# Burden of illness in adults with atopic dermatitis: Analysis of National Health and Wellness Survey data from France, Germany, Italy, Spain, and the United Kingdom

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***Background:*** The disease burden of atopic dermatitis (AD) in European populations is not well known.

***Objective:*** To establish the disease burden in European adult patients with AD.

***Methods:*** Data were from the 2016 National Health and Wellness Survey conducted in France, Germany, Italy, Spain, and the United Kingdom. Bivariate analyses were conducted on outcomes between controls without AD matched to patients with self-reported AD (both n = 1860).

***Results:*** Patients with AD and a subset of patients with inadequately controlled AD (IC-AD) versus controls without AD, respectively, reported significantly higher ($P < .001$) 36-Item Short Form Health Survey Physical and Mental Component Summaries (PCS, MCS), and anxiety (31.9% and 51.7% vs 14.4%), depression (25.8% and 36.2% vs 12.9%), and sleep disorder (22.7% and 39.7% vs 12.6%) prevalences. Patients with IC-AD versus controls without AD reported significantly greater ($P < .001$) overall work (57.1% vs 23.7%) and activity impairment (51.7% vs 26.5%). In addition, 21.6% of patients with AD and 37.9% of patients with IC-AD reported ≥1 emergency department visit in the previous 6 months versus 16.5% of controls without AD, and 93.1% of patients with AD versus 84.2% of those without AD had ≥1 clinician visit (both $P < .001$). Of these, patients with IC-AD showed greater burden on most outcomes than patients with controlled AD.

***Limitations:*** Low response rate, possible selection bias due to survey technology availability, and patient-reported data susceptible to recall bias.

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Conflicts of interest: L.E. and P.M. are employees of and stockholders in Sanofi. S.G. is an associate of Kantar Health, which received research funding from Sanofi/Regeneron Pharmaceuticals, Inc, for the current study. A.G. is an employee of and stockholder in Regeneron Pharmaceuticals, Inc. J.M.G. is an employee of the University of Pennsylvania Perelman School of Medicine, which has received research funding from Sanofi/Regeneron Pharmaceuticals, Inc. In the previous 12 months, J.M.G. served as a consultant for AbbVie, AstraZeneca, Celgene Corp, Coherus, Eli Lilly, Janssen Biologics (formerly Centocor), Sanofi, Merck, Novartis Corp, Regeneron Pharmaceuticals, Inc, Valeant, and Pfizer Inc, receiving honoraria, and received research grants (to the Trustees of the University of Pennsylvania) from AbbVie, Eli Lilly, Janssen, Novartis, Regeneron, Sanofi, and Pfizer Inc, and has received payment for continuing medical education work related to psoriasis. He is also a copatent holder of Resiquimod for the treatment of cutaneous T-cell lymphoma.

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***Conclusion:*** Patients with AD reported significant burden on health, health-related quality of life, productivity, activities, and health care. (J Am Acad Dermatol 2019;81:187-95.)

***Key words:*** atopic dermatitis; disease burden; Europe.

Atopic dermatitis (AD) is a T-helper 2 (TH2) immune disease characterized by chronic skin inflammation and intense pruritus.[1-3] AD usually first manifests in early infancy and childhood.[4,5] For about half of pediatric patients, however, AD persists into adulthood,[6,7] becoming a chronic, lifelong condition,[5] especially for patients with later-onset disease, or presenting with greater severity, or both.[8] AD can also initially appear in adulthood.[7,9-11]

**CAPSULE SUMMARY**

- Limited data exist on the burden of illness associated with atopic dermatitis in Europe.
- In this study, adult patients with atopic dermatitis, especially those with uncontrolled disease, reported a significant burden on health, health-related quality of life, productivity, activities, and health care.

AD prevalence in adults varies according to severity, assessment method, and region. Limited AD prevalence data in European adults indicate prevalence rates between 4.4% and 7.1% (with a range between countries of 2.2%–17.6%)[12,13] and trends of increasing prevalence.[14] Self-reported disease severity prevalence in European adults with AD is 54%, 43%, and 3% for mild, moderate, and severe disease (2.4%, 1.9%, and 0.13% of the European population), respectively.[13]

Moderate-to-severe AD carries a substantial patient burden[13,15] owing to itch, sleep disturbances, functional impairment, depression, anxiety, and reduced overall health-related quality of life (HRQoL).[1,16-19] In addition, AD in adults impairs work productivity and activity.[1,18] Real-world data on the burden of illness among adult patients with AD in Europe are limited. This study aimed to establish the real-world burden of illness in adult patients with AD in 5 European countries (France, Germany, Italy, Spain, and the United Kingdom). We further characterized the burden in patients with AD with inadequate disease control.

