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Prevalence of contact allergy in the general population in different European regions

T.L. Diepgen¹, R.F. Ofenloch¹, M. Bruze², P. Bertuccio³, S. Cazzaniga⁴, P.-J. Coenraads⁵, P. Elsner⁶, M. Goncalo⁷, Å. Svensson⁸, and L. Naldi⁴

¹Dept. of Social Medicine, Occupational and Environmental Dermatology, University Heidelberg, Heidelberg (Germany)

²Department of Occupational and Environmental Dermatology, Skåne University Hospital, Lund University, Malmö (Sweden)

³Department of Epidemiology, Istituto di Ricerche Farmacologiche Mario Negri, IRCCS, Milan (Italy)

⁴Department of Dermatology, Azienda Ospedaliera papa Giovanni XXIII, Bergamo, Centro Studi GISED – FROM Presidio Ospedaliero Matteo Rota, Via Garibaldi 13/15, 24122 Bergamo (Italy)

⁵Department of Dermatology, University of Groningen, University Medical Center Groningen, Groningen (the Netherlands)

⁶Department of Dermatology, University Hospital Jena, Jena (Germany)

⁷Department of Dermatology, Coimbra University Hospital, Faculty of Medicine, University of Coimbra, Coimbra (Portugal)

⁸Department of Dermatology, Skåne University Hospital, Lund University, Malmö (Sweden)

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Corresponding author:

Thomas L. Diepgen
Dept. of Social Medicine
Thibautstraße 3
69115 Heidelberg
Phone: +49 6221 56 87 51
Fax: +49 6221 56 55 84
Email: thomas.diepgen@med.uni-heidelberg.de

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What is already known about this topic?

- There is a high prevalence of contact allergy in clinical settings but most studies are based on in- and out-patients or highly selected populations.
- Data on prevalence of contact allergy in the general population are scarce and the methodology often not comparable across countries.

What does this study add?

- The prevalence of contact allergy in the general population were assessed for the allergens of the European baseline series in different European regions.
- Contact allergy to at least one out of the 32 patch tested allergens of the European standard series was diagnosed in 27.0% (95% CI 25.5-28.5) with a statistically significant higher prevalence in females compared to males.
- In addition, age-standardized prevalence of contact dermatitis, atopic eczema, other eczema, and itchy skin rashes that last longer than three days are reported in the general population.

Abstract (281 words)

Background: Population-based studies about contact allergy are scarce.

Objectives: To obtain reliable estimates of prevalence of contact allergy in the general population in Europe.

Methods: Cross-sectional study of a random sample from the general population, aged 18 to 74 years, in 5 different European countries (Sweden, The Netherlands, Germany, Italy, Portugal). In total 12,377 subjects were interviewed and a random sample (n=3,119) patch tested to TRUE-test panel 1, 2 and 3 plus fragrance mix II, HICC, and sesquiterpene lactone mix. A positive patch test reaction is considered as contact allergy.

Results: In total, 27.0% (95% CI 25.5-28.5) had at least one positive reaction to an allergen of the European baseline series with a significant higher prevalence in females compared to males. The highest age-standardized prevalences ($\geq 1\%$) were found for nickel (14.5%; 95% CI 13.2-15.8), thimerosal (5.0%; 95% CI 4.2-5.8), cobalt (2.2%; 95% CI 1.7-2.7), fragrance mix II (1.9%, 95% CI 1.5-2.5), fragrance mix I (1.8% 95% CI 1.4-2.3), hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC)(1.4%, 95% CI 1.0-1.9), p-tert-butylphenol- formaldehyde-resin (1.3%; 95% CI 0.9-1.7), and p-phenylenediamine (1.0%; 95% CI 0.6-1.3). Only Nickel and Thimerosal showed a statistically significant different prevalence for contact allergy amongst the different European populations. Subjects that reported contact dermatitis in lifetime (age-standardized prevalence 15.1%, 95%CI 13.8-16.3) had an increased risk for contact allergy (OR 1.9, 95% CI 1.5-2.5) the risk of having a contact allergy was not increase in those with atopic dermatitis (prevalence 7.6%, 95% CI 6.7-8.6; OR 1.0, 95% CI 0.7-1.4).

Conclusions: Contact allergy to at least one allergen of the European baseline series was diagnosed in more than one quarter of the general European population. Therefore measures to improve the primary prevention of contact allergy have to be enforced.

Introduction

Contact allergy is caused by skin contact with low molecular weight haptens and may evolve to allergic contact dermatitis (ACD) if a subsequent exposure exceeds the individual elicitation threshold¹. The diagnosis of allergic contact dermatitis ACD is a 3-step procedure². The first step is establishing the diagnosis of contact allergy (immunologically acquired delayed hypersensitivity) followed by the demonstration of present exposure to the sensitizer or possibly

cross-reacting substances. The final step is assessment of clinical relevance which means that the demonstrated exposure should explain/contribute to the dermatitis under investigation with regard to the exposure and localization, type, and course of the dermatitis under investigation on the one hand and the degree of reactivity on the other. Thus, the patch test only measures whether an individual is sensitized or not, and a positive patch test reaction is not necessarily an indicator of allergic contact dermatitis, the clinical disease.

Many studies about contact allergy and ACD are based on highly selected populations that have been patch-tested which usually means that the participants visited a clinic or hospital to be evaluated for contact dermatitis³. However, no information on the incidence or prevalence of contact allergy and ACD in the general population can be derived from these publications. Publications generating incidence-type data for the general population are scarce.

The main objective of this paper was to assess reliable estimates of the prevalence of contact allergies to common allergens in the general population in Europe. Secondary objectives were to evaluate the life time prevalence of different skin diseases. This paper is the first paper presenting the patch test data, and the second in a series of papers on this large prevalence study which was conducted in Europe⁴.

Materials and Methods

Study design

The study design including sample size calculation and the data collection were previously published^{4,5}. Briefly, the European Dermato-Epidemiology Network (EDEN) Fragrance Study was a descriptive epidemiology survey conducted in several European regions, including the metropolitan areas of Malmö (Sweden), Jena, Thüringen (Germany), Heidelberg, Baden-Württemberg (Germany), and the provinces of Groningen (The Netherlands), Bergamo (Italy), and Coimbra (Portugal). A random sample was selected from the general population, based on electoral precincts, aged 18 to 74 years⁴. The study followed a stratified, proportional, sampling-with-replacement design. In total 12,377 subjects were interviewed with a standardized questionnaire and a random sample was patch tested to investigate sensitisation to various

allergens. The interview data were published recently⁴, here we present the patch test data to the different allergens in True Test panel 1, 2, and 3 and additional substances at present included in the European Baseline series. The full phase of the study started in August 2008 and ended in October 2011. Less than 1% of the participants refused to be patch tested. The study was approved by the ethics committee of each participating centres.

