

Title: Prevalence and Trend of Allergen Sensitization in Patients Referred for Patch Testing with a Final Diagnosis of Psoriasis, North American Contact Dermatitis Group Data, 2001-2016

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Abstract

Background: Little is known about the relationship between psoriasis and allergic contact dermatitis (ACD).

Objective: To examine the associations with ACD, related clinical characteristics, and common positive and clinically relevant allergens of patients with a final diagnosis of psoriasis who were referred for patch testing.

Methods: Retrospective analysis of 38,723 patients from the North American Contact Dermatitis Group.

Results: Patients with a final diagnosis of psoriasis had lower proportions of ACD than those without psoriasis (32.7% vs 57.8%). In multivariable logistic regression models, psoriasis was *inversely* associated with female sex, black or Asian race, history of atopic dermatitis and hay fever. Patients with a final diagnosis of psoriasis were less likely to have one or more positive allergic patch test reactions or to have a current clinically relevant patch test reaction to the majority of the most commonly positive and/or relevant allergens. The most clinically relevant allergens included nickel sulfate, methylisothiazolinone, and fragrance mix I.

Conclusion: Approximately one-third of patients who were referred for patch testing with a final diagnosis of psoriasis were also diagnosed with ACD. In select patients with suspected psoriasis who also have a clinical presentation suggestive of ACD, patch testing may be helpful.

1. Introduction

Psoriasis is a chronic inflammatory skin disease affecting approximately 1.5% of adults in North America(1). The link between psoriasis and ACD has been the subject of much debate. Previous epidemiologic(2, 3) and cohort studies(4-6) found inverse associations between psoriasis and ACD, while a recent, large-scale study showed no association(7). However, psoriasis patients may have increased risk of secondary ACD owing to skin-barrier disruption and increased use of topical anti-inflammatory therapy. Yet, little is known about the clinical characteristics of patients referred for patch testing with a final diagnosis of psoriasis.

Few studies analyzed the specific allergen profile among patients with psoriasis(5, 7, 8). A previous UK study found a similar rate of positive reactions in patients with and without psoriasis(7). However, given differences in personal care products and environmental exposures across geographical regions, there is a need to identify the most clinically relevant allergens and their sources in North American patients with both psoriasis and ACD. Using a large, North American cohort of patients referred for patch testing, we sought to examine the proportion of patients with a final diagnosis of both psoriasis and ACD, their associated clinical characteristics and their most commonly positive and clinically relevant allergens.

2. Methods

2.1. Data Source

De-identified data were analyzed from 38,723 patients patched tested by the North American Contact Dermatitis Group (NACDG) from 2001-2016 per previously described standardized guidelines(9-12). Patients were patch tested using the NACDG screening series in 2-year cycles. Data were entered at a centralized location (Access 2010 and Excel 2019; Microsoft). This study was approved by the Institutional Review Board at Northwestern University.

Data was collected on patient demographic characteristics (age, sex, race/ethnicity, and employment), history of atopic disease (atopic dermatitis [AD], asthma, hay fever), sites of dermatitis (up to 3 coded), patch test results including strength of reaction of each allergen, clinical and occupational relevance of each allergen, and the final diagnosis (up to 3 coded). Allergen profile varied by 2-year cycle. Final diagnoses were determined by clinician reading of patch test results at 48 and 72-168 hours after allergen application. Patch test readings were assessed as negative (-), indeterminate (+/-), weak (+), strong (++), and extreme (+++). In addition, a final interpretation was coded as “allergic” or “not allergic.” Indeterminant reactions were coded as allergic or not allergic based on the combination of temporal pattern, other patch test results, and clinical judgement. Clinical relevance was determined by a combination of patch test results and patient history and assessed as definite (positive patch or repeated open application test with product containing allergen), probable (identification of allergen in product used by patient with consistent clinical

presentation), possible (contact with substance possibly containing the allergen), or past relevance (positive patch test with a past exposure).

2.2. Statistical analysis

Data were analyzed using SAS version 9.4 software (SAS Institute, Cary, NC). The frequency and proportion of patients with any (1 of 3) and/or a primary diagnosis of psoriasis were estimated. The proportion of sites affected by dermatitis were estimated in patients with and without psoriasis and compared using Chi-square tests.

Summary statistics were estimated for patient demographics (age, sex, race/ethnicity, employment) and history of atopy (AD, asthma, hay fever) in patients with and without a final diagnosis of psoriasis. Multivariable models were constructed with any diagnosis (yes/no) or a primary final diagnosis of psoriasis (yes/no) as the dependent variable and the aforementioned patient characteristics as independent variables. Additional models were constructed with either ≥ 1 positive allergic reaction (yes/no) or relevant allergic reaction (yes/no) as the dependent variable among patients with a diagnosis of psoriasis. Adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) were estimated.

The frequency and proportion of a final diagnosis of ACD, irritant contact dermatitis (ICD), and AD were estimated and compared between patients with and without a final diagnosis of psoriasis and compared with Chi square tests.

The proportion of patients with at least one positive allergic patch test reaction was estimated and compared between patients with and without a final diagnosis of psoriasis. The mean number $\pm$ standard deviation (SD) of positive allergens was

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estimated and compared using t-test analysis. The proportion of allergens with a positive patch reaction and relevant patch test results were determined in those with and without a final diagnosis of psoriasis and sorted in descending order. To determine the association between each specific allergen with psoriasis, multivariable logistic regression models were constructed with any diagnosis or a primary diagnosis of psoriasis (yes/no) as the dependent variable, and the top 25 most common (yes/no) or most relevant (definite, probable, or possible/negative [past and unknown relevance excluded]) as the independent variable, and age, sex, race/ethnicity, and history of AD, asthma, and hay fever as the covariates.

