INTERNATIONAL AWARDS FOR SOCIAL RESPONSIBILITY IN DERMATOLOGY

CARING *to* INSPIRE SKIN CONFIDENCE

A PARTNERSHIP BETWEEN

L'ORÉAL ILDS 24TH WORLD CONGRESS OF DERMATOLOGY MILAN 2019

Are you a dermatologist working independently, with an organization or in a hospital?

Are you involved in social initiatives, providing support for patients in your community?

The International Awards for Social Responsibility in Dermatology are open to submissions.

TO LEARN MORE & APPLY.

WWW.INSPIRESKINCONFIDENCE.COM

DEADLINE FOR APPLICATION

March 4th, 2019.

European Surveillance System on Contact Allergies (ESSCA): contact allergies in relation to body sites in patients with allergic contact dermatitis

Jart A.F Oosterhaven[1], Wolfgang Uter[2], Werner Aberer[3], José C. Armario-Hita[4], Barbara K. Ballmer-Weber[5], Andrea Bauer[6], Magdalena Czarnecka-Operacz[7], Peter Elsner[8], Juan García-Gavín[9], Ana M. Giménez-Arnau[10], Swen Malte John[11], Beata Krecisz[12], Vera Mahler[13], Thomas Rustemeyer[14], Anna Sadowska-Przytocka[7], Javier Sanchez-Perez[15], Dagmar Simon[16], Skaidra Valiukevičienė[17], Elke Weisshaar[18], Marie L. A. Schuttelaar[1], on behalf of the ESSCA Working Group[19]

Names of the institutions:

[1] University of Groningen, University Medical Center Groningen, Department of Dermatology, The Netherlands.

[2] Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander-University Erlangen/Nürnberg, Erlangen, Germany.

[3] Department of Dermatology, Medical University of Graz, Graz, Austria.

[4] Department of Dermatology, University Hospital of Puerto Real, University of Cádiz, Cádiz, Spain.

[5] Department of Dermatology, University Hospital Zürich and Clinic of Dermatology and Allergology, Kantonsspital St. Gallen, Switzerland.

[6] Department of Dermatology, University Hospital Carl Gustav Carus, University Allergy Center, Technical University Dresden, Dresden, Germany.

[7] Department of Dermatology, Poznan University of Medical Sciences, Poznan, Poland.

[8] Department of Dermatology, University Hospital Jena, Jena, Germany.

[9] Department of Dermatology, University Hospital Complex, Faculty of Medicine, A Coruña, Santiago de Compostela; also: Dermatological Office, Vigo.

[19] The following collaborators from the ESSCA network, in addition to the authors, contributed data (per country, in alphabetical order):
Germany: Ulrike Beiteke, Peter Frosch (Department of Dermatology, Dortmund and University of Witten/Herdecke, Dortmund), Jochen Brasch (Department of Dermatology, University of Schleswig-Holstein, Campus Kiel, Kiel), Thomas Fuchs (Department of Dermatology, University Medicine, Göttingen)
Italy: Anna Balato (Department of Advanced Biomedical Sciences, University of Naples Federico II, Napoli), Fabio Ayala (Department of Dermatology, University of Naples Federico II, Napoli)
Poland: Marta Kieć-Świerczyńska (Department of Dermatology, Nofer Institute of Occupational Medicine, Łodz, Poland)
Spain: Virginia Fernández-Redondo (Department of Dermatology, University Hospital Complex, Faculty of Medicine, A Coruña, Santiago de Compostela), Pedro Mercader (Dermatology Department, Hospital General Universitario Morales Meseguer, Murcia), Inmaculada Ruiz (Department of Dermatology, Complejo Asistencial de León, León), Juan F. Silvestre (Department of Dermatology, Hospital General Universitario de Alicante, Alicante),
Switzerland: Andreas Bircher (Department of Dermatology, Allergy Unit, University Hospital Basel, Basel), Jürgen Grabbe (Department of Dermatology, Kantonsspital Aarau, Aarau)

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/cod.13192

[10] Department of Dermatology. Hospital del Mar, IMIM, Universitat Autònoma, Barcelona, Spain.

[11] Department of Dermatology and Environmental Medicine, Institute for Interdisciplinary Dermatologic Prevention and Rehabilitation (iDerm), Lower Saxony Institute for Occupational Dermatology (NIB), University of Osnabrück, Germany

[12] Faculty of Medicine and Health Science, The Jan Kochanowski University, Kielce, Poland.

[13] Department of Dermatology, University of Erlangen-Nuremberg, Erlangen; Division of Allergology, Paul-Ehrlich-Institut, Langen, Germany.

[14] Amsterdam University Medical Centers, Department of Dermatology and Allergology, The Netherlands.

[15] Department of Dermatology, University Hospital de la Princesa, Madrid, Spain.

[16] Department of Dermatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.

[17] Department of Skin and Venereal Diseases, Lithuanian University of Health Sciences, 44307 Kaunas, Lithuania. Lithuanian University of Health Sciences Hospital, 50009 Kaunas, Lithuania.

[18] Department of Clinical Social Medicine, Environmental and Occupational Dermatology, University of Heidelberg, Germany.

Correspondence to: M.L.A. Schuttelaar, Department of Dermatology, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, the Netherlands, phone: +31 50 361 2520, mail: m.l.a.schuttelaar@umcg.nl, fax: +31 50 361 2624.

Conflicts of interest: There was no funding. WU has received travel reimbursements from cosmetic industry associations and lecture fees from mixed dermatopharmaceutical sponsors and the Paul Ehrlich Institute, respectively, for lectures on patch testing. MCO received honoraria (unrelated to this study) from Pierre Fabre, Bioderma, Berlin Chemie, Galderma, LEO Pharma, Novartis, SVR, CERKO and La Roche Possay. The other authors report no conflicts of interest.

Author contributions: All authors have participated sufficiently to take public responsibility for appropriate proportions of the work and have seen and approved the final, submitted version.

Key words: contact allergy, body site, allergic contact dermatitis, patch test, sensitization.

Abstract

Background: Analyses of the European Surveillance System on Contact Allergies (ESSCA) database have focused primarily on prevalence of contact allergies to the European baseline series; overall and in subgroups of patients. However, affected body sites have hitherto not been addressed.

Objective: To determine prevalence of contact allergies for distinct body sites in patients with allergic contact dermatitis (ACD).

Methods: Analysis of data collected by ESSCA (www.essca-dc.org) in consecutively patch tested patients, 2009-2014, in 8 European countries. Cases were selected based on the presence of minimally one positive patch test to the baseline series, and a final diagnosis of ACD attributed to only one single body site.

Results: *N*=6,255 cases were analyzed. The head and hand were the most common single sites ACD was attributed to. Differences between countries were seen for several body sites. Nickel, fragrance mix I, cobalt and methylchloroisothiazolinone/methylisothiazolinone were the most frequent allergens reported for various body sites.

Conclusion: Distinct allergen patterns per body site were observed. However, contact allergies were probably not always relevant for the dermatitis that patients presented themselves with. Adding possibility to link positive patch test reactions to relevance, along with affected body sites should be a useful addition to data capturing systems.

