

UK trends of allergic occupational skin disease attributed to fragrances 1996–2015

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Summary

Background. Fragrances are well known to cause allergic contact dermatitis (ACD). Occupationally related cases occur, with certain groups being at higher risk.

Objective. To investigate the incidence of occupationally related cases of cutaneous fragrance allergy and to evaluate trends.

Method. Data on incident cases of occupational ACD caused by fragrances between 1996 and 2015 (inclusive) reported to the EPIDERM surveillance scheme were analysed.

Results. Of the cases reported to EPIDERM during the study period, 5.2% had ACD attributed to fragrances. The highest annual incidence rates were observed in women. Hairdressers, beauticians and people working in related occupations had a 47-fold higher incidence rate ratio than the reference category (the average of all other occupations combined). Trends analysis suggested a non-significant increase in fragrance allergy over the study period among all occupations, and beauty and food workers, and a slight decrease in healthcare workers.

Conclusions. Fragrance allergy is a significant problem in an occupational setting. Although there was no significant change in the incidence of fragrance-related allergic occupational contact dermatitis (OCD) during the 20-year study period, this does not mirror the trend in OCD, which is falling. Fragrance allergy continues to be a major contributor to OCD, and contributes to a greater proportion of cases.

Key words: beauticians; epidemiology; food handlers; fragrance allergy; healthcare workers; occupation.

Fragrances are well known to cause allergic contact dermatitis (ACD). At least 2% of the general population are fragrance-allergic (1), and epidemiological studies suggest an increasing prevalence of fragrance allergy (2). Rastogi et al. studied the fragrance constituents in 59 domestic and occupational products. The fragrances most

commonly utilized in these products included limonene (78%), linalool (61%), citronellol (47%), eucalyptol (41%), geraniol (41%), and α -pinene (39%). These results highlight the fact that patch testing with screening fragrances in the baseline series alone may miss important fragrance allergies (2). The present study was aimed at investigating the incidence of occupationally related cases of ACD attributed to fragrances, and evaluating trends as reported to the EPIDERM surveillance scheme within The Health and Occupation Research (THOR) Network (3).

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Methods

We analysed data on incident cases of occupational ACD attributed to fragrances prospectively reported to

EPIDERM between 1996 and 2015 (inclusive). EPIDERM, a component of THOR, is the UK-wide voluntary surveillance scheme, established in February 1993. It enables consultant dermatologists to report incident cases of any skin disease that they believe to have been caused or aggravated by work (3). The diagnosis of ACD was based on positive patch test reactions, with readings on day (D) 2 and D4, and reactions scored in accordance with the ICDRG, alongside a corroborative history of exposures in an occupational setting (4). Physicians participate either on a monthly basis ('core' reporters) or for one randomly selected month per year ('sample' reporters). For each case, the following data were collected: diagnosis, patient demographics, employment, and suspected agents. The scheme does not record the body site affected, and relies on the reporter's option to specify the results for the allergens tested (that is, 'fragrance' would be reported, and not necessarily the individual haptens tested). Data on employment are subsequently coded according to the Standard Industrial Classification and Standard Occupational Classification (SOC) codes (5).

Reports of occupational contact dermatitis (OCD) attributed to fragrances were extracted from EPIDERM on the basis of predetermined search terms to identify fragrance allergy. These included all cases in which fragrances played a role; however, other causes may have been contributory. Extracted cases were reviewed, and those with a diagnosis of irritant dermatitis were excluded. Descriptive analyses were undertaken, with results being presented as 'actual' (sample cases + core cases) and/or 'estimated' ($12 \times$ sample cases + core cases) case counts.

THOR (including EPIDERM) has National Health Service ethics approval given by the North West (Haydock) Research Ethics Committee (11/NW/0832).

Statistical analysis

Annual average incidence rates (per 100 000 persons employed per year) by age and sex were calculated. The numerator was the estimated case count, adjusted to take into account the proportion of UK physicians participating in EPIDERM and the proportion of physicians responding during their reporting month(s) (6). The denominator was the number of persons employed (1996–2015) according to the Labour Force Survey (LFS).

