ORIGINAL REPORT

Clinical Phenotyping of Atopic Dermatitis Using Combined Global Severity (POEM) and Facial Burden (BoFA): A French Population-based Observational Study

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Atopic dermatitis (AD) is characterized by substantial clinical heterogeneity. Global severity is typically assessed using scores such as the POEM; however, lesion localization – particularly on the face – may generate psychosocial consequences partly independent of overall disease severity. This cross-sectional observational study (VISEABLE) included 1,400 French adults with physician-confirmed AD. Severity was measured using the POEM (Clear/Almost Clear: 0–7 vs Moderate–severe: ≥8) and facial involvement using the BoFA (0–109; threshold=36, population median). Six phenotypes were defined through a 2×3 combination. The POEM and BoFA correlation was moderate (r=0.365; ρ=0.389; *p*<0.001). Phenotype Ph3 (Clear/Almost Clear POEM / Severe facial involvement, *n*=58) exhibited stigmatization scores (PUSH-d=21.93) and life trajectory impact (DLLIM=14.76) not significantly different from Ph4 (Moderate–severe POEM/No facial involvement, *n*=527; *p*>0.25 for all comparisons). In multiple regression analysis restricted to patients with facial involvement, BoFA was the dominant independent predictor of stigmatization (β=11.44, *p*<0.001; partial R^2=46.2 %; overall R^2=0.532), superseding POEM (*p*=0.076, ns; partial R^2=0.6%). Mild eczema with severe facial involvement generates a psychosocial burden comparable to that of moderate-to-severe eczema without facial involvement. Systematic BoFA assessment is essential in all patients with AD.

Keywords atopic dermatitis; phenotyping; facial involvement; BoFA; POEM; stigmatization; psychosocial burden.

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Atopic dermatitis (AD) is a chronic inflammatory disease affecting approximately 5–10% of adults in high-income countries (1, 2). AD shows considerable clinical heterogeneity, both in lesion severity and anatomical distribution. This heterogeneity is associated with major psychosocial consequences, including impaired quality of life, difficulties with professional integration and interpersonal relationships and increased rates of depression and anxiety (3, 4). Severity assessment tools such as the POEM (Patient-Oriented Eczema Measure) provide a global, patient-reported evaluation of disease activity over a 7-day period; however, they do not capture location-specific features. POEM was selected as the global severity measure for this study because it is the recommended patient-reported outcome for AD severity in European clinical guidelines (1), demonstrates superior responsiveness and patient acceptability compared with physician-reported scales in real-world settings (5), and its binary categorization (Clear 0–7/Moderate-severe≥8) provides a clinically interpretable anchor for phenotype definition.

Facial involvement constitutes a specific clinical challenge in AD. The permanent visibility of facial lesions exposes patients to heightened social stigmatization, impaired body image and profound repercussions on social and professional functioning. Several recent studies suggest that facial involvement is an independent predictor of psychosocial burden, beyond overall clinical severity (2, 6). In a large international survey of 13,045 patients with visible dermatoses, Richard et al. (6) reported that approximately 30% considered their condition a handicap in their professional, social and intimate lives, with a disease burden on quality of life twice as high as dermatoses localized to less visible areas. While this figure reflects a heterogeneous population and multiple contributing factors, it underscores the disproportionate burden associated with facial involvement. The development and validation of the BoFA (Burden of Face Affected) questionnaire have provided a specific and sensitive instrument to quantify this facial burden (7).

In parallel, Chovatiya et al. demonstrated in 2021, in a prospective American cohort (*n*=592), that combining pruritus severity with lesional severity enabled the definition of 4 distinct clinical phenotypes. Notably,

they identified a group with severe pruritus but mild lesions (SI-ML) with a burden comparable to the group with severe lesions without intense pruritus (MI-SL) (8). This 2-dimensional phenotyping approach illustrates that neither pruritus nor lesions alone fully predict disease burden – it is their combination that matters.