1. Introduction

Previous analyses of the European Surveillance System on Contact Allergies (ESSCA) database have focused primarily on the prevalence of contact allergies. Many papers report on overall prevalence or results in certain subgroups, such as occupational dermatitis patients[1], children/adolescents[2] or particular allergens[3,4]. However, not much attention has been given to affected body sites, apart from describing the overall prevalence of hand, leg and face dermatitis according to the MOAHLFA index. Only facial dermatitis has been highlighted once.[5]

Several papers beyond ESSCA did, however, report on contact allergies linked to specific body sites like the hands, legs, feet and face.[6–12] One publication reported on the frequency of dermatitis at specific body sites, but not on specific contact allergies.[13] Contact allergies linked to various body sites in patients diagnosed with allergic contact dermatitis (ACD) from the ESSCA database have not yet been reported. This study aimed to identify and describe contact allergies related to distinct body sites in patients diagnosed with ACD and patch tested with the European baseline series in the ESSCA network.

2. Methods

2.1 Study design and population

The analysis is based on data collected by the ESSCA network, as described in previous publications[5,14]. Clinical and demographic data, along with patch test results, of all patients patch tested for suspected ACD due to various potential exposures are documented electronically in the departments participating in ESSCA. These use diverse data capture software and partly the multilingual software WinAlldat/ESSCA provided by ESSCA[15]. Standardised patch testing follows international recommendations[16]. The study period was 01/2009 to 12/2014.

Test results with the European baseline series (EBS) valid in the study period, during which methylisothiazolinone (MI) 2000 ppm aq. had been added, and the recommended test concentration of methylchloroisothiazolinone (MCI)/MI had been increased from 100 to 200 ppm, and of formaldehyde from 1 to 2% [17], were analysed.

As the objective of the study was to use a stringent definition of eligible patients – see below – the data analysed are restricted to those departments using the WinAlldat/ESSCA or WinAlldat/IVDK software, as this (i) uses a comparable catalogue of anatomical sites which can be unequivocally mapped to the categories used in the present study and (ii) relies on a documentation where one or two final diagnoses are documented, and up to three sites for each diagnosis. In contrast, other departments use other systems, which, while enabling to use data e.g. for describing the MOAHLFA

index for each department, do not allow selection based on above-mentioned data structure. Thereby, this study used data from eight European countries: Austria, Germany, Italy, Lithuania, Poland, Spain, Switzerland, and the Netherlands.

2.2 Inclusion and exclusion criteria

Inclusion criteria:

- Data documented in the ESSCA database between the years 2009 and 2014 using WinAlldat software (see above).
- Patch tested with the European baseline series.
- Diagnosis of 'allergic contact dermatitis'. Patients were permitted to have additional diagnoses.
- Only one single anatomical site linked to the above ACD diagnosis.

Exclusion criteria:

- More than 1 body site affected.
- No positive patch test to the baseline series.

We have aggregated the body sites in ESSCA into nine larger groups: head, arm, hand, trunk, anogenital, leg, foot, generalized, other. See Supplement S1 for details of this aggregating process. The group with generalized ACD represents patients with widespread eczema. These patients will have more than 3 major body sites affected.

2.3 Statistical analysis

The pseudonymised data delivered by the participating departments are pooled in the ESSCA data center in Erlangen for further analysis[18], using R (version 3.4.2) software (www.r-project.org, last accessed 11 September 2018). The maximum patch test reaction between day 3 and day 5 (inclusive) was aggregated as patch test outcome. Reactions designated as either +, ++ or +++ were classified as

positive (allergic), the remainder as non-allergic. Descriptive statistical analyses, partly stratified for country and site, respectively, followed pertinent guidelines[19,20]. In particular, prevalence estimates concerning baseline series allergens in the different subgroups were age- and sex-adjusted to account for confounding.

3. Results

Figure 1 shows a study flow chart. Overall, 86416 patients had been tested with the baseline series 2009 – 2014[21], of which 44300 were documented using WinAlldat software and were thus utilizable for the present analysis. We only considered the most recent consultation in case of multiple consultations of one patient. Of note:

- Of the 13057 patients with a final diagnosis of ACD, 1997 had no site information attributed to ACD , however, information on the primary (initial) site of dermatitis was mostly available. This was plugged in as appropriate site for the final diagnosis, but only if just one final diagnosis of ACD was made, to avoid ambiguity of the attribution. As such, 12211 patients with information on at least one site linked with a singular ACD diagnosis remained.
- Only one anatomical site (including plugged-in primary (initial) site, see above) had been documented in 8285 patients, while 3230 had two, and 696 had three sites documented. Excluding patients with > 1 site affected, 8285 patients remained in the analysis.
- After a comparison of patient characteristics, all further analyses focused on the subgroup of patients with at least one positive reaction to an allergen of the baseline series, n=6255. The proportion of excluded patients did not vary much between countries (P=0.23, χ^2 test).

Patients with reactions to contact allergens included in an additional series have not been considered further as the tested additional series often have widely varying compositions. Furthermore, among the 13057 patients diagnosed with ACD, 4816 had only one positive reaction, and in this latter subgroup, 1360 (28.8%) had more than one site affected. These 1360 patients were also excluded from further analysis.

A comparison of basic demographic and clinical characteristics between the subgroup positive to at least one baseline series allergen and not being positive to the baseline series is shown in Supplemental table S2 (MOAHLFA index). Males more often had a negative baseline series (χ^2-test: P < 0.0001).

Focusing on the n=6255 patients with at least one positive reaction to contact allergens of the baseline series, the MOAHLFA index for patients, stratified for country is shown in Table 1. The most striking differences are seen for sex (least males in Lithuania, most in Germany) and occupational dermatitis (least cases in Spain, most in Germany). The patch tested population – as restricted in the present analysis – in Italy is strikingly younger than the population from the other countries.

The distribution of anatomical sites in patients with a diagnosis of ACD attributed to one single body site is shown in Table 2, stratified for country. Differences can be seen, mainly for the generalized subgroup ranging from 4.2% in Germany to >20% in the Netherlands and Poland. Head and hand are clearly the most reported single body sites where ACD is attributed to, the anogenital area the least reported site (not taking the 'other' category into account). For head and hand, large differences are seen between the Netherlands and Germany, with the Netherlands reporting head as the most affected single site (39.1%), while for Germany the hand is most reported (45.7%). Conversely, in the head category, Germany reports the lowest percentage (22.7%), while the Netherlands report the lowest percentage in the hand category (22.3%). ACD on the feet as single body site is most reported in Spain (7.7%).

The cases with a positive patch test to the baseline series (n=6255) were subjected to analyses, stratified for body site, concerning patch test results with the European baseline series. The results were adjusted for sex and age. The allergens were sorted by descending prevalence per body site to visualize the most important allergens for each body site, see Table 3. Nickel, fragrance mix I, cobalt and MCI/MI were the most frequent reported allergens for the various body sites. Beyond these, differences between body parts become apparent, including the following observations:

- Particularly frequent positive reactions to MCI/MI in patients with ACD of the hands, e.g. when compared to patients with ACD of the feet.
- A high rating for colophonium and *p-tert*-butylphenol formaldehyde resin (PTBFR) in patients with ACD of the feet.
- Thiuram mix is a common contact allergen in patients with ACD of the hands, while mercapto mix and 2-mercaptobenzathiazole (MBT) are common in patients with ACD on the feet.
- Chromium is a common allergen in patients with ACD on the extremities (arm/hand and leg/feet), and it is the most frequent allergen in patients with ACD of the feet.
- *p*-Phenylenediamine (PPD) contact allergy is often found in patients with ACD of the head, but also in patients with anogenital ACD.
- *Myroxylon pereirae*, colophonium, lanolin alcohol, and paraben mix are contact allergens often found in patients with ACD on the legs.