The significance-prevalence index number (SPIN) was estimated with a weighted calculation using the allergen's prevalence and relevance to determine the relative importance of each allergen ($[\text{proportion of population allergic}] * [1 * \text{percentage with definite relevance} + 0.66 * \text{percentage with probable relevance} + 0.33 * \text{percentage with possible relevance}] * 100$)(13). Among patients with a final diagnosis of psoriasis, SPIN scores for each allergen were estimated biennially, averaged, and sorted in descending order. The most common sources of the top 10 allergens by SPIN and the most common sites of dermatitis by each allergen-source combination were determined.

Complete case analysis was performed. Post-hoc correction was performed for multiple testing using the Bejamini-Hochberg method and yielded a critical P-value of 0.0244.

3. Results

3.1. Population characteristics

Data were analyzed from 38,723 patients (mean age: 48.1±17.0 years), of which 1,675 (4.3%) had of psoriasis as 1 of up to 3 final diagnoses; 1,264 (3.3%) had psoriasis as the primary final diagnosis.

In multivariable logistic regression models, a final diagnosis of psoriasis was *inversely* associated with female sex, black or Asian race, history of AD and hay fever, but not associated with employment or history of asthma (Supplemental Table 1). Prevalence of any diagnosis of psoriasis was lower in age 18-30 years; primary diagnosis of psoriasis was lower in age 18-30 and 31-40 years.

3.2. Sites of dermatitis in patients with final diagnosis of psoriasis

In patients with any final diagnosis of psoriasis, the sites most commonly affected by dermatitis were the feet, arms, legs, face, and a generalized distribution. Patients with vs. without a diagnosis of psoriasis had higher rates of dermatitis affecting the feet (21.8% vs 6.1%, Chi-square: $P<0.0001$), but lower rates of dermatitis in a generalized distribution (19.0% vs 22.5%) or affecting the face (10.8% vs 22.2%), trunk (7.6% vs 12.7%), eyelids (6.3% vs 10.9%), neck (3.9% vs 9.0%), lips (0.9% vs. 4.7%), and areas exposed (0.2% vs 1.6%) and covered by clothes (0.4% vs 1.1%) (all $P\leq 0.01$).

3.3. Comorbid diagnoses in patients with final diagnosis of psoriasis

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Patients with vs. without final diagnosis of psoriasis had lower proportions of a comorbid diagnosis of ACD (32.7% vs 57.8%), ICD (10.5% vs 15.5%), or AD (2.6% vs 15.6%) (all $P < 0.0001$).

3.4. Allergic patch test reactions in patients with final diagnosis of psoriasis

Patients with any diagnosis and a primary diagnosis of psoriasis had lower proportions of at least one positive allergic reaction in patch testing than those without psoriasis (47.6% and 41.4% vs. 65.4%; both $P < 0.0001$) and a lower mean number of positive allergic reactions (1.1 ± 1.7 and 0.8 ± 1.3 vs. 1.8 ± 2.3 ; t-test: both $P < 0.0001$). Those with any diagnosis and a primary diagnosis of psoriasis also had lower proportions of positive reactions to a supplemental non-NACDG screening allergen (17.3% and 7.0% vs. 22.5%; both $P < 0.0001$).

The allergens with highest proportions of positive reactions in patients with any diagnosis of psoriasis included nickel sulfate (14.1%), sodium gold thiosulfate (7.9%), methylisothiazolinone (7.7%), thimerosal (7.3%), fragrance mix I (6.9%), neomycin sulfate (5.9%), *Myroxylon Pereirae* resin (5.1%), cobalt chloride (5.0%), bacitracin (4.6%), and formaldehyde 2.0% aq. (4.6%) (Table 1). Results were similar in patients with a primary diagnosis of psoriasis (Supplemental Table 2).

Patients with any or a primary diagnosis of psoriasis were less likely to have a positive allergic reaction to 7 and 9 of the top 10 most commonly positive allergens, respectively (Table 1, Supplemental Table 2).

3.5. Relevant allergic reactions in patients diagnosed with psoriasis

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Patients with vs. without any diagnosis or primary diagnosis of psoriasis had lower proportions of at least one currently relevant positive allergic reaction than those without psoriasis (34.6% vs. 52.6%; 25.7% vs. 51.0%; both $P < 0.0001$).

The top 10 currently relevant allergens in patients with any diagnosis of psoriasis were nickel sulfate, methylisothiazolinone, fragrance mix I, *Myroxylon Pereirae* resin, formaldehyde 2.0% aq., quaternium-15, fragrance mix II, cobalt chloride, formaldehyde 1.0% aq., and methyldibromoglutaronitrile/ phenoxyethanol 2.0% pet (Table 2). Results were similar in patients with a primary diagnosis of psoriasis (Supplemental Table 3). Individuals with any (Table 2) and primary (Supplemental Table 3) diagnosis of psoriasis had lower odds of a relevant allergic reaction in 6 and 8 of the top 10 most commonly relevant allergens.

Among patients with a final diagnosis of psoriasis, having one or more positive allergic reactions was associated with ages 51-60 years, female sex, and dermatitis affecting the foot and/or arm. Whereas, having one or more currently relevant allergic reaction was associated with female sex and dermatitis of the arm (Table 3).

3.6. SPIN

The top 3 allergens by mean SPIN score in patients with any diagnosis or primary diagnosis of psoriasis were nickel sulfate (61.4 or 44.2), methylisothiazolinone (44.4 or 21.8), and fragrance mix I (17.5 or 12.0). These allergens consistently had the top 3 SPIN scores among patients with psoriasis stratified by sex, age, and sites of dermatitis. The top 10 allergens by SPIN also included methylisothiazolinone, fragrance mix I, *Myroxylon Pereirae* resin, quaternium-15, and formaldehyde 2.0% aq. (Table 4).

3.7. Top allergens and their sources in patients with psoriasis

The top allergens by SPIN were most commonly found in personal care products, e.g. moisturizers, soaps, detergents, and haircare products. Medications (antibiotics, analgesics, and steroids) were the main source for neomycin sulfate and bacitracin. Lastly, jewelry and food products were the main coded sources of nickel sulfate and cobalt chloride.

