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Prevalence of contact allergies in the population compared to a tertiary referral patch test clinic in Jena/Germany

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Conflict of Interests

W. Uter has accepted honoraria for presentations or travel reimbursement from cosmetic industry associations. P. Elsner was study investigator and/or consultant for Leo, Novartis, Pfizer and Pierre Fabre and received speaker's honoraria from Galderma, Leo, Novartis, Pierre Fabre and Sanofi. S. Schliemann was study investigator and/or consultant for LEO Pharma GmbH, Novartis Pharma GmbH, Sanofi GmbH, Pierre Fabre Dermo Cosmetique, Eli

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Collaborators

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Summary

Background. The contact allergy prevalences in patch tested patients are usually higher than those in the population, owing to morbidity-driven selection.

Objectives. To examine the differences between two samples, one from the population, one from the patch test clinic, in one area of Germany (Jena, Thuringia).

Methods. Between August 2008 and October 2011, 519 participants of the population-based EDEN fragrance study were patch tested in Jena using a TRUE Test baseline series extended with some pet.-based (fragrance) allergen preparations. Between 2007 and 2012 (inclusive), 1906 routine patients were patch tested for suspected ACD in the Jena University Hospital Department, of these 1694 (83.2%) with the German baseline series using pet./aq.-based, investigator-loaded allergens.

Results. In the population (clinical) sample, 19.6% (41.1%) were sensitised to at least one of the allergens considered. The most common baseline series allergens in the population/clinical sample were nickel (10.5%/13.2%), fragrance mix (FM) II (2.9%/6.7%), FM I (2.3%/8.3%), and cobalt (1.6%/5%). The clinical sample was slightly older (71.5% vs. 55.9% age 40+) and included less males (36 % vs. 49.3%).

Conclusions. Results are quite similar, although prevalences are usually higher in the clinical setting, with the exception of *p-tert*-butylphenol formaldehyde resin.

Key words

contact allergy, clinical epidemiology, epidemiology, patch testing, RRID:SCR_001905, surveillance

1. Introduction

It is a commonly accepted notion that estimation of morbidity and of the impact of risk factors should preferably be based on population-based epidemiological studies – notwithstanding possible selection bias which may result from possibly inappropriate design of the sampling process or participation bias.¹ However, such studies are costly and, perhaps for this reason, not performed often; certainly, not often enough to be able to serve contact allergy surveillance, which therefore relies on clinical epidemiology, that is, patient-derived data.² It has been criticised that prevalences of sensitisation based on patient data do not represent the frequency of sensitisation in the population, which is certainly true, owing to the morbidity-driven selection process eventually leading to patch testing. While for several objectives of patient-based clinical surveillance this is not an issue, it is nevertheless interesting to compare sensitisation prevalences obtained in a representative population sample with those found in patch tested patients. Such a comparison enables a better description of the selection process, which may perhaps vary e.g. between allergens, or depend on a department's specialties or other regional factors.^{3,4}

Some years ago, the European Dermato-Epidemiology Network (EDEN) fragrance study has been performed in five European countries, combining a survey (interview) on skin problems in a sample of 12377 subjects followed by a patch test of a random sample of this study cohort (n = 3119) with the TRUE Test panels 1–3 as well as, among others, fragrance mix (FM) II, hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) and sesquiterpene lactone mix.⁵ As one of the study centres, Jena (Thuringia, Germany) had contributed 519 participants patch tested from 2008 to 2011. This enabled a comparison with the clinical results of routine patch testing collected in the Department of Dermatology of Jena University, which is a partner of the contact allergy surveillance network “Information Network of Departments of Dermatology” (IVDK; www.ivdk.org) and the European Surveillance System on Contact Allergy (ESSCA), a working group of the ESCD, in a range of years roughly corresponding to the EDEN study period, namely, 2007 to 2012 (inclusive). The present analysis presents and discusses the comparison of these two regionally and temporally matched data sets.

2. Methods

The secondary analysis is based on pseudonymised data obtained in two different contexts, but in the same geographical region and time period: (i) patch test results with a modified European baseline series in a population sample of the EDEN fragrance study, and (ii) patch test results documented in the department of Dermatology and Allergology, University Hospital Jena, as part of the latter department's contribution to the IVDK and ESSCA contact allergy surveillance networks. The two approaches to data management and analysis, using the statistical software R (version 3.6, www.r-project.org, RRID:SCR_001905) are outlined below.

2.1 EDEN study data

The methods of the EDEN fragrance study which, despite its name, also included allergens of a modified European baseline series other than fragrances, have been published in

detail.^{5,6} In brief, a random sample (n=3119) of the 12377 study participants recruited for an initial interview part (54.9% female, age > 40 years 55.4%, atopic dermatitis in 4.1%, hand 2.3%, leg 1.9%, face 2.3%)⁵ was patch tested with 3 panels of the TRUE Test (SmartPractice, Phoenix, Arizona) comprising 29 allergen preparations were tested along with 20 pet.-based allergen preparations of fragrance allergens, including all single constituents of fragrance mix (FM) I and FM II. Moreover, FM I was tested in triplicate: as part of the TRUE Test, as FM I 8% pet. with an *Evernia prunastri* (oak moss absolute) extract with a high content of atranol and chloratranol, and 8% with a low (chlor-)atranol content. A comparison of these diagnostic approaches has been published;⁷ for better comparability with the clinical results, only results with FM I 8% pet. (in both versions) will be used. The allergen preparations considered for the present comparison are shown in **Table 1**, along with their counterpart tested in the clinic. Between August 2008 and October 2011, 519 participants of the population-based EDEN fragrance study were patch tested in Jena, constituting the population sample in the present study. Patch test readings by trained dermatologists on day (D) 3 were used as study outcome.⁵ Readings were performed by trained dermatologists only.

2.2 IVDK data

The Information Network of Departments of Dermatology (IVDK, www.ivdk.org) is a clinical network dedicated to the surveillance of contact allergy, based on routine patch test results. The methods have been described in detail;^{8,9} in brief, patch test results of all patients consulting in the participating departments, including the Jena department, along with pertinent demographic and clinical information, are recorded locally and transmitted, in a pseudonymised fashion, after informed consent of patients, to the IVDK data centre in Göttingen twice per year. After quality checks for completeness and consistency using the statistical software package SAS (version 9.4; SAS Institute, Cary, North Carolina), data are used for scientific analyses. For the present comparative analysis, only results with the German baseline series, age and sex of the Jena department, obtained between 2007 and 2012 (inclusive), in 1694 (83.2%) patients patch tested for suspected ACD with the German baseline series using pet./aq.-based, investigator-loaded allergens were included. The Jena Department used Allmiral Hermal (Reinbek, Germany) allergens in Finn Chambers on Scanpore tape. The duration of patch test exposure was 2 days. Two readings, at D2 and D3, were employed, the latter (or, exceptionally, if no D3 reading was performed, the D4 reading) was used as study outcome.

