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Patients with Negative Patch Tests: Retrospective Analysis of North American Contact Dermatitis Group (NACDG) Data 2001-2016

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Abstract:

Background: Little is known regarding characteristics of patients with negative patch tests (NPTs).

Objective: To characterize patients with NPTs.

Methods: Retrospective cross-sectional analysis of 34,822 patch tested patients. NPTs were defined as negative or irritant final interpretations of all North American Contact Dermatitis Group (NACDG) screening allergens and no relevant allergens on supplemental series.

Results: Almost one-third ($n=10,888$, 31.3%) of patients had negative results. NPT patients were significantly more likely to be male ($p<0.0001$), aged ≤ 40 years ($p=0.0054$), non-Caucasian ($p=0.0005$), and have dermatitis primarily involving the following body sites: scattered generalized ($p=0.0007$), lips ($p=0.0214$), or eyelids ($p=0.0364$). However, absolute differences in age, race, and site were small and may not be clinically meaningful. NPT patients were significantly less likely to have occupationally related skin disease ($p<0.0001$). Overall, 8.3% of NPT patients had occupationally related skin disease with precision production workers/machine operators (28.5%), healthcare workers (17.0%), and mechanics/repairers (7.5%) being the most commonly related occupations. 22.9% of NPT patients had relevant irritants and 41.6% of irritants were occupationally related; cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

Limitations: Retrospective cross-sectional study of tertiary referral population.

Conclusions: Patients with NPTs have distinct characteristics.

Keywords: patch testing; occupational; irritants

Introduction:

The 9-year prevalence of clinical allergic contact dermatitis is estimated to be 7% in the general population.¹ European multi-center studies indicate that the European standard series of 30 allergens yields at least one positive reaction in 40%-50% of individuals referred for patch testing.²⁻⁶ While the North American Contact Dermatitis Group (NACDG) publishes positivity rates for our screening series every two years,⁷⁻¹¹ less is known about the cohort of individuals who test negative. This study characterizes individuals who underwent patch testing by the NACDG and had no positive reactions.

Methods:Database

This study was approved by the Minneapolis Veterans Affairs Medical Center's Human Studies Subcommittee. Methods for patch testing, evaluation of reactions, and data recording by the NACDG have been published.⁷⁻⁹ Allergens (Chemotechnique Diagnostics AB, Malmö, Sweden and allergEAZE SmartPractice, Calgary, Canada) were applied with Finn chambers (SmartPractice, Phoenix, AZ) and Scanpor tape (Norgesplaster Alpha AS, Vennesla, Norway). NACDG members collected the following data shortly following each final patch test visit using a standardized data sheet: sex, age, race, hay fever, eczema (childhood flexural dermatitis), asthma, dermatitis site(s) (3 maximum), final diagnosis/diagnoses (3 maximum), occupational relatedness, and relevant irritants. An expert in occupational classification determined patient occupation and industry using the 3-digit codes published by the 1990 US Department of Commerce Census Industrial and Occupational Classification Codes.¹² Detailed 3-digit source codes were entered for relevant irritants. Only one source was entered per irritant; if multiple sources were present, the most clinically relevant source was recorded.

Study Population

From approximately January 2001 through December 2016, 38,542 patients were patch tested to the NACDG screening series (Figure 1). Individuals with at least one NACDG allergen "not tested" (e.g. individuals with a strong previously positive reaction to nickel may not be retested to nickel) or "unknown" on final interpretation (n=3,720, 9.7%) were excluded. Thus, the study population comprised 34,822 individuals.

Study Design

Data was entered in Access (Access 2010; Microsoft Corp, Redmond, WA) and then analyzed in Excel (Excel 2010; Microsoft Corp). A negative patch test (NPT) was defined as having: 1) “negative” or “irritant” final interpretations for all NACDG screening allergens, and 2) no other relevant allergens from supplemental series. A positive patch test (PPT) was defined as having: 1) an “allergic” final interpretation for one or more NACDG screening allergens, or 2) a positive allergic reaction to a relevant allergen from a supplemental series.

Statistical Analysis

Demographics, occupational relatedness, and relevant irritants were presented using counts and proportions. NPT and PPT populations were compared using chi-square tests. No correction for multiple tests was employed due to the exploratory nature of this analysis; $p < 0.05$ indicated statistical significance. SAS software was used to calculate relative risk (RR) and confidence intervals (CI) (SAS 9.2; SAS, Cary, NC).

Results:Patch Test Results

Of 34,822 patients tested by the NACDG, 68.7% (n=23,934) had ≥ 1 PPT reaction; this included 22,538 patients who had one or more positive reaction(s) to NACDG screening allergen(s) and 1,396 with only positive reaction(s) to non-NACDG supplemental allergen(s). These 23,934 patients were excluded from the study. The study cohort was comprised of 10,888 patients with NPTs (31.3%).