- *N*-Isopropyl-*N*'-phenyl-*p*-phenylenediamine (IPPD) is prevalent in patients with ACD on the head and upper extremities, but not on the trunk and lower extremities.
- Hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC) is prevalent on all body sites, except for in patients with ACD of the feet. Also fragrance mix II, which includes HICC, is a relatively uncommon contact allergen related to the feet.
- Formaldehyde and the formaldehyde-releaser Quaternium 15 are prevalent in patients with ACD of the hands, but mainly in patients with generalized ACD.

Crude prevalences of European baseline series contact allergens have been compiled in Supplement S3. Also, tables have been compiled to stratify for sex and age (dichotomized: <40 years and ≥40 years).

4. Discussion

In this study, we found that in the ESSCA patch test database, the head and hand were the most common distinct body sites ACD was attributed to. Differences between countries were seen for multiple body sites. Nickel, fragrance mix I, cobalt and MCI/MI were the allergens that were most frequently reported for the various body sites. Beyond these, differences between body parts were apparent.

Considering the MOAHLFA criteria, a difference in sex distribution between patients who tested positive to the baseline series and those who did not is obvious: there are more men with an ACD diagnosis based on a positive patch test to an allergen from an additional series. It has been shown that woman are sensitized to allergens from the European baseline series more often, possibly because they tend to use products like cosmetics more than men, of which many constituents are allergens from the European baseline series.[22,23]

The hands and the head were the most common single sites to which a diagnosis of ACD was attributed in our study sample. These sites were also found to be common sites of dermatitis at presentation in other studies.[24,25] This once again justifies the choice of adding facial dermatitis to the MOAHLFA criteria.[26] Also, the feet and legs are common sites in adults[13], as well as in children.[27–29]

4.1 Anatomical site 'Head'

ACD of the head was most often reported in the Netherlands and Lithuania, and least often in Germany and Spain. Of note, in our study "head" includes, but is not limited to, "face" as anatomical site. One large study was performed on facial dermatitis and patch testing by Schnuch et al in 18572

patients.[9] They compared positive patch tests in men and woman. Nickel, fragrance mix, PPD, lanolin alcohol and HICC were significantly more common in woman. Only epoxy resin was significantly more common in men. Other research on facial ACD and patch tests was performed in several smaller studies.[30–37] In these studies, a high prevalence of mainly nickel, fragrances, PPD and MCI/MI contact allergy was found, which corresponds to our results. In the study by Kasemsarn et al the clinical relevance of positive patch tests was determined for each case. Positive patch tests to metals and hairdressing product-related allergens were found to be most often of clinical relevance. Also, positive reactions to colophonium were frequently clinically relevant.[33] In our study, colophonium was not more commonly found in patients with ACD of the head, compared to other body parts. We, however, cannot comment on the clinical relevance of the positive patch tests, which is hitherto not collected in a standardized and systematic way in the ESSCA network. For the thiuram mix, we found a prevalence of 3.5% in patients with ACD of the head, similar to the percentage found by Schwensen et al in Denmark.[38]

4.2 Anatomical site 'Hand'

ACD of the hands was most often diagnosed in Germany and Italy, and least often in the Netherlands. Especially for Germany this might be explained by a higher prevalence of (and focus on) occupational cases, which is often associated with ACD of the hands.[39] Although in Poland also many occupational cases were seen, here, the hands were much less often affected than in Germany. It must be noted that occupational cases can be allergic, as well as irritant in nature. More occupational cases in Poland may therefore have an irritant etiology. In studies performed with >200 subjects with hand eczema tested consecutively with baseline allergens, contact allergy to nickel, preservatives, fragrances and cobalt were most often reported, corresponding to our results.[40–46] In addition, in consecutively tested hospital patients with hand eczema in Portugal and China, chromium and PPD were also often found to be highly prevalent.[47,48] Interestingly, in a cross-sectional analysis of data from the North American Contact Dermatitis Group between 1994 and 2004, Warshaw et al found that the most common allergens in hand eczema patients were the preservatives Quaternium 15 and formaldehyde, before nickel and fragrance mix. In that study, clinical relevance had been determined and these preservatives also proved most often relevant.[7]

4.3 Specific allergens

Contact allergies to nickel, fragrance mix I, cobalt and MCI/MI are common and, as found in our study, not specifically related to certain body sites. This is reflected by the fact that these allergens were the most frequently reported allergens for the various body sites. In other words, one can frequently expect a positive reaction to one of these allergens, regardless of the site of dermatitis.

The finding that MCI/MI was most often found in patients with ACD of the hands is in line with results from a large study with data from North America, in which individuals with MCI/MI and MI allergy were significantly more likely to have hand dermatitis, compared to the general patch tested population.[49] In a worldwide multicenter study, the face was also reported as a frequent localization, next to the hands.[50] The higher prevalence of MCI/MI allergy for these body sites could very well be explained by the fact that the hands and face are preferred locations for leave-on products, which lead to contact allergy more readily than rinse-off products[51]; moreover, both sites are exposed to rinse-off products, too. The high prevalence we found highlights once more how common contact allergy to this preservative has become during the current epidemic and emphasizes the importance of the ban on MI in leave-on products.[52]

Concerning rubber allergens we found distinct patterns for thiuram mix and mercapto mix, respectively: thiuram mix was more often positive in patients with ACD of the hands while contact allergy to mercapto mix was more often diagnosed in patients with ACD of the feet. This is in line with many previous studies[7,10,53–58] and might be explained by a higher release of thiuram mix from rubber gloves (when compared to MBT).[59] Ingredients from the mercapto mix might indeed be more common in shoes and boots (although closely followed by thiuram mix).[60,61] Colophonium and PTBFR are also common ingredients in shoes which frequently cause ACD, which is confirmed again in our data.[60] However, especially concerning gloves, the allergies we found could be due to sensitization in the past. Bergendorff et al showed that there were no thiurams present in protective gloves used in health care in southern Sweden.[62] Uter et al described a downward trend of thiuram allergy for healthcare workers suggesting that most manufacturers may have replaced thiurams by dithiocarbamates.[63] However, patch testing with thiurams is regarded as suitable to diagnose contact allergy to dithiocarbamates, because these substances constitute a redox pair.[64]

Chromium was a common contact allergen in patients with ACD of the extremities and especially so in patients with ACD of the feet. Considering the wide range of sources of chromium exposure, the frequency found for the extremities (including the hands and feet) is not surprising.[65] The most logical explanation for chromium allergy being related to ACD of the feet is that footwear containing leather is the main source of sensitization. In previous studies it was found that chromium was the most common allergen in patients with foot dermatitis[66,67] and that it was significantly associated with leg and foot dermatitis in women.[68] Our finding emphasizes the importance of the European Union directive No. 301/2014 stating that from May 2015, leather articles placed on the markets of European countries that come into contact with the skin should not contain >3 ppm chromium(VI).[69] We therefore expect a decrease of chromium contact allergy in future years.

