

Characteristics of patients patch tested in the European Surveillance System on Contact Allergies (ESSCA) network, 2009–2012

Wolfgang Uter¹, Olaf Gefeller¹, Ana Giménez-Arnau², Peter Frosch³, Jeanne Duus Johansen⁴, Marie-Louise Schuttelaar⁵, Thomas Rustemeyer⁶, Francesca Larese Filon⁷, Aleksandra Dugonik⁸, Andreas Bircher⁹ and Mark Wilkinson¹⁰

¹Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University Erlangen-Nürnberg, 91054 Erlangen, Germany, ²Department of Dermatology, Hospital del Mar, Institut Mar d'Investigacions Mèdiques, Universitat Autònoma, 08003 Barcelona, Spain, ³Department of Dermatology, University of Witten/Herdecke and Klinikum Dortmund (formerly), 44137 Dortmund, Germany, ⁴Department of Dermato-Allergy, National Allergy Research Centre, Gentofte Hospital, University of Copenhagen, 2900 Hellerup, Denmark, ⁵Dermatology, University Medical Centre Groningen, University of Groningen, 9700 RB, Groningen, The Netherlands, ⁶Department of Dermatology, VU University Medical Centre, 1081 HV Amsterdam, The Netherlands, ⁷Department of Public Health, Occupational Medicine, University of Trieste, IT-34129 Trieste, Italy, ⁸Department of Dermatology, University Medical Centre Maribor, 2000 Maribor, Slovenia, ⁹Allergy Unit, Department of Dermatology, University Hospital, 4031 Basel, Switzerland, and ¹⁰Spire Hospital, Leeds, LS8 1NT, UK

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Summary

Background. Patch test results often vary between departments, and also between countries. Such variation may be partly attributable to systematic effects introduced by patient characteristics, differing exposures, patient selection, or methodological differences.

Objective. To examine the amount of variation of patient characteristics in terms of the MOAHLEA index and of the proportion of patients with at least one positive reaction to the (European) baseline series ('P' measure), and to examine potential reasons for the variation.

Methods. A retrospective analysis was performed of patch test data from 63 530 consultations collected by 53 departments from 12 countries participating in the European Surveillance System on Contact Allergies (ESSCA) (www.essca-dc.org) between 2009 and 2012.

Results. Considerable variation in the prevalence of the MOAHLEA factors between departments was found, caused, for example, by differing specializations (e.g. occupational dermatology) or patient characteristics. Notable variation concerning the 'P' measure was observed; however, larger national networks (contributing to the ESSCA) tend to have quite similar ranges of this measure.

Conclusions. Data from one department per country give valuable insights into the spectrum of contact allergy prevalence rates in that country, but are not as representative as national data pooled from several departments.

Key words: clinical epidemiology; contact allergy; patch testing.

Correspondence: Wolfgang Uter, Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University Erlangen-Nürnberg, Waldstr. 4-6, D-91054 Erlangen, Germany. Tel: +49 9131 8522750; Fax: +49 9131 8522721. E-mail: wolfgang.uter@fau.de

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Contributors: The following colleagues contributed data to this analysis (in alphabetical order, by country): Austria: Werner Aberer, Graz. Denmark: Jeanne Duus Johansen, Gentofte/Copenhagen. Finland: Riitta Jolanki and Maria Pesonen, Helsinki; and Tapio Rantanen, Lahti. Germany: Peter Frosch, Dortmund; Thomas Fuchs, Göttingen; Jochen Brasch, Kiel; Andrea Bauer, Dresden; Peter Elsner, Jena; Swen Malte John, Osnabrück; Vera Mahler, Erlangen; and Elke Weisshaar, Heidelberg AKS. Italy: Fabio Ayala and Anna Balato, Napoli; Andrea Peserico, Padova; Anna Belloni Fortina, Padova Paed.; Francesca Larese Filon, Trieste; Maria Teresa Corradin, Pordenone; and Rosella Gallo, Genova. Lithuania: Skaidra Valiukeviciene and Gonda Sliuziaviciene, Kaunas. Poland: Beata Krecicz and Marta Kieć-Swierczyńska, Łódź; Radosław Spiewak, Kraków; Anna Sadowska and Magdalena Czarnecka-Operacz, Poznań. Slovenia: Aleksandra Dugonik, Maribor University; Maja Kalac Pandurovic, Maribor Clinic; Tanja Kmecl, Celje; Marko Vok, Izola; Simona Godnic, Novo Mesto; and Tomaž Lunder, Ljubljana UMC. Spain: Ana Giménez Arnau, Barcelona IMAS; Javier Sánchez-Pérez, Madrid Princesa; Juan Fco. Silvestre, Alicante; Juan García-Gavín and Virginia Fernández-Redondo, Santiago de Compostela; José Carlos Amario-Hita, Cádiz; Pedro Mercader, Murcia; and Inmaculada Ruiz, León. Switzerland: Andreas Bircher, Basel; Dagmar Simon, Bern; Barbara Ballmer-Weber, Zürich; and Philip Spring, Lausanne. The Netherlands: Pieter-Jan Coenraads and Marie-Louise Schuttelaar, Groningen; and Thomas Rustemeyer, Amsterdam VU. United Kingdom: Cathy M. Green, Dundee; Mark Wilkinson, Leeds; Jane E. Sansom, Bristol; Codagh M. King, Liverpool; Helen L. Horne, Middlesbrough; John S. C. English, Nottingham; Graham A. Johnston, Leicester; Barry N. Statham (†), Swansea; Mahbub M. U. Chowdhury, Cardiff; Natalie Stone, Newport; Sue Cooper, Oxford; David J. Gawkrödger, Sheffield; Catherine Holden and Ruth Sabroe, Sheffield; and Anthony D. Ormerod, Aberdeen.

