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APPENDIX S1. Details on instruments and variables used.

- Disease severity of atopic dermatitis was measured using the **Patient Global Assessment (PGA),** a 5-point Likert scale assessing the patient's overall perception of AD severity ("clear/almost clear," "mild," "moderate," and "severe" including extreme severe) (19,27). Higher PGA categories reflected increasing symptom intensity and disease activity. For analytical purposes, responses were grouped into four categories due to few observations and missing values in some original subcategories to ensure sufficient sample size per category.
- **Allergic conditions** (or allergies) were defined as self-reported, physician-diagnosed allergic rhinitis, food allergy, or other allergic diagnoses, excluding asthma. Each condition was coded as a binary indicator (yes/no), and non-responses were treated as missing. Asthma was analysed as a separate variable, although it can represent an allergic condition itself.
  For subgroup analyses, we examined asthma and allergic conditions both individually and jointly. The term *"asthma and allergies"* (or *"asthma and allergic conditions"*) refers to participants reporting asthma together with at least one of the other allergic conditions. These groupings were used when analysing associations with atopic dermatitis (AD) severity, quality of life, and cost outcomes.
- The dermatology-specific QoL questionnaire for adults (**DLQI**-Dermatitis Life Quality Index), is a 10-item questionnaire evaluating the impact of skin disease on daily life, with each item scored from 0 to 3. Total scores range from 0 (no impact) to 30 (maximum impact). (Finlay & Khan (28), HOME 2024 (29)).
  Additional references: Cardiff University. Quality of life questionnaires. School of Medicine. 2023. https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/dermatology-life-quality-index.
- The generic health-related QoL assessment instrument (EuroQoL-5 dimensions-5Levels, **EQ-5D-5L** (30)) measures HRQoL across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each rated on five levels of severity. Health states were converted to index values using the Swedish value set from Sun et al., 2022 (31). It also includes a visual analogue scale (EQ-VAS) from 0 (worst) to 100 (best), used for self-rated health.
- The Patient Benefit Index (**PBI**) (34,35) is a patient-reported tool used to assess treatment benefit by combining pre-treatment goals (Patient Needs Questionnaire, PNQ), which consists of the treatment goal items) and post-treatment outcomes (Patient Benefit Questionnaire, PBQ), which consists of the benefit items measuring the extent to which the treatment goals have been achieved. Both are scored from 0 to 4. Patients rate the importance of treatment goals and how well they were achieved (both on a 0-4 scale). The PNQ used was derived from the study of Wintermann 2025

(36). The global PBI score, ranging from 0 (no benefit) to 4 (maximum benefit), is computed for each patient according to the following algorithm:

$$PBI = \sum_{i=1}^{k} \frac{PNQ_i}{\sum_{i=1}^{k} PNQ_i} PBQ_i$$

Using this algorithm, the importance of each treatment goal is divided by the sum of all importance values of the respective patient and is multiplied with the goal attainment value. The resulting products are added up.
(more details on the PBI in PBI user manual: https://www.patient-benefit-index.com/wp-content/uploads/User-manualPBINovember2024.pdf).

- The **WPAI** (Work Productivity Activity Impairment) questionnaire (33) captures employment status, absenteeism, and overall productivity impairment over the past week.
  Productivity impairment is rated on a scale from 0 (not affected) to 10 (completely prevented), both at work and in daily activities. WPAI scores are expressed as percentages, with higher scores indicating greater impairment. Scoring: 6 questions are asked on the following variables: Q1=currently employed or working for pay, Q2 = hours missed due to health problems, Q3=hours missed due to other reasons, Q4= hours actually worked, Q5=degree affected productivity while working (scale of 0 to 10), Q6=degree affected regular activities (scale of 0 to 10).
  Scores are then calculated as follows:
  1.Percent work time missed (absenteeism): Q2/(Q2+Q4),
  2. Percent impairment while working (presenteeism): Q5/10,
  3.Percent overall work impairment (absenteeism plus presenteeism*): Q2/(Q2+Q4)+((1-(Q2/(Q2+Q4))x(Q5/10)),
  4.Percent activity impairment: Q6/10. Scores are multiplied by 100 to express in percentages.
  Higher WPAI scores indicate greater impairment and less productivity.