PPD is a known common contact allergen for ACD on the head.[70] We also found a quite high prevalence for PPD in patient with anogenital ACD. This might partly be explained by cross-reactions with benzocaine[71], which is used in topical formulations that are applied anally and which we also found to be prevalent for this body site.

The antioxidant/-ozonant IPPD was strikingly more often found in patients with ACD of the head and upper extremities (arm and hand), when compared to the trunk and lower extremities. Although sometimes causing an ACD on the feet because of its presence in heavy boots[72], IPPD is more often reported causing ACD on the upper body parts that come into direct contact with industrial rubbers for heavy-duty applications, like tires.[73,74] Furthermore, it has been shown that that cross-reactions between PPD and IPPD can occur.[71]

A profile of contact allergens associated with the use of topical drugs was found for patients with ACD of the legs (*M. pereirae*, colophonium, lanolin alcohol and paraben mix). This has also been found in previous studies, and mainly in elderly patients, probably because of the use of topical agents in stasis dermatitis and ulceration of the lower legs.[75] However, over the years, a decrease was seen in the frequency of contact allergies in these patients, possibly implicating that the treatment of stasis dermatitis and leg ulceration has improved in terms of using less topical and less allergenic preparations.[12] This might be explained by an increase in the use of wound dressings instead of topical formulations to treat these patients. Conversely, positive patch test reactions to wound dressings are now becoming more common.[11]

The fact that HICC, together with other fragrances, was least often seen in patients with ACD of the feet is in accordance with previous studies.[10,76] Apparently, patients with foot dermatitis are a quite distinctive entity. The most logical explanation could be that patients with foot dermatitis have had less exposure to cosmetic products. We expect the prevalence of HICC contact allergy to decrease in future years, as the European Union directive No. 2017/1410 bans HICC, stating that from August 2021 cosmetic products containing HICC shall not be made available on the Union market.[77]

Formaldehyde is often found in cosmetics. In a recent Danish study it was mostly found in creams, shampoos and soaps.[78] The fact that these products are often used over the whole body most likely explains the prevalence of formaldehyde and Quaternium 15 in patients with generalized ACD and also in patients with ACD of the hands.

A limitation of our study is that it is not certain that the diagnosis of ACD was always based on a clinically relevant positive patch test to an allergen in the European baseline series. Additional series are often tested and the diagnosis could very well been based on a positive test to an allergen from

an additional series, while a positive reaction to a European baseline allergen was also present, but not currently relevant. Another limitation is that relevance of individual positive patch tests was not taken into account as it was not registered systematically in all centers. To overcome this problem in the future an 'extended ESSCA' database has been developed as a concept, providing the possibility to very precisely link positive patch test reactions to body sites, along with current and past relevance for the dermatitis that the patient presented with.[79] Furthermore, a small subgroup was not included in the analyses. This concerns the cases that have only one positive reaction to the European Baseline Series but multiple sites involved. Exclusion of cases with multiple body sites affected removed the possibility of looking into frequent concomitant sites of ACD. Conversely, inclusion would have made it impossible to keep a clean group with isolated affected body sites. We have deliberately included patients with generalized ACD for comparison, although it can be argued generalization does not represent an actual single site. We choose to include this group because it represents patients with widespread eczema, for which it is also important to define the most frequently found contact allergies. Furthermore, the subgroup of patients in our study with generalized ACD (with 'generalized' entered as single body site) represented a substantial percentage of our study population.

In conclusion, in the analysed ESSCA data we found that most cases of ACD concerning a single isolated body site are attributed to the head and hands. Multiple allergen patterns per body site can be observed. Contact allergies to especially nickel, fragrance mix I, cobalt and/or MCI/MI were common for the period between 2009 and 2014. However, contact allergy to these allergens was not found to be specifically related to a certain body site. Adding the possibility to link positive patch test reactions to relevance, along with the affected body sites, should be an important addition to data capturing systems, such as WinAlldat/ESSCA.

References

1 Pesonen M, Jolanki R, Larese Filon F, *et al.* Patch test results of the European baseline series among patients with occupational contact dermatitis across Europe - analyses of the European Surveillance System on Contact Allergy network, 2002-2010. *Contact Dermatitis* 2015; **72**:154–63.

2 Belloni Fortina A, Cooper SM, Spiewak R, *et al.* Patch test results in children and adolescents across Europe. Analysis of the ESSCA Network 2002-2010. *Pediatr Allergy Immunol* 2015; **26**:446–55.

3 Uter W, Spiewak R, Cooper SM, *et al.* Contact allergy to ingredients of topical medications: results of the European Surveillance System on Contact Allergies (ESSCA), 2009-2012. *Pharmacoepidemiol Drug Saf* 2016; **25**:1305–12.

4 Uter W, Larese Filon F, Rui F, *et al.* ESSCA results with nickel, cobalt and chromium, 2009-2012. *Contact Dermatitis* 2016; **75**:117–21.

5 The ESSCA Writing Group. The European Surveillance System of Contact Allergies (ESSCA): results of patch testing the standard series, 2004. *J Eur Acad Dermatol Venereol* 2008; **22**:174–81.

6 Li LF, Wang J. Contact hypersensitivity in hand dermatitis. *Contact Dermatitis* 2002; **47**:206–9.

7 Warshaw EM, Ahmed RL, Belsito D V, *et al.* Contact dermatitis of the hands: cross-sectional analyses of North American Contact Dermatitis Group Data, 1994-2004. *J Am Acad Dermatol* 2007; **57**:301–14.

8 Zug KA, Kornik R, Belsito D V, *et al.* Patch-testing North American lip dermatitis patients: data from the North American Contact Dermatitis Group, 2001 to 2004. *Dermatitis* 2008; **19**:202–8.

9 Schnuch A, Szliska C, Uter W, IVDK. Facial allergic contact dermatitis. Data from the IVDK and review of literature. *Hautarzt* 2009; **60**:13–21.

10 Landeck L, Uter W, John SM. Patch test characteristics of patients referred for suspected contact allergy of the feet--retrospective 10-year cross-sectional study of the IVDK data. *Contact Dermatitis* 2012; **66**:271–8.

11 D'Erme AM, Iannone M, Dini V, Romanelli M. Contact dermatitis in patients with chronic leg ulcers: a common and neglected problem: a review 2000-2015. *J Wound Care* 2016; **25 Suppl 9**:S23-9.

12 Erfurt-Berge C, Geier J, Mahler V. The current spectrum of contact sensitization in patients with chronic leg ulcers or stasis dermatitis - new data from the Information Network of Departments of Dermatology (IVDK). *Contact Dermatitis* 2017; **77**:151–8.

13 Carlsen BC, Andersen KE, Menne T, Johansen JD. Sites of dermatitis in a patch test population: hand dermatitis is associated with polysensitization. *Br J Dermatol* 2009; **161**:808–13.

14 Uter W, Aberer W, Armario-Hita JC, *et al.* Current patch test results with the European baseline series and extensions to it from the 'European Surveillance System on Contact

Allergy' network, 2007-2008. *Contact Dermatitis* 2012; **67**:9–19.

15 Uter W, Arnold R, Wilkinson J, *et al.* A multilingual European patch test software concept: WinAlldat/ESSCA. *Contact Dermatitis* 2003; **49**:270–1.