Patch testing

A detailed description of the patch test materials and procedure can be found in esupplement 1. Briefly, patch testing was performed according to the International Contact Dermatitis Research Group (ICDRG) guidelines. Weak (+), strong (++), and extreme (+++) reactions with an allergic morphology are considered as positive reactions. At least a (+) reaction was considered as a proxy for contact allergy. Both TRUE-test and Finn chambers[®] were used to test a total of 50 allergens (detailed description see esupplement 1).

Data collection

As reported previously, the interview was conducted face-to-face with a trained interviewer and consisted of three parts^{4 5}. The first part recorded demographic and personal characteristics, including age, gender, ethnic group, skin phenotype, body weight, height, personal habits (e.g., smoking), education, occupation, marital status, and family size⁴. The second part recorded any history of skin problems, including localised erythema or itchy skin rashes that lasted more than three days during the last month, the last year (including the last month), or that occurred over their lifetime (including the last month and the last year)⁴. The interviewees were asked whether they thought they had sensitive skin, dry skin, and to describe any previous dermatological diagnoses made by a physician or dermatologist, the treatment received, allergy tests, and any symptoms present at the time of the interview⁴. In order to compare the subsample which was patch tested with the prevalence sample we report the prevalence of atopic eczema, contact dermatitis, other eczema, itchy skin rash, dry skin and sensitive skin for both samples.

Sample size and data analyses

The sample size calculation was described previously⁵: Using data from the pilot clinical phase, we estimated that the 1-year prevalence of a clinically relevant reaction to fragrances was not lower than 1%. Based on this estimate, we performed a power analysis to identify the cut-off for adequate power to investigate the prevalence of contact allergy to fragrances and to document possible differences among countries⁵. Using the exact (Clopper-Pearson) confidence interval method⁶, we estimated that a sample size of 3,000 produces a 2-sided 95% confidence interval with a width equal to 0.08 and a relative standard error of 17% when the sample prevalence is 1.00% (95% confidence interval, 0.06–1.40%; details see⁵). We thus require a sample of 500 individuals interviewed and patch tested per centre, for a total of 3,000 individuals. We further sampled about 1,500 individuals for the interviews per centre (a total of a further 12,000 individuals interviewed)⁵.

All statistical analyses were performed using SPSS 20 (©IBM). Descriptive data are presented as numbers and relative frequencies for demographics and skin complaints of individuals. The prevalence of patch test reactions to different allergens are expressed as numbers and relative frequencies together with the 95% confidence interval (CI). In order to compare prevalences across countries the prevalences were also calculated by country using age standardized estimates. A p-value < 0.01 was considered as statistically significant. Age standardization was performed according to the direct method⁷. This method applies the observed age-specific rates to an age distribution from a standard reference population. For the purpose of our analysis, the chosen reference population was the European Standard Population⁷. The association between the prevalence of contact allergy to at least one allergen of the tested sensitizers and the lifetime prevalence of atopic dermatitis, contact dermatitis, other eczema, dry skin, sensitive skin, and itchy skin rashes (lifetime, last year, last month) are expressed in terms of the Odds Ratio (OR) and 95% CI. OR estimates were obtained with multiple logistic regressions to control for potential confounders (age and gender).

Results

Socio-demographic characteristics

In Table 1 the socio-demographic characteristics of 3,119 subjects patch tested out of 12,377 subjects interviewed in six European regions are presented. These 3,119 subjects are a random sample of 25.2% of the total investigated 12,377 subjects. In each centre between 500 and 546 subjects and at least 25% of the interviewed subjects were patch tested (Bergamo, Italy n=546, Coimbra, Portugal n= 531, Heidelberg, Germany n= 506, Jena, Germany n=518, Groningen, The Netherlands n=500, Malmö, Sweden n=518). Females outnumbered males in all centres (54.9% females overall).

The MOAHLFA index⁸ is as follows: Men (46.1%), Occupational (<1%), Atopic Dermatitis (4.1%), Hand (2.3%), Leg (1.9%), Face (2.3%) and Age > 40 yrs. (54.4%). The calculation is based on the last month prevalence of atopic dermatitis, and of itchy skin rashes lasting longer than three days in different parts of the body like hand, face, leg, respectively.

Contact dermatitis, atopic dermatitis, other eczema, and other skin complains

In Table 2 the age-standardized prevalence of subjects that reported contact dermatitis (any form of contact dermatitis, allergic and/or irritant), atopic dermatitis, other eczema, itchy skin rashes that last longer than three days, dry skin and sensitive skin are shown for the 3,119 subjects patch tested and 12,377 overall interviewed in 6 European regions. Those prevalences of the 12,377 subjects interviewed are very similar to those of the 3,119 subjects patch tested.

A personal history of contact dermatitis (allergic and/or irritant) was reported by 468 (age-standardized prevalence 15.1%, 95% CI 13.8-16.3) of the 3,119 patch tested subjects, in 253 (8.2%) subjects the diagnosis was confirmed by a physician and in 215 (6.9%) subjects it was not confirmed according to the report of the subjects. A personal history of atopic dermatitis was reported by 220 (7.6%, 95% CI 6.7-8.6) of the patch tested subjects, in 209 (7.2%) subjects this diagnosis was confirmed by a physician and in 15 (0.5%) subjects not. Other eczema was

reported by 502 (17.3%, 95% CI 15.9-18.6) out of 3,119 patch tested subjects, in 402 (13.8%) subjects this diagnosis was confirmed by a physician and in 99 (3.4%) not. The diagnosis contact dermatitis (allergic and/or irritant) was confirmed by a physician in 54% (253 out of 468 subjects), atopic dermatitis in 95% (209 out of 220 subjects), and other eczema in 80% (402 out of 502 subjects).

The overall prevalence of itchy skin rashes that last longer than three days in the subsample patch tested was 20.4% (95% CI 19.1-21.6) during the last month preceding the interview, 33.7% (95% CI 31.9-35.3) during the preceding year, and 54.3% (95% CI 52.5-56.0) over a lifetime, with a higher prevalence in females than in males (lifetime prevalence females 58.6%, 95% CI: 57.5-59.8; males 44.8%, 95% CI: 43.5-46.1). A total of 1632 subjects reported they had dry skin (age-standardised prevalence: 54.1%; 95% CI 52.3-55.9), and a total of 1269 subjects reported that they had sensitive skin (age-standardised prevalence: 41.8%; 95% CI 40.1-43.6). The prevalence of dry or sensitive skin was higher in females compared to males (females 60.9%, 95% CI 59.7-62.0 and males 44.4%, 95% CI: 43.1-45.7; respectively: females 51.0%, 95% CI 49.7-52.2, and males 28.6%, 95% CI 27.4-29.8).