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It has generally been recognized that certain characteristics of a patient undergoing patch testing, such as age, sex, and anatomical site of dermatitis, can have a profound impact on the probability of a positive result. Therefore, the distribution of these characteristics in the test population in a department influences the contact allergy prevalence rates observed in that department. Variation in reported prevalence rates of sensitization to specific allergens between departments can thus be indicative of interesting regional differences, potentially giving clues to previously unknown reasons for sensitization, or be a simple consequence of differences in the distribution of the already known factors between the departments. The MOHL index was conceived to provide concise information on these relevant factors in terms of an array of prevalence rates (1), and was later extended to create the MOAHLFA index (2). A few years ago, it was pointed out that the consideration of the percentage of patients with at least one positive reaction to allergens of the baseline series offers additional insights into the selectivity of patch testing in a department, and thus valuable information to enable better interpretation of the prevalences of contact allergies to the single allergens observed in that department (3). The present analysis of data collected in the years 2009–2012 in the European Surveillance System on Contact Allergies (ESSCA) network describes the structure of the patient population (comparing countries and departments) and, especially, the overall yield with the baseline series ('P' measure; the proportion of patients with at least one positive reaction to an allergen included in the baseline series), analyses the factors associated with the 'P' measure, and discusses the implications both for clinical practice and for epidemiological data analysis.

Methods

The retrospective analysis was based on data collected by the ESSCA (www.essca-dc.org) network. The ESSCA network has been described in previous publications (e.g. 4). Briefly, clinical and demographic data, along with patch test results, of all patients patch tested in the departments participating in the ESSCA because of suspected allergic contact dermatitis are documented electronically in the local departments, using diverse data capture software and partly the multilingual software WINALLDAT/ESSCA provided by the ESSCA (5). Patch testing follows international recommendations (6). Data are pooled in the ESSCA data centre in Erlangen for further analysis with R (version 3.1.1) software (7). Pertinent statistical guidelines for the analysis of patch test data (8, 9) are considered. The maximum patch test reaction between day 3 and day 5 (inclusive) is aggregated as the

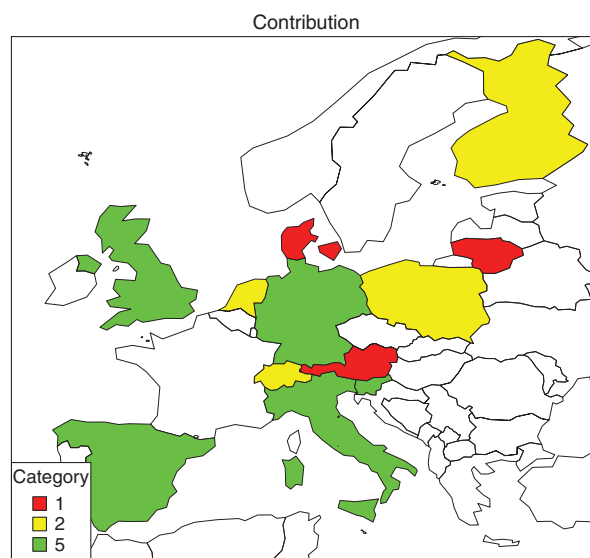


Fig. 1. Number of departments contributing to the European Surveillance System on Contact Allergies network, 2009–2012. Red: one department per country. Yellow: two to four departments per country. Green: Five or more departments per country.

patch test outcome. Reactions designated as either +, ++ or +++ are classified as positive (allergic), and all others as negative (non-allergic). The study period was January 2009 to December 2012; the study including 12 European countries and, in total, 53 departments. The contributions are summarized in Fig. 1.

Altogether, 63 530 consultations were registered. Some patients had not been tested with the baseline series, for example because of a valid patch test with it shortly before. These patients were not considered further in this analysis focusing on baseline series allergens. Altogether, 59 922 consultations involved the baseline series and at least one reading at days 3–5 after application of patch tests. Owing to multiple consultations of some patients in the study period, all involving testing with the baseline series, this number was further slightly reduced to 59 728 single consultations of these patients (the most recent consultation was chosen for analysis). Because of apparent differences in the sensitivity of the TRUE Test[®] (as compared with the investigator-loaded petrolatum-based system used in the overwhelming majority of departments) (e.g. 10), TRUE Test[®] results were separately considered in the analyses addressing the 'P' measure. This affected the data of 2435 consultations in which this test was used. In all departments using it, the TRUE Test[®] was always combined with a set of allergens by use of investigator-loaded chambers, to achieve a better coverage of the desired scope of allergens and

concordance with the European baseline series (EBS), for example including fragrance mix II and hydroxisohexyl 3-cyclohexene carboxaldehyde, methyl dibromoglutaconitrile (MDBGN), sesquiterpene lactone mix, primin, and, more recently, methylisothiazolinone.