Demographics

Table I summarizes standardized demographic information (MOAHLFA¹³) of NPT and PPT patients. NPT patients were significantly more likely to be male (RR [CI] 1.22 [1.19-1.26]), aged ≤ 40 years (RR [CI] 1.05 [1.01-1.09]), and non-Caucasian (RR [CI] 1.08 [1.03-1.12]). NPT patients were significantly less likely to have occupationally related skin disease (RR [CI] 0.69 [0.65-0.73]). There were no significant differences between the NPT and PPT groups for history of atopic dermatitis, seasonal allergies, asthma or any of these three.

The most common primary dermatitis sites for NPT patients were hand (21.8%), scattered generalized (19.4%), and face (14.7%), which were the most common primary dermatitis sites for PPT patients as well. However, when comparing sites (up to three) between these groups, NPT patients were significantly less likely to have dermatitis involving the hands (RR [CI] 0.91 [0.88-0.95]), face (RR [CI] 0.88 [0.85-0.92]), ears (RR [CI] 0.81 [0.71-0.93]), scalp (RR [CI] 0.86 [0.80-0.93]), neck (RR [CI] 0.82 [0.77-0.88]), arms (RR [CI] 0.86 [0.82-0.90]), or anal/genital (RR [CI] 0.87 [0.79-0.96]) areas. When only one body site (the primary dermatitis site) was analyzed, NPT patients were significantly more likely to have dermatitis in a scattered generalized distribution (RR [CI] 1.07 [1.03-1.11]), lips (RR [CI] 1.10 [1.02-1.19]),

eyelids (RR [CI] 1.06 [1.00-1.12]), or other (RR [CI] 1.28 [1.17-1.40]) sites (other meaning not falling into the 18 named categories as shown in Table I). The primary site for NPT patients was significantly less likely to be hands (RR [CI] 0.96 [0.92-1.00]), face (RR [CI] 0.94 [0.90-0.98]), scalp (RR [CI] 0.85 [0.77-0.93]), or anal/genital (RR [CI] 0.86 [0.77-0.97]) areas.

The most common primary final diagnoses for NPT patients were: other dermatitis (28.1%), atopic dermatitis (18.6%), and irritant contact dermatitis (18.0%). For all final diagnoses (up to 3 per patient), NPT patients were significantly less likely to be diagnosed with allergic contact dermatitis (RR [CI] 0.03 [0.03-0.03]) and significantly more likely to have all other diagnoses (irritant contact dermatitis, atopic dermatitis, psoriasis, stasis dermatitis, nummular eczema, other dermatitis, other dermatoses, seborrheic dermatitis, pompholyx, and contact urticaria, p -values ≤ 0.0319 for up to 3 (except for photo dermatitis, $p=0.0893$) and p -values ≤ 0.0003 for primary.

Dermatitis Related to Occupation

Overall 11.6% (4,026/34,822) of patients tested had dermatitis deemed to be related to their occupation. PPT patients were significantly more likely to have occupationally related dermatitis compared to NPT patients (13.1% vs 8.3%, respectively, $p<0.0001$). Of the 902 NPT patients with occupationally related skin disease, the top 7 primary final diagnoses were irritant contact dermatitis (71.1%), atopic dermatitis (7.1%), other dermatitis (4.9%), allergic contact dermatitis (4.3%), psoriasis (3.7%), other dermatoses (3.5%), and contact urticaria (3.5%). The occupations and industries of NPT patients with occupationally related skin disease are listed in Table II. The most common occupations were precision production workers/machine operators (28.5%), healthcare workers (17.0%), and mechanics/repairers (7.5%). The most common

industries were manufacturing (36.3%), professional and related services (22.2%), and retail trade (7.5%).

Relevant Irritants

Of the 10,888 NPT patients, 22.9% (2,489) had relevant irritants. In this subgroup (n=2,489), 41.6% (1,036) had irritants that were occupationally related. Sources of irritants, both occupationally related and non-occupationally related, are summarized in Tables III and IV, respectively. The most common occupationally related sources of irritants were industrial chemicals/chemical products (32.8%); soaps/detergents/cleansers/disinfectants/laundry aids (non-skin) (17.3%); and cosmetics/beauty preparations/skin and health care products (15.5%). The most common non-occupationally related sources of irritants were cosmetics/beauty preparations/skin and health care products (47.9%); animals/plants/minerals/persons (11.9%); and soaps/detergents/cleansers/disinfectants/laundry aids (non-skin) (11.3%).

Discussion:

This study yielded several key findings. First, approximately one-third of patients referred for patch testing had NPTs (31.3%). Second, NPT patients were significantly more likely to be male ($p<0.0001$), aged ≤ 40 ($p=0.0054$), non-Caucasian ($p=0.0005$), and have dermatitis primarily involving scattered generalized ($p=0.0007$), lips ($p=0.0214$), eyelids ($p=0.0364$), or other ($p<0.0001$) sites. Third, while NPT patients were less likely to have occupationally related skin disease than PPT patients, 8.3% had occupationally related skin disease. The most common occupations were precision production workers/machine operators (28.5%), healthcare workers (17.0%), and mechanics/repairers (7.5%). Lastly, almost one-quarter of NPT patients had relevant irritants (22.9%) and 41.6% of these were related to occupation; cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

