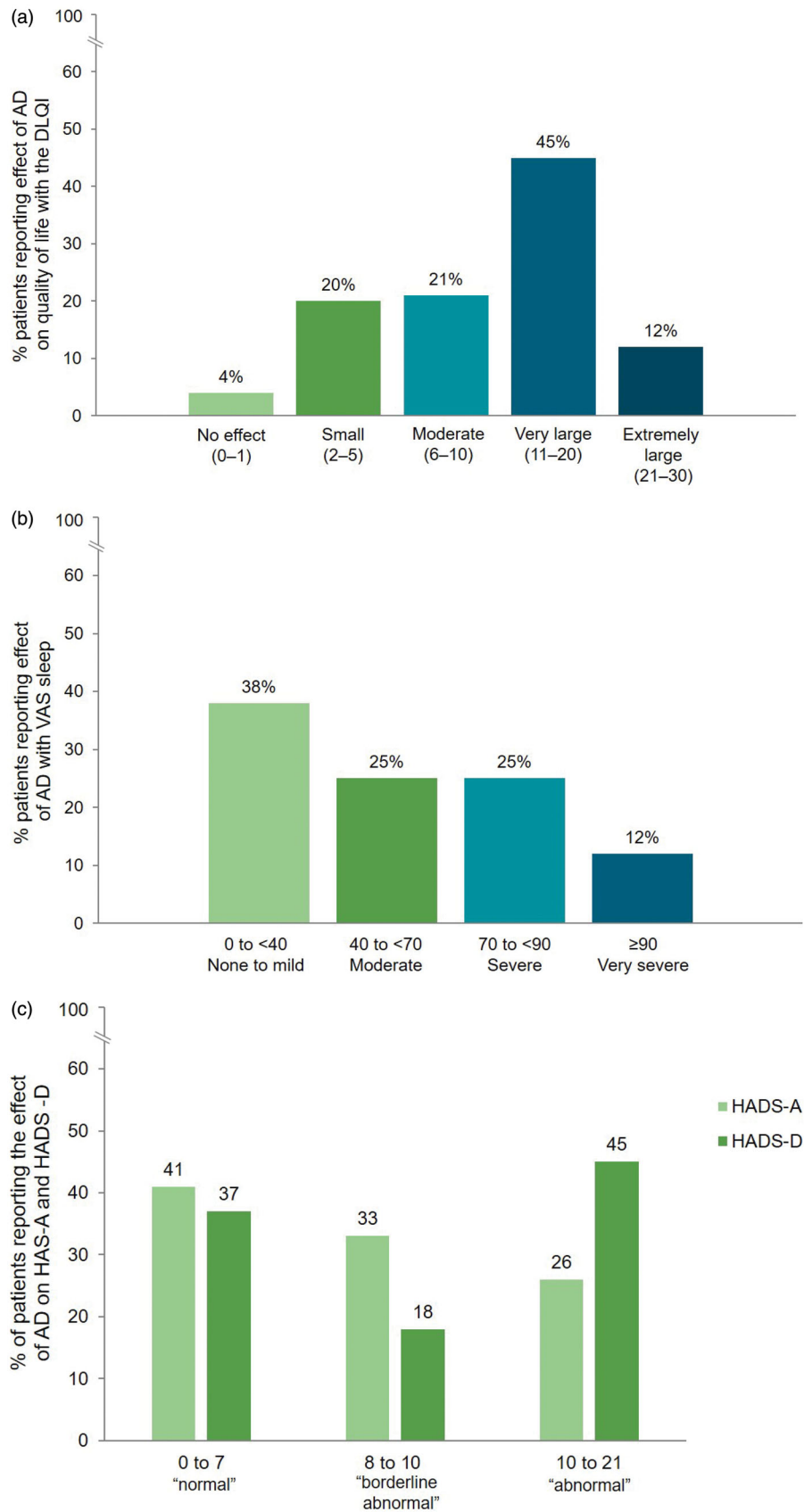


Figure 2. Baseline patient-reported outcomes for (a) DLQI; (b) VAS sleep; (c) HADS-A and HADS-D and (e) POEM. AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; HADS-A, HADS-Anxiety; HADS-D, HADS-Depression; VAS, Visual Analog Scale.