16 Johansen JD, Aalto-Korte K, Agner T, *et al.* European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis* 2015; **73**:195–221.

17 Bruze M, Engfeldt M, Gonçalo M, Goossens A. Recommendation to include methylisothiazolinone in the European baseline patch test series--on behalf of the European Society of Contact Dermatitis and the European Environmental and Contact Dermatitis Research Group. *Contact Dermatitis* 2013; **69**:263–70.

18 Uter W, Schnuch A, Wilkinson M, *et al.* Registries in Clinical Epidemiology: the European Surveillance System on Contact Allergies (ESSCA). *Methods Inf Med* 2016; **55**:193–9.

19 Uter W, Schnuch A, Gefeller O, ESCD working group: European Surveillance System on Contact Allergies. Guidelines for the descriptive presentation and statistical analysis of contact allergy data. *Contact Dermatitis* 2004; **51**:47–56.

20 Gefeller O, Pfahlberg AB, Uter W. What can be learnt from nothing? - A statistical perspective. *Contact Dermatitis* 2013; **69**:350–4.

21 Dittmar D, Uter W, Bauer A, *et al.* European Surveillance System on Contact Allergies (ESSCA): polysensitization, 2009-2014. *Contact Dermatitis* 2018; **78**:373–85.

22 Warshaw EM, Buchholz HJ, Belsito D V., *et al.* Allergic patch test reactions associated with cosmetics: Retrospective analysis of cross-sectional data from the North American Contact Dermatitis Group, 2001-2004. *J Am Acad Dermatol* 2009; **60**:23–38.

23 Uter W, Schwitulla J, Thyssen JP, *et al.* The 'overall yield' with the baseline series - a useful addition to the array of MOAHLFA factors describing departmental characteristics of patch tested patients. *Contact Dermatitis* 2011; **65**:322–8.

24 Bordel-Gómez MT, Miranda-Romero A, Castrodeza-Sanz J. [Epidemiology of contact dermatitis: prevalence of sensitization to different allergens and associated factors]. *Actas Dermosifiliogr* 2010; **101**:59–75.

25 Duarte I, Lazzarini R, Kobata CM. Contact dermatitis in adolescents. *Am J Contact Dermat*

2003; **14**:200–2.

26 Schnuch A, Geier J, Uter W, *et al.* National rates and regional differences in sensitization to allergens of the standard series. Population-adjusted frequencies of sensitization (PAFS) in 40,000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997; **37**:200–9.

27 Clayton TH, Wilkinson SM, Rawcliffe C, *et al.* Allergic contact dermatitis in children: should pattern of dermatitis determine referral? A retrospective study of 500 children tested between 1995 and 2004 in one U.K. centre. *Br J Dermatol* 2006; **154**:114–7.

28 Mortazavi H, Ehsani A, Sajjadi SS, *et al.* Patch testing in Iranian children with allergic contact dermatitis. *BMC Dermatol* 2016; **16**:10.

29 Ortiz Salvador JM, Esteve Martínez A, Subiabre Ferrer D, *et al.* Pediatric Allergic Contact Dermatitis: Clinical and Epidemiological Study in a Tertiary Hospital. *Actas Dermosifiliogr* 2017; **108**:571–8.

30 Katz AS, Sherertz EF. Facial dermatitis: patch test results and final diagnoses. *Am J Contact Dermat* 1999; **10**:153–6.

31 Adisen E, Onder M, Terzioglu Y, *et al.* A retrospective study of patients with facial allergic contact dermatitis patch tested with the European standard series in Turkey. *J Eur Acad Dermatol Venereol* 2009; **23**:704–5.

32 Li L-FF, Liu G, Wang J. Prevalence and 1-year outcome of facial allergic contact dermatitis in patients patch tested in a university hospital. *Contact Dermatitis* 2007; **57**:187–90.

33 Kasemsarn P, Iamphonrat T, Boonchai W. Risk factors and common contact allergens in facial allergic contact dermatitis patients. *Int J Dermatol* 2016; **55**:417–24.

34 Shah M, Lewis FM, Gawkrodger DJ. Facial dermatitis and eyelid dermatitis: a comparison of patch test results and final diagnoses. *Contact Dermatitis* 1996; **34**:140–1.

35 Li LF, Wang J. Patch testing and aeroallergen intradermal testing in facial dermatitis. *Contact Dermatitis* 2000; **43**:90–4.

36 Peng F, Mu Z, He C, *et al.* Patch testing in facial dermatitis using Chinese Baseline Series (60 allergens) and Cosmetic Series (58 allergens). *J Eur Acad Dermatology Venereol* 2018. doi:10.1111/jdv.14822.

37 Murad A, Marren P. Prevalence of methylchloroisothiazolinone and methylisothiazolinone

contact allergy in facial dermatitis: a single centre Irish study. *J Eur Acad Dermatol Venereol* 2016; **30**:60–2.

38 Schwensen JF, Menné T, Johansen JD, Thyssen JP. Contact allergy to rubber accelerators remains prevalent: retrospective results from a tertiary clinic suggesting an association with facial dermatitis. *J Eur Acad Dermatology Venereol* 2016; **30**:1768–73.

39 Goh CL. An epidemiological comparison between hand eczema and non-hand eczema. *Br J Dermatol* 1988; **118**:797–801.

40 Agner T, Andersen KE, Brandao FM, *et al.* Contact sensitisation in hand eczema patients-relation to subdiagnosis, severity and quality of life: a multi-centre study. *Contact Dermatitis* 2009; **61**:291–6.

41 Boonstra MB, Christoffers WA, Coenraads PJ, Schuttelaar ML. Patch test results of hand eczema patients: relation to clinical types. *J Eur Acad Dermatol Venereol* 2015; **29**:940–7.

42 Murphy R, Gawkrodger DJ. Contact allergens in 200 patients with hand dermatitis. *Contact Dermatitis* 2003; **48**:227–8.

43 Skoet R, Olsen J, Mathiesen B, *et al.* A survey of occupational hand eczema in Denmark. *Contact Dermatitis* 2004; **51**:159–66.

44 Veien NK, Hattel T, Laurberg G. Hand eczema: causes, course, and prognosis I. *Contact Dermatitis* 2008; **58**:330–4.

45 Majid I. Contact allergens causing hand eczema in ethnic Kashmiri population: A study of 7-years. *Indian J Dermatol* 2016; **61**:119.

46 Hald M, Agner T, Blands J, *et al.* Allergens associated with severe symptoms of hand eczema and a poor prognosis. *Contact Dermatitis* 2009; **61**:101–8.

47 Magina S, Barros MA, Ferreira JA, Mesquita-Guimarães J. Atopy, nickel sensitivity, occupation, and clinical patterns in different types of hand dermatitis. *Am J Contact Dermat* 2003; **14**:63–8.

48 Ni C, Dou X, Chen J, *et al.* Contact sensitization in Chinese patients with hand eczema. *Dermatitis* 2011; **22**:211–5.

49 Zirwas MJ, Hamann D, Warshaw EM, *et al.* Epidemic of Isothiazolinone Allergy in North America. *Dermatitis* 2017; **28**:204–9.