By transposing this approach to the problem of facial involvement in AD, we hypothesize that combining global severity (POEM) and facial involvement intensity (BoFA) would allow the definition of clinically distinct phenotypes, some of which constitute unrecognized entities with high psychosocial impact. We postulated in particular the existence of a clinical paradox: a patient with mild eczema but severe facial involvement could present a psychosocial burden comparable to that of a patient with moderate-to-severe eczema without facial involvement. Despite prior evidence supporting the importance of facial involvement, no large-scale study has combined a validated global severity measure with a facial-involvement-specific instrument to define and quantitatively characterise distinct psychosocial burden profiles. This gap constitutes the primary rationale for the present study.

The primary objective of this study was to define and characterize AD clinical phenotypes through the POEM×BoFA combination, and to evaluate their respective psychosocial burden in terms of stigmatization (PUSH-d), life trajectory impact (DLLIM/SOL), and mental load (DMLQ). Secondary objectives included identifying the dominant predictors of stigmatization among patients with facial involvement and describing the demographic characteristics of the different phenotypes.

METHODS

Study design and population

This cross-sectional observational study (VISEABLE) was conducted in France among adults (≥18 years) with AD. Diagnosis was established and confirmed by a physician (dermatologist, allergist or general practitioner) and self-reported by participants. Inclusion of diagnoses confirmed by dermatologists, allergists and general practitioners reflects the French care pathway for AD and enhances the generalisability of findings. Recruitment was performed through a panel designed to be representative of the French adult population. Exclusion criteria included inability to complete questionnaires independently and absence of documented medical diagnosis. Electronic informed consent was obtained from all participants. The study protocol was submitted for ethical review in accordance with French regulations and approval from the Ethics Committee (CPP) was obtained.

Assessment instruments

Global AD severity was measured using the POEM (Patient-Oriented Eczema Measure, 0–28; Clear/Almost clear: 0–7; Moderate–severe:≥8) (5, 9). Facial involvement was assessed (n=558) using the BoFA questionnaire (Burden of Face Affected, 0–109), a 20-item self-administered instrument originally developed and validated in systemic sclerosis (7). Although originally validated in systemic sclerosis, the BoFA's 20 items are entirely free of disease-specific content, addressing the functional and psychosocial consequences of visible facial involvement (social interactions, body image, daily activities, self-esteem) irrespective of aetiology. This property enables cross-disease application, as explicitly noted by the instrument developers (7). In the present study, BoFA demonstrated convergent validity with DLQI and POEM scores in the facial involvement subgroup, supporting its construct validity in AD. Items are scored on a 6-point Likert scale; responses of "Sometimes", "Often", "Very often" and "Constantly" are considered positive (impact present), in accordance with the developers' recommendations.

Psychosocial burden was assessed using: the PUSH-d (Perceived Uncertainty in Skin disease – dermatology, perceived stigmatization, 0–68) (10), the DLLIM/SOL (Dermatology Long-Term Life Impact Measure, life trajectory impact) (11), the DMLQ (Dermatological Mental Load Questionnaire, mental load related to AD) (12) and a stress NRS (0–10; 0=no stress, 10=stress completely disrupting daily life). These instruments were selected to address psychosocial dimensions systematically absent from standard AD assessments: PUSH-d specifically measures perceived stigmatization (not captured by DLQI or POEM); DLLIM/SOL captures long-term irreversible life trajectory impact distinct from cross-sectional quality-of-life measures; and DMLQ quantifies the daily cognitive and management burden of living with AD. These instruments are complementary to, not replacements for, standard AD outcomes such as DLQI.