*Overall work impairment is described as absenteeism + presenteeism, but the equation is an 'or' calculation: absenteeism + ((1-absenteeism) x presenteeism).
Reference: ISPOR. Work Productivity and Activity Impairment (WPAI) (Internet). 2024 (cited 2025 Feb 10). Available from: https://www.ispor.org/docs/default-source/intl2024/ispor24patelpcr156handout135924-pdf.pdf

Short explanation of related terms:
Absenteeism: Work time missed due to the health-related issues.
Presenteeism: Reduced productivity due to the specific health issues, while being at work.
Overall work productivity impairment: Combined measure of absenteeism and presenteeism effects on work performance.
Productivity impairment: The overall reduction in an individual's work performance and output due to health-related factors, including both time missed from work (absenteeism) and reduced efficiency while at work (presenteeism).

Productivity losses (costs): The estimated financial cost of reduced work performance due to absenteeism and presenteeism, using the human capital approach (Drummond et al, 2015 (16))
Activity impairment: Limitations in performing daily activities due to health issues, such as household tasks and physical activity.

- Out-of-pocket costs and healthcare consumption data were collected using the adapted **iMTA instrument for economic evaluations** and in particular the Treatment Inventory of Costs in Patients with psychiatric disorders (TIC-P) (37).

APPENDIX S2: Healthcare utilisation & treatment patterns

The average number of healthcare contacts per month was 1.6 (SD=3.1). There was no difference in the number of contacts by age, sex, disease severity, or comorbid conditions. Only the presence of non-atopic conditions showed a statistically significant difference in the number of contacts (p=0.002), with an average of 2.1 (SD=2.2) contacts per month. The majority of contacts were with physicians (47%), followed by nurses (33.9%), and various other professionals (19.1%), such as psychologists/counsellors (9.6%).

The vast majority (83%) of treatments were ointments/creams. Almost 10% of treatments were a type of systemic therapy in the form of tablets or syringes, and almost 2% were phototherapy. Among the systemic therapies, 29% were biologics, 23% were methotrexate, 17.6% were cortisone, and 5.9% were JAK inhibitors.

APPENDIX S3: WTP for symptom relief

This was assessed based on the answers to three questions (shown below), including absolute and relative figures. This approach followed methods from previously published studies (21,44,45) rather than applying a formal shadow pricing* framework (20):

Questions:

How much would you be willing to pay to cure your eczema?

- *Provide an exact amount you would be willing to spend per month:*
  .....
- *Provide an absolute amount you would be willing to spend per month (Choose from: no payment, up to 500, up to 1000, up to 1500, up to 2000, up to 2500, up to 3000, up to 4000, more than 4000):*
  .....
- *Provide a percentage of your monthly income you would be willing to spend (Possible answers: 0-10%, 10-20%, 20-30%, 30-40%, 40-50%, 50-60%, more than 60%):*
  .....

Results:

- On average, participants reported a WTP of €183.70/month (95% CI: €128.70-€256.30) for symptom relief.
- 67.1% of the sample would be willing to pay up to €131.2 per month, 20.3% up to €349.9, and 12.6% even over €350 per month to alleviate their symptoms.
- Around 70% of the sample would be willing to spend up to 10% of their monthly income to receive effective treatment, while 17.5% would be willing to spend up to 20% of their monthly income.

There were no differences in these results based on age, sex, disease severity, or comorbid conditions. Only regarding the question on % of income willing to spend, individuals with asthma (36%) showed higher WTP (>10%) of their monthly income compared to those without asthma (26%), and even 3% would be willing to pay over 50% of their income (p=0.023).However, these results should be interpreted with caution due to low response rates. Also, higher DLQI score was associated with higher WTP in term of percent of monthly income (p=0.033).