Prevalence of contact allergy to allergens in the True Test panel 1, 2, and 3

Table 3 presents the prevalence of contact allergy, defined as a positive patch test reaction (+, ++, +++) to different allergens in TRUE-test panel 1 (Table 3a), panel 2 (Table 3b), panel 3 (Table 3c), and to fragrance mix II, hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC), and sesquiterpene lactone mix (Table 3d) by gender and in total (3,119 patch tested subjects).

At least one positive reaction to at least one allergen of TRUE-test panel 1 was diagnosed in 605 subjects in total (prevalence 19.4%; 95% CI 18.0-20.8), and significantly more frequent in females compared to males (prevalence female: 27.5%, 95% CI 25.3-29.6; prevalence males: 9.6%, 95% CI 8.1-11.1). The most frequent reaction were seen against nickel sulphate (prevalence 14.5%, 95% CI 13.2-15.8), cobalt chloride (prevalence 2.2%, 95% CI 1.7-2.7), fragrance mix I with high atranol and chloratranol (prevalence 1.8%, 95% CI 1.4-2.3), and colophony (prevalence 0.9%, 95% CI 0.6-1.3). To the fragrance mix 1 with low atranol and

chloratranol the prevalence was lower (prevalence 0.9%, 95% CI 0.6-1.3). Contact allergy to nickel, cobalt and colophony were significantly more frequent in females compared to males. For the other allergens of TRUE-test panel 1 the prevalence of contact allergy was not different between females and males. Other allergens of panel 1 with a prevalence $\geq 0.5\%$ were epoxy resin, potassium dichromate, and balsam of Peru (*Myroxylon pereirae*). However, the upper limits of the 95% CI were $> 0.5\%$ for all allergens of panel 1 without quinoline mix (prevalence 0.2%, 95% CI 0.0-0.3).

At least one positive reaction to at least one allergen of TRUE-test panel 2 was diagnosed in 275 subjects (prevalence 8.8%; 95% CI 7.9-9.9) in total, and again significantly more frequent in females compared to males (prevalence females 10.0%, 95% CI 8.6-11.6; prevalence males 7.3%, 95% CI 6.0-8.7). The most frequent reactions with a PR $\geq 0.5\%$ were seen against thimerosal (prevalence 5.0%, 95% CI 4.2-5.8), p-tertiary-butylphenol-formaldehyde resin (PTBP resin) (prevalence 1.3%, 95% CI 0.9-1.7), p-phenyldiamine free base (PPD) (prevalence 1.0%, 95% CI 0.6-1.3), carba mix (prevalence 0.5%, 95% CI 0.3-0.8), MCI/MI (prevalence 0.5%, 95% CI 0.3-0.7), and thiuram mix (prevalence 0.5%, 95% CI 0.3-0.7). In addition the upper limits of the 95% CI of the prevalence of contact allergy were $> 0.5\%$ for quaternium 15, black-rubber-mix, and formaldehyde. The lowest prevalence for contact allergy to an allergen of TRUE-test panel 2 was observed for paraben mix (prevalence 0.1%, 95% CI 0.0-0.2). There were no statistically significant differences between females and males.

At least one positive reaction to at least one allergen of TRUE-test panel 3 was diagnosed in 30 subjects (prevalence 1.0%; 95% CI 0.6-1.3) in total, without a significant gender difference. Allergens with upper limits of the 95% CI for the prevalence of contact allergy to a substance of TRUE-test panel 3 $\geq 0.5\%$ were budesonide, hydrocortison-17-butyrate, and tixocortol-21-pivalate.

In addition, at least one positive reaction to the fragrance mix II was diagnosed in 60 subjects (prevalence 1.9%; 95% CI 1.5-2.5), to HICC in 45 subjects (prevalence 1.4%; 95% CI 1.0-1.9), and to sesquiterpene lactone mix in 3 subjects (prevalence 0.1%; 95% CI 0.0-0.2). At least one

positive reaction to these three additional allergens have been diagnosed in 70 subjects (prevalence 2.2%; 95% CI 1.8-2.8). There was no significant gender difference.

In total, at least one positive patch test reaction (+, ++, +++) (contact allergy) to the 29 allergens of TRUE-test panel 1 (oak moss with a high content of atranol/chloratranol), 2, and 3 were diagnosed in 803 subjects (prevalence 25.7%, 95% CI 24.4-27.2), statistically significantly more frequent in females (prevalence 33.6%, 95% CI 31.4-35.7) compared to males (prevalence 16.2%, 95% CI 14.3-18.0). Regarding the allergens of the European baseline series a positive reaction (contact allergy) to the patch tested 32 allergens was diagnosed in 841 subjects (prevalence 27.0%, 95% CI 25.5-28.5). In females the prevalence of contact allergy to the European baseline series was statistically significant higher compared to males (females prevalence 35.5%, 95% CI 32.7-37.2; males prevalence 17.1%, 95% CI 15.0-19.4. Females had a significantly higher odds ratio for contact allergy (OR 2.6, 95% CI 2.1-3.1) (Logistic regression model adjusted for gender, age, and all skin complains listed in table 5).

The most frequent contact allergy was diagnosed against metals (nickel sulfate, cobalt chloride or potassium dichromate overall prevalence 15.5%, 95%-CI 14.2-16.9, followed by preservatives (thimerosal, MCI/MI, quaternium 15, formaldehyde, parabens mix, diazolidinyl urea or imidazolidinyl urea overall prevalence 6.2, 95%-CI 5.3-7.0 and fragrances (True test technique concerning FM I with high content of atranol/chloratranol, Myroxolon pereirae, colophony and Finn chamber technique concerning FM II, hydroxyisohexyl 3-cyclohexene carboxaldehyde, sesquiterpene lactone mix overall prevalence 4.7, 95%-CI 3.9-5.5) A lower prevalence was observed for rubber chemicals (carba mix 250, thiuram mix, black rubber mix, mercapto mix, mercaptobenzothizole (MBT) overall prevalence 1.4, 95%-CI 1.0-1.8).

Prevalence of contact allergy in different European countries

In Table 4a-d the age-standardized prevalences of contact allergy to the different allergens of True test panel 1, 2, 3 and to fragrance mix II, HICC, and sesquiterpene lactone mix in the different countries are presented. There was a statistically significant difference for contact allergy to nickel, with the lowest age-standardized prevalence in Sweden (prevalence 8.3%,

95% CI 5.9-10.7) and the highest in Portugal (prevalence 18.5%, 95% CI 15.2-21.8). In addition, there was also a statistically significant difference for contact allergy to thimerosal with the highest age-standardized prevalence in Germany and Portugal (prevalence 7.3%) and the lowest in Sweden and the Netherlands (prevalence 1.0% and 1.2% respectively). The prevalence of contact allergies to other allergens, especially fragrance mix I, fragrance mix II, and p-phenyldiamine (PPD) did not differ significantly between countries.