The present analysis was focused on selected demographic and clinical variables of the patch tested patients constituting the MOAHLFA index: 'M', the proportion of male patients; 'O', the proportion of patients with occupation-related contact dermatitis (probable or certain, in our analysis); 'A', the proportion of patients with current or previous atopic eczema; 'H', 'L', and 'F', the proportions of patients with involvement of the hands, the legs, and the face, respectively (in cases of multiple anatomical sites, the 'main' site is considered); and 'A', the proportion of patients who are aged at least 40 years (2). In addition, the 'overall yield' of patch testing with the baseline series as tested locally, that is, with national or departmental additions or omissions, was considered in terms of the 'P' measure, that is, the proportion of patients with at least one positive reaction to the baseline series as used in the department (3) ('P1'). As an alternative outcome, only allergens included in the EBS valid at the time (11), comprising 28 allergens, were included in the analysis ('P2'). In this context, it is important to note that some (national) baseline series did not contain several allergens of the EBS, for various reasons (see Discussion). The following allergens were considered to be equivalent: (i) mercapto mix with three components (cyclohexyl benzothiazolesulfenamide, dibenzothiazyl disulfide, and morpholinyl mercaptobenzothiazole), tested at 1% pet., and mercapto mix also including 2-mercaptobenzothiazole, tested at 2% pet.; (ii) benzocaine (5% pet.) and caine mix III (benzocaine, dibucaine, and tetracaine, 10% pet.); (iii) MDBGN and its combination with 2-phenoxyethanol (Euxyl® K 400), which was initially still tested in some departments; and (iv) *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine 0.1% pet. and 'black rubber mix' (TRUE Test® or 0.6% pet.).

Results

Table 1 shows the number of patients in the single departments, together with some characteristics of the patients tested according to the MOAHLFA index (2, 12), grouped by country, and also aggregated by country in the table row below the respective departments from one country. There was significant variation ($p < 0.0001$) in all MOAHLFA variables between both departments and the departments aggregated to countries. Although the Slovenian departments are prospectively complying with the ESSCA 'minimal dataset', their retrospectively

contributed data did not include information on the anatomical site of dermatitis or occupational causation; thus, this information is lacking in Table 1.

The TRUE Test® was used by the following departments (number of patients): Groningen ($n = 1468$), Amsterdam VU (where the TRUE Test® was applied only exceptionally, $n = 101$), Madrid Princesa ($n = 604$), León ($n = 244$), and Murcia ($n = 18$). In Table 2, the 'P' measure in its two variations 'P1' and 'P2', the latter only including allergens that are included in the EBS, is shown in a similar fashion, that is, per department, and aggregated to the country if there is more than one department per country. As some departments contribute data specifically covering the EBS, the second variant of the 'P' measure is the same as the first one in these departments. Also regarding the 'P' measure, there was significant variation ($p < 0.0001$) both between departments and between countries. This held true both for the 'P1' measure obtained with the full local baseline series and for the 'P2' measure restricted to allergens of the EBS, as recommended. To further elucidate at least some of the underlying frequencies of sensitization to single allergens, the sensitization prevalence rates concerning four important EBS allergens from different groups (metals, fragrances, preservatives, and rubber chemicals) are also shown; detailed results will be presented in separate publications dedicated to these respective groups of allergens. Although some association between the 'P' measure(s) and single sensitizations could be observed, this pattern was certainly not uniform concerning the single allergens of the limited spectrum considered. As a graphical overview of the variation in the 'P1' measure, it is plotted per department in Fig. 2 (the sizes of the circles denote the numbers of contributed patients) and stratified for countries in the columns. The 5% percentile of the estimated 'P1' values in all departments was 33.3%, and the 95% percentile of this distribution was 61.7%. It can be seen that one department (CH-70), which has only recently joined the ESSCA, with an as yet limited number of patients ($n = 74$), showed a very high 'P' measure, namely 91.9 (95% confidence interval 83.2–97%).

To address the question of whether a more extended (longer) baseline series contributes to a high 'P' measure ['The more you test, the more you get?' (13)], the correlation between the average length of a baseline series in a department and its 'P' measure was calculated. Correlation was negligible (Spearman rank correlation coefficient 0.02, $p = 0.89$). Moreover, the 'P' measure was $\leq 58\%$ in all departments using a baseline series with >40 allergens. It should, however, be noted that this analysis only addresses the baseline series, and explicitly not the value of patch testing with additional special test series,

Table 1. Number of patients tested and their basic characteristics according to the MOAHLEA index in the contributing departments, grouped and aggregated by country where more than one department represents a country