***** A **shadow price** is an *estimated monetary value* assigned to something that doesn't have a clear market price, for example, time, environmental impact, or social outcomes.

APPENDIX S4: Productivity losses (costs) & Out-of-pocket costs

Work productivity losses (costs)

To derive annual productivity loss estimates from weekly WPAI data, the following assumptions were applied:

- WPAI reflects impairment during the previous 7 days attributed to atopic dermatitis, capturing weeks with active symptoms rather than continuous year-round burden. Such symptomatic periods vary in frequency and duration across patients and typically increase with disease severity (7,19). Because clinical flare definitions differ in the literature*, these estimates represent symptomatic weeks rather than precise counts of clinical flares and should be interpreted accordingly.

* S.M. Langan, J. Schmitt, H.C. Williams, S. Smith, K.S. Thomas, How are eczema 'flares' defined? A systematic review and recommendation for future studies, *British Journal of Dermatology*, Volume 170, Issue 3, 1 March 2014, Pages 548–556, https://doi.org/10.1111/bjd.12747

Silverberg JL In atopic dermatitis, looks can be deceiving. *Am J Manag Care. 2016.* https://www.ajmc.com/view/burden-of-ad-article. Accessed 1 March 2025

Silverberg JI, Anderson P, Cappelleri JC, Piercy J, Levenberg ME, Myers DE, Gerber RA. Burden of mild and moderate atopic dermatitis in adults: results from a real-world study in the United States. Arch Dermatol Res. 2025;12;317(1):556; https://doi.org/10.1007/s00403-025-03910-y.

- Productivity losses were valued using percentages of impairment during symptomatic weeks derived from WPAI, applying the human capital approach.
- Annual costs were estimated using severity-specific assumptions for symptomatic weeks, ranging from 2 to 8 per year, based on literature and expert consensus. This scenario-based approach reflects variability in flare frequency and provides a type of sensitivity check on annualized estimates.
- National extrapolations assume that the distribution of symptomatic weeks in this sample is broadly comparable to the adult AD population in Sweden.
- Most respondents completed the survey within a relatively narrow calendar window; seasonal variation could not be directly assessed and was handled as an assumption.

The annualised productivity cost per employed participant with atopic dermatitis was €1 972 (95% CI €1 199 to €2 828). These values reflect impairment during symptomatic periods rather than assuming year-round productivity loss (7,19). Extrapolating this cost to adults with atopic dermatitis in Sweden suggests a crude national estimate of approximately €819 million per year (4). These estimates illustrate the potential economic magnitude and should be interpreted with caution given sample representativeness and the episodic nature of the condition.

Presenteeism and total productivity losses were higher among participants with severe atopic dermatitis compared with those reporting mild or moderate disease ($p < 0.001$) while absenteeism related costs did not differ significantly by severity ($p = 0.79$). No significant differences were observed by age group ($p = 0.26$), sex ($p = 0.43$), age at disease onset ($p = 0.81$) or comorbid asthma ($p = 0.98$). Productivity losses were higher among participants with non-atopic comorbidities ($p = 0.042$) particularly those reporting attention deficit hyperactivity disorder ($p = 0.026$) and other allergic conditions ($p = 0.043$).

Productivity losses were moderately associated with lower generic health related quality of life (EQ-5D-5L $r_s = -0.51$) and positively associated with worse dermatology specific health related quality of life (DLQI $r_s = 0.52$), higher activity impairment ($r_s = 0.73$), itch intensity ($r_s = 0.48$), pain intensity ($r_s = 0.41$), perceived treatment benefit (PBI $r_s = 0.57$) and healthcare utilisation ($r_s = 0.45$) with all $p < 0.001$.

Out-of-pocket costs

Out-of-pocket expenses were self-reported for the previous month and included spending on treatments, travel, skin care products and other patient borne costs. Because atopic dermatitis related management needs tend to increase during symptomatic periods, annual totals were estimated using the same symptomatic period, weighting assumptions applied to productivity losses. As month-to-month variation could not be observed directly, this approach reflects plausible periodic fluctuations.