2.3 Corresponding allergen preparations

The allergen preparations included in the European baseline series (EBS) at the time are shown in **Table 1** with comments specific for “pairs” of allergens regarded as identical, similar, or at least grossly comparable. Sesquiterpene lactone (SL) mix and Compositae mix(es) (CM) only partially correspond: SL mix has 3 constituents, namely, alantolactone, dehydrocostus lactone and costunolide, while CM involve natural extracts – resulting in less standardised levels of actual allergens. CM I included *Tanacetum vulgare* (L.) (common tansy) 1% pet., *Arnica montana* (L.) (arnica) 0.5% pet., *Tanacetum parthenium* (L.) Sch. Bip. (feverfew; containing parthenolide) 0.1% pet., *Anthemis nobilis* (L.) (Roman chamomile) 1% pet., and *Achillea millefolium* (L.) (yarrow) 1% pet., and CM II which had to be used later due

to unavailability of CM I included *T. vulgare* 1% pet., *A. montana* 0.5% pet., *T. parthenium* 0.1% pet., *Anthemis nobilis* 1% pet., *Chamomilla recutita* (L.) Rauschert (German chamomile) 1% pet., and *A. millefolium* 1% pet.¹⁰

Some allergens included in the German baseline series during the study period were not included: oil of turpentine, cetearyl alcohol, zinc diethyldithiocarbamate, methyldibromo glutaronitrile, propolis, bufexamac, 2-bromo-2-nitropropan-1,3-diole (Bronopol), *Cananga odorata* (ylang-ylang I and II oil), *Santalum album* (sandalwood oil), and *Jasminum* spp (jasmine absolute). Some allergens of the EBS were neither tested in the EDEN study nor by the IVDK, including clioquinol, primin, and quaternium-15. *p*-Phenylene diamine (PPD) 1% pet. had not been tested in the German baseline series owing to perceived safety concerns,¹¹ and a reduced concentration for screening in the baseline series¹² had not yet been available for routine use. For the calculation of the percentage of participants/patients positive to at least one baseline series allergen, the set of corresponding allergens as shown in **Table 1** were considered.

(Include **Table 1** about here)

2.4 Statistical analysis

Suitable descriptive statistics, including direct age- and sex-standardisation of the prevalences stratified for study subgroup,³ were used to illustrate the differences of sensitisation frequencies between the two sub-samples, IVDK vs. EDEN. Moreover, in order to achieve an adjusted estimate of the increase or decrease of the probability (or risk) of testing positive in the clinical context, compared to the population level, log-binomial regression was utilised. This yielded a prevalence ratio (PR) as effect estimate, accompanied by a 95% confidence interval obtained by the profile likelihood method which provides more valid interval estimates in case of small to medium-sized samples than the standard asymptotic method. Each model (one for each allergen) was adjusted for sex and age, the latter dichotomised as for the MOAHLFA index,¹³ that is, the array of proportions of male patients, those with occupational dermatitis, atopic dermatitis, hand, leg, and face dermatitis, respectively, and the share of patients 40 years or older. This index has been expanded by including the “P measure”, which indicates the proportion of patients who have at least one positive reaction to allergens of the baseline series among those tested with it.¹⁴

3. Results

Regarding the patients patch tested in Jena, 36% were male, 21.1% suffered from occupational dermatitis (IVDK average in that period is approximately 16%),¹⁵ 16.7% had previous or current atopic eczema, 27.6% hand, 7.7% leg, and 13.7% face dermatitis, and 71.5% were age 40 and above. As almost all EDEN study participants were clear of dermatitis when patch tested (see 2.1), only sex and age can sensibly be compared: 48.3% were male and 55.9% age 40 and older. Thus, the distribution of age ($P < .0001$, Wilcoxon test) and sex ($P < .0001$, chi-square test) differed significantly. In view of this observation on the one hand, and the well-known association between age and sensitisation to many allergens, not to the least to the common fragrance allergens,¹⁶ an adjustment of

sensitisation prevalences for age and sex was deemed mandatory. Regarding the “P measure,”¹⁴ in the population sample, 27.2% were sensitised to at least one allergen, while in the clinical sample 44.2% were sensitised to at least one allergen of the full baseline series, that is, also including allergens not in the scope of the present analysis (**Table 1**). If the “P measure” is calculated for the more comparable set of allergens which are part of the European baseline series (**Table 1**), the respective percentages were 19.6% in the population sample and 41.1% in the clinical sample.

Age- and sex-standardised sensitisation prevalences to the scope of allergens considered are presented in **Table 2**, and separately the comparative prevalences for the 10 most common allergens in the EDEN part as **Figure 1**. The rightmost column includes the risk of testing positive if a patient compared to a participant of the EDEN study, adjusted for age and sex. The risk estimate is significant if the 95% confidence interval does not include unity ($PR=1$). For comparison, crude sensitisation prevalences with accompanying 95% CI have been calculated for the two samples (**Online supplemental table 3**) as well as for the two samples further stratified for sex (**Online supplemental table 4**) and age, dichotomised at age 40 (**Online supplemental table 5**), respectively. It is evident that all allergens were more common in the clinical sample, except for *p*-tert-butylphenol formaldehyde resin, which was significantly more often positive in the population sample, adjusted for age and sex, than all other comparisons. Some allergens tested less than twice as often positive in the clinical setting, including nickel, HICC, mercaptobenzothiazole and epoxy resin.

(Include **Table 2** about here)

Looking closer at the 3 most common allergens tested in both subsamples, 43 in the EDEN subgroup were positive only to nickel among all 54 nickel positives (79.6%), while in the IVDK subsample 120 were positive only to nickel among all 226 nickel positives (53.1%). Interestingly, the differences between EDEN and IVDK results especially in females were very small – in contrast to cobalt, which yielded significantly more reactions in female patients than in the female population. The age-stratified results (**Online supplemental table 5**) on the population level seem to indicate that the cohort effect for nickel has eliminated the age gradient while in patients, significantly more young patients (mostly females, see above) are sensitised than those age 40 and above. Regarding FM I, the numbers (percentages) of solitary reactions were 4 among all 12 positives (33.3%), while in the IVDK subsample the share was 35 of 141, ie 24.8%. Lastly in FM II, these numbers (percentages) were 2 among all 15 positives (13.3%), while in the IVDK subsample the share was 21 all 115, ie 18.3%. Thus, nickel was mostly a solitary allergen, particularly in the population.

Finally, the number of positive reactions to the set of allergens considered (**Table 1**) differed between the two subsamples: in the EDEN subsample, 80.4% tested entirely negative, 14% had one single reaction, 3.7% two reactions and 1.9% three or more positive reactions. In the clinical setting, the corresponding proportions were 58.9% being entirely negative, 22.5% with one single reaction, 9.3% with two reactions and 9.3% three or more positive reactions.