Frequency of Negative Patch Tests

The frequency of NPTs in our North American multi-center study was 31.3%. The European Surveillance System on Contact Allergy (ESSCA) is a large multi-center surveillance program that encompasses 12 European countries. The reported frequency of NPTs has varied widely; NPT rates for the European standard series tested by the ESSCA were: 2002-2003: 36% in Italy to 74% in Denmark (10,511 patients);² 2004: 56% overall (11,643 patients),³ 2005-2006: 56.0% in Northeastern Europe to 58.5% in Southern Europe (19,793 patients);⁴ 2007-2008: 46% in Austria to 60% in Denmark (25,181 patients);⁵ and 2009-2012: 46.4% in Poland to 63.4% (59,728 patients).⁶ The frequency of NPTs was higher in the ESSCA (typically 50% to 60%) compared to our data (31.3%). This is likely a reflection of number of allergens (European standard series has 30 allergens, the NACDG screening series has 70 allergens). Previous

calculations of a hypothetical yield of the NACDG screening series as compared with Thin-Layer Rapid Use Epicutaneous (TRUE) Test (35 allergens) found that one-quarter to one-third of allergens identified by the NACDG series would have been missed by testing to TRUE Test.⁷ Additionally, our data accounted for additional relevant allergens; the frequency of negative patch tests for the NACDG screening series alone was 35.3%. Referral patterns and patch test population variations also likely play a significant role.

Demographics

NPT patients were significantly more likely to be male ($p<0.0001$), aged ≤ 40 ($p=0.0054$), and non-Caucasian ($p=0.0005$). These results are not surprising as women have increased skin exposure to allergens compared to men.¹⁴ For example, women have greater exposure to nickel through jewelry.¹⁵ Likewise, older individuals have accumulated more exposures to allergens compared to younger individuals.^{16,17} Our group previously reported significant differences in PPT frequencies to specific allergens for white versus black patients; these differences are likely due to cultural practices and exposures.¹⁸ Importantly, while *statistically* significant, differences in age >40 (65.8% in NPT patients vs. 67.3% in PPT patients) and Caucasian race (85.1% vs. 86.5%, respectively) are small and may not be *clinically* meaningful.

It is not surprising that NPT patients were significantly less likely to have a final diagnosis of allergic contact dermatitis ($p<0.0001$) than PPT patients as patch testing is an important diagnostic tool in the diagnosis of allergic contact dermatitis. These patients may have been diagnosed with allergic contact dermatitis from Repeat Open Application Tests, which is not captured in the NACDG database. We also do not patch test for poison ivy/oak/sumac, which likely accounted for the small number of NPT individuals clinically diagnosed with allergic contact dermatitis.

There were no significant differences in atopic markers between PPT and NPT patients. The relationship between atopy and allergic contact dermatitis is unclear. Our results are similar to other large multi-center studies. The Information Network of Departments of Dermatology (IVDK) and the German Contact Dermatitis Research Group (DKG) showed that frequency of positive patch tests to most allergens differed little between patients with and without eczema;¹⁹ a study from Denmark had similar findings.²⁰

Body Site Location of Dermatitis

We found that NPT patients were more likely to have dermatitis primarily involving scattered generalized distribution ($p=0.0007$), lips ($p=0.0214$), or eyelids ($p=0.0364$). While there are numerous studies of allergens responsible for allergic contact dermatitis in specific body locations, there is little published data for NPT patients. Clinically, it is conceivable that dermatitis in these locations may have other underlying causes. Scattered generalized dermatitis is a common pattern for atopic dermatitis, dermatitis of senescence, or bullous pemphigoid, all of which may have histopathology findings of spongiotic dermatitis with eosinophils. Lip and eyelid dermatitis are often irritant or multifactorial. "Other" sites likely represent patients with conditions with body sites not listed (e.g. burning mouth syndrome, systemic symptoms). Lastly, while absolute differences in site may be statistically significant, clinical relevance may be lacking.

Occupational Considerations

8.3% of NPT patients had occupationally related skin disease and 71.1% of these patients were given a final diagnosis of irritant contact dermatitis. NPT patients were significantly less

likely to have occupationally related skin disease ($p<0.0001$) than PPT patients. While irritant contact dermatitis is more common than allergic contact dermatitis in population-based studies of occupationally related skin disease,²¹⁻²³ typically only those individuals suspected of having allergic contact dermatitis who are referred for patch testing. Therefore, this referral bias may result in an increased number of PPTs compared to NPTs in individuals with occupationally related skin disease.