4. Discussion

We found that approximately one-third of patients with a final diagnosis of psoriasis also had a final diagnosis of ACD. Patients with psoriasis were less likely to have at least one positive allergic reaction and had a lower number of allergic reactions than those without a diagnosis of psoriasis. In addition, those with psoriasis were less likely to have ≥ 1 positive or clinically relevant allergic reaction to many of the most commonly positive or relevant allergens seen among patients without psoriasis.

These findings are consistent with a large-scale Danish study that examined 806 patients at 3 time points between 1990-2006 and found patients with psoriasis were less likely to have ACD (0.581 [0.492-0.685]) than those without psoriasis(14). Similar results were found in a European study of 2,387 patients with psoriasis patch tested from 1996-2015 that found decreased odds of contact sensitization in patients with psoriasis (0.55 [0.50-0.59])(3). In contrast, a UK retrospective study evaluating 2,349 patients with psoriasis from 1984-2014 found similar proportions of positive allergic reactions for each allergen of the extended European baseline series in patients with and without psoriasis(7), though proportions were not controlled for potential confounders and may not be directly comparable. The mechanism for the apparent association is unclear. One theory posits that the distinct immunological milieu of psoriasis and other autoimmune disorders may interfere with the Th1 dominant reaction of ACD. Indeed, previous older studies suggested that those with autoimmune diseases, particularly psoriasis and those on immunosuppressive therapy are more resistant to sensitization(15-19). Another 2014 study found that patch test reactions in 14 patients with psoriasis who were sensitized to nickel were similar phenotypically to

patients without psoriasis, but had a delayed reaction with maximum intensity at day 7 after allergen application(20). Importantly, in the current study of patients undergoing patch testing, psoriasis may have been a diagnosis of exclusion in patients with a negative patch test. Further research is needed to elucidate the complex relationship between psoriasis and ACD.

The most commonly positive allergens in patients with psoriasis were similar to those in patients without psoriasis, including nickel sulfate, sodium gold thiosulfate, methylisothiazolinone, thimerosal, and fragrance mix I. This is consistent with the aforementioned UK study that also showed these allergens to be the most commonly positive among patients with and without psoriasis (excluding thimerosal)(7). In addition, we found that nickel sulfate, methylisothiazolinone, and fragrance mix I also had the highest proportions of clinical relevance and the highest mean SPIN scores, while sodium gold thiosulfate and thimerosal did not. Previous studies showed that rates of sensitization to nickel rose globally(21-24). We found that nickel sensitization rates were similar to patients with and without psoriasis, with jewelry, belts and tools being more common sources of nickel; food/diet was also a source of nickel as shown in previous studies(25). Other studies found sensitization to methylisothiazolinone increased in prevalence among the overall population with cosmetics products as its most common source(26-29). High prevalences of sensitization to fragrance mix I is also largely attributed to personal care products (PCPs)(30, 31). We found PCPs to be the main source of sensitization of methylisothiazolinone and fragrance mix I in a variety of dermatitis distributions.

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Taken together, these findings provide important context for patch testing in patients with psoriasis. First, our study demonstrates that most patients referred for patch testing with a final diagnosis of psoriasis are not also diagnosed with ACD. In general, psoriasis is not an indication for patch testing. Yet, approximately 1 in 3 patients who were referred for patch testing and had a psoriasis diagnosis also had a relevant positive allergic reaction. It is important for clinicians to recognize that concomitant ACD can occur in psoriasis patients irrespective of the controversy over whether ACD is theoretically less likely in psoriasis patients(2-7). Further, 1 in 6 patients with a final diagnosis of psoriasis had a positive allergic reaction to a supplemental non-NACDG screening series allergen, supporting the role of supplemental testing in this very selective patient subset.

In this study, psoriasis patients were *less* likely to be age 18-30, female, black, Asian, or have a history of AD and/or hay fever. These findings are consistent with previous studies that showed lower prevalences of psoriasis among non-white populations(32, 33) and those with AD(34). Though, there is no established association of psoriasis with sex(35, 36); males have a higher prevalence of severe psoriasis(37, 38). The relationship of ACD, sex and severity of psoriasis has yet to be established. Females with psoriasis were more likely to have at least one positive and/or clinically relevant allergic reaction, which was shown in the overall population(39). The inverse association between psoriasis and ages 18-30 years (and 31-40 years in primary diagnosis of psoriasis) may be consistent with a study showing a bimodal pattern of age, most commonly peaking before and after age 40(40, 41).

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This study has several limitations. Data were unavailable for psoriasis phenotype and severity, medications, including biologics and immunosuppressives; or follow-up encounters, precluding analysis of clinical improvement following allergen avoidance. Additionally, the cohort consisted of only of patients referred for patch testing and is not generalizable to all psoriasis patients. Allergens are linked with relevance and source but not specifically to body location.

In conclusion, approximately one-third of patients who were referred for patch testing with a final diagnosis of psoriasis were also diagnosed with ACD. In select patients with suspected psoriasis who also have a clinical presentation suggestive of ACD, patch testing may be helpful.

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Table 1. Most common positive allergic reactions in patients with vs. without a primary or secondary diagnosis of psoriasis.