4. Discussion

The comparison of contact allergy prevalences obtained in the population and in patients tested for suspected ACD, respectively, is interesting because it illustrates selection processes, as discussed below, using some examples. The present comparison benefits from a high degree of methodological standardisation in the EDEN study,⁶ and a presumably largely representative sample, compared to a previous similar comparison in the region of Augsburg, Bavaria (Germany; KORA study)⁴, where, due to the sampling strategy employed, some selection bias by design may be suspected.¹ However, the EDEN study also may not be free of some selection bias, too: participation in initial recruitment had been reported to range between 20.3 and 50.7% in different regions,^{1,17,18} and a participation of less than 70% is considered to jeopardise non-selectiveness.¹ However the age and sex stratified replacement sampling used¹⁸ is capable of evening out numerical deficits appearing in certain strata, and confounding associated with these important variables. A general preference to take part by those having previously suffered from dermatitis (as one possibility of selection biasing prevalence estimates upwards) was avoided by framing the study as being on 'general health'. After taking part in the study all participants were debriefed that the focus was on skin diseases. Still, in conclusion, the extent and direction of putative selection effects can merely be speculated about.

The results, concerning the overall yield, the distribution of the number of positive reactions, and finally the comparison of prevalences for each allergen, confirm the impact of the morbidity-driven selection process, with one exception discussed further below. It needs to be considered, however, that for most allergens, two different test systems had been used, namely, the TRUE Test in the population sample, and investigator-loaded pet. and aq.-based test preparations in the clinic. In initial studies comparing TRUE Test allergens with the same allergens in pet., concordance has, unfortunately, not been adequately addressed for specific allergens. In general terms, it has been reported that among 698 patients, 309 reaction pairs were positive, while in 155 patches, there were discordant reactions.¹⁹ Similarly, in 245 Swedish patients, 121 concordant reaction pairs were observed, and 16 reactions only to TRUE Test, and 19 only with Finn chambers.²⁰ With a few exceptions noted since then, the diagnostic properties of the two test systems can probably be regarded as mostly equivalent. The exceptions are the standard TRUE Test preparation of FM I (however, the pet.-based test preparation[s] employed in the EDEN study have been deliberately used in the present analysis in lieu of this) with its strikingly poor sensitivity,^{7,21} and an apparently higher sensitivity of the MCI/MI TRUE Test preparation than of MCI/MI 0.01% aq. used in the IVDK part.²²

4.1 Metals

It is interesting to note that the most common contact allergen, nickel, is not significantly more commonly positive in the clinical setting, and the risk is just 18% higher than when testing a geographically and temporally matched population sample – and employing adjustment for age and sex, which is mandatory in this and most allergens to avoid confounding. Although selection bias is suspected in the above-mentioned KORA-based Augsburg study, a very similar result has been found there. The interpretation has been that

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contact allergy to nickel may often represent a “chance finding”, meaning this may not often be related to contact dermatitis leading to patch testing. Moreover, nickel allergy or more broadly “metal allergy” can often be self-diagnosed, and metal objects such as fashion jewellery, belt buckles or similar be avoided, preventing recurrences of ACD with some success – notwithstanding the multitude of partly less overt nickel exposures.²³

Continuing to discuss metal allergens, the situation of cobalt is entirely different to nickel: the likelihood of positive reactions is more than three times higher in the clinic than in the general population, and significantly so, very similar to many other allergens. This result may confer that it is less easy to identify and eliminate cobalt exposure for the patient. indeed, dermatologists also face difficulties in establishing clinical relevance of allergic patch test reactions to cobalt, being able to identify, eg, only 20% of reactions as clinically relevant.²⁴ This situation will hopefully improve with the relatively recent availability of a cobalt spot test or of a hand-held X-ray fluorescence device,²⁵ and certainly with more evidence from quantitative analyses of consumer items such as costume jewellery.²⁶ Exposure to chromium-VI (dichromate) has been regulated in Europe first regarding cement exposure and in 2014 regarding exposure by chromium-tanned leather, leading to some decline in sensitisation incidence.²⁷ It may be justified to postulate similar difficulties for the patient to trace eliciting exposures to chromium, hence, the PR very similar to that found for cobalt is plausible.

4.2 Preservatives

The prevalence of sensitisation to MCI/MI also differs by a factor of around 3, still being on the relatively low level before onset of the MI contact allergy epidemic, which also became apparent by drastically increasing the frequency of positive reactions to MCI/MI.²⁸ Sensitisation to formaldehyde is just slightly (and non-significantly) more common in the clinical setting. This may at least be partly explained by a certain share of false-negative reactions using formaldehyde 1% aq. (in the IVDK) and not 2% aq., as recommended.^{29,30} By contrast, positive reactions to parabens are extremely rare in the population, and rare even in the clinical setting; nevertheless, the 6-fold increased risk could be indicative of a certain share of polysensitised patients, possibly with chronic (lower leg) dermatitis, who are more prone to become sensitised by these very weak allergens. Methylidibromo glutaronitrile (MDBGN) has only been tested in the clinical setting; the apparent increase of sensitisation prevalence associated with the use of the 0.3% patch test concentration in lieu of the formerly used 0.2% pet is very likely related to this increase in test concentration.³¹ However, under the synonym 2-bromo-2-(bromomethyl)pentanedinitrile (DBDCB) MDBGN still is one of the permitted preservatives in the EU for “product type 6”, that is, for preservation during storage of products other than foodstuffs, feeding stuffs, cosmetics or medicinal products or medical devices.³² Examples of non-cosmetic exposures associated with MDBGN have been reviewed recently,³³ and hence it may be premature to regard the still high number of patients sensitised to MDBGN³⁴ as an entirely “historical” problem.

4.3 Fragrances

Fragrance mix (FM) I had been tested in triplicate in the EDEN study;⁷ for the present comparison, the “high (chlor)atranol content” version was regarded as most similar to the

regular patch test material, but yielded an identical number of positive reactions in the Jena EDEN subsample (**Table 2**). In the clinical setting, a 3-fold higher prevalence was observed, in contrast to the KORA study, where FM I, similar to nickel, nearly reached the population prevalence in the patch tested patients.⁴ However, as mentioned, the KORA results must be interpreted with caution; specifically, study participants with past rashes due to fragrance allergy may have been over-represented, which would (partly) explain the high population prevalence.¹ Compared to FM I, the sensitisation prevalence to FM II in patients is just twice that of the population sample, and HICC sensitisation is merely 42% more common in patients than in the population setting; hence, the special result for HICC will have an impact on the FM II estimate. The reasons for the relative similarity of HICC sensitisation prevalences are unclear. Many cases of HICC contact allergy may have occurred due to sensitisation and elicitation of ACD by formerly used deodorants, that is, an easily identifiable cause which may have prompted avoidance of fragrance-, and thus HICC-, containing products even without patch test diagnosis, similar to the putative “self-management” discussed regarding nickel. However, this is an entirely speculative explanation. *Myroxylon pereirae* resin (balsam of Peru), although not used as such in perfumes, but only in terms of extracts and distillates thereof,³⁵ is often regarded as an “ill-defined” fragrance marker owing to the fact that several of its single constituents are found in fragrances.³⁶ From this background, it is striking that with a prevalence ratio of almost 10 contact allergy prevalence is much higher in the clinical sample than that of other fragrance allergens. Could this point to sensitising exposures, or perhaps to a greater susceptibility, typical for the polysensitised which may be overrepresented among patients, compared to the population? The present observation adds another facet to this allergen’s enigma.