The most common occupations for NPT patients with occupationally related skin disease were precision production workers/ machine operators (28.5%), healthcare workers (17.0%), and mechanics/repairers (7.5%). Previous studies have found healthcare workers,²¹⁻²³ cleaning occupations,²¹⁻²³ kitchen workers,^{22,23} hairdressers,^{21,22} mechanics,²² metal surface processors,²¹ and craftsmen²³ to be common occupations in populations with occupationally related skin disease that is predominantly irritant in nature. We found manufacturing (36.3%), professional and related services (22.2%), and retail trade (7.5%) to be the most common industries associated with skin disease in NPT patients. In a study analyzing 18,066 cases of irritant-predominant occupational contact dermatitis in the United Kingdom, the most common industries involved were manufacturing, healthcare, and personal services.²² In a study of 965 patients with irritant-predominant occupational skin disease in Singapore, the most common industries involved were metal/engineering, building/construction, and electrical/electronics.²⁴

Relevant Irritants

22.9% of NPT patients had relevant irritants and 41.6% of irritants were occupationally related. The most common sources of occupationally related irritants were chemicals (including solvents, oils, lubricants, and fuels), soaps, and cosmetics/health care products. Previous studies have found soaps/wet work,²²⁻²⁴ solvents,^{22,24} oils/coolants,²²⁻²⁴ petroleum products,²² foods,¹⁹

and gloves¹⁹ to be the most common sources of occupationally related irritants. We found the most common sources of non-occupationally related irritants to be beauty/health care products, animals/plants/minerals/persons, and soaps.

Limitations

Limitations of this study include its retrospective, cross-sectional nature and lack of follow up. Additionally, the patients represent a tertiary referral population. No test is 100% sensitive; it is possible that contact allergy may have been missed if the allergen was not known, suspected, or available for testing. An informal survey of our group indicates that approximately 95% of individuals in this cohort were tested to supplemental allergens in addition to the NACDG screening series. Thus, the number with allergic contact dermatitis to an unidentified allergen is likely low (<5% of patients).

Summary:

This study provides a unique insight into an uncharacterized population. We found that almost one third of patch tested patients had negative results (31.3%). NPT patients were statistically more likely to be male, aged ≤ 40 , and non-Caucasian. Occupationally related skin disease was less common than in PPT patients but of NPT patients with occupationally related skin disease, the most common occupations were precision production workers/machine operators, healthcare workers, and mechanics/repairers. Relevant irritants were found in almost one-quarter of NPT patients; cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

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351 **Abbreviations and Acronyms:**

352 NACDG: North American Contact Dermatitis Group

353 NPT: Negative Patch Test

354 PPT: Positive Patch Test

355 RR: Relative Risk

356 CI: Confidence Interval

357 ESSCA: European Surveillance System on Contact Allergies

358 TRUE Test: Thin-Layer Rapid Use Epicutaneous Test

359 **Figure Legend:**

360 **Figure 1:** *Study population*

361 **Table Legends:**

362 **Table I:** *Patient demographics, negative patch test vs. positive patch test patients*

363 **Table II:** *Occupations and industries of NPT patients with occupationally related skin disease*