Country/department	n (test)	M	O	A	H	L	F	A
AT/Graz	1113	26.1	17	20	26.2	6.8	16.7	63.9
CH/Basel	997	35.5	13.5	13.2	17.8	9.1	15.1	68.9
CH/Bern	1207	43.6	17.4	23.5	30.5	6.5	18.4	64.3
CH/Zürich	2712	38.2	11.7	18.7	27.1	6.5	15.9	65.5
CH/Lausanne	74	31.1	32.4	36.5	39.2	4.1	10.8	60.8
CH total	4990	38.9	13.8	19	26.2	7	16.3	65.8
DE/Dortmund	996	41	21.7	22	33.1	15.2	14.5	75.9
DE/Göttingen	444	34.9	18.7	17.8	29.5	5.4	21.2	72.7
DE/Kiel	1052	35	2.9	4.7	8.3	7.3	4	75.8
DE/Dresden	880	33.9	19.3	28.5	25.1	12.5	12	71.5
DE/Jena	1090	36.7	19.9	15.5	26.6	8.1	12.9	70.8
DE/Osnabrück	1278	52.2	76.1	55.2	87.2	0.5	4.2	64.9
DE/Erlangen	1235	36.3	27.9	21.8	34.8	6.6	20.4	64
DE/Heidelberg AKS	653	51.9	62.9	23	79.2	0.5	0.9	71.7
DE total	7628	40.4	32	24.8	40.9	7.1	11	70.3
DK/Gentofte/Copenhagen	2582	30.4	21.9	18.2	38.8	1.8	27.1	64.9
ES/Barcelona IMAS	1713	31.4	4.7	10.7	17.3	7.6	12.7	64.3
ES/Madrid Princesa	654	35	5.5	19.9	23.4	8.1	20	73.2
ES/Alicante	973	32.2	14	16.5	29.9	10	13.3	62.7
ES/Santiago de Compostela	284	32.7	22.2	9.9	32.7	8.8	15.8	66.5
ES/Cádiz	249	29.3	41.4	16.1	67.5	2	4.8	49.8
ES/Murcia	142	28.9	16.2	17.6	31	8.5	17.6	61.3
ES/León	242	25.6	28.5	8.7	32.2	3.7	10.7	73.1
ES total	4257	31.7	12	13.8	26.4	7.8	13.7	65
FI/Helsinki	512	47.9	61.9	28.5	78.1	0.6	9	51
FI/Lahti	545	28.6	27.5	32.5	42.6	5.7	0	61.8
FI total	1057	37.9	44.2	30.6	59.8	3.2	4.4	56.6
IT/Napoli	2706	35	6.8	14.7	18.2	4.5	7.6	52.3
IT/Padova	1133	32.7	2.5	12.9	23.4	7.8	16.9	54.7
IT/Padova Paed.	957	47	0	57.8	10.8	13.8	20.1	0
IT/Trieste	1503	29	8.1	6	15.4	4	7.8	59.2
IT/Pordenone	999	33.6	3.8	5.9	35.2	8	18.7	59
IT/Genova	1969	28.4	2.9	14.7	28.3	9.6	12.7	62.4
IT total	9267	33.4	4.6	16.6	21.6	7.3	12.3	51.2
LT/Kaunas	865	19.5	13.3	11.3	25.1	11.2	22.9	63.7
NL/Groningen	1465	33.2	19.9	40.5	30	4.1	27	54.7
NL/Amsterdam VU	2920	34.5	17.7	31.5	15.7	4.8	15.5	57.8
NL total	4385	34	18.4	34.5	20.5	4.5	19.4	56.8
PL/Lodz	610	27.7	23.6	19	44.3	2.3	17.4	59.7
PL/Krakow	646	22.6	0	22.8	0	0	0	44.4
PL/Poznan	1572	31.9	31.1	7.1	35.4	6.2	20.4	59.7
PL total	2828	28.9	22.4	13.2	29.2	3.9	15.1	56.2
SI/Maribor University	1612	31.3	–	–	–	–	–	63.7
SI/Maribor Clinic	925	27.1	–	–	–	–	–	53.3
SI/Celje	1261	35.1	–	–	–	–	–	59.5

Table 1. Continued

Country/department	n (test)	M	O	A	H	L	F	A
SI/Izola	610	26.7	–	–	–	–	–	58.4
SI/Novo Mesto	225	23.6	–	–	–	–	–	63.6
SI/Ljubljana UMC	591	31.8	–	–	–	–	–	51.1
SI total	5224	30.7	–	–	–	–	–	58.8
UK/Dundee	2076	30.4	7.2	28.5	26.6	6.4	28.2	60.1
UK/Leeds	2611	32.2	9.7	40.1	28.8	4.5	27.6	52.8
UK/Bristol	509	30.5	12.2	34.8	31.2	6.9	32.2	59.5
UK/Liverpool	624	28.7	8.5	39.4	27.1	8.3	26.3	63
UK/Middlesbrough	1172	31.1	9	28.1	35	6.6	29.4	60.1
UK/Leicester	1155	28.1	11.4	37.7	24.5	5.4	30	62.6
UK/Nottingham	698	35.1	10.9	39.7	25.8	8.6	28.9	53.9
UK/Swansea	378	33.9	18.3	23.3	45	6.9	18.8	61.9
UK/Cardiff	1238	32.2	10.5	33.6	34.8	6.1	27.5	57
UK/Newport	2543	35.1	9.2	32.2	25.4	6.8	23.6	61.5
UK/Oxford	983	28.8	10.2	36.6	22.3	9	31.5	61
UK/Sheffield	1138	31.9	11.3	38.2	22.4	4.3	29.6	52.1
UK/Aberdeen	407	35.4	5.4	38.1	29.2	7.1	21.1	53.6
UK total	15 532	31.9	9.7	34.6	28	6.3	27.5	58.2

AT, Austria; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; IT, Italy; LT, Lithuania; NL, The Netherlands; PL, Poland; SI, Slovenia; UK, United Kingdom.

Slovenia provided retrospective data not including information on anatomical site of dermatitis and occupational causation ('–').

tailored to the individual patient's history (see Discussion).