50 Isaksson M, Ale I, Andersen KE, *et al.* Multicenter Patch Testing With Methylisothiazolinone and Methylchloroisothiazolinone/Methylisothiazolinone Within the International Contact Dermatitis Research Group. *Dermatitis* 2017; **28**:210–4.

51 Gerberick GF, Robinson MK, Felter SP, *et al.* Understanding fragrance allergy using an exposure-based risk assessment approach. *Contact Dermatitis* 2001; **45**:333–40.

52 European Commission. Commission Regulation (EU) 2016/1198 of 22 July 2016 amending Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products (Text with EEA relevance) [WWW Document]. 2016.URL https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32016R1198 [accessed on 5 June 2018].

53 Duarte I, Terumi Nakano J, Lazzarini R. Hand eczema: evaluation of 250 patients. *Am J Contact Dermat* 1998; **9**:216–23.

54 Veien NK, Hattel T, Laurberg G. Hand eczema: causes, course, and prognosis II. *Contact Dermatitis* 2008; **58**:335–9.

55 Hald M, Veien NK, Laurberg G, Johansen JD. Severity of hand eczema assessed by patients and dermatologist using a photographic guide. *Br J Dermatol* 2007; **156**:77–80.

56 Warshaw EM, Schram SE, Belsito D V, *et al.* Shoe allergens: retrospective analysis of cross-sectional data from the north american contact dermatitis group, 2001-2004. *Dermatitis* 2007; **18**:191–202.

57 Templet JT, Hall S, Belsito D V. Etiology of hand dermatitis among patients referred for patch testing. *Dermatitis* 2004; **15**:25–32.

58 Chen H-H, Sun C-C, Tseng M-P. Type IV Hypersensitivity from Rubber Chemicals: A 15-Year Experience in Taiwan. *Dermatology* 2004; **208**:319–25.

59 Geier J, Lessmann H, Uter W, *et al.* Occupational rubber glove allergy: results of the Information Network of Departments of Dermatology (IVDK), 1995-2001. *Contact Dermatitis* 2003; **48**:39–44.

60 Matthys E, Zahir A, Ehrlich A. Shoe Allergic Contact Dermatitis. *Dermatitis* 2014; **25**:163–71.

61 Goossens A, Taylor JS. Shoes. In: *Contact Dermatitis* (Johansen JD, Frosch PJ, Lepoittevin JP, eds), 5th ed. Berlin-Heidelberg, Springer-Verlag, 2011; 819–30.

62 Bergendorff O, Persson C, Hansson C. High-performance liquid chromatography analysis of

rubber allergens in protective gloves used in health care. *Contact Dermatitis* 2006; **55**:210–5.

63 Uter W, Hegewald J, Pfahlberg A, *et al.* Contact allergy to thiurams: multifactorial analysis of clinical surveillance data collected by the IVDK network. *Int Arch Occup Environ Health* 2010; **83**:675–81.

64 Crepy M-N, Lecuen J, Ratour-Bigot C, *et al.* Accelerator-free gloves as alternatives in cases of glove allergy in healthcare workers. *Contact Dermatitis* 2018; **78**:28–32.

65 Bregnbak D, Johansen JD, Jellesen MS, *et al.* Chromium allergy and dermatitis: prevalence and main findings. *Contact Dermatitis* 2015; **73**:261–80.

66 Nardelli A, Taveirne M, Drieghe J, *et al.* The relation between the localization of foot dermatitis and the causative allergens in shoes: a 13-year retrospective study. *Contact Dermatitis* 2005; **53**:201–6.

67 Hansen MB, Menné T, Johansen JD. Cr(III) reactivity and foot dermatitis in Cr(VI) positive patients. *Contact Dermatitis* 2006; **54**:140–4.

68 Lejding T, Mowitz M, Isaksson M, *et al.* A retrospective investigation of hexavalent chromium allergy in southern Sweden. *Contact Dermatitis* 2018; **78**:386–92.

69 European Commission. Commission Regulation (EU) No 301/2014 of 25 March 2014 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards chromi [WWW Document]. 2014.URL https://publications.europa.eu/en/publication-detail/-/publication/93044ae6-b4bc-11e3-86f9-01aa75ed71a1/language-en [accessed on 31 May 2018].

70 Mukkanna KS, Stone NM, Ingram JR. Para-phenylenediamine allergy: current perspectives on diagnosis and management. *J Asthma Allergy* 2017; **10**:9–15.

71 Thomas BR, White IR, McFadden JP, Banerjee P. Positive relationship-intensity of response to p-phenylenediamine on patch testing and cross-reactions with related allergens. *Contact Dermatitis* 2014; **71**:98–101.

72 Nishioka K, Murata M, Ishikawa T, Kaniwa M. Contact dermatitis due to rubber boots worn by Japanese farmers, with special attention to 6-ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (ETMDQ) sensitivity. *Contact Dermatitis* 1996; **35**:241–5.

73 Warburton KL, Bauer A, Chowdhury MMU, *et al.* ESSCA results with the baseline series, 2009-2012: rubber allergens. *Contact Dermatitis* 2015; **73**:305–12.

74 Uter W, Rühl R, Pfahlberg A, *et al.* Contact allergy in construction workers: results of a multifactorial analysis. *Ann Occup Hyg* 2004; **48**:21–7.

75 Uter W, Geier J, Pfahlberg A, Effendy I. The Spectrum of Contact Allergy in Elderly Patients with and without Lower Leg Dermatitis. *Dermatology* 2002; **204**:266–72.

76 Bennike NH, Zachariae C, Johansen JD. Non-mix fragrances are top sensitizers in consecutive dermatitis patients - a cross-sectional study of the 26 EU-labelled fragrance allergens. *Contact Dermatitis* 2017; **77**:270–9.

77 Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (European Commission) EC. Commission Regulation (EU) 2017/1410 of 2 August 2017 amending Annexes II and III to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products (Text with EEA relevance) [WWW Document]. 2017.URL https://publications.europa.eu/en/publication-detail/-/publication/f14047b3-7814-11e7-b2f2-01aa75ed71a1/language-en [accessed on 5 June 2018].

78 Fasth IM, Ulrich NH, Johansen JD. Ten-year trends in contact allergy to formaldehyde and formaldehyde-releasers. *Contact Dermatitis* 2018; **79**:263–9.

79 Uter W, Bauer A, Bensefa-Colas L, *et al.* Pilot study on a new concept of documenting the clinical relevance of patch test results in contact dermatitis patients. *Contact Dermatitis* 2018. doi:10.1111/cod.13097.

Figure legend:

Figure 1. Study flow diagram. ACD, allergic contact dermatitis.