Mean annual out-of-pocket expenses were €900 (95% CI €401 to €1 758). Extrapolating this estimate to the adult population with atopic dermatitis in Sweden suggests a crude national burden of approximately €747 million per year (4), recognising uncertainty in prevalence and severity distribution.

Out-of-pocket costs were moderately associated with PBI (rs = 0.43) and weak to moderately associated with pain intensity (rs = 0.31) and activity impairment (r_s = 0.35) with all $p < 0.05$. No significant differences were observed by sex, age group or disease duration ($p > 0.05$), and there was no significant association with willingness to pay ($p > 0.05$).

Interpretation notes

• Annual values reflect flare-linked symptomatic burden rather than continuous disease activity

• National extrapolations are indicative and depend on prevalence, severity distribution, employment rates, healthcare system factors.

APPENDIX S5: Results Regression DLQI

A log-transformed linear regression model was applied to examine factors associated with quality of life, as measured by the DLQI, in individuals with AD. The analysis assessed how various variables relate to the natural logarithm of total DLQI scores among participants.

Results from the Analysis of Variance (ANOVA) are summarized in table 1 below. The overall model was statistically significant ($F(13, 69) = 8.561$, $p < 0.001$), suggesting that the included predictors account for a meaningful proportion of the variability in DLQI scores. The model yielded an R^2 of 0.617 and an adjusted R^2 of 0.545.

Parameter estimates for the individual predictors are presented in table 2 below. Among the variables analysed, percentage of activity impairment ($B = 1.268$, $p < 0.001$) and itch severity ($B = 0.095$, $p < 0.001$) showed statistically significant associations with DLQI scores. Based on the log-transformed model, a one-unit increase in activity impairment was associated with an estimated 126.8 percent increase in DLQI scores, while a one-unit increase in itch severity was linked to an estimated 9.5 percent increase.

Other variables, including age group, sex, age of onset of AD, presence of non-atopic conditions, and comorbid asthma or allergies, were not statistically significant in this model.

Overall, the results indicate that functional limitations and symptom severity are closely related to variations in DLQI. These findings highlight the potential relevance of managing these factors in efforts to improve patient-reported outcomes.

Tests of Between-Subjects Effects
Parameter Estimates

Dependent Variable: natural logarithm total result DLQI adults

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	23,377[a]	13	1,798	8,561	<,001	,617
Intercept	5,060	1	5,060	24,092	<,001	,259
age	,344	4	,086	,409	,802	,023
sex	,154	1	,154	,732	,395	,010
Age AD start	,034	2	,017	,082	,922	,002
having_non_atopic_conditions	,117	1	,117	,558	,458	,008
activity_impairment	4,730	1	4,730	22,521	<,001	,246
itch_severity	3,372	1	3,372	16,055	<,001	,189
having_asthma_and allergies	,043	1	,043	,205	,652	,003
AD_severity_	,026	1	,026	,124	,726	,002
Error	14,493	69	,210			
Total	432,422	83				
Corrected Total	37,869	82				

a. R Squared = ,617 (Adjusted R Squared = ,545). Note: “Allergic conditions” include allergic rhinitis, food allergy, or other allergic diagnoses (excluding asthma). “Asthma and allergies” refers to respondents reporting asthma together with at least one of the other allergic conditions.

The parameter estimates for the predictors are presented in the table 2 below. Significant predictors included activity impairment (B = 1.268, p < 0.001) and itch (B = 0.095, p < 0.001), indicating that these factors have a substantial impact on DLQI scores. Other predictors, such as age categories, sex, start of AD, having non-atopic conditions, and asthma/allergies, were not significant.