Allergen	Primary or Secondary Diagnosis of Psoriasis						Adjusted OR (95% CI)	P-value
	No			Yes				
	No. of pts tested	Allergic reaction, n (%)	Rank order	No. of pts tested	Allergic reaction, n (%)	Rank order		
Nickel sulfate hexahydrate, 2.5% pet.	36906	6608 (17.9%)	1	1670	235 (14.1%)	1	0.89 (0.769-1.03)	0.11842
Gold sodium thiosulfate, 0.5% pet.	9601	945 (9.8%)	5	406	32 (7.9%)	2	0.9 (0.611-1.324)	0.59155
Methylisothiazolinone, 0.2% aq. (2000 ppm)	10194	1187 (11.6%)	2	401	31 (7.7%)	3	0.623 (0.429-0.905)	0.01288
Thimerosal 0.1% pet.	4721	490 (10.4%)	3	177	13 (7.3%)	4	0.804 (0.451-1.432)	0.45867
Fragrance mix I, 8.0% pet.	36985	3699 (10%)	4	1673	115 (6.9%)	5	0.672 (0.552-0.817)	<0.0001
Neomycin sulfate, 20.0% pet.	36977	3293 (8.9%)	7	1673	98 (5.9%)	6	0.612 (0.492-0.76)	<0.0001
<i>Myroxylon Pereirae</i> resin (Balsam of Peru), 25.0% pet.	37023	3135 (8.5%)	8	1674	86 (5.1%)	7	0.551 (0.44-0.689)	<0.0001
Cobalt (ii) chloride hexahydrate, 1.0% pet.	36983	2774 (7.5%)	10	1672	83 (5%)	8	0.745 (0.593-0.936)	0.01167
Bacitracin, 20.0% pet.	36992	2822 (7.6%)	9	1673	77 (4.6%)	9	0.594 (0.468-0.754)	<0.0001
Formaldehyde, 2.0% aq.	5384	503 (9.3%)	6	196	8 (4.1%)	10	0.408 (0.2-0.835)	0.01417

Table 2. Most common relevant allergens in adults with a primary or secondary diagnosis of psoriasis.

Allergen	Rank order of allergen relevance in primary/secondary diagnosis of psoriasis	Primary /secondary diagnosis of psoriasis	Relevance of allergens - freq. (%)					Adjusted OR (95% CI)*	P-value
			Not relevant allergen	Definite	Probable	Possible	Past		
Nickel sulfate hexahydrate, 2.5% pet.	1	No	30205 (83.8%)	126 (0.3%)	1258 (3.5%)	2379 (6.6%)	2095 (5.8%)	1.00 [ref]	-
		Yes	1438 (87.4%)	5 (0.3%)	36 (2.2%)	119 (7.2%)	48 (2.9%)	1.032 (0.87-1.225)	0.71647
Methylisothiazolinone, 0.2% aq. (2000 ppm)	2	No	8924 (88.3%)	89 (0.9%)	600 (5.9%)	469 (4.6%)	27 (0.3%)	1.00 [ref]	-
		Yes	368 (91.8%)	1 (0.2%)	26 (6.5%)	5 (1.2%)	1 (0.2%)	0.662 (0.458-0.956)	0.02799
Fragrance mix I, 8.0% pet.	3	No	32950 (90.2%)	84 (0.2%)	1138 (3.1%)	2204 (6%)	163 (0.4%)	1.00 [ref]	-
		Yes	1548 (93.7%)	1 (0.1%)	11 (0.7%)	88 (5.3%)	4 (0.2%)	0.61 (0.496-0.751)	<0.0001
Myroxylon Pereirae Resin (Balsam of Peru), 25.0% pet.	4	No	33443 (91.4%)	46 (0.1%)	1007 (2.8%)	1960 (5.4%)	118 (0.3%)	1.00 [ref]	-
		Yes	1569 (94.9%)	0 (0%)	12 (0.7%)	68 (4.1%)	5 (0.3%)	0.526 (0.419-0.662)	<0.0001
Formaldehyde, 2.0% aq.	5	No	4901 (92.9%)	5 (0.1%)	108 (2%)	252 (4.8%)	9 (0.2%)	1.00 [ref]	-
		Yes	187 (95.9%)	0 (0%)	0 (0%)	8 (4.1%)	0 (0%)	0.563 (0.274-1.155)	0.11707
Quaternium 15, 2.0% pet.	6	No	34277 (93.2%)	73 (0.2%)	770 (2.1%)	1537 (4.2%)	106 (0.3%)	1.00 [ref]	-
		Yes	1604 (96.4%)	1 (0.1%)	20 (1.2%)	37 (2.2%)	2 (0.1%)	0.493 (0.378-0.643)	<0.0001
Fragrance mix II, 14.0% pet.	7	No	21947 (95.3%)	27 (0.1%)	433 (1.9%)	593 (2.6%)	32 (0.1%)	1.00 [ref]	-
		Yes	1025 (97.1%)	0 (0%)	3 (0.3%)	26 (2.5%)	2 (0.2%)	0.584 (0.401-0.85)	0.00496
Cobalt (ii) chloride hexahydrate, 1.0% pet.	8	No	34183 (94.5%)	24 (0.1%)	247 (0.7%)	1015 (2.8%)	702 (1.9%)	1.00 [ref]	-
		Yes	1591 (96.5%)	0 (0%)	6 (0.4%)	38 (2.3%)	13 (0.8%)	0.826 (0.608-1.123)	0.22363
Formaldehyde, 1.0% aq.	8	No	34191 (93.5%)	31 (0.1%)	705 (1.9%)	1584 (4.3%)	67 (0.2%)	1.00 [ref]	-
		Yes	1618 (97.2%)	0 (0%)	8 (0.5%)	37 (2.2%)	1 (0.1%)	0.379 (0.281-0.512)	<0.0001
Methylidibromoglutaronitrile/P-henoxyethanol, (Euxyl K 400), 2.0% pet.	10	No	35089 (96.3%)	40 (0.1%)	406 (1.1%)	830 (2.3%)	81 (0.2%)	1.00 [ref]	-
		Yes	1613 (97.2%)	0 (0%)	11 (0.7%)	31 (1.9%)	5 (0.3%)	0.634 (0.463-0.866)	0.00423

* Multivariable logistic regression models were constructed with specific allergen relevance (definite/probable/possible vs. not relevant; excluding past or unknown relevance) as the dependent variable and primary or secondary diagnosis of psoriasis (yes vs. no) as the independent variable, and age (continuous), race/ethnicity (white, non-Hispanic/black/Hispanic/Asian/other), sex, employment, and history of AD, asthma, and hay fever.