Prevalence of contact allergy observed in different skin diseases

Table 5 presents the prevalence of contact allergy, defined as at least one positive patch test reaction (+, ++, +++) to different allergens in True Test panel 1 to 3 and to the 32 allergens of the European baseline series in subgroups of patients that reported contact dermatitis (allergic and/or irritant), atopic dermatitis, other eczema, itchy skin rashes that last longer than three days, dry skin and sensitive skin in the patch tested subjects. In addition the odds ratios for a contact allergy are given in comparison with subject that did not report those skin diseases or skin complains. The odds ratios were calculated in a multiple logistic regression model controlling for gender, age and all skin complains presented in the table. Significantly increased odds ratios for contact allergy were found for subjects that reported contact dermatitis (allergic and/or irritant) (OR 1.9, 95% CI 1.5-2.5) and itchy skin rashes that last longer than three days over lifetime (OR 1.3, 95% CI 1.1-1.6). This means that subjects with a history of contact dermatitis (allergic and/or irritant) have about two times higher risk of having contact allergy. If we consider only subjects with a physician diagnosed contact dermatitis (allergic and/or irritant) in the logistic regression analysis the OR for contact allergy is even higher (OR 2.4, 95% CI 1.8-3.3). In contrast to contact dermatitis, subjects with a personal history of atopic dermatitis had no increased or decreased risk of contact allergy (OR 1.0, 95% CI 0.7-1.4). In our study there was no significant increase in nickel contact allergy (OR 0.8, 95% CI 0.6-1.3) or fragrance contact allergy (OR 0.8, 95% CI 0.4-1.6) in subjects that reported atopic dermatitis.

Discussion

This study is the largest of its kind ever conducted. Over 12.000 subjects participated and a random sample of more than 3,000 subjects (or 25%) was patch tested. As demonstrated in Table 1 there is no substantial difference to the socio-demographic characteristics of 12,377

subjects interviewed and previously reported by Naldi et al⁴ and the 3,119 patch tested subjects. It demonstrates that the 3,119 subjects patch tested are a random sample of the 12,377 subjects interviewed and are representative for the prevalence sample of the general population. As demonstrated by Naldi et al⁴ the age and gender distribution is consistent with the general population data obtained from Eurostat 2010. There is also no substantial difference in the prevalence of subjects that reported different skin complains between the patch tested 3,119 and the 12,377 interviewed subjects (see Table 2). Also the prevalence of physician confirmed diagnoses of AD (7.0%), contact dermatitis (allergic and/or irritant) (8.4%) and other eczema (13.4%) recently reported by Naldi et al⁴ in the interviewed 12,377 subjects are very similar to the reported prevalence of physician diagnosed skin disease in the 3,119 patch tested subjects (AD prevalence 7.2%, contact dermatitis prevalence 8.2%, other eczema prevalence 13.8%).

The study employed the highest methodological quality in population-based patch test studies so far. Based on the experience gained from a pilot study, some amendments to the original design were incorporated. A peer-reviewed publication confirming the feasibility of the methodology in assessing human contact allergy in the pilot study was published in 2010⁵. There was a standardization of all aspects of the study including standardised interviews from a trained medical professional, application and reading of patch tests and all test substances were from the same batch and lot in all six centres. An expert in the technique of patch testing visited each of the six sites to monitor the patch testing techniques and to assure that they were conducted in a uniform manner and according to the protocol used based on consideration of 16 factors of possible significance for the patch test result in multicentre patch test studies⁹. Besides listing the 16 factors a scoring system is also suggested with various scores based on the relative importance of each factor for the quality of the multicentre patch test study. In the current study the highest scores were obtained for all factors except for lack of control of occlusion after 48 h and only one test reading on day 3. In spite of this, the total score rendered this study to be classified as a multicentre patch test study with excellent quality⁹.

In total, contact allergy to at least one out of the 32 patch tested allergens of the European standard series was diagnosed in 27.0% with a statistically significant higher prevalence in females compared to males. The highest age-standardized prevalences ($\geq 1\%$) were found for

nickel sulfate (14.5%), thimerosal (5.0%), cobalt chloride (2.2%), fragrance mix II (1.9%), fragrance mix I (high atranol and chloratranol) (1.8%), HICC (1.4%), p-tert-butylphenol-formaldehyde resin (PTBP resin 1.3%), and p-phenylenediamine (1.0%). The most frequent contact allergy was diagnosed against metals (nickel sulfate, cobalt chlorid or potassium dichromate), followed by preservatives (thimerosal, MCI/MI, quaternium 15, formaldehyde, parabens mix, diazolidinyl urea or imidazolidinyl urea), fragrances (FM I with high content of atranol/chloratranol, Myroxolon pereirae, colophony, FM II, hydroxyisohexyl 3-cyclohexene carboxaldehyde or sesquiterpene lactone mix and rubber chemicals (carba mix 250, thiuram mix, black rubber mix, mercapto mix, mercaptobenzothizole (MBT)). Between the countries there only were statistically significant differences in the age-standardized prevalence for nickel and thimerosal but not for the other allergens.

Thyssen et al¹⁰ reviewed published studies mainly from North America and Western Europe investigating the prevalence of contact allergy in the general population and in unselected subgroups of the general population. This review is based on 17 published studies on contact allergy in the general population conducted between 1966 and 2007 in different countries (4 from Denmark, 3 from Sweden, 2 from Germany, 2 from Norway, 2 from US, 1 from Italy, Hungary, Portugal, and Thailand). The sample size varied between 93 and 1236 subjects and there are many methodological differences regarding the allergens used for patch testing, the patch test instruments and techniques, the selected population (e.g. school children, twins, cadets, general population, etc.) and the age and gender distribution of the population which makes it difficult or even impossible to compare or summarize the results of the different studies. The major limitations of that study are those that are typical of a meta-analysis study¹¹. In summary, the median prevalence of contact allergy to at least one contact allergen was reported to be 21.2% (range 12.5% to 40.5%), and the weighted average prevalence was 19.5%, based on data collected on all age groups and all countries between 1966 and 2007. However in none of the studies were fragrance mix II or HICC patch tested. The most prevalent contact allergens were nickel, thimerosal, and fragrance mix I. The median nickel allergy prevalence based on all studies was 8.6% (range 0.7-27.8%), and was higher among females than males (17.1%, range 3.9-38.8% versus 3%, range 0.7-6.8%). In addition, cobalt, chromium, PPD, and MCI/MI were prevalent allergens in several studies¹⁰.

