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A systematic review of vigorous physical activity in eczema

Running Header: Eczema and physical activity.

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Abbreviations used: CI=confidence interval, OR=odds ratio, AD=atopic dermatitis

JI Silverberg and A Kim full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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What's known about this topic?

Previous studies found conflicting results about the impact of eczema on level of physical activity.

What does this study add?

This systematic review revealed few high quality studies of the association between eczema and physical activity.

To the editor:

The hallmark of atopic dermatitis (AD) is intense itch that can disturb all aspects of patients' lives. Sweating is one of the most commonly reported exacerbants of itch in AD^{1,2}. Thus, AD patients may avoid exercise or vigorous physical activity, which are typically accompanied by increased sweating, in order to avoid worsening itch. If patients with AD have a lower physical activity profile, they could potentially be at higher risk for obesity and cardiovascular disease. It is therefore important to understand the relationship between AD and physical activity and develop clinical interventions to improve AD patients' overall health. We conducted a systematic review of the literature and meta-analysis to explore the relationship between AD and vigorous physical activity.

We searched the following databases through March 11, 2015: PubMed (1946-present), EMBASE (1947-present), Scopus (1823-present), GREAT (all years) and the Cochrane Library (1992-present). The search strategy was based on a previous Cochrane review³ (Supplemental Table 1). Studies were excluded based on the title and/or abstract if there was no clear indication they were investigating

physical activity in AD patients or if they were case series, i.e. there was no patient group without AD.

There were no relevant studies in foreign languages.

Both reviewers, AK and JS, independently performed data extraction from these studies and differences were resolved by discussion. The following data items collected were: first author name; year of publication; location; study design; how AD was diagnosed; number of patients in study; level of physical activity; age range; and percent of males in the study. Two studies presented total the odds ratios (OR) of AD for level of activity^{4,5}, but frequencies were not presented thereby precluding inclusion in the meta-analysis. Repeated attempts to obtain the data were made for all these studies, though unsuccessfully. One study presented total group sizes for eczema classification and the odds ratios (OR) of physical activity⁶. The frequencies of AD within each level of physical activity were reconstructed as previously described⁷.

The exposures were level of physical activity and the dependent variable was AD. The definitions for physical activity varied by study. AD was also defined differently throughout studies, where some used the clinical criteria and others various questions from the International Study of Allergy and Asthma in Children⁸, or other definitions. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-Analysis was used to assess study quality based on selection criteria, between-group comparability and study outcome using a 9-star scoring system^{9,10}. We only included studies with NOS ≥ 7 in the meta-analysis.

Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC). Studies of AD and vigorous physical activity or exercise were combined. OR of AD in exercise or vigorous physical activity ≥ 1 or ≥ 3 times a week with 95% confidence interval (CI) were estimated. Forest-plots were constructed for studies included in the meta-analysis. Pooled OR were estimated using both fixed-effect models, as well as random-effect models that account for variability between studies. Egger regression, Begg rank correlation and funnel plot regression were used to assess for potential publication bias. A 2-sided P-value of 0.05 was taken as significant.

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The literature search yielded 4,993 non-duplicate articles. After review of the titles and abstracts, 229 full-text articles were reviewed and 7 manuscripts including 8 studies were included in the final analysis^{4,6,11-14}. Of these, 5 manuscripts had sufficient data for inclusion in a meta-analysis^{6,11-14}. The PRISMA flow diagram is presented in Figure 1. The studies were all cross-sectional, either retrospective or prospective data collection, included both males and females, and encompassed subjects of all ages. Published years of studies ranged from 2008-2014. Quality assessment using the NOS scale revealed that 5 of 8 studies had scores ≥ 7 (good quality) (Supplemental Table 2).

Three studies found a positive association between AD and physical activity^{4,11,12}; three found an inverse association^{5,6,14}; and one found no association¹³. No published studies of the association between exercise or physical activity and eczema severity were found. There were 4 studies with NOS ≥ 7 included in the meta-analysis encompassing 61,974 patients, including 3,065 children and 61,974 adults, of which 5,434 (8.8%) had AD. Overall, 3,298 (8.7% [range, 7.5–47.3%]) of patients with less than once weekly exercise, 2,136 (8.8% [6.8–51.0%]) of patients with at least once weekly exercise and 147 (23.8% [14.9–47.9%]) of patients with at least thrice weekly exercise had a history of AD.