Figure 2. Continued. Baseline patient-reported outcomes for (d) Peak Pruritus NRS; and (e) POEM. AD, atopic dermatitis; NRS, numerical rating scale; POEM, Patient-Oriented Eczema Measure.

subsequent disease activity and outcomes as the EUROSTAD study continues. The generalizability of the findings in EUROSTAD participants to a broader adult population with moderate-to-severe AD may be limited by the requirement to have recent systemic therapy initiation or changes, the low sample sizes available for certain subgroups, and regulatory restrictions in the different countries that may influence the prescription of therapies. Dupilumab was not listed in the systemic treatment inclusion criterion because it was not commercially available when the EUROSTAD study started; however, some patients were prescribed dupilumab after the study started but during the 12-month enrollment period. An additional limitation of the study is that comorbidities were reported by the patients and not confirmed by a physician diagnosis.

The demographics, baseline clinical characteristics, and disease activity of patients enrolled in EUROSTAD reflect a relatively young adult population with a substantial disease burden from long-standing moderate-to-severe AD. A comprehensive impact on various domains of health and life is evident, along with

atopic and non-atopic comorbidities, despite continuous use of topical drugs, emollients, and systemic therapies. Patients reported a notable impact on non-clinical aspects of life, including mental health, sleep, work, and activities of daily living. As more systemic therapies are designed for AD specifically, proactive treatment of this debilitating condition may become more advanced. EUROSTAD will continue to follow European adults with moderate-to-severe AD, including their treatment patterns and outcomes, offering a longitudinal contribution to the understanding of the course of AD and the impact of therapy on real-world patient outcomes.

Disclosure statement

Dr. de Bruin-Weller has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme, and UCB.

Table 5. Baseline AD-related healthcare resource use and indirect costs in the previous 12 months.

	Overall (N = 308)
Direct costs – healthcare resource utilization	
AD-related healthcare provider office visits	n = 287
Total	8.8 (9.7)
Attributed to flares	
Mean (SD)	5.7 (9.3)
Median (range)	4.0 (0–87)
Not attributed to flares	
Mean (SD)	3.1 (4.5)
Median (range)	2.0 (0–31)
AD-related emergency department admissions	n = 308
Total	0.2 (0.7)
Attributed to flares	
Mean (SD)	0.2 (0.6)
Median (range)	0 (0–5)
Not attributed to flares	
Mean (SD)	0 (0.3)
Median (range)	0 (0–3)
AD-related hospitalizations	n = 308
Total	0.1 (0.5)
Attributed to flares	
Mean (SD)	0.1 (0.5)
Median (range)	0 (0–4)
Not attributed to flares	
Mean (SD)	0 (0.2)
Median (range)	0 (0–3)
Monthly medication cost (EUR) to patient, n (%) [*]	n = 288
0–10	66 (22.9)
>10–100	166 (57.6)
>100–200	48 (16.7)
>200	8 (2.8)
Indirect costs – productivity	
AD-related sick leave, mean (SD), days	n = 290
Total among patients currently employed	4.1 (13.7)
Total, all patients	3.2 (11.8)
Attributed to flares	n = 290
Mean (SD)	2.6 (11.1)
Median (range)	0 (0–140)
Not attributed to flares	n = 289
Mean (SD)	0.6 (3.6)
Median (range)	0 (0–30)
AD-related days off from usual activities	n = 288
Total	16.8 (38.7)
Attributed to flares	n = 286
Mean (SD)	11.4 (25.9)
Median (range)	0 (0–104)
Not attributed to flares	n = 287
Mean (SD)	5.5 (18.8)
Median (range)	0 (0–99)

Healthcare resource utilization and indirect costs were based on reported experience in the 12 months prior to enrollment. AD: atopic dermatitis; SD: standard deviation.

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Dr. Ferrucci is speaker and consultant for Drex Pharma, Menarini, Novartis, Pierre Fabre Laboratories, Sanofi Genzyme, and SVR Pharma; and Principal Investigator for Eli Lilly, Novartis, Regeneron Pharmaceuticals, Inc., and Sanofi Genzyme.

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Drs. Jayawardena and Eckert, are employees of Sanofi and may hold stock and/or stock options in the company.

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Data availability statement

Qualified researchers may request access to study documents (including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan) that support the methods and findings reported in this manuscript. Individual anonymized participant data will be considered for sharing once the product and indication has been approved by major health authorities (e.g. FDA, EMA, PMDA, etc), if there is legal authority to share the data and there is not a reasonable likelihood of participant re-identification. Submit requests to <https://vivli.org/>.

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