In 6 out of the 17 studies reviewed by Thyssen et al¹⁰ the TRUE-test was used for patch testing but no study used panel 1, 2 and 3. Only in three studies, however, a sample of the general population was investigated: in Denmark n= 567 subjects¹² and n=469¹³, and in Norway n=1236¹⁴. In the other three studies, 85 infants in the US¹⁵, 1146 school children in Denmark¹⁶, and 627 Danish Twins¹⁷ were investigated. The prevalence of positive reactions to at least 1 allergen in those studies investigating the general population in Denmark^{12,13} and Norway¹⁴ varied between 15.2% and 26.3%. For nickel, the prevalence varied between 6.7% and 17.6%; for Thimerosal, between 1.9% and 3.1%; and, for fragrance mix I, between 1.1% and 2.3%.

Patch testing with TRUE-test[®] panels 1 and 2 in 1146 Danish 8th grade school children (age 12-16 years) showed that 15.2% (girls 19.4% vs. boys 10.3%) had contact allergy to at least one contact allergen. Contact allergy was most common to nickel (8.6%) and fragrance mix I (1.8%)¹⁶. Nickel allergy was clinically relevant in 69% and fragrance allergy in 29% of cases. A significant association was found between contact allergy and hand eczema while no association was found between contact allergy and atopic dermatitis or inhalant allergy¹⁸. The authors did a 15 years follow-up study to estimate the incidence rates and persistence of contact allergy from adolescence to adulthood, and the point prevalence in adulthood¹⁹. 442 subjects could be again patch tested with TRUE-test[®] panels 1 and 2. The point prevalence of contact allergy was 20.1%. Nickel was the most common contact allergen (11.8%), followed by cobalt (2.3%), colophony (2.0%), thimerosal (1.4%), p-phenylenediamine (1.1%), and fragrance mix I (0.7%). Most nickel reactions were persistent, and a significant number of new nickel sensitizations were found. However, fragrance mix I reactions from adolescence could not be reproduced.

Bryld et al¹⁷ performed patch testing with TRUE-test in 627 Danish twins without hand eczema. The prevalence of at least 1 positive reaction (contact allergy) was 21.4%, contact allergy to nickel was 12.8%, thimerosal 2.2%, colophony 1.3%, and fragrance mix 1.3%.

Contact allergy to allergens of the TRUE-test panel 1 and 2 was investigated in the Danish general population in 1990 and 2006²⁰. The overall prevalence decreased significantly from 15.5% in 1990 to 10.0% in 2006, mainly as a result of a decrease in thimerosal allergy from

3.4% to 0.8%. Furthermore, the prevalence of cobalt allergy and rubber-related allergens decreased from 1.1% to 0.2% and from 1.5% to 0.2%, respectively. However the prevalence of fragrance allergy (fragrance mix I) increased from 1.1% in 1990 to 1.6% in 2006.

It is very important to mention that a positive patch test reaction, which we consider as contact allergy, is not a disease but an immunologically acquired reaction pattern (delayed hypersensitivity) which may manifest as allergic contact dermatitis, a clinical disease, as the patch test only measures whether the individual is sensitized or not^{2,10,21}. It is generally acknowledged that the patch test holds some biological as well as technical limitations¹⁰, and many variables like the patch test material used (e.g. TRUE-test, Epiquick or standard allergens different suppliers), the patch test concentrations, the anatomical application site, the time of patch test reading, the knowledge and experience of the reading person may influence the number of positive patch test reactions and should be accounted for. Therefore a high standardization of all these variables like we did in this European study is very important⁹. Although the exact sensitivity and specificity of patch testing is unknown, it has been estimated that the reproducibility is generally high^{22,23}. However, it also has to be considered that the diagnostic performance of patch testing is different when patch testing is carried out in a population with low disease prevalence, that is a low positive predictive value and a high proportion of false-positive reactions²⁴.

Conclusion

Contact allergy to at least one allergen of the European baseline series was diagnosed in more than one quarter of the general European population. The TRUE-test panels and petrolatum preparations tested for all contact sensitizers in the European baseline series at the time when the study was performed²⁵ except primin and methyl dibromo glutaronitrile (MDBGN).

Unfortunately, between 2008-2011 other emerging contact allergens were not introduced into the study such as methylisothiazolinone and it would be very interesting to know the prevalence of this contact allergy in the general population. Patch testing is very important and every subject with contact dermatitis but also with an unclear dermatitis will benefit from patch testing. Even subjects with a lifetime prevalence of an itchy skin rash lasting longer than three days had a significantly increased prevalence of contact allergy and might benefit from patch testing.

Population-based epidemiological studies on contact allergy and allergic contact dermatitis are needed to provide important risk data to government agencies, industries, and consumer-oriented groups. Epidemiological data and knowledge based on carefully conducted representative studies are essential when the safety and benefits of different consumer goods are balanced against the risk of causing contact allergy and allergic contact dermatitis. These data are also prerequisites in the surveillance of national and international contact allergy epidemics. Therefore similar studies are needed, especially from other parts of the world, like America and Asia.

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Table 1: Socio-demographic characteristics of 3,119 subjects patch tested (out of 12,377 interviewed subjects) in 6 European regions. In addition the socio-demographic characteristics of the interviewed subjects are given according to Naldi et al. 2013

		prevalence sample*		subsample patch tested	
		(n=12,377) ¹		(n=3,119) ¹	
		N	%	N	%
Gender	Male	5701	46.1%	1405	45.1%
	Female	6669	53.9%	1712	54.9%
Age	18 - 30 years	3498	28.3%	828	26.5%
	31 - 45 years	3314	26.8%	824	26.4%
	46 - 60 years	3150	25.5%	855	27.4%
	61 - 74 years	2415	19.5%	612	19.6%
Occupation	Working	7035	56.9%	1684	54.2%
	Student	1869	15.1%	473	15.2%
	unemployed	519	4.2%	181	5.8%
	Retired	1919	15.5%	520	16.7%
	homemaker (male or female)	540	4.4%	136	4.4%

	Others	471	3.8%	111	3.6%
marital status	married / common law	6838	55.5%	1720	55.5%
	divorced / widowed	1192	9.7%	336	10.8%
	Single	4282	34.8%	1044	33.7%
Smoking	non-smoker	6830	55.3%	1698	54.6%
	ex-Smoker	2705	21.9%	678	21.8%
	Smoker	2818	22.8%	736	23.7%
BMI ²	<20	1025	8.3%	263	8.5%
	20-25	6059	49.2%	1482	47.9%
	25-30	3736	31.3%	990	32.0%
	30<	1373	11.2%	360	11.6%

*according to Naldi et al. (2013)

¹frequencies in each category may not up to the total due to missing values

²BMI: Body Mass Index

Table 2: Age-standardized prevalence of subjects that reported contact dermatitis (allergic and/or irritant), atopic dermatitis, other eczema, itchy skin rashes that last longer than three days, dry skin and sensitive skin in of 3,119 subjects patch tested and 12,377 interviewed in 6 European regions.