Phenotype definition and statistical analyses

Six phenotypes were defined by combining 2POEM (Clear/Almost clear vsBoFA (Absent / Mild<36 vs Severe≥36). The BoFA threshold of 36 corresponds to the median value observed in the population with facial involvement (n=558). This threshold is exploratory, based on the population median, and has not been externally anchored on clinical criteria. Sensitivity analyses with alternative thresholds (T1=22 and T2=50, corresponding to approximate tertiles of the BoFA distribution in the facial involvement subgroup) are presented in Table SI. The 6-phenotype structure was chosen a priori to capture 3 clinically distinct situations

on the facial involvement axis (absent/mild/severe) that a binary design would conflate, thereby obscuring the paradoxical protective effect of mild facial involvement.

Statistical analyses included Pearson and Spearman correlations between POEM and BoFA, 1-way ANOVAs followed by post-hoc comparisons with Tukey test, 2-tailed *t*-tests for pairwise comparisons, and multiple linear regression analyses to identify predictors of PUSH-d (standardized POEM, standardized BoFA, sex and standardized age). The significance threshold was set at α=0.05 (2-tailed). Analyses were conducted using Python 3.12 (pandas, scipy, statsmodels). Missing data were excluded (complete case analysis).

RESULTS

Population characteristics (N = 1,400)

The population included 62.5% women, with a mean age of 42.7±14.8 years. Facial involvement was reported by 558 patients (39.9%), with a mean BoFA score of 37.3±24.7 in this subgroup. Subgroups of patients with and without facial involvement were comparable in terms of age, sex, POEM severity and stress levels (p>0.10 for all), except for a slight overrepresentation of self-employed workers in the facial involvement subgroup (5.4% vs 2.5%, p=0.008). Baseline characteristics are presented in **Table I**.

The equivalence of global stress NRS between patients with and without facial involvement (6.2±2.4 in both subgroups, p=0.646) reflects the fact that both groups experience high global stress through distinct pathways: pruritus, sleep disruption and treatment burden in non-facial patients; stigmatization, social avoidance and visibility concerns in facial patients. This convergence underlines why multidimensional assessment is needed to differentiate these subgroups.

POEM and BoFA correlation

In the subpopulation with facial involvement (n=558), the correlation between POEM score and BoFA was r=0.365 (Pearson, p<0.001) and ρ=0.389 (Spearman, p<0.001). According to Dancey and Reidy criteria (13), this correlation is classified as moderate – confirming that the 2 axes measure related but non-redundant dimensions, which legitimizes their combination for defining independent phenotypes.

Distribution of the six phenotypes

The dominant phenotype was Ph4 (Moderate/severe POEM/No facial involvement, n=527, 37.6%), followed by Ph1 (Clear/Almost clear POEM/No facial involvement, n=315, 22.5%). Phenotype Ph3 (Clear/Almost clear POEM/Severe facial involvement) was the least frequent (n=58, 4.1%) but represented a clinically unexpected and highly relevant entity (**Fig. 1**).

Table I. Main characteristics according to presence of facial involvement

	Facial involvement		
Variable	YES (n=558)	NO (n=842)	p
Mean age±SD	42.0±14.5	43.2±15.0	0.127 n.s.
Women (%)	63.6%	61.6%	0.488 n.s.
POEM clear/almost clear (%)	35.3%	37.4%	0.457 n.s.
POEM Moderate–severe (%)	64.7%	62.6%	0.457 n.s.
Mean POEM score±SD	11.1±6.4	10.6±6.4	0.148 n.s.
Mean BoFA±SD	37.3±24.7	N/A	—
Mean PUSH-d±SD	16.7±16.6	15.5±16.4	0.174 n.s.
Mean stress NRS±SD	6.2±2.4	6.2±2.4	0.646 n.s.
Specific treatment yes (%)	80.3%	N/A	—
Camouflage yes (%)	40.5%	N/A	—

N/A: not applicable; n.s.: not significant.