Table 3. Association of one or more positive and currently relevant allergic reactions with demographics, atopic history, and most common distributions of dermatitis in patients with psoriasis.

Variable	Overall (n=1675) Freq (%)	Psoriasis							
		≥1 Positive Allergic Reaction				≥1 Currently Relevant Allergic Reaction			
		No (n=877) Freq (%)	Yes (n=798) Freq (%)	Adjusted OR (95% CI)	P	No (n=1096) Freq (%)	Yes (n=579) Freq (%)	Adjusted OR (95% CI)	P
<i>Age (yr)</i>									
0-7	55 (3.3%)	36 (65.5%)	19 (34.5%)	1.000 [ref]	-	40 (72.7%)	15 (27.3%)	1.000 [ref]	-
8-30	125 (7.5%)	69 (55.2%)	56 (44.8%)	1.711 (0.863-3.395)	0.1241	82 (65.6%)	43 (34.4%)	1.487 (0.717-3.084)	0.286
31-40	194 (11.6%)	106 (54.6%)	88 (45.4%)	1.614 (0.828-3.146)	0.1594	133 (68.6%)	61 (31.4%)	1.267 (0.62-2.586)	0.5163
41-50	371 (22.1%)	211 (56.9%)	160 (43.1%)	1.573 (0.832-2.971)	0.163	259 (69.8%)	112 (30.2%)	1.215 (0.615-2.4)	0.5742
51-60	497 (29.7%)	234 (47.1%)	263 (52.9%)	2.374 (1.273-4.427)	0.0066	311 (62.6%)	186 (37.4%)	1.678 (0.864-3.258)	0.1264
61-70	298 (17.8%)	148 (49.7%)	150 (50.3%)	2.029 (1.089-3.783)	0.0259	183 (61.4%)	115 (38.6%)	1.733 (0.894-3.361)	0.1034
≥70	135 (8.1%)	73 (54.1%)	62 (45.9%)	1.847 (0.947-3.602)	0.072	88 (65.2%)	47 (34.8%)	1.523 (0.748-3.1)	0.2464
<i>Sex</i>									
Female	961 (57.4%)	464 (48.3%)	497 (51.7%)	1.441 (1.176-1.767)	0.0004	596 (62%)	365 (38%)	1.426 (1.15-1.769)	0.0012
Male	713 (42.6%)	412 (57.8%)	301 (42.2%)	1.000 [ref]	-	499 (70%)	214 (30%)	1.000 [ref]	-
<i>Race/ethnicity</i>									
White	1537 (92.1%)	795 (51.7%)	742 (48.3%)	1.000 [ref]	-	992 (64.5%)	545 (35.5%)	1.000 [ref]	-
Black	32 (1.9%)	22 (68.8%)	10 (31.3%)	0.444 (0.2-0.989)	0.0469	26 (81.3%)	6 (18.8%)	0.381 (0.144-1.013)	0.053
Hispanic	21 (1.3%)	15 (71.4%)	6 (28.6%)	0.442 (0.168-1.161)	0.0975	19 (90.5%)	2 (9.5%)	0.208 (0.048-0.904)	0.0362
Asian	46 (2.8%)	24 (52.2%)	22 (47.8%)	0.922 (0.494-1.72)	0.7975	30 (65.2%)	16 (34.8%)	0.928 (0.483-1.78)	0.8213
Other	32 (1.9%)	17 (53.1%)	15 (46.9%)	1.103 (0.539-2.257)	0.7876	24 (75%)	8 (25%)	0.698 (0.308-1.581)	0.3888
<i>Occupation</i>									
Unemployed	571 (35%)	297 (52%)	274 (48%)	1.000 [ref]	-	366 (64.1%)	205 (35.9%)	1.000 [ref]	-
Employed	1061 (65%)	560 (52.8%)	501 (47.2%)	0.969 (0.757-1.24)	0.8017	700 (66%)	361 (34%)	0.981 (0.758-1.268)	0.8807
<i>Atopic disease</i>									
<i>Atopic dermatitis</i>									
No	1477 (88.3%)	772 (52.3%)	705 (47.7%)	1.000 [ref]	-	962 (65.1%)	515 (34.9%)	1.000 [ref]	-
Yes	196 (11.7%)	103 (52.6%)	93 (47.4%)	0.994 (0.717-1.377)	0.9688	132 (67.3%)	64 (32.7%)	0.983 (0.696-1.389)	0.9223
<i>Asthma</i>									
No	1505 (90%)	791 (52.6%)	714 (47.4%)	1.000 [ref]	-	975 (64.8%)	530 (35.2%)	1.000 [ref]	-
Yes	168 (10%)	84 (50%)	84 (50%)	1.146 (0.809-1.622)	0.4437	119 (70.8%)	49 (29.2%)	0.78 (0.534-1.138)	0.1975
<i>Hay fever</i>									
No	1391 (83.1%)	729 (52.4%)	662 (47.6%)	1.000 [ref]	-	903 (64.9%)	488 (35.1%)	1.000 [ref]	-
Yes	283 (16.9%)	147 (51.9%)	136 (48.1%)	1.027 (0.773-1.365)	0.8546	192 (67.8%)	91 (32.2%)	0.94 (0.695-1.271)	0.6854
<i>Distribution</i>									
No	1309 (78.2%)	695 (53.1%)	614 (46.9%)	1.000 [ref]	-	854 (65.2%)	455 (34.8%)	1.000 [ref]	-
Yes	365 (21.8%)	182 (49.9%)	183 (50.1%)	1.331 (1.04-1.703)	0.023	241 (66%)	124 (34%)	1.143 (0.882-1.48)	0.312
<i>Generalized</i>									
No	1356 (81%)	717 (52.9%)	639 (47.1%)	1.000 [ref]	-	897 (66.2%)	459 (33.8%)	1.000 [ref]	-
Yes	318 (19%)	160 (50.3%)	158 (49.7%)	1.265 (0.973-1.645)	0.0791	198 (62.3%)	120 (37.7%)	1.353 (1.03-1.778)	0.0298
<i>Acral</i>									
No	1421 (84.9%)	762 (53.6%)	659 (46.4%)	1.000 [ref]	-	955 (67.2%)	466 (32.8%)	1.000 [ref]	-
Yes	253 (15.1%)	115 (45.5%)	138 (54.5%)	1.433 (1.076-1.906)	0.0137	140 (55.3%)	113 (44.7%)	1.736 (1.3-2.319)	0.0002