## METHODS

### Study design

This study used a cross-sectional study design to evaluate the burden of AD in adult patients. Patient-level data were obtained from the 2016 National Health and Wellness Survey (NHWS), a large general population survey administered to individuals aged ≥18 years using a self-administered, Internet-based questionnaire. A random, stratified sampling framework on which the NHWS is designed ensures that the survey is representative of the demographic composition of the general population.

The 2016 NHWS was approved by the centralized Pearl Institutional Review Board (Indianapolis, IN). Individuals who completed the survey gave informed consent online for their anonymized data to be used for research purposes. The present cross-sectional study was a pooled analysis of February 2016 to May 2016 NHWS data sets from France, Germany, Italy, Spain, and the United Kingdom.

### Study population

Patients with AD were identified by self-reported presence of AD and self-reported presence of a physician diagnosis by answering "yes" to the questions whether "they had ever experienced atopic dermatitis" or "had experienced atopic dermatitis in the past 12 months" and whether "their atopic dermatitis had been diagnosed by a physician." These questions, which required affirmative answers, ensured the sample provided a true representative population of patients with self-reported AD. Adults who did not meet the criteria above were allocated to the control group without AD.

### Outcomes

AD burden was measured across patient-reported outcomes: comorbidities, HRQoL, work and productivity impairment, and health care resource utilization (HCRU). Also recorded were self-reported comorbidities such as mood disorders, including anxiety, depression, and sleep disorders. The survey asked patients, "Which of the following conditions have you experienced in the past 12 months?" or "Which of the following conditions have you ever experienced?" For each condition identified, respondents also had to answer "yes" to the question, "Has your condition been diagnosed by a physician?"

HRQoL was assessed using the 36-Item Short Form Health Survey version 2 (SF-36v2)[20] and the

*Abbreviations used:*

| | |
|---|---|
| AD: | atopic dermatitis |
| C-AD: | controlled atopic dermatitis |
| DLQI: | Dermatology Life Quality Index |
| ED: | emergency department |
| HCRU: | health care resource utilization |
| HRQoL: | health-related quality of life |
| IC-AD: | inadequately controlled atopic dermatitis |
| MCS: | Mental Component Summary |
| NHWS: | National Health and Wellness Survey |
| PCS: | Physical Component Summary |
| SF-36v2: | 36-Item Short Form Health Survey version 2 |
| US: | United States |

dermatology-specific 10-question Dermatology Life Quality Index (DLQI).[21] Both questionnaires have been linguistically validated for the languages across the study countries.[22,23] Patient responses to the SF-36v2 Mental Component Summary (MCS) and Physical Component Summary (PCS) covered the period for the previous 4 weeks, with higher scores indicating better health status. For the DLQI, patients provided information on their HRQoL regarding the previous week, with higher scores indicating increased impairment in HRQoL.

A subset of participants with self-reported AD who provided a DLQI score were also examined between those who reported DLQI >10 (indicating a "very large effect on patient's life"[24]) and categorized as patients with inadequately controlled AD (IC-AD) and those who reported DLQI ≤10 categorized as controlled AD (C-AD).

The Work and Productivity Impairment questionnaire was used to evaluate work productivity and activity impairment, during the past 7 days, across 4 domains[25]: absenteeism (percentage of work time missed owing to a health problem), presenteeism (percentage of work time impaired), overall work impairment (percentage of overall work impairment: absenteeism plus presenteeism), and activity impairment (percentage of activity impairment).

HCRU over the previous 6 months was determined using responses to the following survey questions:

- "How many visits did you make to the following traditional health care provider(s) in the past 6 months?"
- "How many times have you been to the emergency room for your own medical condition in the past 6 months?"
- "How many times have you been hospitalized for your own medical condition in the past 6 months?"