Parameter Estimates

Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared
					Lower Bound	Upper Bound	
Intercept	1,131	,342	3,311	,001	,450	1,813	,137
(age_categories=1,00)	-,050	,202	-,247	,806	-,452	,353	,001
(age_categories=2,00)	-,047	,170	-,277	,783	-,387	,292	,001
(age_categories=3,00)	-,036	,193	-,188	,852	-,421	,349	,001
(age_categories=4,00)	,116	,182	,638	,526	-,246	,478	,006
sex	,120	,141	,855	,395	-,160	,401	,010
Start_AD=1,00	-,029	,255	-,114	,909	-,538	,479	,000
Start_AD=2,00	-,076	,267	-,287	,775	-,608	,455	,001
Having non-atopic conditions	,091	,122	,747	,458	-,152	,334	,008
PBI	,018	,077	,234	,816	-,135	,171	,001
Acitivity impairment*	**1,268**	**,267**	**4,746**	**<,001**	**,735**	**1,801**	**,246**
Itch severity*	**,095**	**,024**	**4,007**	**<,001**	**,048**	**,142**	**,189**
Having asthma and allergies	,073	,162	,452	,652	-,250	,396	,003
AD severity	-,032	,090	-,352	,726	-,210	,147	,002

*statistically significant. Note: “Allergic conditions” include allergic rhinitis, food allergy, or other allergic diagnoses (excluding asthma). “Asthma and allergies” refers to respondents reporting asthma together with at least one of the other allergic conditions.

Appendix S6: Regression model for out-of-pocket costs

A generalized linear model (GLM) with a gamma distribution and log-link function was applied to explore factors associated with out-of-pocket costs in adults with AD. The model included variables such as age, sex, presence of asthma and allergies, WTP, PBI score, itch severity, overall AD severity, percentage of activity impairment, and DLQI score.

Model fit indicators, including a deviance-to-degrees-of-freedom ratio of 1.018 and a Pearson Chi-Square-to-degrees-of-freedom ratio of 0.813, suggest that the model represents the data adequately. Additionally, the Omnibus Test yielded a statistically significant result ($p < 0.001$), indicating that the model overall accounts for a meaningful portion of the variability in reported out-of-pocket expenses.

Among the variables included, both the PBI score ($B = 0.518$, $p = 0.004$) and the percentage of activity impairment ($B = 1.305$, $p = 0.04$) were statistically associated with higher cost estimates. For the PBI, the Exp(B) value was 1.679, which corresponds to an estimated 67.9 percent increase in out-of-pocket costs for each one-unit increase in PBI. For activity impairment, Exp(B) was 3.688, reflecting an estimated 268.8 percent increase in costs per unit increase in impairment.

These associations point to the relevance of treatment-related perceived benefit and functional limitation in understanding variability in personal health expenditures among adults with AD. Further exploration may clarify whether these relationships persist across different populations or care settings.

Parameter Estimates

Parameter			95% Wald Confidence Interval		Hypothesis Test			95% Wald Confidence Interval for Exp(B)		
	B	Std. Error	Lower	Upper	Wald Chi-Square	df	Sig.	Exp(B)	Lower	Upper
(Intercept)	4,819	,7070	3,434	6,205	46,472	1	<,001	123,902	30,995	495,290
Sex(=1,00)	,304	,3783	-,437	1,046	,647	1	,421	1,356	,646	2,846
Age	,014	,0090	-,004	,031	2,284	1	,131	1,014	,996	1,032
Having asthma and allergies	-,202	,4099	-1,005	,602	,242	1	,623	,817	,366	1,825
WTP	,000	,00005	-,00001	,000	3,201	1	,074	1,000	1,000	1,000
Itch severity	-,065	,0905	-,242	,112	,516	1	,472	,937	,785	1,119
Activity Impairment*	**1,305**	**,6454**	**,040**	**2,570**	**4,089**	**1**	**,043**	**3,688**	**1,041**	**13,065**
DLQI score	-,060	,0332	-,126	,005	3,300	1	,069	,941	,882	1,005
PBI*	**,518**	**,1806**	**,164**	**,872**	**8,241**	**1**	**,004**	**1,679**	**1,179**	**2,393**
AD Severity	,422	,2354	-,040	,883	3,209	1	,073	1,525	,961	2,419
(Scale)	,739[a]	,1297	,524	1,042						

a. Maximum likelihood estimate, *statistically significant. Note: “Allergic conditions” include allergic rhinitis, food allergy, or other allergic diagnoses (excluding asthma). “Asthma and allergies” refers to respondents reporting asthma together with at least one of the other allergic conditions.