4.4 Plant- and animal-derived materials

The crude prevalence ratio for colophonium is around 15, and the adjusted PR considerably higher, which is indicative of some confounding by age and sex. At any rate, colophonium is the allergen with the greatest discrepancy between population and clinical results, with just one positive test reactions among the former vs. a prevalence of 4.57% which is just slightly higher than that found in the IVDK overall (3.47% [95% CI: 3.3–3.64%] in males and 4.0% [95% CI: 3.86–4.14%] in females).¹⁵ The comparison between sesquiterpene lactone mix (SLM) and Compositae mix I (CM I) results are difficult to interpret, owing to the differing constituents. In an IVDK study, 250 patients reacted both to one of the CMs and SLM, 89 only to SLM, and 283 only to CM;¹⁰ hence, the sensitivity of CM may be higher, thereby partly explaining the higher sensitisation prevalence found in clinical testing. Lanolin alcohol has been a dominating allergen in the previous Augsburg-centred comparison, with 7.9% positives, explained by a strong phlebological/leg dermatitis background at that department,⁴ while, in contrast, the prevalence in Jena is certainly higher than on the population level (PR=4.72), and also higher than in the IVDK average (2.1% in males [95% CI: 1.97–2.24%], 2.39% in females [95% CI: 2.29–2.5%])¹⁵ but not to such an outstanding extent as in Augsburg.

4.5 Rubber, resins and other contact allergens

The medicaments included in the EBS, namely, neomycin sulfate, budesonide, tixocortol-21-pivalate, and benzocaine (or, starting 2019, caine mix III)³⁰ have not been (during the study

period), and are not part of the German baseline series; thus, a comparison with clinical sensitisation prevalences is not possible. Among the rubber chemicals, thiuram mix was a significantly more common contact allergen in the clinical sample, probably indicating that hand eczema due to gloves, as most likely eliciting exposure, may have been the reason for many consultations for patch testing. The picture for the two benzothiazole test preparations, which are less frequent allergens, is less clear, but similar. A striking observation is a much higher yield of positive reactions to IPPD than to black rubber mix (PR=7.74) despite the fact that IPPD is only one of the three ingredients of black rubber mix (along with N-cyclohexyl-N'-phenyl-*p*-phenylenediamine and N, N'-diphenyl *p*-phenylenediamine), and thus exhibit a lower sensitivity, as cross-reactivity between IPPD and the two other derivatives is limited.³⁷ Thus, the high prevalence of IPPD patch test reactions in patients of the Jena department of 1.42% (slightly in excess of the IVDK average: 0.95% [95%CI: 0.86–1.04] in males and 0.62% [95%CI: 0.56–0.68] in females)¹⁵ may to some extent be due to the slightly higher share of patients with occupational dermatitis in Jena, compared to the IVDK average, IPPD often being an occupational allergen. Epoxy resin (in terms of the diglycidyl ether of bisphenol A tested in the baseline series) is also often an occupational allergen. Thus, the relatively high prevalence of contact allergy in the population of 1.33%, not significantly different from the prevalence found in patients (1.75%), is surprising. Optical industries in or near Jena may be an explanation for some background sensitisation, as these use epoxy resin systems in lens manufacture. The only allergen which was significantly more common on the population level than in patients tested for suspected ACD was *p*-*tert*-butylphenol formaldehyde resin, an adhesive often used in the production of shoes. An even higher prevalence of 1.9% contact allergy – interestingly, also using the TRUE Test material – has been noted in a population-based study of adolescents in Sweden, where PTBFR was the third most common contact allergen.³⁸ Hence the question arises whether this somewhat counter-intuitive difference in Jena, and generally the high prevalence in the population, may be related to the use of this particular patch test material.

5. Conclusion

The observed differences mostly confirm notions of morbidity-driven selection, which may also vary between departments, owing to their specialties and catchment areas, respectively. For instance, the phlebological background of the department was reflected in such differences in a previous, similar study centred around Augsburg, Germany.⁴ Differences between different allergens are obvious, and several more or less hypothetical interpretations have been discussed above. Also based on the EDEN study results of one department (Groningen, The Netherlands), sensitisation prevalences to PPD have been compared between population (1.3%) and patients (3.3%), and causative exposures been investigated,³⁹ albeit addressing only this one allergen from the EBS so far.

More comparisons between clinical and population-based patch test data would be highly desirable to possibly arrive at a more general understanding of the selection process until patch testing. This could also help validating the CE-DUR approach of extrapolating patch test results from a sufficiently large and representative national network to a putative population prevalence or incidence of specific contact allergies.^{40,41}

Figure 1: Comparative prevalences of the 10 most common EDEN study contact allergens (dark shade) and the corresponding sensitization prevalences in the IVDK part of the study (light shade). CI, confidence interval; HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; PTBFR, *p*-*tert*-butylphenol formaldehyde resin; PR, prevalence ratio (adjusted for age and sex, see Table 2).

Table 1: Baseline series allergens included in the present comparative analysis. Conc., concentration; pet., petrolatum; TT, TRUE Test matrix as vehicle.

EDEN		IVDK	
Allergen preparation	Conc., vehicle	Allergen preparation	Conc., vehicle
Metals			
Nickel sulfate	0.2 mg/cm ²	Nickel sulfate	5% pet.
Cobalt chloride	0.02 mg/cm ²	Cobalt chloride	1% pet.
Potassium dichromate	0.023 mg/cm ²	Potassium dichromate	0.5% pet.
Preservatives			
Cl+Me-isothiazolinone (MCI/MI)	0.004 mg/cm ²	MCI/MI	0.01% aq.
Formaldehyde	0.18 mg/cm ²	Formaldehyde	1% aq.
Parabens mix	1.0 mg/cm ²	Paraben mix	16% pet.
		Methyldibromo glutaronitrile	0.2%/0.3% pet.
Fragrances			
Fragrance mix (FM) I ^{a)}	8% pet.	FM I	8% pet.
FM I ^{b)}	8% pet.		
FM II	14% pet.	FM II	14% pet.
HICC	5% pet.	HICC	5% pet.
<i>Myroxylon pereirae</i> (balsam of Peru)	0.8 mg/cm ²	<i>Myroxylon pereirae</i>	25% pet.
Plants (other)			
Colophony 850 (Rosin)	1.2 mg/cm ²	Colophonium	20% pet.
Sesquiterpene lactone mix	0.1% pet.	Compositae mix I/II	5% pet.
Medicaments, excipients			
Wool alcohols (lanolin)	1.0 mg/cm ²	Lanolin alcohols	30% pet.
Neomycin sulfate	0.23 mg/cm ²		
Budesonide	0.001 mg/cm ²		

EDEN		IVDK	
Tixocortol-21-pivalate	0.33 mg/cm ²		
Caine mix	0.63 mg/cm ²		
Rubber additives			
Thiuram mix	0.025 mg/cm ²	Thiuram mix	1% pet.
Mercaptobenzothiazole (MBT)	0.0075 mg/cm ²	MBT	2% pet.
Mercapto mix	0.075 mg/cm ²	Mercapto mix (CBS, MOR, CBT)	1% pet.
Black rubber mix	0.075 mg/cm ²	IPPD	0.1% pet.
Resins and miscellaneous			
Epoxy resin	0.05 mg/cm ²	epoxy resin	1% pet.
PTBFR	0.045 mg/cm ²	PTBRF	1% pet.
<i>p</i> -Phenylenediamine (PPD)	0.09 mg/cm ²		

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PTBFR, *p*-*tert*-butylphenol formaldehyde resin;

^{a)} high concentration of atranol and chloratranol

^{b)} low concentration of atranol and chloratranol

Table 2: Patch test results with the baseline series in the EDEN and IVDK subsamples, respectively, in Jena. pos, age- and sex-standardised prevalence with accompanying confidence interval (CI). The rightmost column includes a prevalence ratio (PR) with accompanying 95% CI quantifying the risk of testing positive to the allergen in question in the clinical vs. the population setting, adjusted for age (dichotomised at 40) and sex. For concentration and vehicle, see Table 1.