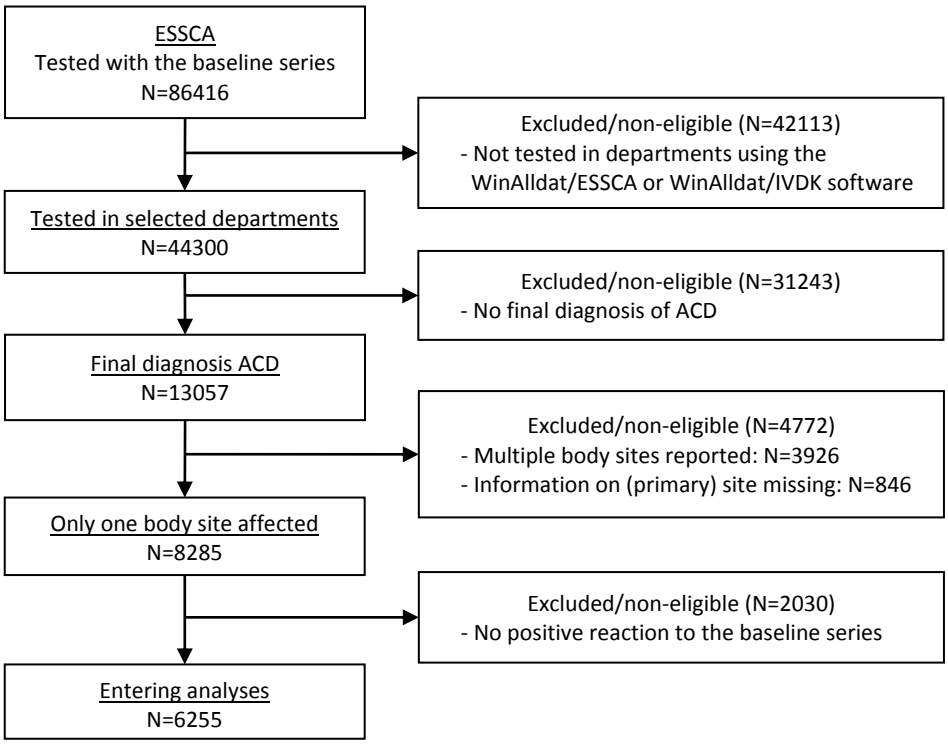

Figure 1. Study flow diagram. ACD, allergic contact dermatitis.

Table 1: MOAHLFA index for the n=6255 patients positive to the baseline series with a diagnosis of allergic contact dermatitis attributed to a single body site, stratified for country.

	AT	CH	DE	ES	IT	LT	NL	PL
Male	23.4	32.8	37.5	27.3	23.2	14.5	27.8	19.6
Occupational	24.5	21.1	41.2	15.9	23.6	19.7	18.6	35.9
Atopic Eczema	24.5	17.8	26.4	9.1	11.2	7.4	34.7	9.3
Site of ACD: Hand	34.8	29.3	45.7	24.9	38.2	26.2	22.3	26.7
Site of ACD: Leg	9.2	8.7	10.0	7.3	2.7	9.5	2.9	5.5
Site of ACD: Face	20.3	26.0	16.4	12.1	12.6	27.1	20.9	13.3
Age 40+	62.8	66.5	71.8	65.8	39.0	61.2	63.3	58.0
Total (n)	282	1002	981	1375	259	461	1293	602

All figures are percentages. Of note, the 3 sites (hand, leg, face) do not relate to the primary site of contact dermatitis (irrespective of other information such as diagnosis or patch test reactions) normally used for the MOAHLFA index, but to the same single sites used elsewhere in this analysis. ACD, allergic contact dermatitis; AT, Austria; CH, Switzerland; DE, Germany; ES, Spain; IT, Italy; LT, Lithuania; NL, the Netherlands; PL, Poland. *P*-value of χ^2 test for heterogeneity across countries: $P < .0001$ for all MOAHLFA items.

Table 2: Distribution of anatomical sites of allergic contact dermatitis of a single body site in n=6255 patients positive to the baseline series, stratified for country.

Country	tested	Head	Arm	Hand	Trunk	anogenital	Leg	Foot	generalised
AT	282	96 (34.0)	17 (6.0)	98 (34.8)	19 (6.7)	7 (2.5)	26 (9.2)	5 (1.8)	12 (4.3)
CH	1002	339 (33.8)	50 (5.0)	294 (29.3)	58 (5.8)	52 (5.2)	87 (8.7)	38 (3.8)	73 (7.3)
DE	981	223 (22.7)	34 (3.5)	448 (45.7)	57 (5.8)	20 (2.0)	98 (10.0)	45 (4.6)	41 (4.2)
ES	1375	325 (23.6)	125 (9.1)	342 (24.9)	239 (17.4)	35 (2.5)	100 (7.3)	106 (7.7)	91 (6.6)
IT	259	78 (30.1)	13 (5.0)	99 (38.2)	28 (10.8)	1 (0.4)	7 (2.7)	15 (5.8)	17 (6.6)
LT	461	163 (35.4)	10 (2.2)	121 (26.2)	23 (5.0)	34 (7.4)	44 (9.5)	8 (1.7)	48 (10.4)
NL	1293	505 (39.1)	23 (1.8)	288 (22.3)	41 (3.2)	29 (2.2)	37 (2.9)	63 (4.9)	306 (23.7)
PL	602	177 (29.4)	20 (3.3)	161 (26.7)	39 (6.5)	12 (2.0)	33 (5.5)	31 (5.1)	128 (21.3)
Total	6255	1906 (30.5)	292 (4.7)	1851 (29.6)	504 (8.1)	190 (3.0)	432 (6.9)	311 (5.0)	716 (11.4)

Figures are shown as overall number (percentage within country). n=53 (0.8%) patients with “other” single sites not shown. AT, Austria; CH, Switzerland; DE, Germany; ES, Spain; IT, Italy; LT, Lithuania; NL, the Netherlands; PL, Poland.

Table 3 Sex and age adjusted prevalences of positive reactions to the baseline series haptens stratified for body site