Table 4. Sources and dermatitis distributions of the allergens with the top 10 highest mean SPIN scores of patients with psoriasis.							
Rank Order by SPIN	Allergen						
1	Nickel Sulfate Hexahydrate	Source	Jewelry 158 (78.6%)	Belt 8 (4.0%)	Food products 7 (3.5%)	Tools 4 (1.9%)	Misc. Consumer Items 3 (1.5%)
		Distribution Rank	1. Arm 2. Face 3. Scalp	1. Trunk 2. Generalized 3. Arm/Face	1. Foot 2. Legs/ Generalized	1. Neck/Eyelids/ Foot	1. Generalized/ Arm/Eyelid
2	Methylisothiazolinone	Source	Haircare products 29 (85.3%)	Unspecified PCP 2 (5.9%)	Soaps 1 (2.9%)	Wipes 1 (2.9%)	Sunscreen 1 (2.9%)
		Distribution Rank	1. Arm 2. Leg 3. Scalp	1. Foot/Generalized	1. Face	1. Foot	1. Trunk
3	Fragrance Mix I	Source	Unspecified PCP 23 (37.1%)	Moisturizer 20 (32.3%)	Detergents 3 (4.8%)	Shampoo 3 (4.8%)	Soaps 3 (4.8%)
		Distribution Rank	1. Generalized 2. Face 3. Neck/Leg/Foot	1. Face/Generalized/ Arm/Foot	1. Ears 2. Arm	1. Arm 2. Face/Generalized/ Leg	1. Generalized 2. Leg 3. Foot
4	Myroxylon Pereirae Resin	Source	Unspecified PCP 16 (38.1%)	Food Products 7 (16.7%)	Cosmetics 5 (11.9%)	Moisturizers 4 (9.5%)	Soaps 2 (4.8%)
		Distribution Rank	1. Foot 2. Generalized/ Arm	1. Foot 2. Generalized 3. Arm/Trunk/Leg	1. Generalized 2. Arm	1. Generalized 2. Arm/Leg/Foot	1. Leg
5	Quaternium-15	Source	Moisturizers 16 (40.0%)	Unspecified PCP 8 (20.0%)	Soaps 5 (12.5%)	Cosmetics 4 (10.0%)	Shampoo 4 (10.0%)
		Distribution Rank	1. Arm 2. Generalized 3. Leg	1. Face/ Generalized/ Under Clothing	1. Generalized/ Anogenital	1. Generalized/ Foot/ Leg	1. Generalized/ Scalp 2. Face/Arm/ Neck/Leg
6	Neomycin Sulfate	Source	Topical Antibiotics 70 (95.9%)	Steroids 3 (4.1%)			
		Distribution Rank	1. Foot 2. Generalized 3. Arm/Leg	1. Arm/Trunk/ Foot/ Ear			
7	Bacitracin	Source	Antibiotics 54 (91.5%)	Analgesics 5 (8.5%)			
		Distribution Rank	1. Foot 2. Generalized 3. Arm/Leg	1. Leg 2. Arm 3. Eyelids/Trunk/			

				Anogenital			
8	Formaldehyde 2.0% aq.	Source	Unspecified PCP 1 (50.0%)	Moisturizers 1 (50.0%)			
		Distribution Rank	1. Generalized	1. Generalized/ Foot			
9	Cobalt Chloride	Source	Jewelry 24 (60.0%)	Food products 2 (5.0%)	Medication 2 (5.0%)	Other 12 (30.0%)	
		Distribution Rank	1. Arm 2. Leg 3. Foot	1. Generalized	1. Generalized	1. Generalized 2. Arm/Leg/Foot	
10	Methyldibromoglutaronitrile/Phenoxyethanol, (Euxyl K 400), 2.0% pet.	Source	Unspecified PCP 11 (39.3%)	Moisturizers 11 (39.3%)	Cosmetics 4 (14.3%)	Haircare products 1 (3.6%)	Wipes 1 (3.6%)
		Distribution Rank	1. Generalized 2. Foot 3. Trunk/Neck/ Scalp/ Anogenital	1. Face/ Generalized 2. Arm/Neck	1. Face/ Generalized/ Arm Trunk/Neck/ Leg	1. Foot	1. Foot

Only data from patch test results with a recorded allergen source were included.

PCP, personal care product

Allergen sources are listed for allergens with past or current relevance.

Supplemental Tables for: "Prevalence and Trend of Allergen Sensitization in Patients Referred for Patch Testing with a Final Diagnosis of Psoriasis, North American Contact Dermatitis Group Data, 2001-2016"

Contact Dermatitis
Silverberg JI, et al.