364 **Table III:** *Sources of occupationally related irritants*

365 **Table IV:** *Sources of non-occupationally related irritants*

	Overall, n (%)	Negative patch test, ^Δ n (%)	Positive patch test, ^Ψ n (%)	Negative patch test vs. positive patch test	
	N=34822	N=10888	N=23934	RR (95% CI)	p-value
Sex					
Male [#]	11424 (32.8)	4073 (37.4)	7351 (30.7)	1.22 (1.19-1.26)	<0.0001*
Age					
Mean (y)	48.0	48.0	48.1		
>40 [#]	23270 (66.9)	7160 (65.8)	16110 (67.3)	0.95 (0.92-0.99)	0.0054*
>18	33127 (95.2)	10321 (94.9)	22806 (95.3)	0.94 (0.87-1.01)	0.0734
19-29	3819 (11.0)	1247 (11.5)	2572 (10.8)		
30-39	5388 (15.5)	1704 (15.7)	3684 (15.4)		
40-49	6967 (20.0)	2107 (19.4)	4860 (20.3)		
50-59	7755 (22.3)	2333 (21.4)	5422 (22.7)		
≥60	9198 (26.4)	2930 (26.9)	6268 (26.2)		
Race					
Caucasian	29766 (86.1)	9234 (85.1)	20532 (86.5)	0.93 (0.89-0.97)	0.0005*
Non-Caucasian					
Black	1788 (5.2)	637 (5.9)	1151 (4.9)		
Asian	1732 (5.0)	516 (4.8)	1216 (5.1)		
Hispanic	689 (2.0)	258 (2.4)	431 (1.8)		
Other	597 (1.7)	200 (1.8)	397 (1.7)		
Atopy					
Hay fever	10161 (29.3)	3216 (29.6)	6945 (29.1)	1.01 (0.98-1.05)	0.4026
Eczema	8228 (23.7)	2601 (24.0)	5627 (23.6)	1.01 (0.98-1.05)	0.5234
Asthma	5264 (15.2)	1673 (15.4)	3591 (15.1)	1.02 (0.98-1.06)	0.4109
Any of 3 above [#]	15314 (44.0)	4829 (44.4)	10485 (43.9)	1.01 (0.98-1.05)	0.3934
Site (up to 3 per patient)					
Scattered generalized	7783 (22.4)	2426 (22.3)	5357 (22.4)	1.00 (0.96-1.03)	0.8499
Hand [#]	9223 (26.5)	2692 (24.8)	6531 (27.3)	0.91 (0.88-0.95)	<0.0001*
Foot	2362 (6.8)	750 (6.9)	1612 (6.7)	1.02 (0.96-1.08)	0.5911
Face [#]	7537 (21.7)	2128 (19.6)	5409 (22.6)	0.88 (0.85-0.92)	<0.0001*
Lips	1582 (4.5)	517 (4.8)	1065 (4.5)	1.05 (0.97-1.13)	0.2117
Nose	42 (0.1)	13 (0.1)	29 (0.1)	0.99 (0.63-1.56)	0.9659
Eyelids	3760 (10.8)	1193 (11.0)	2567 (10.7)	1.02 (0.97-1.07)	0.5098
Eyes	274 (0.8)	89 (0.8)	185 (0.8)	1.04 (0.88-1.23)	0.6609
Ears	638 (1.8)	162 (1.5)	476 (2.0)	0.81 (0.71-0.93)	0.0013*
Scalp	1895 (5.4)	512 (4.7)	1383 (5.8)	0.86 (0.80-0.93)	<0.0001*
Neck	3057 (8.8)	799 (7.3)	2258 (9.4)	0.82 (0.77-0.88)	<0.0001*
Arm	5333 (15.3)	1469 (13.5)	3864 (16.2)	0.86 (0.82-0.90)	<0.0001*
Leg [#]	3803 (10.9)	1161 (10.7)	2642 (11.0)	0.97 (0.93-1.02)	0.3038
Trunk	4338 (12.5)	1303 (12.0)	3035 (12.7)	0.96 (0.91-1.00)	0.0636
Anal/genital	992 (2.9)	271 (2.5)	721 (3.0)	0.87 (0.79-0.96)	0.0066*
Most exposed areas	531 (1.5)	151 (1.4)	380 (1.6)	0.91 (0.79-1.04)	0.1576
Only under clothing	371 (1.1)	106 (1.0)	265 (1.1)	0.91 (0.78-1.07)	0.2617
Erythroderma	35 (0.1)	15 (0.1)	20 (0.1)	1.37 (0.94-2.01)	0.1386
Other	1006 (2.9)	376 (3.5)	630 (2.6)	1.20 (1.11-1.30)	<0.0001*
Primary site					
Scattered generalized	6377 (18.3)	2107 (19.4)	4270 (17.9)	1.07 (1.03-1.11)	0.0007*
Hand [#]	7841 (22.5)	2371 (21.8)	5470 (22.9)	0.96 (0.92-1.00)	0.0269*
Foot	1112 (3.2)	337 (3.1)	775 (3.2)	0.97 (0.88-1.06)	0.4862
Face [#]	5398 (15.5)	1596 (14.7)	3802 (15.9)	0.94 (0.90-0.98)	0.0035*
Lips	1211 (3.5)	415 (3.8)	796 (3.3)	1.10 (1.02-1.19)	0.0214*
Nose	19 (0.1)	7 (0.1)	12 (0.1)	1.18 (0.65-2.12)	0.5994
Eyelids	3014 (8.7)	993 (9.1)	2021 (8.5)	1.06 (1.00-1.12)	0.0364*

