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Atopic dermatitis is associated with less physical activity in US adults

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Title: Atopic dermatitis is associated with less physical activity in US adults.

Running Title: Atopic dermatitis and less physical activity.

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Abbreviations used: AD = atopic dermatitis; NHANES = National Health and Nutrition Examination Survey

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Abstract: In the present study, we demonstrate that adult atopic dermatitis is associated with decreased moderate-vigorous and overall physical activity as judged by actigraphy. Such decreased activity may place atopic dermatitis patients at higher risk for cardiovascular disease.

To the editor:

Patients with atopic dermatitis (AD) have multiple potential risk factors for decreased physical activity. First, heat, sweat and exercise were found to be the most commonly reported exacerbants of AD in children (1, 2). Second, patients with eczematous lesions affecting the hands and feet may have limitations of physical activities. Third, comorbid fatigue, sleep disturbances and depression might all be indirectly associated with decreased physical activity in AD. We previously found that adult AD is associated with lower odds of self-reported daily vigorous physical activity and lower frequency of vigorous activity (3). Moreover, adult AD was associated with significantly higher cardiovascular risk (3, 4). However, no studies examined physical activity in adult AD patients using objective measures. Self-report of physical activity is limited because respondents' perceptions of activity intensity vary and periods of physical activity may be difficult to recall and quantify. We sought to confirm whether adults with AD have decreased vigorous physical activity using objective measures.

We used the 2005-2006 National Health and Nutrition Examination Survey (NHANES). Written informed consent was obtained from all participants or proxies. Household surveys were administered in-person in English and Spanish, followed by health examinations in mobile examination centers (5). Then, all participants ≥ 6 years of age, who reported no walking impairments during the health examination, were invited to wear the uniaxial ActiGraph AM-7164 (ActiGraph, Ft. Walton Beach, FL) strapped around the waist to assess ambulatory physical activity (6).

History of AD was assessed by a positive response to the question, "Has a doctor or other health professional ever told (you/sample person) that (you have/sample person has) eczema?" We previously validated this question and found it to have very good specificity and positive

predictive value (7). Subjects who reported a health care provider diagnosis of psoriasis were excluded from analyses.

Participants were instructed to wear the monitor for seven consecutive days over their right hip and to remove the monitor before going to bed and during showers or other water activities. The monitors were returned to the NHANES contractor to download data, and check the monitor calibration (6). The accelerometer output is an activity count, which is the weighted sum of the number of accelerations over a minute, where weights are proportional to the magnitude of acceleration. A sedentary minute and a moderate-vigorous minute are analytically identified by activity counts/minute of <100 and ≥ 2020 respectively (6). Non-wear time was defined as intervals of at least 60 consecutive minutes of 0 counts with allowance for up to 2 consecutive minutes of counts between 0-100. A valid day of monitoring was defined as 10 or more wear hours (6). To provide reliable physical activity estimates, we restricted analyses to participants with at least four valid days of accelerometer monitoring (6). Children were excluded from the analysis because of different definitions of physical activity levels, as well as potential differences between pediatric and adult AD.

Bivariate and multivariate survey weighted linear regression was performed in SAS version 9.4 (SAS institute, Cary, NC). The dependent variables were average daily activity, sedentary time, light and moderate-vigorous physical activity time (all in minutes). The independent variable was history of AD. Multivariate models included age, sex, race, education level, US birthplace, type of home, BMI and actigraph wear time. Additional models controlled for asthma, sleep disturbance (difficulty falling asleep, difficulty staying asleep, waking up early, not having restful sleep) or comorbid depression (SIGECAPS criteria). Domain analysis was performed to yield appropriate estimates of variance for non-missing values. Two-way

interaction terms between AD and covariates were tested and included in final models if $P < 0.01$ and modification of estimates $> 20\%$. A 2-sided $P < 0.05$ was taken to indicate statistical significance. Results were weighted to represent the population of US adults using data from the U.S. Census Bureau. Approval by the Northwestern University institutional review board was waived.

A total of 3,252 adults ages 18-85 (58.5% of the cohort) were included in this analysis; 344 (6.2%) had AD, of whom 57.7% were women, 68.2% white, 84.9% completed high school or higher education, 89.9% were born in the US, 25.9% overweight, 37.6% obese and 29.3% had a history of asthma or hay fever.

In multivariate models, adult AD was associated with significantly lower average total counts of daily activity (adjusted beta [95% CI]: -15994 [-30536.00—1452.74], $P = 0.03$) and moderate-vigorous physical activity (-2.12 [-3.92—-0.33], $P = 0.02$), but no association with sedentary time (12.74 [-4.30—29.79], $P = 0.13$) or light physical activity (-7.91 [-27.39—6.35], $P = 0.20$) (Table 1). The association between AD and total daily activity and moderate-vigorous physical activity also remained significant in models that controlled for sleep disturbance, comorbid asthma and depression. Moreover, there were no significant two-way interactions between AD and any of the covariates as predictors of physical activity levels ($P \geq 0.36$ for all).