Incidence rate ratios (IRRs) were calculated to quantify the extent of variation in incidence among occupations. IRRs were calculated for occupations (grouped to the three-digit SOC minor group level) with ≥ 20 actual cases. The numerator was the estimated case count for each occupation, and the denominator was the number

Table 1. Total estimated cases (and annual average incidence rate per 100 000 employed) per year for occupational contact allergy to fragrances by age and sex, as reported by dermatologists to EPIDERM, 1996–2015

Age (years)	Male	Female	Total
16–24	14 (0.07)	226 (1.15)	240 (0.59)
25–34	83 (0.23)	274 (0.84)	357 (0.50)
35–44	97 (0.22)	223 (0.64)	320 (0.41)
45–54	144 (0.36)	305 (0.87)	449 (0.61)
55–64	149 (0.64)	182 (1.02)	331 (0.80)
≥ 65	30 (0.65)	19 (0.76)	50 (0.71)
Total ^a	519 (0.30)	1256 (0.86)	1776 (0.56)

^aOne case had no sex assigned, and 7 cases had no age assigned.

of persons employed in that occupation according to the LFS. The reference category was the average of all other occupations (i.e. the total working population minus the occupation in question) combined. For the calculation of 95% confidence intervals (CIs), a method was used that allowed for the increased uncertainty generated by sample reporting and included a finite population correction to allow for the fact that only a proportion of eligible (UK) physicians reported to EPIDERM (7).

Trends in the incidence of ACD attributed to fragrances were estimated for industry overall and for the three groups for which numbers were sufficient to permit meaningful analyses: health and social care, hairdressers and related occupations, and 'food' (which encompassed both manufacturing and retail). The methods used to analyse trends in THOR surveillance data have been described previously (8). The change in incidence of dermatologist-diagnosed ACD attributed to fragrances was estimated, with the STATA software command `xtnbreg` being used to fit longitudinal, negative binomial (i.e. overdispersed) models (also known as multilevel models). The dependent variable was the number of actual cases, including zeros, per reporter per month. The main predictor of interest, calendar time, was represented as a continuous variable with a scale of years or as a categorical variable with 1996 as the reference year. In the latter, the statistical uncertainty is presented in such a way as to allow the reader to assess the significance of the difference between any 2 years (9). This approach assigns a confidence (or comparison) interval to the reference category (1996), and reduces the width of the confidence (comparison) intervals of non-reference categories. Variables representing 'season', 'reporter type' ('core' or 'sample'), 'first month as a new reporter' and 'first month as a new 'core' reporter' were also included (8). To account for changes in the population base, an offset variable representing the number of persons working in

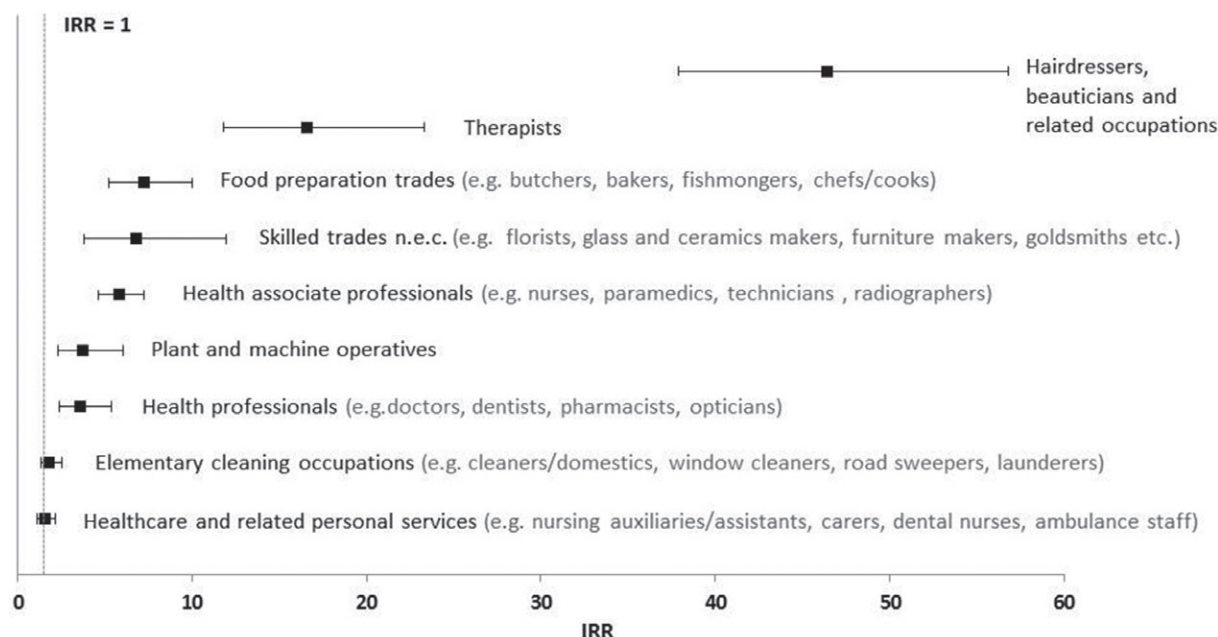


Fig. 1. Incidence rate ratios (IRRs) for occupational contact allergy to fragrances by occupation, based on estimated case counts reported by dermatologists to EPIDERM, 1996–2015. n.e.c., not elsewhere classified.

each of the occupational groups (obtained from the LFS) for each year was included in the model (10).