Discussion

The present descriptive analysis presents, in some detail, differences between departments and countries joined in the ESSCA network concerning the well-known, albeit quite non-specific, surrogate markers associated with the risk of sensitization to a number of important allergens termed the MOAHLFA index (2). Moreover, the recently suggested addition to the array of MOAHLFA factors, the 'P' measure, has been analysed regarding variation between departments and countries. The amount of variation is similar to that in a previous analysis, in which the 'P' measure ranged between approximately 20% and 65% in the departments of the Information Network of Departments of Dermatology (IVDK) (3).

The differences in patient characteristics of some specialized departments are at least partly reflected in MOAHLFA results (Table 1); for instance, a prevalence of >60% patients with occupational dermatitis, and a prevalence of hand dermatitis of ~80%, in Heidelberg, Osnabrück, and Helsinki, all of which are specialized occupational departments. The paediatric department in Padova evidently has a distinct pattern of demographic variables, including a very high proportion of patients with atopic eczema. However, according to this description, other departments are much less specialized, and

there is thus much less impact of their specialization on the spectrum of allergens diagnosed. Moreover, some characteristics cannot be directly related to one of the MOAHLFA factors, for example the selection process for the department. Some of the departments are tertiary referral or national reference centres, whereas others provide care, if not at the primary level, then at least in a less preselected way.

As a first observation concerning the 'P' measure, for example based on Fig. 2, the more or less pronounced variation between departments within one country is evident. Such variation implies that, for those countries represented by only one department, the 'P' measure of this one department may not be representative of a country. Those countries represented by a substantial number of departments (for example, arbitrarily, at least five, with a green colour code in Fig. 1) offer a more precise estimate of the country-specific 'normal' proportion of patients positive for at least one allergen of the baseline series. Reassuringly, four of these five well-represented countries show a fairly similar distribution of the 'P' measure. In contrast, two of the six contributing Slovenian departments have a rather low 'P' measure, with no apparent differences concerning the sex and age distribution (the prospective contribution from Slovenia will also include the other MOAHLFA factors site and occupational causation). In Slovenia, the indication for patch testing is generally quite liberal, with the exception of the departments in Ljubljana

Table 2. The 'P' measure in two variations: 'P1', considering the full local baseline series; and 'P2', considering only allergens included in the European baseline series