### Statistical methods

Patients with AD were propensity score matched 1:1 with controls without AD using the following variables: country, age, sex, education, income, employment status, body mass index, smoking status, and Charlson Comorbidity Index. Patients with IC-AD were analyzed as a separate subgroup. Propensity score matching was conducted using variables that were statistically different between the groups with and without AD at baseline and during iterations of the propensity matching process. Relevant variables were entered into a logistic regression model using the SAS/STAT LOGISTIC procedure to generate the propensity score. Matching was completed using the greedy matching technique.[26] This approach ensures that the algorithm makes the "best" matches first (highest digital match on propensity score; 5 decimal points), followed by the "next-best" matches, continuing in a hierarchical sequence until no further matches are possible (0 decimal points). The best matches have the least absolute difference in matched propensity score.

Between-group comparisons of categorical and continuous variables were conducted using $\chi^2$ and $t$ tests, respectively, with the 2-tailed significance level ($\alpha$) set at 0.05. Analyses were performed using SAS 9.3 software (SAS Institute, Inc, Cary, NC).

## RESULTS

### Demographic and clinical characteristics

Of 971,854 adults contacted, 80,600 completed the survey (Table I). Another 21,168 respondents left the survey during the screening, refused informed consent, or did not meet the inclusion criteria.

Subsequently, 1860 adults with a self-reported diagnosis of AD, including 441 who reported a DLQI score, of which 58 (3.1%) were IC-AD and 383 were C-AD, were propensity score matched to 1860 individuals with no diagnosis of AD (Table I). Most respondents, with or without a diagnosis of AD, were from Spain (37.0%), followed by Italy (24.6%), France (19.0%), Germany (10.6%), and the United Kingdom (8.9%). Most patients (69.3%) were women, and their mean age was 44 years. The matching process resulted in good comparability between the groups with and without AD at baseline ($P > .10$) (Table I).

### Comorbidities

Self-reported comorbidities were significantly more prevalent in patients with AD and with IC-AD compared with those in controls without AD (Fig 1).

**Table I.** Baseline characteristics in patients with atopic dermatitis (AD) and inadequately controlled AD (IC-AD) versus controls without AD

| Characteristics | Controls without AD (n = 1860) | Patients with AD (n = 1860) | *P* value vs controls | Patients with IC-AD (n = 58) | *P* value vs controls |
|---|---|---|---|---|---|
| Age, mean (SD), y | 43.6 (15.0) | 43.9 (14.5) | .44 | 37.9 ± 14.6 | .004 |
| Female sex, No. (%) | 1266 (68.1) | 1312 (70.5) | .10 | 35 (60.3) | .22 |
| Body mass index, mean (SD), kg/m$^2$ | 25.3 (5.5) | 25.3 (5.5) | .75 | 25.3 ± 5.8 | .95 |
| Employed, No. (%) | 1172 (63.0) | 1140 (61.3) | .28 | 38 (65.5) | .70 |
| College educated, No. (%) | 1017 (54.7) | 1014 (54.5) | 1.00 | 25 (43.1) | .19 |
| Married/living with partner, No. (%) | 1152 (61.9) | 1119 (60.2) | .45 | 34 (58.6) | .76 |
| Annual household income ≥€50,000/£, No. (%) | 282 (15.2) | 292 (15.7) | .72 | 9 (15.5) | .48 |
| Charlson Comorbidity Index, mean (SD) | 0.4 (1.1) | 0.4 (0.9) | .12 | 1.3 ± 4.5 | <.001 |
| Dermatology Life Quality Index >10, No. (%) | … | 58 (13.2) | … | 58 (100) | |

*SD*, Standard deviation.

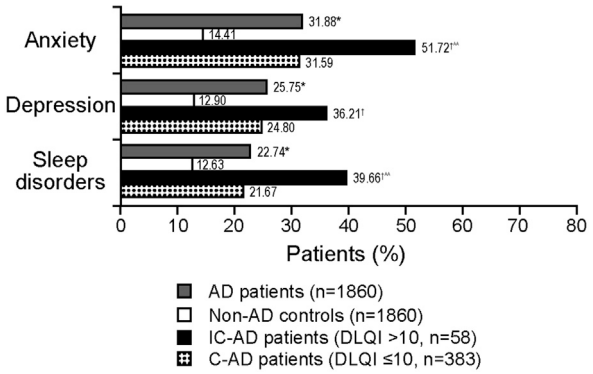


**Fig 1.** Self-reported prevalence of comorbidities in patients with atopic dermatitis (*AD*), controlled AD (*C-AD*), and inadequately controlled AD (*IC-AD*) versus controls without AD (*Non-AD*). *DLQI*, Dermatology Life Quality Index. *$P < .001$ between the cohorts with and without AD. †$P < .001$ between the cohort without AD and patients with IC-AD (DLQI >10). ^$P = .003$ between patients with C-AD and patients with IC-AD (DLQI >10).