Psychosocial burden by phenotype

ANOVAs revealed highly significant differences among the 6 phenotypes across all instruments (PUSH-d: F=79.1, η^2=0.221, p<0.001; DLLIM: F=75.5, η^2=0.213, p<0.001; Stress NRS: F=49.9, η^2=0.143, p<0.001; DMLQ: F=99.4, η^2=0.263, p<0.001). Mean scores are reported in **Fig. 2**. The central finding was the Ph3 ≈ Ph4 paradox: despite clinically mild eczema (POEM Clear/Almost Clear), Ph3 patients exhibited levels of perceived stigmatization, life trajectory impact and mental load not significantly different from Ph4 patients with moderate-to-severe eczema. Only stress NRS differed slightly, with lower stress in Ph3 (6.22 vs 6.75, p=0.040) (**Table II**).

Protective effect of mild facial involvement (Ph2 and Ph5)

A second unexpected finding was observed among patients with mild facial involvement. At both POEM severity levels, these patients reported significantly lower stigmatization scores than those without facial involvement (Ph2<Ph1: PUSH-d 3.89 vs 9.07, p<0.001; Ph5<Ph4: PUSH-d 8.53 vs 19.27, p<0.001). This protective effect was found across all burden instruments (p<0.001 in both POEM strata), except for stress NRS between Ph1 and Ph2 (p=0.826, ns).

Predictors of stigmatization in patients with facial involvement

In multivariable linear regression analyses restricted to patients with facial involvement (n=558), the model explained 53.2% of the variance in PUSH-d (R^2=0.532). BoFA emerged as the dominant independent predictor of stigmatization (β=11.44, t=21.78, p<0.001; partial R^2=46.2%), whereas POEM lost significance when controlling for BoFA (β=0.93, t=1.78, p=0.076; partial R^2=0.6%). Younger age was independently associated with higher stigmatization (β = −1.34, p=0.007), while sex was not (p=0.716). Results are presented in **Table III**.