Eyes	171 (0.5)	55 (0.5)	116 (0.5)	1.03 (0.83-1.28)	0.7979
Ears	338 (1.0)	97 (0.9)	241 (1.0)	0.92 (0.77-1.09)	0.3076
Scalp	1188 (3.4)	316 (2.9)	872 (3.6)	0.85 (0.77-0.93)	0.0004*
Neck	622 (1.8)	196 (1.8)	426 (1.8)	1.01 (0.90-1.13)	0.8907
Arm	1719 (4.9)	531 (4.9)	1188 (5.0)	0.99 (0.92-1.06)	0.7356
Leg [#]	1464 (4.2)	464 (4.3)	1000 (4.2)	1.01 (0.94-1.10)	0.7132
Trunk	1989 (5.7)	637 (5.9)	1352 (5.7)	1.03 (0.96-1.10)	0.4466
Anal/genital	736 (2.1)	199 (1.8)	537 (2.2)	0.86 (0.77-0.97)	0.0125*
Most exposed areas	443 (1.3)	129 (1.2)	314 (1.3)	0.93 (0.80-1.08)	0.3285
Only under clothing	329 (0.9)	97 (0.9)	232 (1.0)	0.94 (0.80-1.12)	0.4853
Erythroderma	26 (0.1)	12 (0.1)	14 (0.1)	1.48 (0.97-2.24)	0.1012
Other	794 (2.3)	316 (2.9)	478 (2.0)	1.28 (1.17-1.40)	<0.0001*
Final diagnosis (up to 3 per patient)					
Allergic contact dermatitis	19510 (56.2)	392 (3.6) [^]	19118 (80.1)	0.03 (0.03-0.03)	<0.0001*
Irritant contact dermatitis	5687 (16.4)	2491 (23.0)	3196 (13.4)	1.52 (1.47-1.58)	<0.0001*
Atopic dermatitis	5549 (16.0)	2292 (21.1)	3257 (13.6)	1.41 (1.36-1.46)	<0.0001*
Psoriasis	1695 (4.9)	796 (7.3)	899 (3.8)	1.54 (1.46-1.63)	<0.0001*
Stasis dermatitis	280 (0.8)	104 (1.0)	176 (0.7)	1.19 (1.02-1.39)	0.0319*
Nummular eczema	725 (2.1)	356 (3.3)	369 (1.5)	1.59 (1.48-1.72)	<0.0001*
Photo dermatitis	480 (1.4)	167 (1.5)	313 (1.3)	1.12 (0.99-1.26)	0.0893
Other dermatitis	5810 (16.7)	3291 (30.4)	2519 (10.5)	2.17 (2.11-2.23)	<0.0001*
Other dermatoses	3821 (11.0)	2051 (18.9)	1770 (7.4)	1.89 (1.82-1.95)	<0.0001*
Seborrheic dermatitis	771 (2.2)	420 (3.9)	351 (1.5)	1.77 (1.66-1.90)	<0.0001*
Pompholyx	278 (0.8)	152 (1.4)	126 (0.5)	1.76 (1.58-1.96)	<0.0001*
Contact urticaria	287 (0.8)	125 (1.2)	162 (0.7)	1.40 (1.23-1.60)	<0.0001*
Primary final diagnosis					
Allergic contact dermatitis	16283 (46.9)	290 (2.7)	15993 (67.0)	0.03 (0.03-0.03)	<0.0001*
Irritant contact dermatitis	3345 (9.6)	1949 (18.0)	1396 (5.8)	2.06 (1.99-2.13)	<0.0001*
Atopic dermatitis	4059 (11.7)	2013 (18.6)	2046 (8.6)	1.72 (1.66-1.79)	<0.0001*
Psoriasis	1179 (3.4)	655 (6.0)	524 (2.2)	1.83 (1.73-1.93)	<0.0001*
Stasis dermatitis	185 (0.5)	93 (0.9)	92 (0.4)	1.62 (1.40-1.87)	<0.0001*
Nummular eczema	583 (1.7)	321 (3.0)	262 (1.1)	1.79 (1.66-1.93)	<0.0001*
Photo dermatitis	328 (0.9)	133 (1.2)	195 (0.8)	1.30 (1.14-1.49)	0.0003*
Other dermatitis	4882 (14.1)	3051 (28.1)	1831 (7.7)	2.39 (2.33-2.46)	<0.0001*
Other dermatoses	2924 (8.4)	1754 (16.2)	1170 (4.9)	2.10 (2.03-2.17)	<0.0001*
Seborrheic dermatitis	547 (1.6)	347 (3.2)	200 (0.8)	2.07 (1.93-2.21)	<0.0001*
Pompholyx	222 (0.6)	135 (1.2)	87 (0.4)	1.96 (1.76-2.18)	<0.0001*
Contact urticaria	184 (0.5)	100 (0.9)	84 (0.4)	1.75 (1.53-2.00)	<0.0001*
Occupationally related ^{#§}	4026 (11.6)	902 (8.3)	3124 (13.1)	0.69 (0.65-0.73)	<0.0001*

Table I: Patient demographics, negative patch test vs. positive patch test patients

RR=relative risk, CI=confidence interval, y=years

[#]Male, occupational, atopic, hand, leg, face, age>40 years, positive patch test (MOAHLFAP) index¹³

[§]Refers to overall skin disease being occupationally related.

[^]Likely comprised of patients with poison ivy/oak/sumac allergic contact dermatitis; we do not patch test urushiol.

^ΔNegative patch test patients: sex missing for 1 patient, age missing for 10 patients, race missing for 33 patients, hay fever status missing for 13 patients, eczema status missing for 28 patients, asthma status missing for 22 patients, site missing for 13 patients, final diagnosis missing for 47 patients, and occupational relatedness missing for 19 patients. Denominators adjusted accordingly.

^υPositive patch test patients: sex missing for 4 patients, age missing for 9 patients, race missing for 207 patients, hay fever status missing for 94 patients, eczema status missing for 127 patients, asthma status missing for 82 patients, site missing for 18 patients, final diagnosis missing for 54 patients, and occupational relatedness missing for 51 patients. Denominators adjusted accordingly.

*Indicates statistical significance, p-value <0.05.

Occupation	%	Number	Industry	%	Number
Precision production workers and machine operators	28.5	257	Manufacturing	36.3	327
Healthcare workers	17.0	153	<i>Metal, machinery, and equipment n=204</i>		
Mechanics and repairers	7.5	68	<i>Chemicals and allied products n=30</i>		
Transportation and material moving occupations	6.3	57	<i>Food and kindred products n=24</i>		
Construction occupations	5.4	49	<i>Lumber, wood, stone, clay, glass, and concrete products n=23</i>		
Food preparation and service occupations	4.8	43	<i>Printing, publishing, and allied industries n=17</i>		
Personal service occupations	4.3	39	<i>Textile and paper products n=16</i>		
<i>Not otherwise specified n=9</i>			<i>Petroleum, coal, rubber, and plastics products n=13</i>		
<i>Hairdressers and cosmetologists n=30</i>			Professional and related services	22.2	200
Management occupations	3.5	32	<i>Not elsewhere classified n=194</i>		
Administrative occupations	2.8	25	<i>Physician clinics n=6</i>		
Technicians	2.5	23	Retail trade	7.5	68
Cleaning and building service occupations	2.1	19	Personal services	5.0	45
Engineers and scientists	1.8	16	Construction	4.9	44
Protective service and military occupations	1.4	13	Finance, insurance, real estate, business, and repair services	4.7	42
Sales occupations	1.3	12	Transportation, communications, utilities, and sanitary services	4.5	41
Agricultural occupations	1.3	12	Public administration	2.1	19
Writers, artists, entertainers, and athletes	0.7	6	Agriculture, forestry, fisheries, and mining	1.8	16
Teachers	0.7	6	Wholesale trade	1.4	13
(Unknown or uncodable)	8.0	72	Entertainment and recreation services	1.0	9
Total		902	(Unknown or Other)	8.6	78
			Total		902