Depression was more prevalent in patients with AD, affecting 25.8% and 36.2% of those with AD and IC-AD, respectively, compared with 12.9% of controls without AD ($P < .001$ for both comparisons) (Fig 1).

The rate of anxiety was also higher in patients with AD than in controls without AD (31.9% vs 14.4%, respectively; $P < .001$), particularly in those with IC-AD (51.7%, $P < .001$) versus controls without AD and patients with C-AD (31.6%, $P = .003$) (Fig 1). The pattern was similar for sleep disorders, which were reported by 22.7% and 39.7% of patients with AD and IC-AD, respectively, versus 12.6% of controls without AD ($P < .001$ for both comparisons) and 21.7% versus patients with C-AD ($P = .003$) (Fig 1).

## Health-related quality of life

Patients with AD and IC-AD both had significantly reduced HRQoL, indicated by lower mean SF-36v2 MCS scores, 41.96 and 34.78, respectively, versus 44.23 in controls without AD (both $P < .001$) and mean PCS scores of 49.41 and 43.87, respectively, versus 51.15 in controls without AD (both $P < .001$) (Fig 2, *A*). In addition, patients with IC-AD had significantly reduced MCS (42.52) and PCS (49.52) scores (both $P < .001$) versus patients with C-AD.

Fig 2, *B* shows a comparison of mean MCS and PCS scores between patients with AD and patients with IC-AD versus normative populations in each study country.[20,27] The patients with AD, IC-AD, and C-AD reported MCS and PCS scores that were lower than the normative scores in each of the study countries.

## Activity and work impairment

The presence of AD and IC-AD had a significant ($P < .001$) impact on work productivity (ie, presenteeism and overall work impairment) and the ability to undertake activities. Presenteeism rates were 24.7% for patients with AD and 53.5% for patients with IC-AD versus 21.2% for controls without AD ($P = .002$ and $P < .001$, respectively). Overall work impairment rates were 27.0% for patients with AD and 57.1% for patients with IC-AD versus 23.7% for controls without AD ($P = .009$ and $P < .001$, respectively) (Fig 3). Significant activity impairment was also reported by 31.8% of patients with AD and 51.7% of those with IC-AD versus 26.5% for controls without AD (both $P < .001$) (Fig 3). In contrast, rates of absenteeism did not differ significantly between those with and without AD but were numerically higher for patients with IC-AD (Fig 3).

For patients with C-AD versus IC-AD, absenteeism (10.2%) was not significant, but differences in the rates of presenteeism (21.8%), overall work impairment (23.6%), and activity impairment (31.2%) were significant (all $P < .001$) (Fig 3).