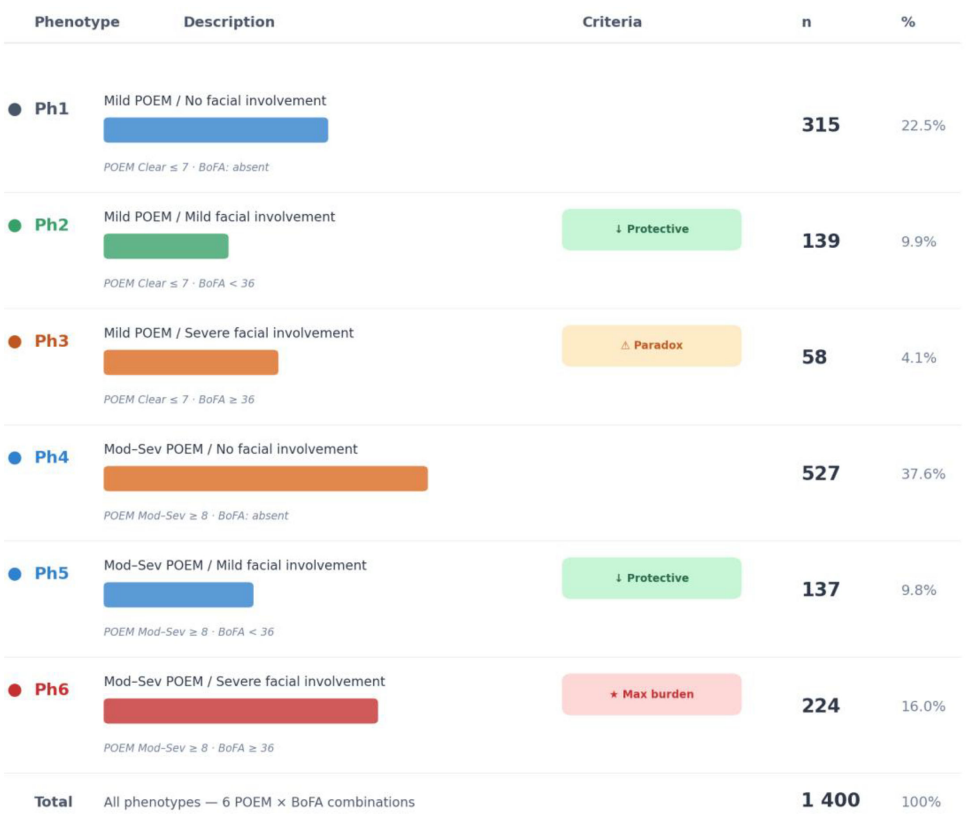

Fig. 1. Distribution of the six clinical phenotypes obtained by crossing global disease severity (POEM) with facial-involvement severity (BoFA) in 1,400 adults with atopic dermatitis. Each phenotype is a row with a horizontal bar whose length is proportional to the number of patients; the phenotypes sum to the full sample. Ph1, clear-to-mild POEM (≤7) with no facial involvement, comprises 315 patients (22.5%). Ph2, POEM ≤7 with mild facial involvement (BoFA <36), comprises 139 patients (9.9%) and is annotated as protective. Ph3, POEM ≤7 with severe facial involvement (BoFA ≥36), is the smallest group at 58 patients (4.1%) and is annotated as the paradox phenotype. Ph4, moderate-to-severe POEM (≥8) with no facial involvement, is the largest group at 527 patients (37.6%). Ph5, POEM ≥8 with mild facial involvement (BoFA <36), comprises 137 patients (9.8%) and is annotated as protective. Ph6, POEM ≥8 with severe facial involvement (BoFA ≥36), comprises 224 patients (16.0%) and is annotated as the maximum-burden phenotype. Total: 1,400 patients (100%).Ph1: Clear POEM / No facial involvement (n=315, 22.5%); Ph2: Clear POEM/Mild facial involvement BoFA<36 (n=139, 9.9%); Ph3: Clear POEM/Severe facial involvement BoFA≥36 (n=58, 4.1%); Ph4: Moderate–severe POEM / No facial involvement (n=527, 37.6%); Ph5: Moderate–severe POEM/Mild facial involvement (n=137, 9.8%); Ph6: Moderate–severe POEM / Severe facial involvement (n=224, 16.0%).

Demographic characteristics and resource utilization

Ph6 (moderate–severe POEM/severe facial involvement) was the youngest phenotype (mean age 39.0 years); Ph2 was the most female-predominant (69.1%). Among patients with facial involvement, 80.3% reported use of specific treatment for facial lesions and 40.5% reported cosmetic camouflage use. Camouflage use was similar among treated (40.1%) and untreated patients (40.6%) (p=ns), suggesting that it represents a strategy independent of medical treatment.

Camouflage use by phenotype

Among patients with facial involvement (n=558), camouflage use increased monotonically with BoFA severity: Ph2 23.0% vs Ph3 48.3% (p=0.0008); Ph5 32.1% vs Ph6 54.5% (p=0.0001). Patients in the protective phenotypes (Ph2, Ph5) used significantly less camouflage than their severe-involvement counterparts, ruling out a proactive coping mechanism as the primary explanation for their lower stigmatization. These data are presented in **Table IV**.

DISCUSSION

Bidimensional phenotyping: Parallel with Chovatiya et al. (8)

Our study builds directly on the methodological framework of Chovatiya et al. (8), proposing a bidimensional phenotyping approach adapted to the specific issue of facial involvement in AD. Several parallels emerge: a moderate correlation between axes (r=0.365 vs ρ=0.32–0.62 in Chovatiya et al.), a protective phenotype with minimal burden (Ph2/Ph5 vs MI-ML), and a central paradox between a "visible but clinically mild" phenotype and a "severe but non-visible" phenotype (Ph3 ≈ Ph4 vs. SI-ML ≈ MI-SL). In both studies, the highest psychosocial burden was observed in patients combining elevated severity across both dimensions.