Analysis of the pattern of missing values for actigraphy data in NHANES revealed that missing values were more likely in women, blacks, those who did not complete high school education, had a $BMI \geq 35$ and < 18 ($P < 0.05$), but were not associated with age, birthplace in the US, history of AD or asthma. Therefore, sensitivity analyses were performed that excluded these subgroups in adults. The associations for average daily activity remained significant in models

that excluded women ($P=0.04$), blacks ($P=0.049$), those who did not complete high school education ($P=0.007$) and had $BMI \geq 35$ and <18 ($P=0.02$).

The results of this study confirm and expand on previous studies that found less self-reported vigorous physical activity among adults with AD from 2 different cohorts (7). In that study, however, physical activity was assessed by self-report, which may not be a reliable predictor of activity levels. Moreover, a recent systematic review found no significant association between history of AD and physical activity (8). However, there were very few studies, with considerable heterogeneity, different regions and inconsistent measures of self-reported physical activity. The present study further suggests that adult AD is associated with less physical activity, particularly moderate-vigorous activity, in a different cohort. Moreover, this study used objective measures of physical activity, i.e. actigraphy. Physical activity levels were neither related to comorbid asthma, sleep disturbances or depression. It is well established that regular physical activity decreases acquired cardiovascular risk factors, including obesity, diabetes, hypertension and hyperlipidemia (9). Thus, decreased physical activity in adults with AD may contribute toward increased cardiovascular risk.

This study has several strengths, including being US population-based, with complex survey weighting, a very large diverse sample and objective measurement of physical activity and BMI. However, this study has potential limitations. History of AD was self-reported and not assessed clinically or verified with any diagnostic testing. However, we previously validated the question used in this study and found it to have very good specificity and positive predictive value (7). Nevertheless, the validation study was performed in the dermatology setting and may not be representative of the US population. Moreover, we were not able to measure whether the adults with a history of AD had recently active disease or remitted. Future studies of the

association between AD and physical activity are needed with objective confirmation of active AD and assessment of AD severity. Despite the large sample size, there were smaller sample sizes with occasionally inflated estimates and broader confidence intervals for some individual subsets analyses. The activity monitors were not waterproof, precluding monitoring of activities such as swimming and water aerobics. Additionally, the device records uniaxial movement, which may be not as accurate in activities primarily involving upper body movement. Finally, we were unable to assess AD severity and its impact on physical activity. Future studies are needed to verify these associations and determine the role of AD severity on physical activity. Finally, further studies are needed to determine effective strategies for improving physical activity in adults with AD.

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Table 1. Association of atopic dermatitis with physical activity as measured by daytime actigraphy in adults.						
Variable	Atopic dermatitis					
	No (n=3,061)	Yes (n=189)				
	Mean (95% CI)	Mean (95% CI)	Crude beta (95% CI)	P	Adj beta (95% CI)	P
Average daily activity (count)*	261275 (254825.6–267725.3)	239245 (222411.3– 256079.4)	-19562 (-35498 – -3627.32)	0.02	-15994 (-30536 – -1452.74)	0.03
Average sedentary time (min)	489.7 (485.0–494.4)	510.6 (494.8–526.4)	15.83 (-1.83 – 33.50)	0.08	12.74 (-4.30 – 29.79)	0.13
Average light activity (min)	344.4 (338.5–350.3)	329.6 (311.9–347.2)	-14.19 (-31.41 – 3.04)	0.10	-7.91 (-27.39 – 6.35)	0.20
Average moderate-vigorous activity (min)	21.2 (20.0–22.4)	17.9 (15.5–20.4)	-2.68 (-5.42 – -0.06)	0.04	-2.12 (-3.92 – -0.33)	0.02

Survey linear regression models were constructed with minutes of average daily activity, sedentary time, light activity and moderate-vigorous activity as measure by actigraphy being the dependent (outcome) continuous variables and history of atopic dermatitis (binary) as the independent (explanatory) variable. Multivariate models included age (continuous), gender (binary), race/ethnicity (white vs. other), birthplace in the US (binary), highest level of education in the household (less than high school vs. high school or greater), type of home (house vs. other), body mass index (<18, 18-24, 25-29, ≥30) and daily wear time of the actigraph (continuous) as covariates. Domain analysis was performed to yield appropriate estimates of variance. Crude and adjusted beta and 95% confidence intervals (95% CI) were determined.

* Average daily activity is the average total daily accelerometer count.