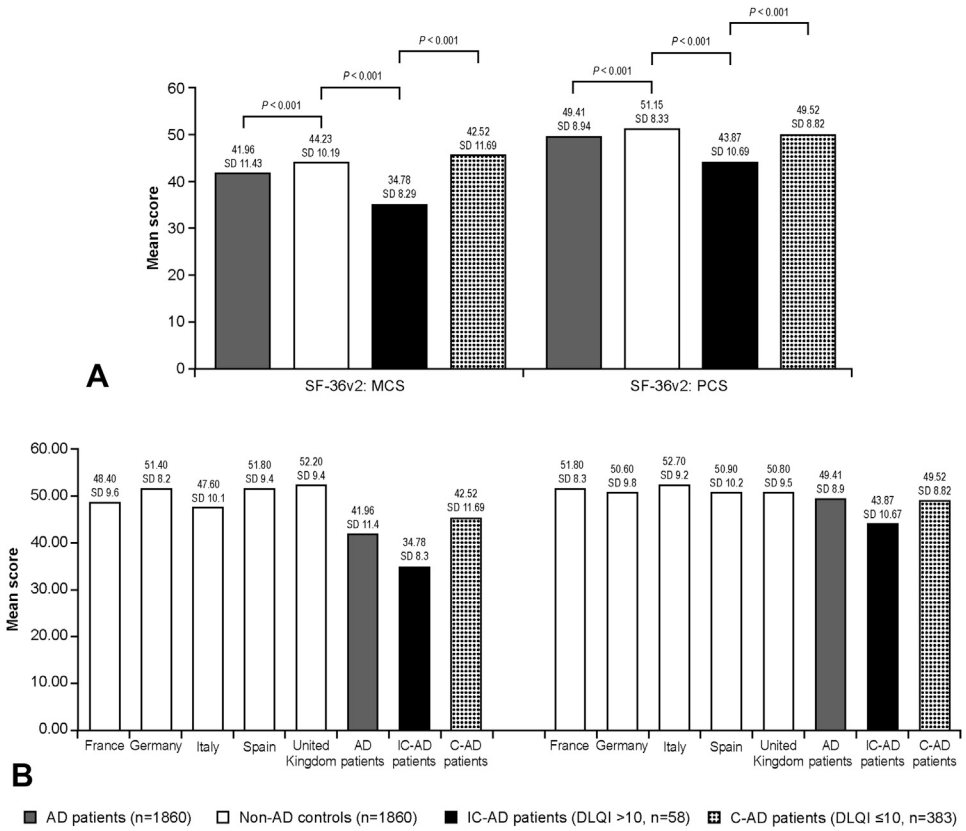


**Fig 2.** Health-related quality of life in (A) patients with atopic dermatitis (*AD*), controlled AD (*C-AD*), and inadequately controlled AD (*IC-AD*) versus controls without AD (*Non-AD*) and (B) patients with AD, C-AD, and IC-AD versus normative populations in France, Germany, Italy, Spain, and the United Kingdom, respectively. Lower scores imply more impairment in health-related quality of life. *DLQI*, Dermatology Life Quality Index; *MCS*, Mental Component Summary; *PCS*, Physical Component Summary; *SD*, standard deviation; *SF-36v2*, 36-Item Short Form Health Survey, version 2.

### Health care resource utilization

The proportion of patients with ≥1 traditional provider visit in the previous 6 months was higher in patients with AD (93.1%; mean number of visits, 7.4 ± 11.2; $P < .001$) and IC-AD (94.8%; mean number of visits, 13.9 ± 17.8; $P = .027$) than in controls without AD (84.2%; mean number of visits, 4.5 ± 7.2; $P < .001$ for both comparisons) (Fig 4).

Similarly, the proportion of patients with ≥1 emergency department (ED) visits was 21.6% for patients with AD, 37.9% for patients with IC-AD, and 16.5% for controls without AD (both $P < .001$). The proportion of patients with ≥1 hospitalization was similar in patients with AD and controls without AD (9.0% and 8.7%, respectively), but significantly higher in those with IC-AD (19.0%; $P = .007$) (Fig 4). The mean number of health care provider visits, ED visits, and hospitalizations for patients with IC-AD (13.9 ± 17.8, 0.9 ± 1.7, and 0.4 ± 1.4, respectively) compared with controls without AD (4.5 ± 7.2, 0.3 ± 1.5, and 0.1 ± 0.6, respectively) were all significantly higher ($P < .001$, $P < .001$, and $P = .003$, respectively).

There were also significant differences in HCRU between patients with IC-AD and those with C-AD for at least 1 ED visit (37.9% vs 20.9%; $P = .004$) and at least 1 hospitalization (19.0% vs 9.1%; $P = .022$), respectively (Fig 4). The mean number of health care provider visits (13.9 ± 17.8 vs 7.6 ± 9.3), ED visits (0.9 ± 1.7 vs 0.4 ± 0.9), and hospitalizations (0.4 ± 1.4 vs 0.1 ± 0.5) was also greater for patients with IC-AD than for those with C-AD (all $P < .001$).

## DISCUSSION

This study of adult patients with AD from France, Germany, Italy, Spain, and the United Kingdom indicates that AD is associated with a significant disease burden and higher prevalence of atopic and psychological comorbidities, impaired HRQoL, lower work productivity, increased activity impairment, and increased health care utilization. The burden is even higher among patients with IC-AD.