Fig. 2. Mean psychosocial burden scores by phenotype (*N*=1,400). PUSH-d (stigmatization), DLLIM (life-course impact), DMLQ (quality of life), and Stress NRS; higher values indicate greater burden. Ph1, mild POEM with no facial involvement (n=315): PUSH-d 9.1, DLLIM 7.5, DMLQ 15.4, Stress 4.9. Ph2, mild POEM with mild facial involvement (n=139, annotated protective): PUSH-d 3.9, DLLIM 3.8, DMLQ 14.6, Stress 5.0. Ph3, mild POEM with severe facial involvement (n=58, annotated paradox): PUSH-d 21.9, DLLIM 14.8, DMLQ 18.9, Stress 6.2. Ph4, moderate-to-severe POEM with no facial involvement (n=527): PUSH-d 19.3, DLLIM 14.6, DMLQ 18.9, Stress 6.9. Ph5, moderate-to-severe POEM with mild facial involvement (n=137, annotated protective): PUSH-d 8.5, DLLIM 6.5, DMLQ 16.6, Stress 6.0. Ph6, moderate-to-severe POEM with severe facial involvement (n=224, annotated maximum burden): PUSH-d 28.2, DLLIM 19.1, DMLQ 21.2, Stress 7.2. One-way ANOVAs across phenotypes are significant for every instrument (PUSH-d F=79.1; DLLIM F=75.5; DMLQ F=99.4; Stress NRS F=49.9; all p<0.001). Ph3 and Ph4 show statistically equivalent burden on all instruments except Stress NRS, illustrating the central paradox: mild eczema with severe facial involvement carries the same psychosocial burden as moderate-to-severe eczema without facial involvement. Six small-multiple bar charts of mean psychosocial burden (PUSH-d, DLLIM, DMLQ, Stress) across atopic dermatitis phenotypes. Burden rises with facial involvement: Ph6 highest (PUSH-d 28.2), Ph2 lowest (3.9). Ph3 equals Ph4 except on stress. ANOVA p<0.001.

Table II. Central paradox – Ph3 (Clear/Almost Clear POEM/Severe facial involvement) vs Ph4 (Moderate–severe POEM/Absent/Mild facial involvement)

Instrument	Ph3 (n=58)	Ph4 (n=527)	Difference (95% CI)	Cohen d	p	Conclusion
PUSH-d	21.93	19.27	+2.66 [−1.57;+6.89]	0.16	0.257 n.s.	No significant difference
DLLIM/SOL	14.76	14.58	+0.18 [−2.47;+2.82]	0.02	0.908 n.s.	No significant difference
DMLQ	18.88	18.91	−0.03 [−1.06;+0.99]	−0.01	0.950 n.s.	No significant difference
Stress NRS	6.22	6.93	−0.71 [−0.98;+0.19]	−0.30	0.040*	Ph3 slightly<Ph4

*p<0.05. Cohen d thresholds: |d| < 0.20 = negligible; 0.20–0.49 = small; 0.50–0.79 = moderate.
CI: confidence interval on mean difference.; n.s.: not significant; Ph:Phenotype.

These converging findings support the concept that the psychosocial burden of AD cannot be adequately predicted by a single disease dimension. Each dimension – pruritus intensity, global lesional severity or facial involvement – contributes complementarily to the total burden, and their combination reveals phenotypes impossible to identify through examination of each dimension separately. This observation supports a shift in clinical AD assessment from unidimensional to systematically multidimensional evaluation.

The facial paradox: Clinical implications

The burden equivalence between Ph3 and Ph4 represents one of the most clinically impactful findings of this study. This paradox can be explained by a well-documented mechanism whereby the visibility of facial lesions triggers social stigmatization, discrimination and isolation independent of overall clinical disease intensity. Grosperrin et al. demonstrated, in a systematic review of 41 studies including 12,373 patients with visible dermatoses, that depression and anxiety prevalence reached 38.7% and 43.9% on average, respectively, with rates systematically higher than in healthy controls (3). Germain et al. proposed a conceptual model of stigmatization in visible dermatoses, emphasizing that perceived stigmatization constitutes a central mediator between lesion visibility and psychosocial distress, independent of objective clinical severity (14).