	Prevalence Sample (n=12,377)		Subsample patch tested (n=3,119)	
	n	Prevalence (95% CI ¹)	n	Prevalence (95% CI ¹)
Contact Dermatitis	1911	15.5% (14.8-16.1)	468	15.1% (13.8-16.3)
Atopic Dermatitis	883	7.8% (7.3-8.3)	204	7.1% (6.1-8.0)
Other eczema	1594	14.0% (13.3-14.6)	502	17.3% (15.9-18.6)
Itchy skin rash: last MONTH	2411	19.5% (18.8-20.2)	632	20.4% (19.1-21.6)
Itchy skin rash: last YEAR	3954	32.1% (31.3-32.9)	1039	33.7% (31.9-35.3)
Itchy skin rash: LIFETIME	6463	52.3% (51.4-53.2)	1683	54.3% (52.5-56.0)
Dry skin	6468	53.3% (52.5-54.2)	1632	54.1% (52.3-55.9)
Sensitive skin	4941	40.7% (39.8-41.6)	1269	41.8% (40.1-43.6)

¹CI = confidence interval

Table 3a-d: Prevalence of contact allergy (defined as at least one + reaction in the patch test) to different allergens in True Test panel 1 (3a), panel 2 (3b), panel 3 (3c), and additional allergens of the European baseline series (3d) by gender and in total (3,118 patch tested subjects).

Substance (concentration)	Males (n=1405)		Females (n=1712)		Total (n=3119)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
*Nickel sulfate (0.20 mg/cm ²)	73	*5.2% (4.1-6.4)	378	*22.2% (20.1-24.1)	451	14.5% (13.2-15.8)
*Cobalt dichloride (0.02 mg/cm ²)	16	*1.1% (0.6-1.7)	52	*3.0% (2.3-3.9)	68	2.2% (1.7-2.7)
*Colophony 850 (Rosin; 1.2 mg/cm ²)	6	*0.4% (0.1-0.8)	24	*1.4% (0.9-2.0)	30	0.9% (0.6-1.3)
*Fragrance Mix 1 (0.43 mg/cm ²)	7	*0.5% (0.1-0.9)	22	*1.3% (0.8-1.9)	29	0.9% (0.6-1.3)
Epoxy resin (0.05 mg/cm ²)	13	0.9% (0.4-1.4)	15	0.9% (0.5-1.3)	28	0.9% (0.6-1.2)
Potassium dichromate(0.023 mg/cm ²)	13	0.9% (0.5-1.4)	12	0.7% (0.4-1.1)	25	0.8% (0.5-1.1)
Balsam of Peru (Myroxylon pereirae; 0.8 mg/cm ²)	6	0.4% (0.1-0.8)	17	1.0% (0.5-1.5)	23	0.7% (0.4-1.1)
Wool alcohols (1.0 mg/cm ²)	5	0.4% (0.1-0.7)	9	0.5% (0.2-0.9)	14	0.4% (0.2-0.7)
Caine mix 630 (0.63 mg/cm ²)	3	0.2% (0.0-0.5)	10	0.6% (0.2-0.9)	13	0.4% (0.2-0.6)
Neomycin sulfate (0.23 mg/cm ²)	5	0.4% (0.1-0.7)	6	0.4% (0.1-0.7)	11	0.4% (0.2-0.6)

Ethylenediamine dihydrochloride (0.05 mg/cm ²)	5	0.4% (0.1-0.7)	6	0.4% (0.1-0.6)	11	0.4% (0.2-0.6)
Quinoline mix (0.19 mg/cm ²)	2	0.1% (0.0-0.4)	3	0.2% (0.0-0.4)	5	0.2% (0.0-0.3)
*At least one reaction to an allergen of True Test Panel 1	126	*9.0% (7.5-10.4)	462	*27.0% (24.9-29.1)	588	18.9% (17.5-20.2)

*differences between males and females are significant (p<0.05)

¹CI = confidence interval

Table 3b: Prevalence of contact allergy to a substance of True test panel 2 by gender and total

Substance (concentration)	Males (n=1405)		Females (n=1712)		Total (n=3119)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
Thimerosal; 0.008 mg/cm ²)	61	4.3% (3.4-5.4)	94	5.5% (4.4-6.6)	155	5.0% (4.2-5.8)
p-tert-butylphenol-formaldehyde resin (PTBP resin; 0.045 mg/cm ²)	13	0.9% (0.4-1.5)	26	1.5% (1.0-2.2)	39	1.3% (0.9-1.7)
p-phenylenediamine (PPD; 0.09 mg/cm ²)	12	0.9% (0.4-1.4)	18	1.1% (0.6-1.6)	30	1.0% (0.6-1.3)
Carba mix 250 (0.25 mg/cm ²)	5	0.4% (0.1-0.7)	12	0.7% (0.3-1.2)	17	0.5% (0.3-0.8)
CL+Me-isothiazolinone (MCI/MI; 0.0040 mg/cm ²)	5	0.4% (0.1-0.7)	10	0.6% (0.3-1.0)	15	0.5% (0.3-0.7)
Thiuram mix (0.025 mg/cm ²)	7	0.5% (0.1-0.9)	8	0.5% (0.2-0.8)	15	0.5% (0.3-0.7)

Quaternium 15 (0.1 mg/cm ²)	5	0.4% (0.1-0.7)	7	0.4% (0.1-0.8)	12	0.4% (0.2-0.6)
Black rubber mix (0.075 mg/cm ²)	3	0.2% (0.0-0.5)	8	0.5% (0.2-0.9)	11	0.4% (0.2-0.6)
Formaldehyde (0.18 mg/cm ²)	3	0.2% (0.0-0.5)	8	0.5% (0.2-0.8)	11	0.4% (0.2-0.6)
Mercaptobenzothiazole (MBT; 0.0075 mg/cm ²)	4	0.3% (0.1-0.6)	3	0.2% (0.0-0.4)	7	0.2% (0.1-0.4)
Mercapto mix (0.075 mg/cm ²)	4	0.3% (0.1-0.6)	3	0.2% (0.0-0.4)	7	0.2% (0.1-0.4)
Parabens mix (1.0 mg/cm ²)	0	0.0% (0.0-0.2)	3	0.2% (0.0-0.4)	3	0.1% (0.0-0.2)
*At least one reaction to an allergen of True Test Panel 2	103	*7.3% (6.0-8.7)	172	*10.0% (8.6-11.6)	275	8.8% (7.9-9.9)