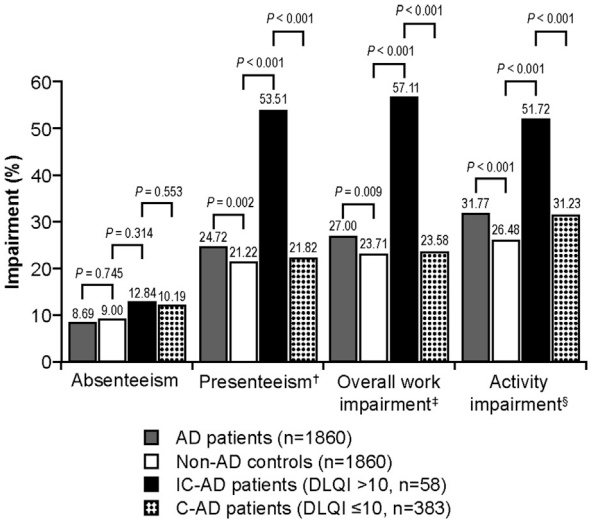


**Fig 3.** Work and Productivity Impairment questionnaire scores in patients with atopic dermatitis (*AD*), controlled AD (*C-AD*), and inadequately controlled AD (*IC-AD*) versus controls without AD (*Non-AD*). *DLQI*, Dermatology Life Quality Index. †Presenteeism: percentage reduced productivity while at work. ‡Overall work impairment: percentage of overall work impairment (absenteeism plus presenteeism). §Activity impairment: percentage reduced everyday activity.

The importance of disease burden in AD and the limitation of European data in this field have been recognized by the European Federation for Allergy and Airways Diseases Patients' Associations, which has initiated a survey in 9 member states to obtain better information about the impact of AD in Europe.[28] Our findings highlight the burden of AD in Europe, consistent with the patient-reported burden of AD in the United States[19,29,30] and Japan[31] and another study based on DLQI data in Spain.[32] These studies support conclusions by the World Health Organization, based on the 2010 Global Burden of Disease survey, that AD is associated with the highest number of disability-adjusted life-years of all skin disorders.[33,34] Our results are also consistent with global epidemiologic studies highlighting the public health importance and burden of skin diseases, including AD.[35,36]

Furthermore, our results are in line with an analysis of participants in a multinational clinical trial, including patients from 4 European countries, that revealed the multifactorial impact of AD on patients.[17] The results also support the known link between AD and other conditions.[2,37,38] AD is often the first manifestation of atopic disease, with patients subsequently developing other atopic conditions such as food allergies, allergic rhinitis (hay fever), and asthma, known as the "allergic march."[39,40]

This study found depression and anxiety were common in patients with AD versus controls without AD. Higher rates of depression in European patients have been reported previously[16] and are confirmed by our findings. For HRQoL, all patients with AD had substantially lower SF-36v2 MCS scores than scores for normative populations in each study country,[20] highlighting the negative psychological impact of AD. For patients with IC-AD, PCS scores were also substantially lower than scores for the normative populations. The minimal clinically important difference in SF-36v2 MCS and PCS scores is not known for AD, but values of 3 to 5 points have been reported for other chronic diseases.[41-45] Compared with this reference marker of the minimal clinically important difference, the 6-point to 9-point differences in these scores between non-AD and IC-AD suggest important decrements in HRQoL related to AD. Impaired HRQoL in adults with AD compared with that in the general population has previously been reported.[46-48]

Consistent with US[29,30] and Japanese[31] NHWS data, work productivity and activities of European patients with AD were negatively affected by the presence of AD, in particular for patients with IC-AD. Given the deleterious impact of AD on society in reduced national levels of productivity, effective AD treatment is important not just for individual patients but also for society as a whole. As one of the variables used in the propensity score matching was employment status, it is possible that the impact of AD on work life may have been underestimated in this study.