Significant heterogeneity was identified between studies that assessed once weekly (Cochrane Q P -value <0.001 ; $I^2=87.5\%$), but not thrice weekly vigorous activity or exercise ($P=0.37$; $I^2=4.3\%$).

Vigorous physical activity or exercise at least once weekly (OR [95% CI] for random-effects model: 1.04 [0.92–1.17]) or thrice weekly (1.11 [0.88–1.40], $P=0.40$) were not associated with AD in random-effects models. Publication bias was not detected as judged by non-significant Egger regression, Begg rank correlation or funnel plot regression for any of the above mentioned outcomes ($P\geq 0.27$).

It is interesting that some studies found associations between AD and increased physical activity^{4,11}. Al Sahab et al. noted that, in Lebanon, people are mostly physically active outdoors and thereby exposed to airborne pollutants that could exacerbate AD¹¹. Further, the frequency and types of physical activity and exercise performed are likely modified by a number of factors, including access to

parks and recreational spaces, adiposity, functional limitation from medical disorders such as asthma or arthritis, socio-cultural factors and attitudes toward healthfulness.

This systematic review revealed few high-quality studies, with varying definitions of exercise and vigorous physical activity and it appears that none of the self-reported assessments of physical activity were previously validated. Thus, there is insufficient evidence to make solid conclusions. Future studies are needed to address the knowledge gaps about the association of AD and physical activity, including using objective measures, longitudinal studies to determine the temporal relationship, stratification of results by different socio-demographic groups, including race/ethnicity and gender, and exploration of the mechanisms of association.

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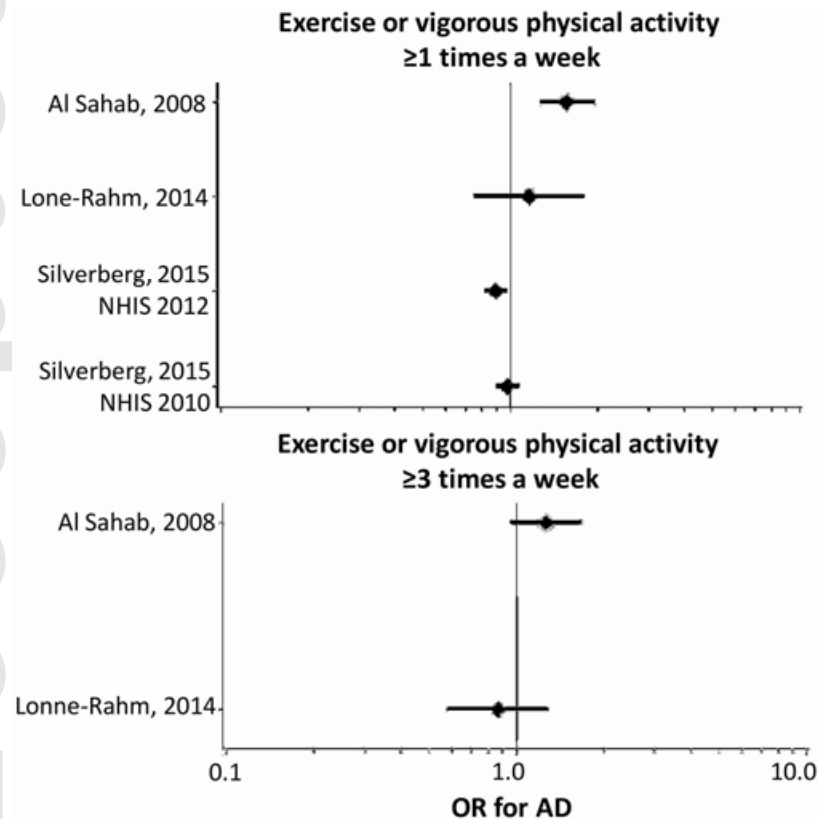
Abbreviations used: CI=confidence interval, OR=odds ratio, AD=atopic dermatitis; NHIS= National Health Interview Survey