In clinical practice, this paradox suggests that a patient with a low POEM score but marked facial burden (e.g. POEM=5; BoFA=55) is likely to experience psychosocial distress comparable to that of a patient with POEM=14 but no facial involvement. POEM alone is therefore likely to underestimate the burden of patients with severe facial involvement, risking under-management – particularly regarding psychological support, aesthetic medicine and recognition of disability.

The protective effect of mild facial involvement: The social legitimacy hypothesis

The paradoxical protective effect of mild facial lesions (Ph2<Ph1 and Ph5<Ph4 across all stigmatization scores) warrants in-depth discussion. Our camouflage data directly test the competing hypotheses that have been proposed. If proactive coping were driving the protective effect, Ph2/Ph5 patients would be expected to use more camouflage than Ph3/Ph6. The opposite is observed: camouflage use is significantly lower in Ph2 than Ph3 (23.0% vs 48.3%, p=0.0008) and in Ph5 than Ph6 (32.1% vs 54.5%, p=0.0001). This rules out the proactive coping hypothesis and supports the social legitimacy mechanism: mild but visible facial involvement appears to confer external recognition of the disease, sparing patients from the burden of "invisible illness" – a well-described source of internalized stigma in AD without visible lesions. Patients without facial lesions may feel unrecognized or disbelieved in their suffering, generating a different type of stigmatization that is internalized and self-imposed. Qualitative investigation through semi-structured interviews remains warranted to explore the precise mechanisms underlying this protective effect.

BoFA as a clinically relevant tool

The finding that BoFA emerged as the dominant independent predictor of perceived stigmatization (β=11.44; partial R^2=46.2 % vs 0.6 % for POEM – a 77-fold difference) with loss of POEM significance when controlling for BoFA is a major finding. It validates the clinical relevance of BoFA as a tool for

Table III. Multiple linear regression – PUSH-d predictors (n=558, patients with facial involvement)

Predictor	β (unstandardized)	SE	t	p	Partial R^2	Significance
Constant	16.91	0.80	21.07		—	***
BoFA (standardized)	11.44	0.52	21.78		46.2%	***
POEM score (standardized)	0.93	0.52	1.78	0.076	0.6%	n.s. (trend)
Age (standardized)	−1.34	0.50	−2.71	0.007	1.3%	**
Female sex	−0.37	1.01	−0.36	0.716	0.0%	n.s.

Overall model R^2 = 0.532; F(4, 553)=157.2, p<0.001. ***p<0.001; **p<0.01.
n.s.: not significant.

Table IV. Camouflage use by phenotype (patients with facial involvement only, *n*=558)

Phenotype	n	Camouflage (%)	Comparison	*p*-value
Ph1 – Clear POEM / No facial involvement	315	N/A	—	—
Ph2 – Clear POEM / Mild facial (BoFA<36)	139	23.0%	vs Ph3	0.0008***
Ph3 – Clear POEM / Severe facial (BoFA≥36)	58	48.3%	—	—
Ph4 – Mod-Sev POEM / No facial involvement	527	N/A	—	—
Ph5 – Mod-Sev POEM / Mild facial (BoFA<36)	137	32.1%	vs Ph6	0.0001***
Ph6 – Mod-Sev POEM / Severe facial (BoFA≥36)	224	54.5%	—	—

Chi-squared test. ***p < 0.001.
N/A: not applicable (no facial involvement); Ph:Phenotype.

psychosocial risk stratification in AD patients with facial involvement. Recent studies have confirmed the psychometric properties of BoFA (responsiveness to change, convergent validity with DLQI and POEM) (7), but our study is, to our knowledge, the first to demonstrate its superior predictive value for stigmatization compared with a global severity score.

Heratizadeh et al. (15) had previously suggested, in a German cohort, that facial involvement was an independent predictor of quality-of-life impact. Our study goes further by precisely quantifying this predominance and demonstrating its independence of sex and age (R^2=0.532). These findings argue for systematic integration of BoFA, or at minimum a structured question about facial involvement, in clinical assessments and therapeutic decision algorithms for AD.