Country/department	P1 (95%CI)	P2 (95%CI)	% Ni-positive (95%CI)	% FM I- positive (95%CI)	% MCI/MI positive (95%CI)	% Thiuram-mix- positive (95%CI)
AT/Graz	52.6 (49.6–55.5)	49.4 (46.4–52.4)	21.6 (19.2–24.1)	14.7 (12.6–16.9)	6.5 (5.1–8.1)	3.5 (2.5–4.8)
CH/Basel	47.7 (44.6–50.9)	41.8 (38.7–45)	16.3 (14.1–18.8)	11.7 (9.7–13.9)	2.2 (1.4–3.4)	2 (1.2–3.1)
CH/Bern	51.2 (48.3–54.1)	48.9 (46–51.7)	18.6 (16.5–21)	13.9 (12–16)	4.6 (3.5–6)	2.7 (1.9–3.8)
CH/Zürich	54.1 (52.2–56)	47.9 (46–49.8)	23 (21.4–24.6)	10.4 (9.3–11.7)	4.8 (4–5.7)	2 (1.5–2.6)
CH/Lausanne	91.9 (83.2–97)	89.2 (79.8–95.2)	45.2 (33.5–57.3)	26 (16.5–37.6)	8.2 (3.1–17)	2.7 (0.3–9.5)
CH total	52.7 (51.3–54.1)	47.6 (46.2–49)	20.9 (19.8–22.1)	11.8 (10.9–12.7)	4.3 (3.7–4.9)	2.2 (1.8–2.6)
DE/Dortmund	34.2 (31.3–37.3)	30.9 (28.1–33.9)	11.9 (10–14.1)	4.8 (3.5–6.3)	2.8 (1.9–4.1)	2.1 (1.3–3.2)
DE/Göttingen	49.8 (45–54.5)	43.7 (39–48.4)	15.7 (12.3–19.5)	7.7 (5.3–10.6)	7.2 (4.9–10.1)	3.2 (1.8–5.4)
DE/Kiel	50.9 (47.8–53.9)	47.5 (44.5–50.6)	13 (11–15.1)	14.4 (12.3–16.7)	3.1 (2.2–4.4)	2.5 (1.6–3.6)
DE/Dresden	35 (31.8–38.3)	29.8 (26.8–32.9)	8.4 (6.6–10.4)	6 (4.5–7.9)	2.9 (1.9–4.3)	1.8 (1–2.9)
DE/Jena	44.4 (41.4–47.4)	39.1 (36.2–42.1)	11.3 (9.4–13.4)	9.4 (7.7–11.3)	2.6 (1.8–3.8)	3.5 (2.5–4.8)
DE/Osnabrück	39.7 (37–42.4)	36.3 (33.7–39)	8 (6.4–9.8)	8.5 (6.9–10.4)	5.6 (4.3–7.1)	4.7 (3.5–6.1)
DE/Erlangen	47.6 (44.8–50.4)	43.2 (40.4–46)	15.4 (13.4–17.5)	10.2 (8.6–12)	2.7 (1.9–3.8)	2 (1.3–3)
DE/Heidelberg AKS	43.6 (39.8–47.5)	42.1 (38.3–46)	12.9 (10.4–15.7)	10 (7.8–12.6)	5.4 (3.8–7.4)	5.3 (3.7–7.3)
DE total	42.9 (41.7–44)	38.8 (37.7–39.9)	11.9 (11.2–12.7)	9.1 (8.4–9.7)	3.7 (3.3–4.2)	3 (2.7–3.5)
DK/Copenhagen (Gentofte)	36.6 (34.7–38.5)	36.6 (34.7–38.5)	12.6 (11.3–14)	8.6 (7.5–9.8)	1.6 (1.2–2.2)	2.6 (2–3.3)
ES/Barcelona IMAS	41.9 (39.6–44.3)	39.2 (36.9–41.6)	21.3 (19.4–23.4)	5 (4–6.1)	3.3 (2.4–4.3)	1.5 (1–2.2)
ES/Madrid Princesa	60.6 (56.7–64.3)	54.6 (50.7–58.5)	37.6 (32.5–42.9)	4.8 (3.3–6.7)	11.5 (9–14.3)	1.2 (0.5–2.4)
ES/Alicante	50.7 (47.5–53.9)	44.4 (41.2–47.6)	27.4 (24.6–30.3)	4.6 (3.4–6.1)	5.6 (4.2–7.2)	1.7 (1–2.7)
ES/Santiago de Compostela	43 (37.1–48.9)	39.1 (33.4–45)	23.6 (18.8–29)	3.2 (1.5–5.9)	–	2.5 (1–5)
ES/Cádiz	42.2 (36–48.6)	42.2 (36–48.6)	30.1 (24.5–36.2)	6.4 (3.7–10.2)	2.4 (0.9–5.2)	2 (0.7–4.6)
ES/Murcia	52.8 (44.3–61.2)	44.4 (36–52.9)	23.8 (17.1–31.6)	9.1 (4.9–15)	0 (0–18.5)	2.1 (0.4–6)
ES/León	63.6 (57.2–69.7)	58.7 (52.2–64.9)	43.4 (37.1–49.9)	3.3 (1.4–6.4)	1.7 (0.5–4.2)	0.8 (0.1–3)
ES total	48.5 (46.9–50)	44.2 (42.7–45.7)	26.4 (25–27.8)	4.9 (4.2–5.6)	5.1 (4.4–5.9)	1.6 (1.2–2)
FI/Helsinki	48.2 (43.8–52.7)	46.3 (41.9–50.7)	16.8 (13.6–20.4)	5.7 (3.8–8)	3.7 (1.7–6.9)	3.3 (2–5.3)
FI/Lahti	57.6 (53.3–61.8)	55 (50.8–59.3)	27.5 (23.7–31.5)	8.3 (6.1–10.9)	3.7 (2–6.2)	1.8 (0.9–3.4)
FI total	53.1 (50–56.1)	50.8 (47.7–53.9)	22.4 (19.8–25)	7 (5.5–8.7)	3.7 (2.3–5.5)	2.6 (1.7–3.7)
IT/Napoli	40.7 (38.8–42.6)	40.2 (38.3–42)	26.2 (24.6–27.9)	2.6 (2–3.3)	2 (1.5–2.6)	1.2 (0.8–1.7)
IT/Padova	53.6 (50.6–56.5)	49.2 (46.3–52.2)	24 (21.5–26.6)	5.2 (4–6.7)	5.1 (3.9–6.6)	0.8 (0.4–1.6)
IT/Padova Paed.	40.4 (37.3–43.6)	39.6 (36.5–42.8)	21.4 (18.9–24.2)	0.4 (0.1–1.1)	2.5 (1.6–3.7)	–
IT/Trieste	45.6 (43–48.1)	44.3 (41.8–46.9)	30 (27.7–32.4)	5.9 (4.8–7.2)	2.4 (1.7–3.3)	1.5 (0.9–2.2)
IT/Pordenone	49.6 (46.5–52.8)	47.5 (44.4–50.7)	24.5 (21.9–27.3)	9.5 (7.8–11.5)	3.7 (2.6–5.1)	2.7 (1.8–3.9)
IT/Genova	44.3 (42.1–46.5)	43.5 (41.3–45.7)	27.6 (25.6–29.6)	6.2 (5.2–7.4)	5.7 (4.7–6.8)	1.2 (0.7–1.7)
IT total	44.8 (43.7–45.8)	43.4 (42.4–44.4)	26.2 (25.3–27.1)	4.8 (4.4–5.3)	3.5 (3.1–3.9)	1.4 (1.1–1.7)
LT/Kaunas	43.8 (40.5–47.2)	43.6 (40.2–47)	14.3 (12.1–16.8)	5.1 (3.7–6.8)	1.8 (1.1–3)	0.5 (0.1–1.2)
NL/Groningen	40.5 (38–43)	39.5 (36.9–42)	17.7 (15.5–20)	3.7 (2.8–4.9)	7.8 (6.5–9.3)	1.7 (1.1–2.5)
NL/Amsterdam VU	69.8 (68.1–71.4)	55.9 (54.1–57.7)	20.1 (18.6–21.6)	12.8 (11.6–14.1)	9.1 (8.1–10.2)	2.7 (2.2–3.4)
NL total	60 (58.5–61.4)	50.4 (48.9–51.9)	19.4 (18.2–20.7)	9.9 (9–10.8)	8.7 (7.9–9.6)	2.4 (2–2.9)
PL/Lodz	47.9 (43.8–51.9)	41.5 (37.5–45.5)	24.9 (21.5–28.5)	5.2 (3.6–7.3)	2 (1–3.4)	2.6 (1.5–4.2)
PL/Krakow	60.7 (56.8–64.5)	59.4 (55.5–63.3)	32.5 (28.9–36.3)	6.2 (4.5–8.4)	1.9 (1–3.2)	0.8 (0.3–1.8)
PL/Poznan	55.6 (53.1–58.1)	55.6 (53.1–58.1)	22 (20–24.1)	4.8 (3.8–6)	2.4 (1.7–3.3)	1.1 (0.6–1.7)
PL total	55.1 (53.2–56.9)	53.4 (51.6–55.3)	25 (23.4–26.7)	5.2 (4.4–6.1)	2.2 (1.7–2.8)	1.3 (1–1.8)