We observed an additional burden: compared with controls without AD, patients with objectively defined markers of poor disease control also revealed increased HCRU, including significantly higher rates of ED and traditional health care visits. The survey questions relating to HCRU were not specific for AD to allow a full comparison of resource use by individuals with and without AD. These results were in line with a US-based study of AD-related HCRU, with severity defined on clinical variables.[49] A previous comparison of HCRU in patients with AD based on the US NHWS did not find any significant difference between those with self-reported moderate-to-severe versus mild disease, but small numbers of patients reporting the higher level of disease severity might have limited the power of the analysis.[29] Regional differences in health care systems and clinical practice are another possible contributor to the differences in study findings.

The key strength of this study lies in the NHWS sampling approach, which was defined to ensure

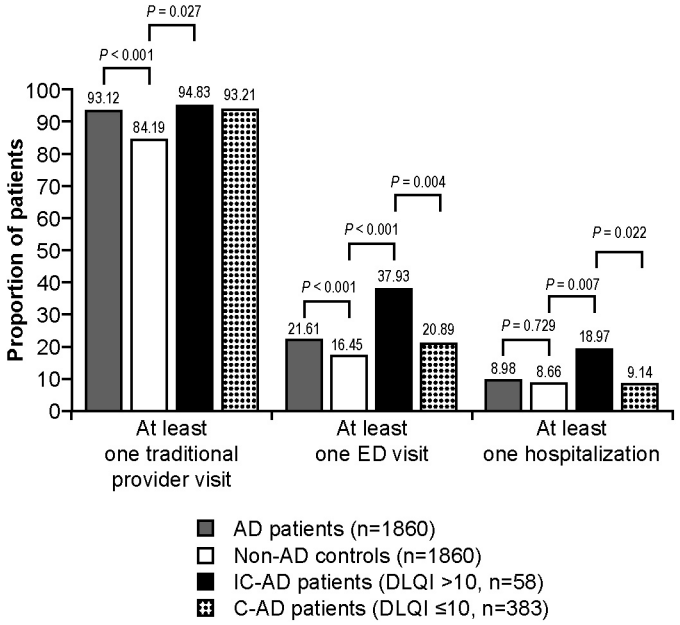


**Fig 4.** Health care resource utilization over the previous 6 months in patients with atopic dermatitis (AD), controlled AD (*C-AD*), and inadequately controlled AD (*IC-AD*) versus controls without AD (*Non-AD*). *DLQI*, Dermatology Life Quality Index; *ED*, emergency department.

that the sample was representative of the general adult populations of the study countries. The use of propensity score matching of the groups with and without AD reduced the chances of confounding differences in baseline demographic characteristics between the groups. However, the frequency of self-reported AD in this study was 2.3% (1860 of 80,600), which is on the low side of point prevalence of AD in adults reported in the literature, which ranges from 4.4% to 7.1%.[12,50] This may be attributable to the case definition, because AD is a more specific term than eczema, which is more commonly recognized by the general population.

Study limitations include technology limitations that may have biased the sample to favor younger, healthier adults, hence under-representing patients with AD, particularly those with more severe AD. In addition, the sample of patients reporting a DLQI score was limited to only 441.

Although a random, stratified sampling framework was used, those without access to a computer or the Internet were likely not to have been contacted or to have participated in the study. In addition, those hospitalized or extremely ill may have not been healthy enough to complete a 30-minute survey. Finally, only 6% of patients offered the survey completed it. They may not be representative of the entire population; in particular, patients in the middle part of life, busy with their jobs and family life, may not have had the time to participate in the study. The sociodemographic data for the full population of contacted individuals indicate the most prevalent age groups across countries was 18 to 29 years.

Another potential limitation of the study is that the presence of AD was largely based on patient reporting. Although previous research has reported discrepancies of up to 30% in physician and patient assessments of AD,[51] patient-reported data are imperative for obtaining the patient perspective in the evaluation of disease outcomes.[52] Diagnoses and other clinical variables were not confirmed by review of patient medical records owing to the self-reported nature of the data; therefore, the present data may have been susceptible to recall bias.[53] Furthermore, patients with AD were matched to controls by country rather than geographic region. Because region can affect access to health care and therefore use of health care resources, this may have affected our findings.

As a representation of the populations in 5 European countries, this study has provided evidence on the impact of disease severity and overall burden in adult patients with AD in Europe, for which data are currently sparse.

## CONCLUSION

This study highlights the significant disease burden associated with IC-AD in a European adult population, suggesting the need for more effective AD management strategies.

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