For each of the selected industries, trends in ACD attributed to fragrances were compared with trends in incidence of ACD attributed to agents other than fragrances (based on case reports to EPIDERM over the same time period). To assess whether there were differences between these two groups, a statistical interaction term for group (fragrance; not fragrance) and calendar time was added to the model.

Results

Fifteen thousand five hundred and ten actual (33 000 estimated) incident cases of OCD were reported to EPIDERM, equating to 82% of the actual cases reported during the study period. Eight hundred and sixty-two actual patients (6%) were identified as having a fragrance allergy contributing to their OCD. Of these, 59 were excluded: 52 because of a diagnosis of irritant dermatitis caused by a fragranced product, and 7 because of insufficient data, resulting in 808 actual (1776 estimated) cases being selected for analysis.

Table 1 shows the estimated cases and annual average incidence rate per year according to sex and age group. A much larger number of cases were observed in women. In females, the highest annual incidence rate was seen in those aged 16–24 years, with a second peak between 55

and 64 years. In men, the highest annual incidence rates were seen in patients aged > 55 years.

The IRRs for ACD caused by fragrances by occupation are shown in Fig. 1. Hairdressers, beauticians and those working in related occupations had a 47-fold higher IRR than the reference category (the average of all other occupations combined). When we analysed data for hairdressers and beauticians separately, we found IRRs of 23 (95%CI: 18–31) for hairdressers and 87 (95%CI: 67–112) for beauticians and those working in related occupations, suggesting a much higher incidence for the latter group. Therapists (including physiotherapists, occupational therapists, speech and language therapists, and aromatherapists) had the next highest IRR, which was 16-fold higher than that of the reference category. Restricting therapists to aromatherapists only gave an IRR of 33.5 (95%CI: 22.3–50.4), that is, 33-fold higher than that of the reference category.

Table 2 and Fig. 2 show the annual average percentage changes in incidence and relative rates by year (as compared with the reference year, 2015), respectively, for ACD attributed to fragrance allergy versus ACD not attributed to fragrance allergy for industry overall and (Table 2 only) for specific occupational groups. For fragrance-related ACD, an annual average increase in incidence was suggested for industry overall and for each of the three occupational groups studied, but none of these results was statistically significant. Figure 2,

Table 2. Average annual percentage change in reported incidence of work-related allergic contact dermatitis attributed to fragrances and not attributed to fragrances, 1996–2015

Group	Attributed to fragrances		Not attributed to fragrances	
	Number ^a	% change (95%CI)	Number ^a	% change (95%CI)
Health and social care	265	0.4 (–2.6 to 3.6)	855	–8.3 (–9.9 to –6.7)
Beauty	202	3.1 (–0.2 to 6.5)	738	1.4 (–0.5 to 3.2)
Food	100	1.3 (–3.1 to 5.9)	332	–3.7 (–6.1 to –1.3)
All industry	808	1.1 (–0.8 to 3.0)	5309	–5.5 (–6.2 to –4.7)

CI, confidence interval.

The model included variables for calendar time (a continuous time variable measured on a scale of years), reporter type (taking the value of '1' if core reporter, or '0' if sample reporter), season (indicator variables for each month with June as the reference month), and harvesting (taking the value '1' if it was the first month the reporter had reported, and '0' for all other months).

Population offset included in the model.

^aNumber of actual cases, 1996–2015.

which shows the year-on-year variation in incidence (industry overall only), suggests a relatively flat trend in fragrance-related ACD until 2010, followed by a slight increase in incidence thereafter (although the CIs for the individual year estimates were wide and overlapping). In comparison, for ACD attributed to agents other than fragrances, a statistically significant annual average decrease in incidence was observed for industry overall and for two of the occupational groups, that is, health and social care and beauty. Figure 2 suggests that much of the decrease in the incidence of non-fragrance-related ACD (for industry overall) occurred in the earlier part of the time period (1996–2007). Tests for significance suggested that the two trends (ACD attributed to fragrance and ACD not attributed to fragrance) were statistically different for all industries, health and social care ($p < 0.001$) and for food ($p < 0.05$), but not for beauty ($p = 0.19$).

Discussion

Our results support previous reports stating that fragrance allergy is reported more frequently in certain occupations. ACD caused by cosmetics has been reported for nearly two decades, owing to fragrances in skin care products (11, 12). 'Essential oils' are substances derived from many different plants, and represent a wide range of chemical groups; commonly terpenoids. These are becoming increasingly popular with the trend towards the use of 'natural' products, and are increasingly being recognized as an occupational problem (13, 14). The incidence of OCD caused by fragrances was higher in females. This mirrors the fact that occupations with the highest IRRs are predominantly female-orientated, namely hairdressing, beauty, and related occupations.