Allergen	EDEN				IVDK				PR (95% CI)
	tested	n(pos)	pos.	(95% CI)	tested	n(pos)	pos.	(95% CI)	
Nickel sulfate	515	54	12.31	(9.2–15.43)	1662	225	14.83	(12.95–16.72)	1.18 (0.90- 1.57)
Cobalt chloride	515	8	1.51	(0.4–2.61)	1680	85	5.73	(4.45–7.01)	3.30 (1.71- 7.39)
Potassium dichromate	515	6	1.32	(0.2–2.44)	1676	70	3.68	(2.75–4.61)	3.39 (1.61- 8.74)
MCI/MI	515	3	0.75	(0–1.63)	1699	35	1.96	(1.25–2.66)	3.34 (1.20- 13.85)
Formaldehyde	515	3	0.62	(0–1.31)	1687	25	1.15	(0.68–1.63)	2.54 (0.90- 10.65)
Paraben mix	514	1	0.21	(0–0.61)	1688	21	1.11	(0.58–1.64)	6.36 (1.32- 114.41)
Methyldibromo glutaronitrile (0.2%)					1186	31	2.08	(1.3–2.85)	
Methyldibromo glutaronitrile (0.3%)					528	25	3.38	(2.1–4.66)	
Fragrance mix (FM) I ^{a)}	504	12	2.32	(0.96–3.67)	1688	141	7.79	(6.43–9.15)	3.34 (1.95- 6.35)
FM I ^{b)}	515	12	2.55	(1.07–4.03)					
FM II	515	15	3.02	(1.47–4.56)	1698	114	6.05	(4.87–7.23)	2.08 (1.27- 3.70)
HICC	515	12	2.23	(0.94–3.52)	1691	64	3.33	(2.46–4.2)	1.42 (0.80- 2.76)
<i>Myroxylon pereirae</i> (balsam of Peru)	515	5	0.83	(0.09–1.57)	1677	171	8.88	(7.48–10.27)	9.69 (4.45- 27.20)
Colophonium	515	1	0.3	(0–0.89)	1695	80	4.57	(3.49–5.65)	23.85 (5.31- 420.74)

Allergen	EDEN				IVDK				PR (95% CI)
	tested	n(pos)	pos.	(95% CI)	tested	n(pos)	pos.	(95% CI)	
SL / Compositae mix	515	1	0.21	(0–0.61)	1403	43	2.46	(1.7–3.22)	13.46 (2.97- 237.94)
Compositae mix II					310	11	3.24	(1.11–5.36)	
Lanolin alcohols	515	4	1.04	(0–2.08)	1684	69	3.73	(2.78–4.68)	4.72 (1.96- 15.50)
Neomycin sulfate	515	1	0.3	(0–0.89)					
Budesonide	515	3	0.64	(0–1.4)					
Tixocortol-21-pivalate	515	3	0.55	(0–1.17)					
Caine mix III	515	3	0.56	(0–1.2)					
Thiuram mix	515	5	1.09	(0.09–2.09)	1695	50	3.06	(2.14–3.98)	
Mercaptobenzothiazole	515	2	0.41	(0–0.98)	1701	10	0.6	(0.19–1.02)	1.55 (0.40- 10.29)
Mercapto mix	515	1	0.15	(0–0.44)	1701	11	0.66	(0.23–1.08)	3.81 (0.72- 70.56)
Black rubber mix / IPPD	515	1	0.13	(0–0.4)	1686	23	1.42	(0.77–2.06)	7.74 (1.61- 139.21)
Epoxy resin	515	7	1.33	(0.31–2.36)	1686	36	1.75	(1.13–2.37)	1.49 (0.70- 3.66)
PTBFR	515	8	1.51	(0.4–2.61)	1690	8	0.33	(0.1–0.56)	0.29 (0.11- 0.80)
<i>p</i> -Phenylenediamine	515	3	0.71	(0–1.53)					

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PTBFR, *p*-*tert*-butylphenol formaldehyde resin; SL, sesquiterpene lactone