Supplemental Table 1. Association of psoriasis with demographics and atopic history.									
Variable	Overall (n=38723)	Psoriasis							
		Psoriasis coded as any of up to 3 Diagnoses				Psoriasis coded as the Primary Diagnosis			
		No (n=37048)	Yes (n=1675)	Adjusted OR (95% CI)	P	No (n=37428)	Yes (n=1264)	Adjusted OR (95% CI)	P
	Freq (%)	Freq (%)	Freq (%)			Freq (%)	Freq (%)		
<i>Age (yr)</i>									
0-17	1631 (4.2%)	1576 (96.6%)	55 (3.4%)	1.000 [ref]	-	1586 (97.3%)	44 (2.7%)	1.000 [ref]	-
18-30	4932 (12.7%)	4807 (97.5%)	125 (2.5%)	0.615 (0.439-0.862)	0.0048	4842 (98.2%)	89 (1.8%)	0.508 (0.346-0.747)	0.0006
31-40	6107 (15.8%)	5913 (96.8%)	194 (3.2%)	0.757 (0.547-1.047)	0.0924	5966 (97.8%)	137 (2.2%)	0.62 (0.429-0.895)	0.0108
41-50	8033 (20.8%)	7662 (95.4%)	371 (4.6%)	1.066 (0.782-1.451)	0.6868	7746 (96.5%)	281 (3.5%)	0.934 (0.66-1.321)	0.6991
51-60	8539 (22.1%)	8042 (94.2%)	497 (5.8%)	1.334 (0.987-1.803)	0.0605	8150 (95.6%)	378 (4.4%)	1.175 (0.838-1.647)	0.3497
61-70	5772 (14.9%)	5474 (94.8%)	298 (5.2%)	1.144 (0.846-1.547)	0.381	5541 (96.1%)	227 (3.9%)	1.043 (0.744-1.462)	0.8058
>70	3686 (9.5%)	3551 (96.3%)	135 (3.7%)	0.753 (0.544-1.043)	0.0878	3574 (97.1%)	108 (2.9%)	0.738 (0.514-1.061)	0.1009
<i>Sex</i>									
Female	26030 (67.2%)	25069 (96.3%)	961 (3.7%)	0.705 (0.636-0.781)	<.0001	25292 (97.3%)	715 (2.7%)	0.692 (0.616-0.778)	<.0001
Male	12689 (32.8%)	11976 (94.4%)	713 (5.6%)	1.000 [ref]	-	12133 (95.7%)	548 (4.3%)	1.000 [ref]	-
<i>Race/ethnicity</i>									
White	33230 (86.3%)	31693 (95.4%)	1537 (4.6%)	1.000 [ref]	-	32050 (96.5%)	1155 (3.5%)	1.000 [ref]	-
Black	1941 (5.0%)	1909 (98.4%)	32 (1.6%)	0.343 (0.238-0.494)	<.0001	1913 (98.7%)	26 (1.3%)	0.373 (0.248-0.561)	<.0001
Hispanic	749 (1.9%)	728 (97.2%)	21 (2.8%)	0.607 (0.391-0.941)	0.0258	729 (97.5%)	19 (2.5%)	0.754 (0.475-1.196)	0.2302
Asian	1909 (5.0%)	1863 (97.6%)	46 (2.4%)	0.541 (0.397-0.736)	<.0001	1871 (98.2%)	35 (1.8%)	0.551 (0.386-0.786)	0.001
Other	659 (1.7%)	627 (95.1%)	32 (4.9%)	1.114 (0.775-1.6)	0.5597	634 (96.2%)	25 (3.8%)	1.18 (0.786-1.774)	0.4246
<i>Occupation</i>									
Unemployed	14365 (38.4%)	13794 (96%)	571 (4%)	1.000 [ref]	-	13934 (97.1%)	421 (2.9%)	1.000 [ref]	-
Employed	23071 (61.6%)	22010 (95.4%)	1061 (4.6%)	1.112 (0.982-1.259)	0.0945	22245 (96.5%)	805 (3.5%)	1.201 (1.04-1.388)	0.0127
<i>Atopic disease</i>									
<i>Atopic dermatitis</i>									
No	29385 (76.2%)	27908 (95%)	1477 (5%)	1.000 [ref]	-	28238 (96.2%)	1121 (3.8%)	1.000 [ref]	-
Yes	9183 (23.8%)	8987 (97.9%)	196 (2.1%)	0.551 (0.469-0.647)	<.0001	9037 (98.5%)	141 (1.5%)	0.531 (0.44-0.64)	<.0001
<i>Asthma</i>									
No	32745 (84.8%)	31240 (95.4%)	1505 (4.6%)	1.000 [ref]	-	31576 (96.5%)	1142 (3.5%)	1.000 [ref]	-
Yes	5873 (15.2%)	5705 (97.1%)	168 (2.9%)	0.937 (0.787-1.116)	0.4678	5749 (98%)	120 (2%)	0.888 (0.723-1.091)	0.2576
<i>Hay fever</i>									
No	27283 (70.7%)	25892 (94.9%)	1391 (5.1%)	1.000 [ref]	-	26208 (96.1%)	1052 (3.9%)	1.000 [ref]	-
Yes	11330 (29.3%)	11047 (97.5%)	283 (2.5%)	0.556 (0.483-0.64)	<.0001	11111 (98.1%)	211 (1.9%)	0.565 (0.48-0.664)	<.0001

Missing values were encountered in 23 (0.06%) for age, 4 (0.01%) for sex, 235 (0.61%) for race/ethnicity, 1287 (3.3%) for occupation, 155 (0.40%) for history of eczema, 105 (0.27%) for history of asthma and 110 (0.28%) for history of hay fever.

Supplemental Table 2. Most common positive allergic reactions in patients with vs. without a primary diagnosis of psoriasis.