Table 2. Continued

Country/department	P1 (95%CI)	P2 (95%CI)	% Ni-positive (95%CI)	% FM I- positive (95%CI)	% MCI/MI positive (95%CI)	% Thiuram-mix- positive (95%CI)
SI/Maribor University	43.4 (41–45.9)	43.4 (41–45.9)	19.9 (17.9–22)	5.2 (4.1–6.5)	2.1 (1.4–2.9)	1 (0.6–1.6)
SI/Maribor Clinic	37.7 (34.6–40.9)	37.7 (34.6–40.9)	14.6 (12.3–17.1)	3.7 (2.6–5.2)	2.2 (1.4–3.5)	0.4 (0.1–1.1)
SI/Celje	30.4 (27.8–33)	30.4 (27.8–33)	9.8 (8.1–11.7)	4.4 (3.3–5.8)	1 (0.5–1.8)	2.1 (1.3–3.1)
SI/Izola	52.8 (48.7–56.8)	52.8 (48.7–56.8)	24 (20.3–27.9)	9.1 (6.7–11.9)	6.3 (4.3–8.7)	1.1 (0.4–2.4)
SI/Novo Mesto	25.8 (20.2–32)	25.8 (20.2–32)	14.7 (10.3–20)	2.2 (0.7–5.1)	2.7 (1–5.7)	0.4 (0–2.5)
SI/Ljubljana UMC	47 (43–51.2)	47 (43–51.2)	21.3 (18.1–24.8)	9.3 (7.1–11.9)	3.4 (2.1–5.2)	2.2 (1.2–3.7)
SI total	40 (38.7–41.4)	40 (38.7–41.4)	16.9 (15.9–18)	5.5 (4.9–6.2)	2.5 (2.1–3)	1.3 (1–1.6)
UK/Dundee	47.9 (45.7–50.1)	40.9 (38.8–43.1)	16 (14.5–17.7)	7.9 (6.7–9.1)	–	2.2 (1.6–2.9)
UK/Leeds	39.9 (38–41.8)	34.4 (32.6–36.3)	13.3 (12–14.7)	7.5 (6.5–8.5)	–	1.8 (1.3–2.4)
UK/Bristol	45.8 (41.4–50.2)	43.8 (39.4–48.2)	22.7 (19.1–26.6)	5.3 (3.5–7.6)	4.9 (3.2–7.2)	1.6 (0.7–3.1)
UK/Liverpool	36.5 (32.8–40.5)	33.8 (30.1–37.7)	17.1 (14.3–20.3)	6 (4.3–8.1)	2.2 (1.2–3.7)	1.7 (0.9–3.1)
UK/Middlesbrough	47.1 (44.2–50)	44.4 (41.5–47.3)	20.7 (18.4–23.2)	5.9 (4.7–7.5)	3 (2.1–4.1)	2 (1.2–2.9)
UK/Leicester	41.4 (38.5–44.3)	38.6 (35.8–41.5)	19.2 (17–21.6)	5.7 (4.4–7.2)	4.8 (3.6–6.2)	1.6 (0.9–2.5)
UK/Nottingham	31.7 (28.2–35.3)	30.1 (26.7–33.6)	13.2 (10.8–15.9)	4.2 (2.8–5.9)	3 (1.9–4.6)	2.3 (1.3–3.7)
UK/Swansea	42.3 (37.3–47.5)	39.2 (34.2–44.3)	23.2 (19–27.8)	5.6 (3.5–8.4)	0 (0–1)	1.9 (0.7–3.8)
UK/Cardiff	49.6 (46.8–52.4)	45.7 (42.9–48.5)	22.9 (20.5–25.3)	5.9 (4.7–7.4)	5.3 (4.1–6.6)	2.2 (1.4–3.2)
UK/Newport	42.4 (40.5–44.4)	39.9 (38–41.8)	16.3 (14.9–17.8)	6.7 (5.7–7.7)	4.2 (3.5–5.1)	1.8 (1.4–2.5)
UK/Oxford	50.3 (47.1–53.4)	45.2 (42–48.3)	21.7 (19.2–24.4)	7.2 (5.6–9)	2.1 (1.3–3.3)	1.4 (0.8–2.4)
UK/Sheffield	35.6 (32.8–38.4)	33.1 (30.4–35.9)	11.7 (9.9–13.7)	5.6 (4.3–7)	2.7 (1.9–3.8)	1.3 (0.7–2.1)
UK/Aberdeen	58 (53–62.8)	52.1 (47.1–57)	26.7 (22.4–31.2)	9.3 (6.7–12.5)	5.1 (3.2–7.7)	0.5 (0.1–1.8)
UK total	43.4 (42.6–44.2)	39.4 (38.6–40.2)	17.4 (16.8–18)	6.6 (6.2–7)	3.6 (3.3–4)	1.8 (1.6–2)

AT, Austria; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; IT, Italy; LT, Lithuania; NL, The Netherlands; PL, Poland; SI, Slovenia; UK, United Kingdom.