*differences between males and females are significant (p<0.05)

¹CI = confidence interval

Table 3c: Prevalence of contact allergy to a substance of True test panel 3 by gender and total

Substance (concentration)	Males (n=1405)		Females (n=1712)		Total (n=3119)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
Budesonide (0.001 mg/cm ²)	9	0.6% (0.3-1.1)	4	0.2% (0.1-0.5)	13	0.4% (0.2-0.6)
Hydrocortisone-17-butyrate (0.02 mg/cm ²)	9	0.6% (0.3-1.1)	4	0.2% (0.1-0.5)	13	0.4% (0.2-0.6)
Tixocortol-21-pivalate(0.33 mg/cm ²)	5	0.4% (0.1-0.7)	5	0.3% (0.1-0.6)	10	0.3% (0.1-0.5)
Imidazolidinyl urea (Germall 115; 0.6 mg/cm ²)	2	0.1% (0.0-0.4)	4	0.2% (0.1-0.5)	6	0.2% (0.1-0.4)
Diazolidinyl urea (Germall I; 0.55 mg/cm ²)	2	0.1% (0.0-0.4)	4	0.2% (0.1-0.5)	6	0.2% (0.1-0.4)
At least one reaction to an allergen of True Test Panel 3	15	1.1% (0.6-1.6)	15	0.9% (0.5-1.3)	30	1.0% (0.6-1.3)

¹CI = confidence interval

Table 3d: Prevalence of contact allergy to additional allergens of the European baseline series

Substance (concentration)	Males (n=1405)		Females (n=1712)		Total (n=3119)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
FM 2 (14% pet)	18	1.3% (0.7-1.9)	42	2.5% (1.8-3.2)	60	1.9% (1.5-2.5)
Lyr al (5% pet)	12	0.9% (0.4-1.4)	33	1.9% (1.3-2.6)	45	1.4% (1.0-1.9)
Sesquiterpenelactone mix (0.1% pet)	1	0.1% (0.0-0.2)	2	0.1% (0.0-0.3)	3	0.1% (0.0-0.2)
At least one positive reaction to the allergens	23	1.6% (1.1-2.4)	47	2.7% (2.0-3.6)	70	2.2% (1.8-2.8)

¹CI = confidence interval; ²pet = petrolatum

Table 4a: Prevalence of True Test Panel 1 by country (age standardized)

	Germany (n=1024)		Italy (n=546)		The Netherlands (n=500)		Portugal (531)		Sweden (n=518)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
*Nickel sulfate (0.20 mg/cm ²)	143	13.9% (11.8-16.0)	87	16.4% (13.2-19.4)	78	15.8% (12.5-18.9)	98	18.5% (15.2-21.8)	42	8.3% (5.9-10.7)
*Cobalt dichloride (0.02 mg/cm ²)	24	2.3% (1.3-3.2)	5	0.9% (0.1-1.7)	19	3.8% (2.1-5.5)	13	2.5% (1.1-3.8)	6	1.1% (0.2-2.1)
Fragrance Mix 1 (0.43 mg/cm ²)	12	1.2% (0.6-2.0)	5	0.9% (0.1-1.8)	5	0.9% (0.1-1.8)	5	1.0% (0.1-1.8)	4	0.7% (0.0-1.5)
Epoxy resin (0.05 mg/cm ²)	13	1.3% (0.5-1.8)	3	0.5% (0.0-1.1)	6	1.2% (0.3-2.2)	2	0.4% (0.0-0.9)	5	1.0% (0.1-1.8)
*Colophony 850 (Rosin; 1.2 mg/cm ²)	7	0.7% (0.2-1.2)	7	1.3% (0.3-2.3)	10	2.0% (0.8-3.3)	1	0.2% (0.0-0.6)	4	0.7% (0.0-1.5)
Balsam of Peru (Myroxylon pereirae; 0.8 mg/cm ²)	10	1.0% (0.4-1.6)	1	0.2% (0.0-0.6)	4	0.8% (0.0-1.6)	4	0.7% (0.0-1.5)	4	0.9% (0.0-1.7)
Potassium dichromate(0.023 mg/cm ²)	12	1.1% (0.5-1.8)	2	0.4% (0.0-0.9)	2	0.4% (0.0-0.9)	7	1.3% (0.4-2.3)	1	0.2% (0.0-0.7)
Caine mix 630 (0.63 mg/cm ²)	9	0.9% (0.3-1.4)	1	0.2% (0.0-0.6)	3	0.5% (0.0-1.1)	1	0.2% (0.0-0.6)	1	0.1% (0.0-0.4)
Wool alcohols (1.0 mg/cm ²)	5	0.5% (0.0-0.9)	1	0.3% (0.0-0.7)	3	0.5% (0.0-1.1)	5	0.9% (0.1-1.8)	0	0.0% (0.0-0.5)
Neomycin sulfate (0.23 mg/cm ²)	2	0.2% (0.0-0.4)	1	0.1% (0.0-0.5)	1	0.3% (0.0-0.7)	3	0.6% (0.0-1.2)	4	0.8% (0.0-1.6)
Ethylenediamine	4	0.4% (0.0-0.8)	0	0.0% (0.0-0.6)	3	0.7% (0.0-1.4)	0	0.0% (0.0-0.6)	3	0.6% (0.0-1.3)

dihydrochloride (0.05 mg/cm ²)										
Quinoline mix (0.19 mg/cm ²)	2	0.2% (0.0-0.4)	1	0.1% (0.0-0.5)	0	0.0% (0.0-0.6)	1	0.2% (0.0-0.6)	1	0.1% (0.0-0.4)
*At least one reaction to True Test Panel 1	198	19.2% (16.8-21.6)	103	19.2% (15.9-22.6)	107	21.3% (17.7-24.9)	119	22.4% (18.8-25.9)	60	11.9% (9.0-14.7)

*differences are significant (p<0.05)

¹CI = confidence interval

Table 4b: Prevalence of True Test Panel 2 by country (age standardized)