^{a)} high concentration of atranol and chloratranol

^{b)} low concentration of atranol and chloratranol

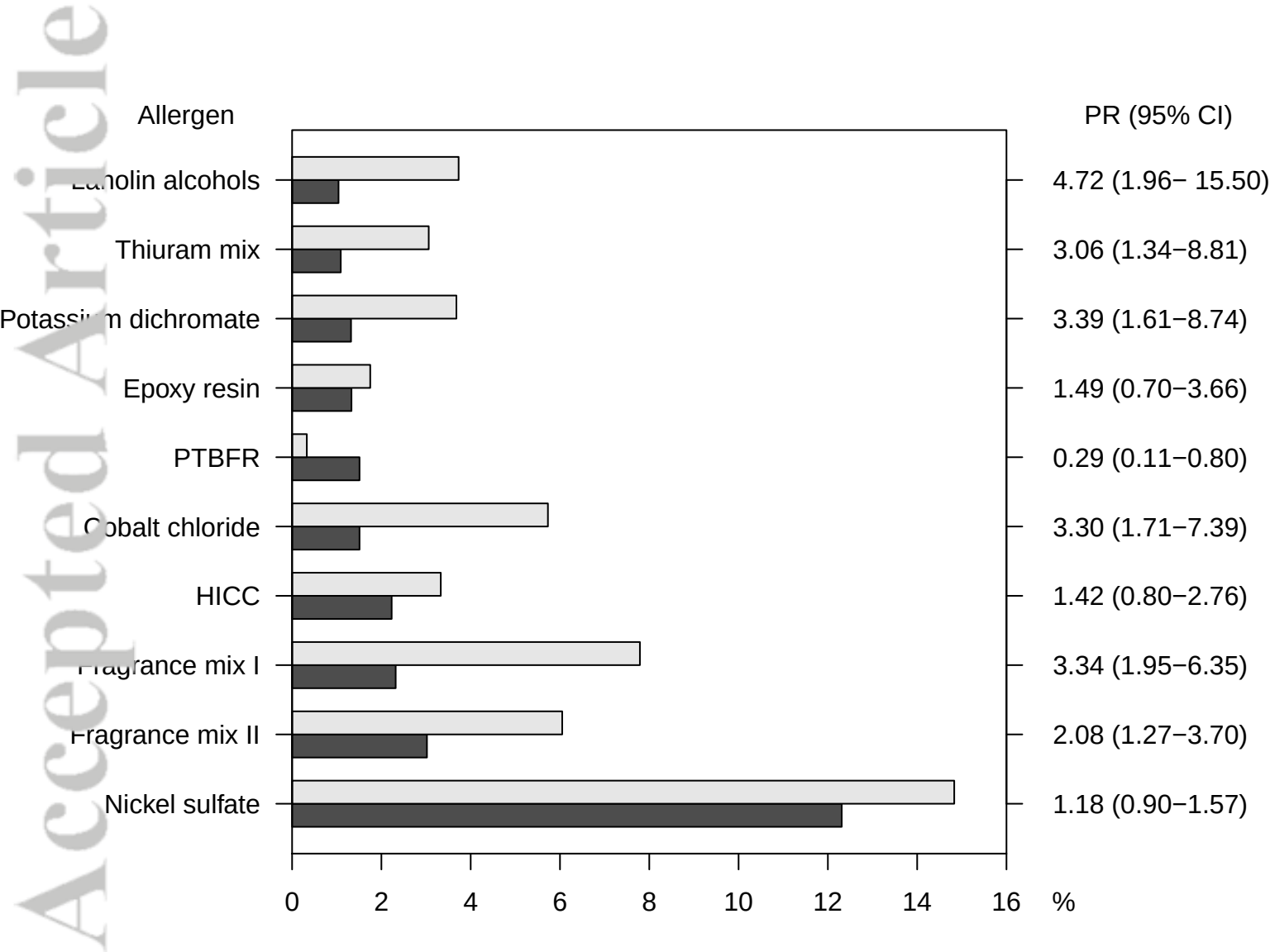
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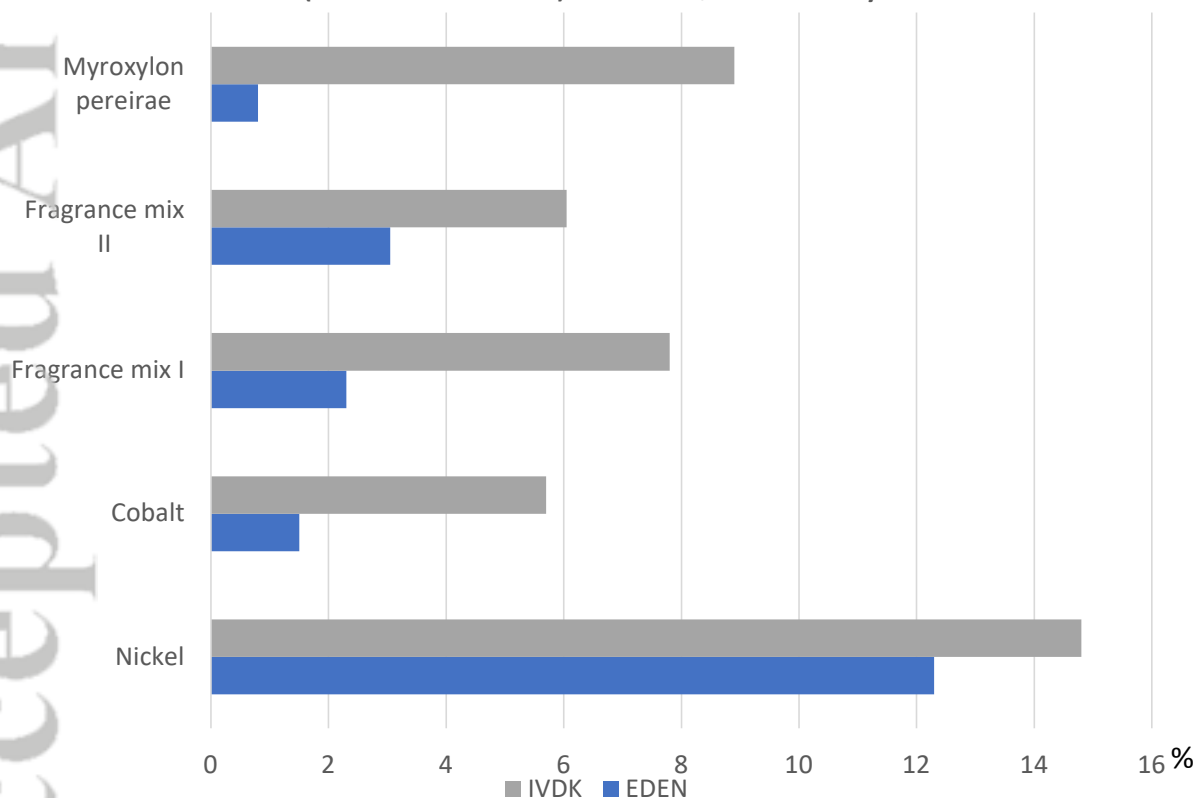
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Comparative prevalences of sensitisation between a population sample (EDEN study) and clinical patients (IVDK network) in Jena, Germany



- Generally, contact allergy prevalences are higher in the clinic owing to morbidity-driven selection
- If exposure to an individual allergen can be avoided by self-management (e.g., in nickel allergy), resulting allergic contact dermatitis may less often be a reason to consult, and prevalences may be more similar – compared e.g. to cobalt
- In the clinic, older and polysensitised patients are over-represented, and with them, multiple, strongly age-associated contact allergies, e.g., to *Myroxylon pereirae* (balsam of Peru)

Online supplemental table 3: Patch test results with the baseline series in the EDEN and IVDK subsamples, respectively, in Jena., presenting crude prevalences with accompanying confidence interval (CI). For concentration and vehicle, see Table 1.

Allergen	EDEN				IVDK			
	tested	n(pos)	pos.	(95% CI)	tested	n(pos)	pos.	(95% CI)
Nickel sulfate	515	54	10.49	(7.98–13.46)	1662	225	13.54	(11.93–15.28)
Cobalt chloride	515	8	1.55	(0.67–3.04)	1680	85	5.06	(4.06–6.22)
Potassium dichromate	515	6	1.17	(0.43–2.52)	1676	70	4.18	(3.27–5.25)
MCI/MI	515	3	0.58	(0.12–1.69)	1699	35	2.06	(1.44–2.85)
Formaldehyde	515	3	0.58	(0.12–1.69)	1687	25	1.48	(0.96–2.18)
Paraben mix	514	1	0.19	(0–1.08)	1688	21	1.24	(0.77–1.9)
Methyldibromo glutaronitrile (0.2%)					1186	31	2.61	(1.78–3.69)
Methyldibromo glutaronitrile (0.3%)					528	25	4.73	(3.09–6.91)
Fragrance mix (FM) I ^{a)}	504	12	2.38	(1.24–4.12)	1688	141	8.35	(7.08–9.78)
FM I ^{b)}	515	12	2.33	(1.21–4.03)				
Fragrance mix II	515	15	2.91	(1.64–4.76)	1698	114	6.71	(5.57–8.01)
HICC	515	12	2.33	(1.21–4.03)	1691	64	3.78	(2.93–4.81)
<i>Myroxylon perei</i> (balsam of Peru)	515	5	0.97	(0.32–2.25)	1677	171	10.2	(8.79–11.75)
Colophonium	515	1	0.19	(0–1.08)	1695	80	4.72	(3.76–5.84)
SL / Compositae mix	515	1	0.19	(0–1.08)	1403	43	3.06	(2.23–4.11)
Compositae mix II					310	11	3.55	(1.78–6.26)
Lanolin alcohols	515	4	0.78	(0.21–1.98)	1684	69	4.1	(3.2–5.16)
Neomycin sulfate	515	1	0.19	(0–1.08)				
Budesonide	515	3	0.58	(0.12–1.69)				