The rightmost four columns present the crude percentage positive patch test reactions to the four key allergens: nickel sulfate hexahydrate, 5% pet. (Ni); fragrance mix I, 8% pet. (FM I); methylchloroisothiazolinone/methylisothiazolinone 3:1, 0.01% aq. (in the departments with a dash, the test concentration had been 0.02% aq. throughout the study period) (MCI/MI); and thiuram mix (1% pet.).

UMC and Izola, where more selected patients are being tested. These are the departments with the highest 'P' measure (Table 2). Interestingly, the one southern Italian department (Napoli), the largest contributor in Italy, has a 'P' measure that is quite similar to that of the other departments in the north of Italy.

Concerning the TRUE Test[®], at least some of the allergens are regarded as less sensitive than the pet./aq.-based allergen preparations used in investigator-loaded systems, for example fragrance mix I [discussed in (10, 14)]. However, a systematic difference between the TRUE Test[®] and the investigator-loaded system is not apparent from our analysis, probably at least partly because the TRUE Test[®] is routinely supplemented with pet.-based allergens, which is expected to increase the overall yield of positive reactions. Moreover, it is evident from Fig. 2 that, although the Groningen department has a lower 'P' measure than the Amsterdam department, the two Spanish departments with the highest 'P' measure are those using the TRUE Test[®] in their baseline series – which is, however, much expanded with pet.-based and aq.-based allergens.

Possible reasons for variation in the 'P' measure, both between departments and between countries, and the limitations of including this measure as an 'adjustment factor' for actual sensitization prevalence rates in the different countries or departments, have already been discussed (3). We consider it plausible that the amount of variation is (slightly) larger in a network covering very different European countries than within a more homogeneous network, for example the IVDK (3) or the British Society for Cutaneous Allergy (BSCA) (15).

Often, the EBS is supplemented with one or more allergens that are considered to be important at a national level; the usefulness of such an addition has been confirmed, for example, by a previous analysis of the BSCA, in which the 12 (at that time) additional allergens yielded sensitization prevalence rates between 2.4% (MDBGN) and 0.4% (chloroxylonol) (15). In the IVDK, temporary additions to the (German) baseline series, termed 'monitor series', are used to evaluate the importance of certain allergens as an evidence base for deciding whether they should be included in the baseline series (16).

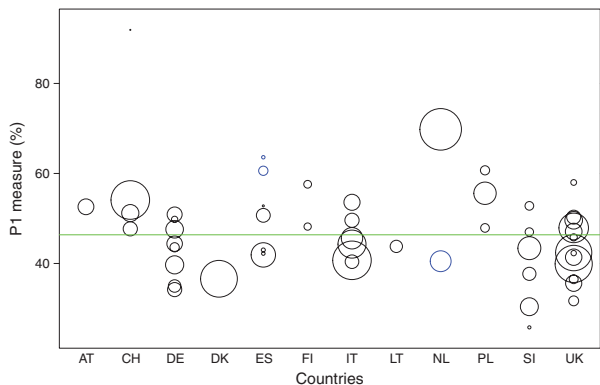


Fig. 2. The 'P1' measure (proportion of patients with at least one positive reaction to the baseline series as used in the department) across the departments participating in the European Surveillance System on Contact Allergies, grouped by country. The sizes of the circles indicate the numbers of patients tested in the departments during the study period 2009–2012. Blue circles indicate departments in which at least 80% of the patients have been patch tested with a baseline series including, but not limited to, TRUE Test® allergens. AT, Austria; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; IT, Italy; LT, Lithuania; NL, The Netherlands; PL, Poland; SI, Slovenia; UK, United Kingdom.

In fact, a comparison of the 'P1' (full baseline series with supplements) and the 'P2' (only allergens from the EBS) measures allows, in those departments and countries employing such additions, an evaluation of their effectiveness at a general level. However, national contact dermatitis groups may also decide that some allergens of

the EBS may not be appropriate for testing and remove these from their national baseline series. For instance, in the study period, the German baseline series, used by the Austrian, German and Swiss members of the ESSCA, did not include nine allergens recommended in the EBS (11), namely, *p*-phenylenediamine (because of safety concerns regarding the 1% patch test concentration 17, and not because *p*-phenylenediamine is regarded to be an unimportant allergen), neomycin sulfate, benzocaine, clioquinol, sesquiterpene lactone mix, quaternium-15, primin, and the two corticosteroid markers, budesonide and tixocortol pivalate. Thereby, the 'P2' measure refers to a slightly restricted EBS in these departments, which will exaggerate the differences between 'P1' and 'P2'.

In conclusion, any comparison of the 'P' measure needs to take into account the number of allergens in the baseline series examined, and its composition. However, the mere number of allergens is a poor predictor of the overall yield, as shown by our results, and the appropriateness of the set of allergens, together with the local/national selectivity of patch testing in general, appears to be the major determinant of the overall yield 'P'. Moreover, it is very important to use additional special patch test series, as appropriate from the patient's history, which will enable the detection of additional (occupationally) relevant contact allergies (e.g. 18, 19). For instance, during diagnostic work-up, 34.6% of relevant contact allergies have been identified beyond the baseline series (19).

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