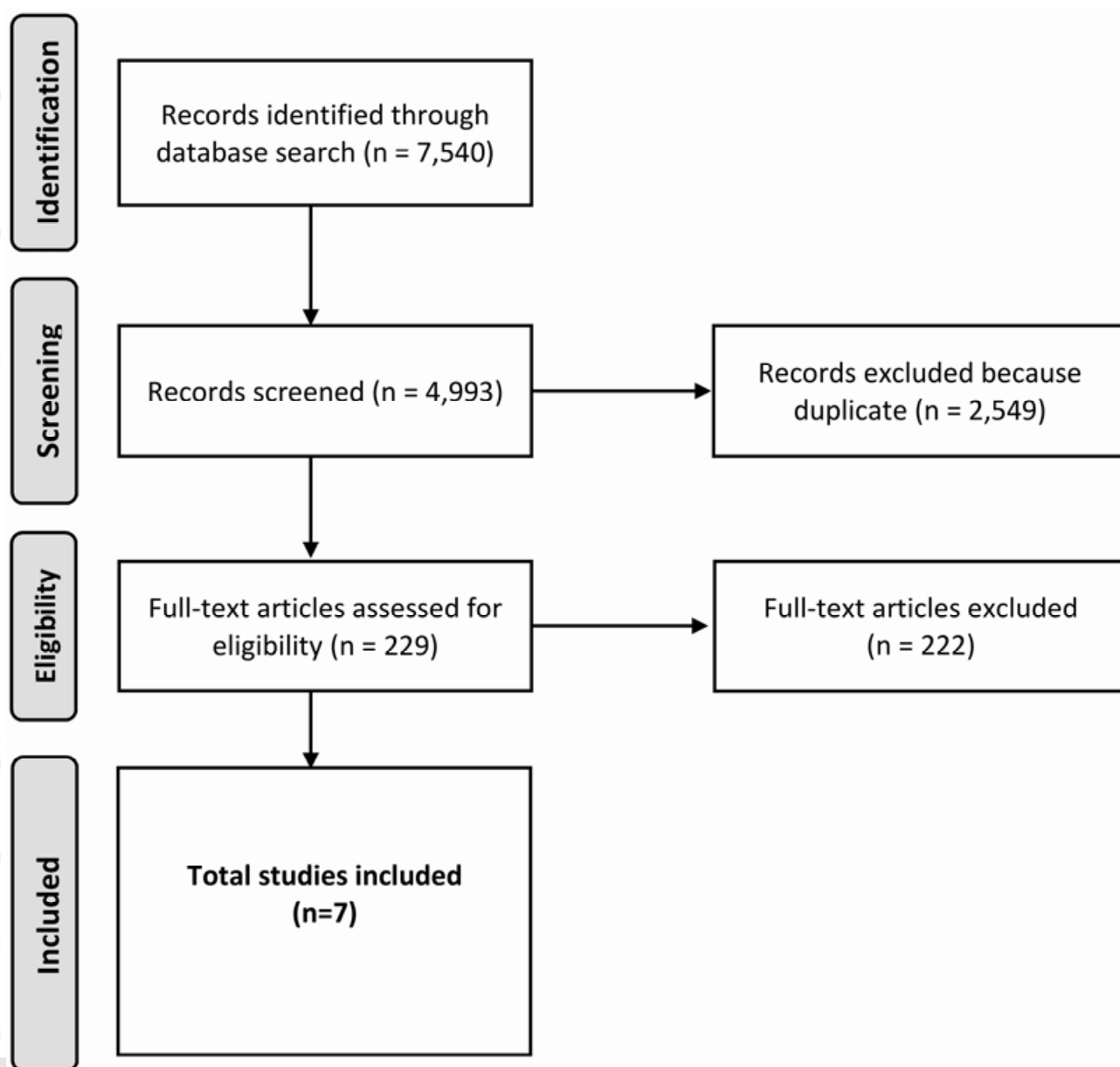
Figure legends.

Figure 1. PRISMA flow diagram of literature search and study selection for meta-analysis of AD, exercise and vigorous activity.

AD=atopic dermatitis.

Figure 2. Association between AD, exercise and vigorous activity. Forest Plot are presented for the log-odds ratios and 95% CI of AD in patients with at least once weekly or thrice weekly exercise and vigorous activity compared.