Allergen	Head *n*=1906	Arm *n*=292	Hand *n*=1851	Trunk *n*=504	anogenital *n*=190	Leg *n*=432	Foot *n*=311	generalised *n*=716
Nickel	38 (35.6–40.3)	48.4 (42.9–53.9)	34.4 (32.3–36.4)	53.8 (49.5–58.2)	30.9 (24.3–37.5)	30.5 (24.2–36.9)	31.7 (26.4–37.0)	43 (39.2–46.8)
Cobalt	10.7 (9.1–12.4)	14.6 (10.2–19.0)	16.0 (14.3–17.7)	14.8 (11.5–18.2)	10.1 (5.4–14.8)	13.1 (8.0–18.2)	24.5 (19.4–29.6)	18.2 (15.0–21.3)
Chromium	5.0 (3.8–6.2)	10.3 (6.6–14.1)	10.2 (8.8–11.6)	7.2 (4.8–9.6)	3.3 (0.2–6.5)	15.1 (9.6–20.6)	42.8 (37.0–48.6)	13.5 (10.8–16.2)
Fragrance mix I	22.2 (19.6–24.7)	16.5 (12.3–20.6)	16.2 (14.5–17.9)	16.9 (13.6–20.3)	25.9 (19.0–32.8)	25.8 (20.2–31.4)	9.4 (6.2–12.7)	19.5 (16.5–22.5)
Fragrance mix II	10.5 (8.8–12.2)	10.3 (6.7–13.8)	10.1 (8.7–11.4)	11.8 (8.9–14.7)	17.9 (11.6–24.3)	11.9 (7.9–15.9)	4.1 (1.9–6.3)	13.5 (10.9–16.1)
HICC	5.5 (4.2–6.8)	3.6 (1.4–5.9)	4.8 (3.8–5.7)	4.7 (2.8–6.6)	5.6 (1.1–10.2)	3.4 (0.6–6.2)	1.0 (0.0–2.0)	4.5 (2.9–6.0)
Myroxylon pereirae (balsam of Peru)	15 (12.8–17.2)	9.0 (5.8–12.2)	11.5 (10.1–13.0)	12.2 (9.4–15.1)	21.7 (15.1–28.4)	27.6 (22.1–33.1)	11.8 (8.2–15.4)	14.2 (11.7–16.7)
Colophonium	6.7 (5.2–8.2)	4.2 (1.8–6.6)	8.3 (7.0–9.5)	6.2 (3.9–8.4)	6.1 (2.1–10.0)	14.1 (9.1–19.0)	12.9 (9.0–16.9)	7.3 (5.4–9.3)
Formaldehyde	3.2 (2.1–4.4)	2.9 (0.8–4.9)	5.6 (4.6–6.7)	4.4 (2.5–6.4)	3.0 (0.8–5.2)	1.2 (0.4–2.0)	3.2 (1.1–5.2)	6.2 (4.3–8.0)
Paraben Mix	1.7 (0.9–2.4)	1.3 (0.0–2.7)	1.5 (0.9–2.1)	1.8 (0.6–3.0)	5.6 (1.3–9.9)	4.9 (2.3–7.4)	0.9 (0.0–2.0)	2.5 (1.4–3.6)
Quaternium 15	1.1 (0.4–1.8)	0.0 (0.0–1.0)	1.4 (0.9–2.0)	0.4 (0.0–1.0)	0.4 (0.0–1.1)	1.2 (0.0–2.8)	0.5 (0.0–1.5)	2.2 (1.1–3.4)
MCI/MI	15.4 (13.3–17.4)	9.4 (5.9–12.8)	22.4 (20.5–24.4)	13.8 (10.7–17.0)	15.6 (10.2–20.9)	9.3 (5.5–13.1)	6.1 (3.2–9.0)	18.2 (15.2–21.2)
MI	8.0 (6.5–9.4)	5.3 (2.6–8.0)	9.8 (8.5–11.2)	8.0 (5.5–10.5)	3.8 (0.4–7.2)	5.5 (2.2–8.8)	4.8 (2.2–7.3)	9.9 (7.6–12.2)
MDBGN	6.8 (5.2–8.4)	3.5 (1.4–5.6)	7.1 (5.9–8.3)	6.5 (4.4–8.6)	6.9 (3.5–10.4)	9.1 (5.5–12.6)	3.6 (1.4–5.8)	10.0 (7.8–12.2)
PPD	9.6 (8.0–11.2)	5.2 (2.4–8.0)	5.5 (4.5–6.6)	4.7 (2.9–6.5)	8.6 (4.1–13.1)	3.5 (1.6–5.4)	3.4 (1.5–5.3)	5.7 (3.9–7.4)
Benzocaine	1.0 (0.3–1.6)	1.2 (0.0–2.5)	0.4 (0.1–0.7)	1.1 (0.3–1.9)	4.1 (1.4–6.8)	1.2 (0.4–2.0)	0.5 (0.0–1.1)	0.4 (0.0–0.8)
Clioquinol	0.8 (0.1–1.6)	0.0 (0.0–1.0)	0.2 (0.0–0.4)	0.4 (0.0–1.0)	1.7 (0.0–3.5)	0.5 (0.0–1.1)	0.3 (0.0–0.8)	0.6 (0.1–1.1)
Budesonide	1.2 (0.3–2.0)	1.9 (0.2–3.6)	0.8 (0.4–1.2)	1.7 (0.6–2.9)	1.6 (0.0–3.4)	0.9 (0.2–1.6)	1.3 (0.0–2.5)	1.3 (0.4–2.3)
Tixocortol pivalate	0.9 (0.4–1.3)	1.0 (0.0–2.4)	0.7 (0.3–1.1)	1.6 (0.6–2.7)	1.0 (0.0–2.4)	1.6 (0.0–3.3)	1.0 (0.0–2.1)	2.1 (1.0–3.2)
Neomycin sulfate	1.4 (0.7–2.1)	1.5 (0.0–2.9)	1.0 (0.5–1.4)	2.1 (0.8–3.4)	2.0 (0.0–4.0)	2.1 (1.1–3.2)	0.4 (0.0–1.2)	2.5 (1.3–3.7)
Thiuram mix	3.3 (2.1–4.5)	5.1 (2.5–7.7)	12.6 (11.1–14.2)	2.5 (1.1–4.0)	2.1 (0.0–4.9)	3.0 (1.8–4.2)	5.1 (2.5–7.7)	3.3 (1.9–4.7)
2-MBT	0.8 (0.2–1.4)	0.3 (0.0–0.8)	3.1 (2.3–3.9)	0.7 (0.0–1.6)	0.4 (0.0–1.1)	0.9 (0.2–1.6)	7.9 (4.6–11.2)	1.6 (0.7–2.6)
Mercapto mix	0.5 (0.2–0.8)	0.5 (0.0–1.2)	2.8 (2.1–3.6)	1.1 (0.1–2.1)	0.5 (0.0–1.4)	1.2 (0.4–2.0)	8.1 (4.8–11.4)	1.2 (0.5–2.0)
IPPD	2.1 (1.3–2.8)	2.6 (0.5–4.7)	2.3 (1.6–2.9)	0.3 (0.0–0.7)	0.4 (0.0–1.1)	0.5 (0.0–1.1)	0.5 (0.0–1.2)	2.1 (0.9–3.3)
Lanolin alcohol	5.6 (4.1–7.2)	3.4 (1.3–5.5)	4.1 (3.2–5.0)	3.1 (1.6–4.7)	5.2 (2.1–8.2)	10.1 (6.5–13.7)	5.7 (3.0–8.4)	6.8 (4.8–8.8)
SL mix	1.0 (0.2–1.9)	0.5 (0.0–1.6)	1.3 (0.8–1.9)	0.8 (0.1–1.4)	0.8 (0.0–1.8)	0.7 (0.1–1.3)	1.1 (0.0–2.3)	1.3 (0.4–2.2)
Primin	0.3 (0.1–0.5)	0.0 (0.0–1.0)	0.2 (0.0–0.4)	0.0 (0.0–0.6)	0.8 (0.0–1.8)	0.0 (0.0–0.7)	0.0 (0.0–1.0)	0.9 (0.1–1.7)
Epoxy resin	4.2 (2.7–5.7)	3.5 (1.2–5.7)	4.0 (3.1–5.0)	2.1 (0.7–3.5)	2.8 (0.5–5.1)	3.6 (0.7–6.4)	2.1 (0.4–3.8)	3.7 (2.2–5.1)
PTBFR	1.3 (0.8–1.8)	2.2 (0.4–3.9)	1.5 (0.9–2.0)	1.9 (0.6–3.2)	0.8 (0.0–2.0)	2.8 (0.5–5.2)	8.5 (5.3–11.7)	2.6 (1.4–3.8)

n=6255 patients tested with all 29 allergens included in this analysis, and positive to at least one of these. *n*=53 patients with "other" single sites not shown.
HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, N-isopropyl-N-phenyl-p-phenylenediamine; MBT, mercaptobenzathiazole; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; MDBGN, methyldibromo glutaronitrile (dibromodicyanobutane); PPD, p-phenylenediamine; PTBFR, p-tert-butylphenol formaldehyde resin; SL, sesquiterpene lactone.