Table II: Occupations and industries of NPT patients with occupationally related skin disease

Source	%	Number
Chemicals and chemical products	32.8	340
NOS n=35		
Coatings, adhesives, dyes, inks, photographic and copying chemicals n=72		
NOS n=4		
Coatings (paint, lacquer, shellac, varnish, stains) n=19		
Adhesives, glues, bonding agents n=41		
Dyes, coloring agents, inks, photographic chemicals n=8		
Solvents, oils, lubricants, fuels n=205		
NOS n=32		
Coal, coal products, gasoline, diesel, jet fuel, kerosene, heating oil n=7		
Solvents, degreasers, petroleum distillates n=66		
Lubricating oils and greases n=23		
Automotive oils and fluids n=23		
Metalworking fluid, cutting oils n=54		
Miscellaneous (acrylic, epoxy, urethane, and formaldehyde resins) n=28		
Soaps, detergents, cleansers, disinfectants, laundry aids (non-skin)	17.3	179
NOS n=23		
Soaps and detergents, miscellaneous n=119		
Laundry detergents and aids n=2		
Disinfectants n=35		
Cosmetics, beauty preparations, skin and health care products	15.5	161
NOS n=6		
Hair care products n=34		
Nail care products n=3		
Cosmetics n=5		
NOS n=3		
Moisturizers, lotions, creams n=2		
Soaps and cleansers (personal hygiene) n=109		
NOS n=58		
Disinfectants (e.g. alcohol, povidone-iodine) n=41		
Hand sanitizers n=10		
Dentistry materials and products n=4		
Building and construction materials, tools, equipment, supplies	8.8	91
NOS n=10		
Building materials n=33		
Bricks, blocks, stone n=2		
Cement, concrete, mortar n=15		
Wood, lumber n=16		
Sealants, caulking, and insulating materials n=17		
Tools, equipment, instruments, miscellaneous supplies n=9		
Paper products and supplies n=22		
Clothing, wearing apparel, protective equipment, textiles	7.9	82
Clothing n=68		
NOS n=11		

Gloves n=40		
Shoes, boots, sandals, slippers n=6		
Shirts, pants, blouses, dresses, skirts n=8		
Suits, coats, jackets n=3		
Glasses and contact lenses n=1		
Safety equipment, miscellaneous (e.g. masks, respirators) n=6		
Animals, plants, minerals, persons	4.1	42
Animals and plants n=13		
Food products n=15		
Minerals and persons n=14		
Sewage, waste, debris, scrap	2.1	22
Machinery and vehicles	1.2	12
Environmental, water	1.0	10
Furniture, fixtures, structures, and surfaces	0.4	4
Medications	0.2	2
(Unknown or Other)	8.8	91
Total		1036