Allergen	EDEN				IVDK			
	tested	n(pos)	pos.	(95% CI)	tested	n(pos)	pos.	(95% CI)
Tixocortol-21-pivalate	515	3	0.58	(0.12–1.69)				
Caine mix III	515	3	0.58	(0.12–1.69)				
Thiuram mix	515	5	0.97	(0.32–2.25)	1695	50	2.95	(2.2–3.87)
Mercaptobenzothiazole	515	2	0.39	(0.05–1.4)	1701	10	0.59	(0.28–1.08)
Mercapto mix	515	1	0.19	(0–1.08)	1701	11	0.65	(0.32–1.15)
Black rubber mix / IPPD	515	1	0.19	(0–1.08)	1686	23	1.36	(0.87–2.04)
Epoxy resin	515	7	1.36	(0.55–2.78)	1686	36	2.14	(1.5–2.94)
PTBFR	515	8	1.55	(0.67–3.04)	1690	8	0.47	(0.2–0.93)
<i>p</i> -Phenylenediamine	515	3	0.58	(0.12–1.69)				

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PTBFR, *p*-*tert*-butylphenol formaldehyde resin; SL, sesquiterpene lactone

a) high concentration of atranol and chloratranol

b) low concentration of atranol and chloratranol

Online supplemental table 4: Patch test results with the baseline series in the EDEN and IVDK subsamples, respectively, in Jena, presenting crude prevalences in the two strata according to sex with accompanying confidence interval (CI). For concentration and vehicle, see Table 1.

Allergen	EDEN: male		IVDK: male		EDEN: female		IVDK: female	
	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)
Nickel sulfate	9/249	3.61 (1.67–6.75)	33/615	5.37 (3.72–7.45)	45/266	16.92 (12.62–21.97)	193/1048	18.42 (16.11–20.9)
Cobalt chloride	5/249	2.01 (0.66–4.62)	22/612	3.59 (2.27–5.39)	3/266	1.13 (0.23–3.26)	64/1069	5.99 (4.64–7.58)
Potassium dichromate	3/249	1.2 (0.25–3.48)	31/608	5.1 (3.49–7.16)	3/266	1.13 (0.23–3.26)	40/1069	3.74 (2.69–5.06)
MCI/MI	1/249	0.4 (0.01–2.22)	12/619	1.94 (1.01–3.36)	2/266	0.75 (0.09–2.69)	23/1081	2.13 (1.35–3.18)
Formaldehyde	0/249	0 (0–1.47)	9/612	1.47 (0.67–2.77)	3/266	1.13 (0.23–3.26)	16/1076	1.49 (0.85–2.4)
Paraben mix	0/248	0 (0–1.48)	12/610	1.97 (1.02–3.41)	1/266	0.38 (0.01–2.08)	9/1079	0.83 (0.38–1.58)
Methyldibromo glutaronitrile (0.2%)	/		14/444	3.15 (1.73–5.23)	/		17/742	2.29 (1.34–3.64)
Methyldibromo glutaronitrile (0.3%)	/		9/178	5.06 (2.34–9.38)	/		16/350	4.57 (2.64–7.32)
Fragrance mix (FM) I ^{a)}	5/243	2.06 (0.67–4.74)	52/617	8.43 (6.36–10.91)	7/261	2.68 (1.08–5.45)	89/1072	8.3 (6.72–10.12)
FM I ^{b)}	3/249	1.2 (0.25–3.48)	/		9/266	3.38 (1.56–6.33)	/	
Fragrance mix II	4/249	1.61 (0.44–4.06)	37/618	5.99 (4.25–8.16)	11/266	4.14 (2.08–7.28)	78/1081	7.22 (5.75–8.92)

Allergen	EDEN: male		IVDK: male		EDEN: female		IVDK: female	
	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)	pos/tested	% pos. (95% CI)
HICC	5/249	2.01 (0.66–4.62)	18/612	2.94 (1.75–4.61)	7/266	2.63 (1.06–5.35)	46/1080	4.26 (3.13–5.64)
<i>Myroxylon pereirae</i> (balsam of Peru)	3/249	1.2 (0.25–3.48)	63/612	10.29 (8–12.98)	2/266	0.75 (0.09–2.69)	109/1066	10.23 (8.47–12.2)
Colophonium	0/249	0 (0–1.47)	30/616	4.87 (3.31–6.88)	1/266	0.38 (0.01–2.08)	50/1080	4.63 (3.46–6.06)
SL / Compositae mix I	0/249	0 (0–1.47)	15/618	2.43 (1.36–3.97)	1/266	0.38 (0.01–2.08)	39/1082	3.6 (2.58–4.89)
Compositae mix II	/		3/114	2.63 (0.55–7.5)	/		8/196	4.08 (1.78–7.88)
Lanolin alcohols	1/249	0.4 (0.01–2.22)	21/611	3.44 (2.14–5.21)	3/266	1.13 (0.23–3.26)	48/1074	4.47 (3.31–5.88)
Neomycin sulfate	0/249	0 (0–1.47)	/		1/266	0.38 (0.01–2.08)	/	
Budesonide	1/249	0.4 (0.01–2.22)	/		2/266	0.75 (0.09–2.69)	/	
Tixocortol-21- pivalate	1/249	0.4 (0.01–2.22)	/		2/266	0.75 (0.09–2.69)	/	
Caine mix III	1/249	0.4 (0.01–2.22)	/		2/266	0.75 (0.09–2.69)	/	
Thiuram mix	2/249	0.8 (0.1–2.87)	19/616	3.08 (1.87–4.77)	3/266	1.13 (0.23–3.26)	31/1080	2.87 (1.96–4.05)
Mercapto- benzothiazole	0/249	0 (0–1.47)	5/619	0.81 (0.26–1.87)	2/266	0.75 (0.09–2.69)	5/1083	0.46 (0.15–1.07)
Mercapto mix	1/249	0.4 (0.01–2.22)	3/618	0.49 (0.1–1.41)	0/266	0 (0–1.38)	8/1084	0.74 (0.32–1.45)