Allergen	Primary Diagnosis of Psoriasis						Adjusted OR (95% CI)	P-value
	No			Yes				
	No. of pts tested	Allergic reaction, n (%)	Rank order	No. of pts tested	Allergic reaction, n (%)	Rank order		
Nickel sulfate hexahydrate, 2.5% pet.	37285	6678 (17.9%)	1	1260	161 (12.8%)	1	0.81 (0.681-0.963)	0.01709
Thimerosal 0.1% pet.	4765	493 (10.3%)	3	132	10 (7.6%)	2	0.841 (0.436-1.623)	0.60647
Fragrance mix I, 8.0% pet.	37364	3734 (10%)	4	1263	77 (6.1%)	3	0.585 (0.461-0.742)	<0.0001
Gold sodium thiosulfate, 0.5% pet.	9682	954 (9.9%)	5	323	22 (6.8%)	4	0.751 (0.471-1.196)	0.22783
Methylisothiazolinone, 0.2% aq. (2000 ppm)	10279	1203 (11.7%)	2	295	15 (5.1%)	5	0.394 (0.233-0.665)	0.0005
Neomycin sulfate, 20.0% pet.	37356	3330 (8.9%)	7	1263	59 (4.7%)	6	0.472 (0.357-0.624)	<0.0001
<i>Myroxylon Pereirae</i> resin (Balsam of Peru), 25.0% pet.	37404	3168 (8.5%)	8	1263	52 (4.1%)	7	0.428 (0.322-0.571)	<0.0001
Bacitracin, 20.0% pet.	37371	2847 (7.6%)	9	1263	50 (4%)	8	0.493 (0.366-0.664)	<0.0001
Cobalt (ii) chloride hexahydrate, 1.0% pet.	37362	2807 (7.5%)	10	1262	48 (3.8%)	9	0.557 (0.413-0.752)	0.00013
Formaldehyde, 2.0% aq.	5428	506 (9.3%)	6	148	5 (3.4%)	10	0.338 (0.138-0.829)	0.01779

Supplemental Table 3. Most common relevant allergens in patients with a primary diagnosis of psoriasis.

Allergen	Rank order of allergen relevance in primary diagnosis of psoriasis	Primary diagnosis of psoriasis	Relevance of allergens - freq. (%)					Adjusted OR (95% CI)*	P-value
			Not relevant allergen	Definite	Probable	Possible	Past		
Nickel sulfate hexahydrate, 2.5% pet.	1	No	30512 (83.7%)	127 (0.3%)	1273 (3.5%)	2424 (6.7%)	2101 (5.8%)	1.00 [ref]	-
		Yes	1104 (89%)	4 (0.3%)	19 (1.5%)	73 (5.9%)	41 (3.3%)	0.807 (0.651-1.002)	0.05167
Methylisothiazolinone, 0.2% aq. (2000 ppm)	2	No	8992 (88.2%)	90 (0.9%)	614 (6%)	471 (4.6%)	27 (0.3%)	1.00 [ref]	-
		Yes	279 (94.6%)	0 (0%)	12 (4.1%)	3 (1%)	1 (0.3%)	0.404 (0.239-0.683)	0.00071
Fragrance mix I, 8.0% pet.	3	No	33290 (90.2%)	85 (0.2%)	1145 (3.1%)	2233 (6%)	163 (0.4%)	1.00 [ref]	-
		Yes	1180 (94.8%)	0 (0%)	3 (0.2%)	58 (4.7%)	4 (0.3%)	0.483 (0.371-0.628)	<0.0001
Myroxylon Pereirae Resin (Balsam of Peru), 25.0% pet.	4	No	33785 (91.4%)	46 (0.1%)	1013 (2.7%)	1985 (5.4%)	119 (0.3%)	1.00 [ref]	-
		Yes	1198 (95.8%)	0 (0%)	5 (0.4%)	43 (3.4%)	4 (0.3%)	0.411 (0.307-0.551)	<0.0001
Formaldehyde, 2.0% aq.	5	No	4942 (92.9%)	5 (0.1%)	108 (2%)	255 (4.8%)	9 (0.2%)	1.00 [ref]	-
		Yes	142 (96.6%)	0 (0%)	0 (0%)	5 (3.4%)	0 (0%)	0.467 (0.19-1.149)	0.09736
Fragrance mix II, 14.0% pet.	6	No	22180 (95.3%)	27 (0.1%)	435 (1.9%)	603 (2.6%)	32 (0.1%)	1.00 [ref]	-
		Yes	766 (97.7%)	0 (0%)	1 (0.1%)	15 (1.9%)	2 (0.3%)	0.431 (0.261-0.71)	0.00096
Quaternium 15, 2.0% pet.	6	No	34623 (93.2%)	74 (0.2%)	782 (2.1%)	1557 (4.2%)	107 (0.3%)	1.00 [ref]	-
		Yes	1229 (98%)	0 (0%)	7 (0.6%)	17 (1.4%)	1 (0.1%)	0.264 (0.176-0.397)	<0.0001
Methyldibromoglutaronitrile/P henoxylethanol, (Euxyl K 400), 2.0% pet.	8	No	35444 (96.3%)	40 (0.1%)	412 (1.1%)	844 (2.3%)	82 (0.2%)	1.00 [ref]	-
		Yes	1227 (97.9%)	0 (0%)	5 (0.4%)	17 (1.4%)	4 (0.3%)	0.43 (0.281-0.659)	0.00011
Cinnamic aldehyde, 1.0% pet.	9	No	31575 (97.1%)	17 (0.1%)	342 (1.1%)	557 (1.7%)	27 (0.1%)	1.00 [ref]	-
		Yes	1107 (98.3%)	1 (0.1%)	0 (0%)	18 (1.6%)	0 (0%)	0.58 (0.366-0.918)	0.02018
Cobalt (ii) chloride hexahydrate, 1.0% pet.	10	No	34527 (94.5%)	24 (0.1%)	248 (0.7%)	1036 (2.8%)	705 (1.9%)	1.00 [ref]	-
		Yes	1218 (97.6%)	0 (0%)	4 (0.3%)	16 (1.3%)	10 (0.8%)	0.49 (0.314-0.767)	0.00178

* Multivariable logistic regression models were constructed with specific allergen relevance (definite/probable/possible vs. not relevant; excluding past or unknown relevance) as the dependent variable and primary diagnosis of psoriasis (yes vs. no) as the independent variable, and age (continuous), race/ethnicity (white, non-Hispanic/black/Hispanic/Asian/other), sex, employment, and history of AD, asthma, and hay fever.