Table III: Sources of occupationally related irritants

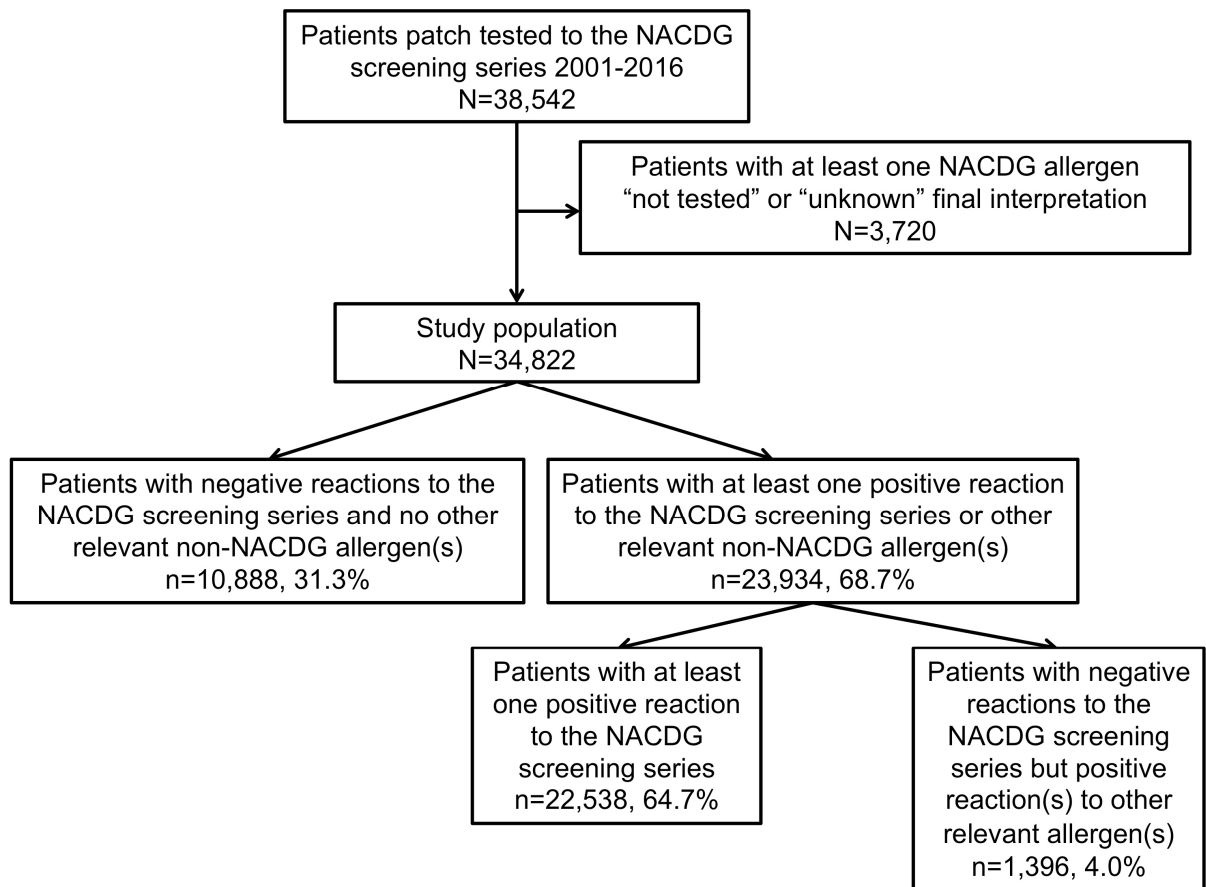
NOS=not otherwise specified

Source	%	Number
Cosmetics, beauty preparations, skin and health care products	47.9	696
NOS n=186		
Hair care products n=82		
Nail care products n=5		
Cosmetics n=171		
NOS n=41		
Moisturizers, lotions, creams n=49		
Make-up n=47		
Perfumes and fragrances n=5		
Tattoos n=1		
Deodorants and antiperspirants n=17		
Lipsticks n=11		
Soaps and cleansers (personal hygiene) n=86		
NOS n=72		
Disinfectants (e.g. alcohol, povidone-iodine) n=12		
Wipes (baby wipes, toilettes, etc.) n=2		
Sunscreens n=37		
Eye care products n=20		
Oral hygiene products n=12		
Dentistry materials and products n=25		
Miscellaneous health aids n=72		
NOS n=10		
Tapes, band-aids, adhesives aids n=22		
Essential oils, massage oils, aromatherapy n=25		
Orthopedic implants, prostheses, medical and misc. health devices n=15		
Animals, plants, minerals, persons	11.9	173
Animals and plants n=10		
Food products n=6		
Minerals and persons n=157		
Soaps, detergents, cleansers, disinfectants, laundry aids (non skin)	11.3	164
NOS n=11		
Soaps and detergents, miscellaneous n=138		
Laundry detergents and aids n=5		
Disinfectants n=9		
Air fresheners, deodorizers n=1		
Clothing, wearing apparel, protective equipment, textiles	6.4	93
Clothing n=79		
NOS n=34		
Gloves n=5		
Shoes, boots, sandals, slippers n=34		
Shirts, pants, blouses, dresses, skirts n=6		
Jewelry, watches n=7		
Safety equipment, miscellaneous (e.g. masks, respirators) n=7		
Building and construction materials, tools, equipment, supplies	5.2	75
NOS n=8		

<i>Tools, equipment, instruments, miscellaneous supplies n=60</i>		
<i>Paper products and supplies n=7</i>		
Medications	3.8	55
Chemicals and chemical products	2.1	30
<i>NOS n=7</i>		
<i>Coatings, adhesives, dyes, inks, photographic and copying chemicals n=12</i>		
<i>Coatings (paint, lacquer, shellac, varnish, stains) n=4</i>		
<i>Adhesives, glues, bonding agents n=8</i>		
<i>Solvents, oils, lubricants, fuels n=11</i>		
Environmental, water	1.8	26
Sewage, waste, debris, scrap	0.6	8
Miscellaneous consumer items	0.2	3
<i>Coins, currency n=1</i>		
<i>Personal grooming devices, applicators n=2</i>		
Furniture, fixtures, structures, and surfaces	0.1	1
(Unknown or Other)	8.9	129
Total		1453

Table IV: Sources of non-occupationally related irritants

NOS=not otherwise specified



Capsule Summary:

- We characterized patients with negative patch tests; this population has not been studied.
- Patients with negative patch tests have distinct characteristics. They are more likely to be male and have irritant dermatitis, and less likely to have occupationally related skin disease when compared to patients with positive patch tests.