Ph6: The reference phenotype for clinical management

Ph6 (Moderate–severe POEM/Severe facial involvement), representing 16% of the study population, concentrated the highest level of vulnerabilities and should constitute a priority target for interventions. This phenotype was characterized by the greatest perceived stigmatization (PUSH-d=28.24 vs 9.07 for Ph1) and youngest mean age (39.0 years), making it a high-priority intervention group. The relative youth of this phenotype is of particular concern, as it corresponds to a critical period of professional integration and identity construction during which visible stigmatization may have long-lasting consequences on life trajectories. Recent clinical trials have demonstrated that biological therapies (dupilumab, tralokinumab, lebrikizumab) and JAK inhibitors (abrocitinib, upadacitinib) significantly improve not only clinical scores but also patient-reported quality-of-life outcomes (16–19). Ensuring appropriate access to these therapies for patients in this high-burden phenotype may therefore represent an important opportunity to mitigate both clinical and psychosocial impact.

Strengths and limitations

Key strengths of this study include its large nationally representative sample size (N=1,400), the simultaneous use of 5 validated burden instruments including 2 specific tools targeting stigmatization and facial burden (BoFA, PUSH-d), and a bidimensional phenotyping approach anchored in published methodology (8). Several limitations should be acknowledged. The cross-sectional design prevents assessment of phenotype temporal stability and precludes causal inference; reverse causation cannot be excluded, as psychosocial burden may influence self-reported BoFA scores. Longitudinal studies are required to confirm phenotype stability and establish causal pathways. The BoFA threshold of 36 is exploratory, based on the population median. Sensitivity analyses with alternative thresholds (T1=22, T2=50) confirm the robustness of the Ph3 ≈ Ph4 paradox at all configurations (Table SI); prospective validation using ROC curve analysis anchored on clinical outcomes is needed to define an optimal evidence-based cut-off. BoFA administration was limited to patients reporting facial involvement, and recruitment through a population panel may have resulted in possible overrepresentation of patients with moderate-to-severe eczema.

Conclusion

This study demonstrates, for the first time in a large French cohort, that combining POEM and BoFA enables the definition of 6 clinical AD phenotypes with radically different psychosocial burden profiles. The central paradox – equivalent stigmatization in patients with mild eczema and severe facial involvement compared with those with moderate-to-severe eczema without facial involvement – challenges the exclusive use of POEM as a burden assessment tool in AD. Camouflage data support the social legitimacy mechanism as the primary explanation for the paradoxical protective effect of mild facial involvement.

These findings argue for 3 changes in clinical practice: (*i*) systematic assessment of facial involvement using BoFA in all AD patients, regardless of POEM severity; (*ii*) integration of BoFA into therapeutic decision-making – if BoFA≥36, refer for psychosocial support regardless of POEM; and (*iii*) recognition of Ph3 (Mild POEM / Severe facial involvement) as a clinically deceptive phenotype at high risk of under-recognition and under-management. Prospective validation of these recommendations and qualitative

exploration of the paradoxical protective effect of mild facial lesions represent key future research directions.

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Data availability statement: The datasets generated and/or analysed during this study are available from the authors upon reasonable request.

Ethics committee: The project was reviewed by a French ethics committee and found to be in accordance with the ethical standards set forth by that committee. 24.00998.000323-MS01.1 [Committee for the Protection of Individuals Est III]. This pragmatic study was designed and conducted in accordance with the Declaration of Helsinki (2013) and CIOMS guidelines (2016). All participants confirmed their consent after being informed of the study's objectives and of its expected contribution to improved clinical assessment of patients with atopic dermatitis. No individual therapeutic benefit was anticipated or promised. Data were collected and processed in accordance with data protection regulations, including the GDPR.

Conflict of interest: Audrey Bourne Chastel is employed by Leo Pharma.

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