Appendix S7: Regression model for productivity losses

This GLM regression examines total productivity losses among adults by accounting for both presenteeism and absenteeism. It incorporates various factors including sex, age, presence of asthma and allergies, itch intensity, disease severity, percentage of activity impairment, EQ-5D-5L health index, and frequency of healthcare contact.

Several variables were statistically associated with differences in productivity-related costs. Percentage of activity impairment showed the strongest association, with each unit increase corresponding to an estimated sixfold rise in costs (Exp(B) = 5.851, p = .003). Itch severity also showed a significant relationship, where each one-point increase on the 0 to 10 scale was linked to a 13.9 percent increase in costs (Exp(B) = 1.139, p = .013). Gender appeared relevant as well, with male participants showing 31.9 percent lower costs compared to females (Exp(B) = 0.681, p = .033).

Other variables such as age, disease severity, healthcare contact frequency, asthma or allergy status, EQ-5D-5L scores, and skin pain were not statistically significant. Still, some patterns, such as lower estimated costs among individuals with asthma or allergies (Exp(B) = 0.510) and a negative trend between EQ-5D-5L scores and costs (Exp(B) = 0.717), may be noteworthy in larger samples.

Overall, the model suggests that itch severity and activity impairment are closely associated with productivity loss. These findings support the potential benefit of focusing on symptom control and functional well-being in clinical care, as these factors may have more influence on indirect economic outcomes than general health measures or pain levels when examined concurrently.

Parameter Estimates

Parameter	B	Std. Error	95% Wald Confidence Interval Lower	95% Wald Confidence Interval Upper	Hypothesis Test Wald Chi-Square	df	Sig.	Exp(B)	95% Wald Confidence Interval for Exp(B) Lower	95% Wald Confidence Interval for Exp(B) Upper
(Intercept)	5,554	1,2986	3,009	8,099	18,292	1	<,001	258,260	20,262	3291,742
(sex=1,00)	**-,385**	**,1800**	**-,737**	**-,032**	**4,567**	**1**	**,033***	**,681**	**,478**	**,969**
age	,007	,0058	-,005	,018	1,358	1	,244	1,007	,995	1,018
severity	-,203	,1510	-,498	,093	1,800	1	,180	,817	,607	1,098
% Activity Impairment*	**1,767**	**,6015**	**,588**	**2,946**	**8,627**	**1**	**,003***	**5,851**	**1,800**	**19,022**
Itch severity*	**,130**	**,0522**	**,028**	**,232**	**6,196**	**1**	**,013***	**1,139**	**1,028**	**1,261**
Pain severity	,013	,0731	-,130	,156	,031	1	,860	1,013	,878	1,169
Health care contacts frequency	,048	,0398	-,030	,126	1,474	1	,225	1,049	,971	1,135
Having asthma and allergies	-,674	,3863	-1,431	,083	3,046	1	,081	,510	,239	1,086
EQ-5D- 5L health index	-,333	,8628	-2,024	1,358	,149	1	,700	,717	,132	3,890
(Scale)	,092[a]	,0261	,053	,160						

a. Maximum likelihood estimate, *statistically significant. Note: “Allergic conditions” include allergic rhinitis, food allergy, or other allergic diagnoses (excluding asthma). “Asthma and allergies” refers to respondents reporting asthma together with at least one of the other allergic conditions.

Omnibus Test[a]		
Likelihood Ratio Chi-Square	df	Sig.
44,782	9	<,001