Allergen	EDEN: male pos/tested	% pos. (95% CI)	IVDK: male pos/teste d	% pos. (95% CI)	EDEN: female pos/tested	% pos. (95% CI)	IVDK: female pos/tested	% pos. (95% CI)
Black rubber mix / IPPD	1/249	0.4 (0.01–2.22)	10/610	1.64 (0.79–2.99)	0/266	0 (0–1.38)	13/1077	1.21 (0.64–2.06)
Epoxy resin	3/249	1.2 (0.25–3.48)	19/610	3.11 (1.89–4.82)	4/266	1.5 (0.41–3.81)	17/1077	1.58 (0.92–2.52)
PTBFR	5/249	2.01 (0.66–4.62)	3/613	0.49 (0.1–1.42)	3/266	1.13 (0.23–3.26)	5/1078	0.46 (0.15–1.08)
<i>p</i> -Phenylene- diamine	0/249	0 (0–1.47)	/		3/266	1.13 (0.23–3.26)	/	

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, *N*-isopropyl-*N'*-phenyl-*p*-phenylendiamin; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PTBFR, *p*-*tert*-butylphenol formaldehyde resin; SL, sesquiterpene lactone

a) high concentration of atranol and chloratranol

b) low concentration of atranol and chloratranol

Online supplemental table 5: Patch test results with the baseline series in the EDEN and IVDK subsamples, respectively, in Jena, presenting crude prevalences in the two strata according to age, dichotomised into < 40 vs. 40+, with accompanying confidence interval (CI). For concentration and vehicle, see Table 1.

Allergen	EDEN: <40		IVDK: <40		EDEN: 40+		IVDK: 40+	
	pos/test ed	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tested	% pos. (95% CI)
Nickel sulfate	22/227	9.69 (6.17–14.31)	87/487	17.86 (14.56–21.56)	32/288	11.11 (7.73–15.32)	139/1176	11.82 (10.03–13.8)
Cobalt chloride	4/227	1.76 (0.48–4.45)	37/485	7.63 (5.43–10.36)	4/288	1.39 (0.38–3.52)	49/1196	4.1 (3.05–5.38)
Potassium dichromate	4/227	1.76 (0.48–4.45)	13/486	2.67 (1.43–4.53)	2/288	0.69 (0.08–2.49)	58/1191	4.87 (3.72–6.25)
MCI/MI	3/227	1.32 (0.27–3.81)	9/497	1.81 (0.83–3.41)	0/288	0 (0–1.27)	26/1203	2.16 (1.42–3.15)
Formaldehyde	0/227	0 (0–1.61)	2/487	0.41 (0.05–1.48)	3/288	1.04 (0.22–3.01)	23/1201	1.92 (1.22–2.86)
Paraben mix	0/226	0 (0–1.62)	4/486	0.82 (0.22–2.09)	1/288	0.35 (0.01–1.92)	17/1203	1.41 (0.83–2.25)
Methyldibromo glutaronitrile (0.2%)	/		3/341	0.88 (0.18–2.55)	/		28/845	3.31 (2.21–4.75)
Methyldibromo glutaronitrile (0.3%)	/		0/158	0 (0–2.31)	/		25/370	6.76 (4.42–9.81)
Fragrance mix (FM) I ^{a)}	3/225	1.33 (0.28–3.85)	31/498	6.22 (4.27–8.72)	9/279	3.23 (1.49–6.04)	110/1191	9.24 (7.65–11.02)
FM I ^{b)}	4/227	1.76 (0.48–4.45)	/		8/288	2.78 (1.21–5.4)	/	
Fragrance mix II	4/227	1.76 (0.48–4.45)	22/498	4.42 (2.79–6.61)	11/288	3.82 (1.92–6.73)	93/1201	7.74 (6.3–9.4)
HICC	3/227	1.32 (0.27–3.81)	11/487	2.26 (1.13–4.01)	9/288	3.12 (1.44–5.85)	53/1205	4.4 (3.31– 5.71)

Allergen	EDEN: <40		IVDK: <40		EDEN: 40+		IVDK: 40+	
	pos/test ed	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tested	% pos. (95% CI)
<i>Myroxylon pereirae</i> (balsam of Peru)	1/227	0.44 (0.01–2.43)	27/485	5.57 (3.7–8)	4/288	1.39 (0.38–3.52)	145/1193	12.15 (10.35–14.14)
Colophonium	1/227	0.44 (0.01–2.43)	21/497	4.23 (2.63–6.39)	0/288	0 (0–1.27)	59/1199	4.92 (3.77–6.3)
SL / Compositae mix I	0/227	0 (0–1.61)	6/498	1.2 (0.44–2.6)	1/288	0.35 (0.01–1.92)	48/1202	3.99 (2.96–5.26)
Compositae mix II	/		2/83	2.41 (0.29–8.43)	/		9/227	3.96 (1.83–7.39)
Lanolin alcohols	3/227	1.32 (0.27–3.81)	14/487	2.87 (1.58–4.78)	1/288	0.35 (0.01–1.92)	55/1198	4.59 (3.48–5.93)
Neomycin sulfate	1/227	0.44 (0.01–2.43)	/		0/288	0 (0–1.27)	/	
Budesonide	1/227	0.44 (0.01–2.43)	/		2/288	0.69 (0.08–2.49)	/	
Tixocortol-21-pivalate	0/227	0 (0–1.61)	/		3/288	1.04 (0.22–3.01)	/	
Caine mix III	1/227	0.44 (0.01–2.43)	/		2/288	0.69 (0.08–2.49)	/	
Thiuram mix	3/227	1.32 (0.27–3.81)	17/496	3.43 (2.01–5.43)	2/288	0.69 (0.08–2.49)	33/1200	2.75 (1.9–3.84)
Mercaptobenzothiazole	0/227	0 (0–1.61)	3/498	0.6 (0.12–1.75)	2/288	0.69 (0.08–2.49)	7/1204	0.58 (0.23–1.19)
Mercapto mix	1/227	0.44 (0.01–2.43)	3/498	0.6 (0.12–1.75)	0/288	0 (0–1.27)	8/1204	0.66 (0.29–1.31)
Black rubber mix / IPPD	0/227	0 (0–1.61)	7/486	1.44 (0.58–2.95)	1/288	0.35 (0.01–1.92)	16/1201	1.33 (0.76–2.15)
Epoxy resin	2/227	0.88	4/485	0.82	5/288	1.74	32/1202	2.66

Allergen	EDEN: <40		IVDK: <40		EDEN: 40+		IVDK: 40+	
	pos/test ed	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tes ted	% pos. (95% CI)	pos/tested	% pos. (95% CI)
		(0.11–3.15)		(0.23–2.1)		(0.57–4)		(1.83–3.74)
PTBFR	4/227	1.76 (0.48–4.45)	0/487	0 (0–0.75)	4/288	1.39 (0.38–3.52)	8/1204	0.66 (0.29–1.31)
<i>p</i> -Phenylenediamine	1/227	0.44 (0.01–2.43)	/		2/288	0.69 (0.08–2.49)	/	

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; IPPD, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; PTBFR, *p*-*tert*-butylphenol formaldehyde resin; SL, sesquiterpene lactone

a) high concentration of atranol and chloratranol

b) low concentration of atranol and chloratranol