# Assessment of major comorbidities in adults with atopic dermatitis using the Charlson comorbidity index

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***Background:*** There is a growing interest in comorbidities of adults with atopic dermatitis (AD).

***Objectives:*** To examine the burden of comorbidities in adult patients with AD using the Charlson comorbidity index (CCI) in nationwide registries.

***Methods:*** All Danish patients ≥18 years on January 1, 2012 with AD diagnosed by a hospital dermatologist were included. Patients were age-and sex-matched in a 1:4 ratio with general population controls. Severity was determined by systemic AD treatment and analyzed by conditional logistic regression.

***Results:*** In total, 10,738 adult patients with AD and 42,952 controls were analyzed. CCI score was significantly increased in smokers with AD compared with controls (0.41 vs 0.13, $P < .001$). Nonsmokers with AD had a similar CCI score as controls (0.09 vs 0.08, $P = .12$). In analyses restricted to patients with severe AD, a stronger difference in CCI score was observed for smokers (0.48 vs 0.14, $P < .001$) than for nonsmokers (0.10 vs 0.08, $P = .01$).

***Limitations:*** Observational studies do not establish cause and effect.

***Conclusion:*** On the basis of nationwide data, the risk for major comorbidities was significantly increased in adult patients with AD compared with controls. The risk difference was predominantly found in patients with severe disease and among smokers. (J Am Acad Dermatol 2017;76:1088-92.)

***Key words:*** atopic dermatitis; comorbidity; epidemiology; risk; smoking.

Atopic dermatitis (AD) affects about one fifth of children,[1] with many still having the disease in adulthood.[2] Patients with AD not only have increased risk for atopic and psychiatric comorbidities[3,4] but also certain autoimmune diseases.[5-8] Recently, cardiovascular (CV) risk factors and comorbidities were associated with AD,[9-12] although lifestyle factors such as increased alcohol consumption and smoking might explain the increased risk of CV disease (CVD).[13-15] The Charlson comorbidity index (CCI) allows for a comparison of comorbidities based on the International

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Classification of Diseases (ICD) diagnostic codes. Based on adjusted risk for mortality or resource use,[16] selected major systemic comorbidities have an associated weight from 1 to 6. The sum of all the weights results in a single comorbidity score for a patient, and a score of 0 indicates that no comorbidities exist. We compared the CCI in adults with AD and matched controls.

**CAPSULE SUMMARY**

- Despite the growing literature on atopic dermatitis comorbidities, systematic analyses of comorbidities remain scarce.
- Adults with atopic dermatitis had an overall higher occurrence of comorbidities when nationwide data were analyzed with the Charlson comorbidity index. The increased risk was restricted to patients with severe disease, and in particular smokers.
- Sedentary lifestyle and modifiable risk factors should be targets for intervention when assessing comorbidities in patients with atopic dermatitis.

## MATERIALS AND METHODS

### Data sources and study population

Danish nationwide registries can be linked at the individual level.[17] The Danish National Patient Register[18] contains information on in- and outpatient (ambulatory) hospital consultations according to the ICD classification. The Danish Registry of Medicinal Products Statistics[19] records information on all pharmacy-dispensed medications according to the international Anatomical Therapeutic Chemical classification.

Medication dispensed during hospitalization or given directly from ambulatory clinics is recorded in the Danish National Patient Register. Tax-reported household income is recorded by Statistics Denmark.[20] The source population comprised all adults ≥18 years alive and resident in Denmark on December 31, 2012. We identified all adults with an AD diagnosis (ICD-8 691 and ICD-10 L20) after their 18th birthday. To ensure accuracy of the AD diagnosis, we only included diagnoses given by a hospital dermatologist. Each patient was matched on age and sex with 4 control subjects from the general population. Patients were classified as outpatients (ie, seen in an ambulatory setting) unless they had been hospitalized at least once due to AD. Patients were classified with severe disease if they received systemic therapy for AD (methotrexate, azathioprine, mycophenolate mofetil, systemic corticosteroids, psoralen plus ultraviolet A, or cyclosporine), and if not, they were classified as mild. We calculated an age-standardized index of socioeconomic status based on the mean gross annual income during the 5-year period before December 31, 2012. Smoking data was collected using a data retrieval algorithm, which has been described extensively elsewhere.[21] Major medical comorbid disease burden was evaluated by means of the CCI.[22] Comorbidity for up to 5 years before December 31, 2012, was identified, and use of the CCI in the Danish National Patient Register has an overall positive predictive value of 98%.[23]

### Statistical analysis

Sample characteristics and CCI scores were summarized descriptively. Characteristics of individuals with or without AD were compared by using either the $\chi^2$ for dichotomous variables and the Fisher's exact test for continuous variables. The associations between AD and comorbid diseases were estimated by conditional logistic regression, inherently adjusting for the matched factors, ie, age and sex. The Benjamini-Hochberg procedure was used to adjust for multiple comparisons of the examined outcomes, with differences considered significant at $P < .05$ in 2-sided tests. All analyses were performed with SAS v9.4 (SAS Institute Inc, Cary, NC, USA) and STATA v13.0 (StataCorp, College Station, TX, USA). The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology recommendations.[24]

## RESULTS

A total of 10,738 adult patients with AD and 42,952 age- and sex-matched controls were analyzed (Table I). Higher proportions of patients with AD belonged to the highest socioeconomic class. About half of patients with AD had severe disease. The proportion of smokers was significantly higher among AD patients than among controls (11.2% vs 7.6%, $P < .001$). Tables II and III show the CCI scores for patients with AD and controls. Overall, AD patients had a significantly higher CCI score than controls (0.13 vs 0.09, $P < .001$), but in subanalyses stratified by severity, we found that only severe AD (0.17 vs 0.10, $P < .001$) and not mild AD (0.07 vs 0.07, $P = .98$) was associated with higher CCI scores than controls. Stratification by hospitalization status showed that both inpatients (0.16 vs 0.11, $P < .001$) and outpatients (0.11 vs 0.08, $P < .001$) had significantly higher CCI scores than controls. The CCI score was only significantly increased in smokers with AD compared with control subjects (0.41 vs 0.13,