	Germany (n=1025)		Italy (n=546)		The Netherlands (n=500)		Portugal (531)		Sweden (n=518)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
*Thimerosal; 0.008 mg/cm ²)	75	7.3% (5.7-8.9)	30	5.5% (3.6-7.6)	6	1.2% (0.4-2.2)	39	7.3% (5.2-9.6)	5	1.0% (0.2-1.9)
*p-tert-butylphenol-formaldehyde resin (PTBP resin; 0.045 mg/cm ²)	16	1.6% (0.8-2.3)	8	1.5% (0.6-2.5)	11	2.2% (1.0-3.6)	4	0.8% (0.2-1.5)	1	0.2% (0.0-0.6)
p-phenylenediamine (PPD; 0.09 mg/cm ²)	8	0.8% (0.3-1.4)	4	0.7% (0.0-1.5)	6	1.2% (0.4-2.3)	6	1.1% (0.4-2.1)	6	1.2% (0.4-2.2)
Carba mix 250 (0.25 mg/cm ²)	5	0.5% (0.1-1.0)	2	0.4% (0.0-0.9)	5	1.0% (0.2-1.9)	3	0.6% (0.0-1.3)	2	0.4% (0.0-1.0)
CL+Me-isothiazolinone (MCI/MI; 0.0040 mg/cm ²)	6	0.6% (0.2-1.2)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.6)	4	0.8% (0.2-1.5)	3	0.6% (0.0-1.3)
Thiuram mix (0.025 mg/cm ²)	7	0.7% (0.2-1.3)	3	0.5% (0.0-1.3)	1	0.2% (0.0-0.6)	3	0.6% (0.0-1.3)	1	0.2% (0.0-0.6)
Quaternium 15 (0.1 mg/cm ²)	4	0.4% (0.1-0.8)	0	0.0% (0.0-0.5)	4	0.8% (0.2-1.6)	2	0.4% (0.0-1.0)	2	0.4% (0.0-1.0)

Black rubber mix (0.075 mg/cm ²)	4	0.4% (0.1-0.8)	0	0.0% (0.0-0.5)	2	0.4% (0.0-1.0)	3	0.6% (0.0-1.3)	2	0.4% (0.0-1.0)
Formaldehyde (0.18 mg/cm ²)	3	0.3% (0.0-0.7)	0	0.0% (0.0-0.5)	3	0.6% (0.0-0.6)	2	0.4% (0.0-1.0)	3	0.6% (0.0-1.3)
Mercaptobenzothiazole (MBT; 0.0075 mg/cm ²)	3	0.3% (0.0-0.7)	0	0.0% (0.0-0.5)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.6)	2	0.4% (0.0-1.0)
Mercapto mix (0.075 mg/cm ²)	2	0.2% (0.0-0.5)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.6)	2	0.4% (0.0-1.0)	1	0.2% (0.0-0.6)
Parabens mix (1.0 mg/cm ²)	1	0.1% (0.0-0.3)	0	0.0% (0.0-0.5)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.6)	0	0.0% (0.0-0.5)
*At least one positive reaction to True Test Panel 2	115	11.2% (9.4-13.3)	45	8.2% (5-9-10-7)	34	6.8% (4.6-9.1)	61	11.5% (8.9-14.2)	21	4.1% (2.4-5.7)

*differences are significant (p<0.05)

¹CI = confidence interval;

Table 4c: Prevalence of True Test Panel 3 by country (age standardized)

	Germany (n=1025)		Italy (n=546)		The Netherlands (n=500)		Portugal (531)		Sweden (n=518)	
	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)	N	Prevalence (95%-CI ¹)
Hydrocortisone-17-butyrate (0.02 mg/cm ²)	5	0.5% (0.0-0.9)	2	0.4% (0.0-0.9)	5	1.0% (0.1-1.9)	0	0.0% (0.0-0.5)	2	0.5% (0.0-1.1)
Budesonide (0.001 mg/cm ²)	4	0.4% (0.0-0.8)	2	0.4% (0.0-0.9)	5	1.0% (0.1-1.9)	0	0.0% (0.0-0.5)	2	0.4% (0.0-0.9)
Tixocortol-21-pivalate(0.33 mg/cm ²)	6	0.6% (0.1-1.0)	1	0.1% (0.0-0.5)	1	0.3% (0.0-0.7)	0	0.0% (0.0-0.5)	2	0.4% (0.0-0.9)
Imidazolidinyl urea (Germall 115; 0.6 mg/cm ²)	2	0.2% (0.0-0.5)	1	0.1% (0.0-0.5)	0	0.0% (0.0-0.5)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.7)
Diazolidinyl urea (Germall I; 0.55 mg/cm ²)	2	0.2% (0.0-0.4)	1	0.1% (0.0-0.5)	1	0.2% (0.0-0.6)	1	0.2% (0.0-0.6)	1	0.1% (0.0-0.4)
At least one positive reaction to True Test Panel 3	12	1.2% (0.5-1.8)	3	0.6% (0.0-1.3)	7	1.5% (0.5-2.6)	1	0.2% (0.0-0.6)	6	1.1% (0.2-2.0)

*differences are significant (p<0.05)

¹CI = confidence interval; ²not available

Table 5: Prevalence of contact allergy to at least one allergen of True test panel 1, 2, and 3 in subjects that reported different dermatological diagnoses and skin complains.

		Total	At least one positive reaction to True Test Panel 1		At least one positive reaction to True Test Panel 2		At least one positive reaction to True Test Panel 3		At least one positive reaction to True Test Panel 1-3		
		n	n	Prevalence	n	Prevalence	n	Prevalence	n	Prevalence	OR ¹ (95% CI ²)
Atopic	yes	207	43	20,8%	29	14,0%	3	1,4%	62	30,0%	1.0 (0.7 -1.4)
Dermatitis	no	2712	497	18,3%	236	8,7%	22	0,8%	670	24,7%	
Contact	yes	462	153	33,1%	56	12,1%	8	1,7%	183	39,6%	1.9 (1.4-2.5)*
Dermatitis	no	2658	435	16,4%	220	8,3%	22	0,8%	608	22,9%	
Other	yes	497	103	20,7%	46	9,3%	7	1,4%	137	27,6%	1.0 (0.8-1.3)
eczema	no	2441	442	18,1%	219	9,0%	18	0,7%	599	24,5%	
Itchy skin	yes	1682	378	22,5%	174	10,3%	18	1,1%	496	29,5%	1.3 (1.1-1.6)*
rash	no	1438	210	14,6%	102	7,1%	12	0,8%	295	20,5%	
lifetime											
Dry skin	yes	1627	330	20,3%	159	9,8%	16	1,0%	439	27,0%	0.9 (0.8-1.1)
	no	1409	237	16,8%	112	7,9%	12	0,9%	329	23,3%	
Sensitive	yes	1252	298	23,8%	119	9,5%	12	1,0%	371	29,6%	1.1 (0.9-1.3)
skin	no	1803	279	15,5%	151	8,4%	18	1,0%	408	22,6%	
Total		3119 ³	588	18,9%	276	8,8%	30	1,0%	791	25,4%	

¹ calculated in a multiple logistic regression controlling for gender, age and all variables presented in the rows. *significant value (p<0.05)

² CI = confidence interval

³ frequencies in each category may not up to the total due to missing values