Supplemental Table 1. Literature search scheme for OVID MEDLINE.
1. explode DERMATITIS, ATOPIC/ 2. atopic dermatitis.mp. 3. dermatitis atopic.mp. 4. explode ECZEMA/ or eczema.mp 5. childhood eczema.mp. 6. infantile eczema.mp. 7. neurodermatitis.mp. or exp Neurodermatitis/ 8. Besnier's prurigo.mp 9. or/1-8 10. exercise 11. physical activity 12. sedentary 13. sports 14. 10-13 15. 9 and 14

Supplemental Table 2. Study characteristics.

#	First author, Year published	Location	No physical activity		Physical activity		Age (yr)	Sex	Study design	Assessment of AD	Assessment of physical activity	NOS score *
			Total #	# (%) with AD	Total #	# (%) with AD						
1	Al-Sahab, 2008	Lebanon	1823	191 (10.5%)	791	126 (15.9%)	13-14	48% M	Cross-sectional	ISAAC questionnaire - ever history of eczema	Self-report of exercise 1-2 times a week vs. never or rarely	8
					451	67 (14.9%)					Self-report of exercise ≥3 times a week vs. never or rarely	
2	Foliaki, 2008	Samoa, Fiji, Tokelau, French Polynesia and New Caledonia	19212	2498 (13.0%)	1655	242 (14.6%)	13-14	47.5% M	Cross-sectional	ISAAC questionnaire - ever history of eczema	Self-report of exercise ≥3 times a week vs. 0-2 times a week	6
3	Lonne-Rahm, 2014	Sweden	110	52 (47.3%)	123	68 (55.3%)	20-34	39.2% M	Cross-sectional	Clinically-diagnosed AD	Self-report of more strenuous exercise at least once a week vs. very little / a few walks / light physical activity	8
					167	80 (47.9%)					Self-report of regular hard training or competition / everyday exercise vs. very little / a few walks / light physical activity	
4	Mitchell, 2013	73 centers from 35 countries	NP	NP	NP	OR (95% CI): 1.02 (0.95,1.11)	6-7	NP	Cross-sectional	ISAAC questionnaire - Ever itchy rash coming and going for 6 months, and 'in the	Caregiver-report of exercise 1-2 times a week vs. never or occasionally	8

					NP	0.97 (0.88,1.06)				past 12 months' and flexural distribution.	Caregiver-report of exercise ≥3 times a week vs. never or occasionally	
			NP	NP	NP	1.18 (1.11,1.26)	13-14				Self-report of exercise 1-2 times a week vs. never or occasionally	
					NP	1.24 (1.15,1.34)					Self-report of exercise ≥3 times a week vs. never or occasionally	
5	Brescianini, 2009	Italy	223	26 (11.7%)	234	24 (9.3%)	11-15	49.3% M	Cross-sectional	ISAAC questionnaire - ever diagnosis of eczema OR ever itchy rash, coming and going, for at least 6 monthss	Self-report of ≥1 hr of physical activity a week vs. <1 hr a week	5
6	Font-Ribera, 2011	United Kingdom	NP	NP	NP	OR (95% CI): 0.66 (0.42,1.02)	7	50.7% M	Cross-sectional	ISAAC questionnaire - eczema in past 12 months	Self-report of ever swimming before age 4 yr and high swimming score at 4–7 yr vs. never swimming before age 4 yr or 4–7 yr	6
			NP	NP	NP	0.86 (0.53, 1.39)	10					
7	Silverberg, 2015	United States NHIS 2012	20441	1537 (7.7%)	13651	923 (6.7)	18-85	46.1% M	Cross-sectional	Self-reported history of diagnosed eczema in the past year	Self-report of vigorous activity ≥1 time a week vs. <1 time a week	8
8	Silverberg, 2015	United States NHIS 2010	15398	1518 (10.4%)	9019	872 (10.1%)	18-85	44.1% M	Cross-sectional	Self-reported history of itchy red rash in the past year	Self-report of vigorous activity ≥1 time a week vs. <1 time a week	8

* Newcastle-Ottawa Scale: Poor quality: 0-1 for selection and outcome, 0 for comparability; Fair quality: 2 for selection, ≥1 for comparability, ≥2 for outcome; Good quality: ≥3 for selection, ≥2 for comparability and outcome.