Data on contact allergy collected by the European Surveillance System on Contact Allergy from 11 European countries found the highest rates of ACD

in hairdressers and beauticians (15). However, in this study fragrance allergy was not reported as a significant causative agent. Thiuram rubber accelerators were the commonest causes of ACD in beauty occupations, as well as *p*-phenylenediamine in hairdressers (15). Our data suggest that, although other allergens may cause OCD more frequently overall, fragrance allergy is more frequently relevant in the beauty industry than in other occupations.

Therapists had the second highest IRR. However, this group includes aromatherapists. In this occupation, fragrance exposure is extremely high, especially to essential oils. Chefs and food handlers are well known to have high rates of occupational skin disease. Predominantly, this is irritant contact dermatitis (ICD), but ACD is also a problem. We found the third highest IRR in workers in food preparation trades. Bakers have been reported to have higher rates of ACD than other food handlers (16). OCD caused by spices has been previously reported (17). These contain natural fragrance allergens, namely cinnamal and cinnamic alcohol. Ackermann et al. reported a case series of 6 patients, who were bakers and restaurant workers, with occupational ACD caused by cinnamon. In one patient, contact allergy was deemed to be airborne (18). This highlights the fact that other patterns of eczema may be seen in an occupational context, and not just hand eczema. Previously, fragrance mix has been found to be an important indicator allergen for allergy to spices, especially paprika, nutmeg, and cloves (17).

We also found fragrance contact allergies in many skilled trades, with the IRR being just below the IRRs in food preparation trades. Historically, fragrances were commonly found in water-based metal-working fluids to mask odour. In this group, ICD was even more of a problem than ACD, owing to both the persistent wet work and the alkaline pH of the water-based metal-working fluid (19).

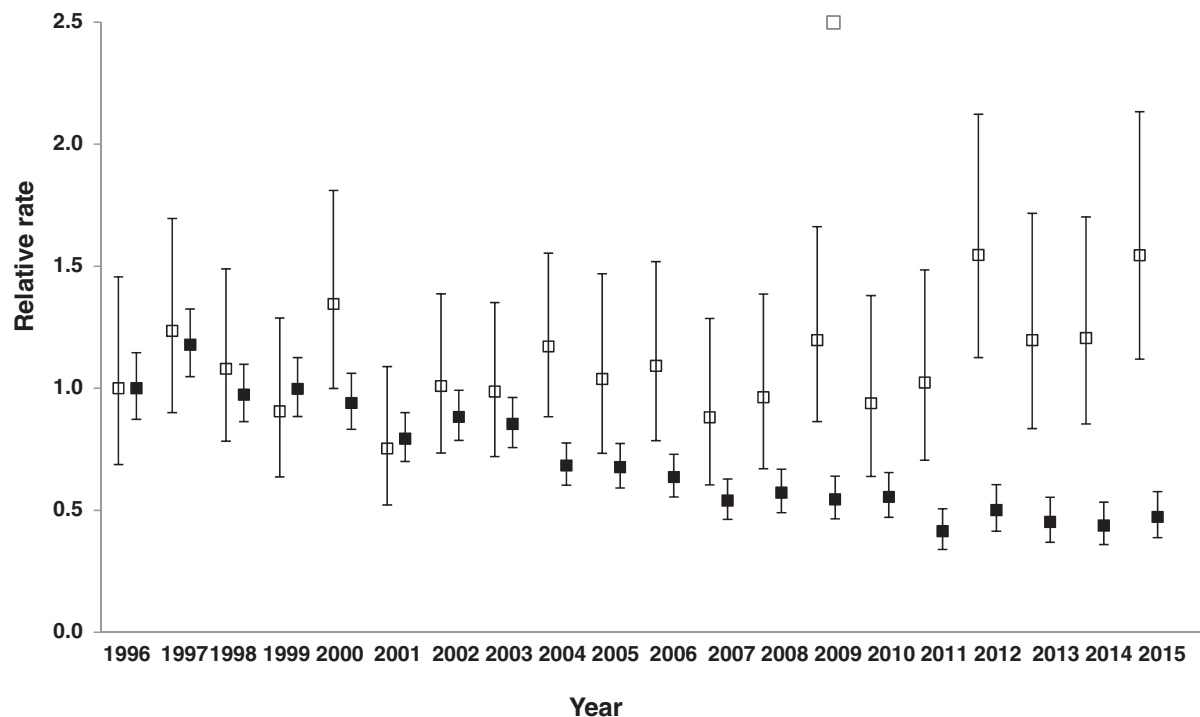


Fig. 2. Relative rates by year (1996 estimate = 1), with 95% comparison intervals, of dermatologist-reported allergic contact dermatitis attributed to fragrances [□] and not attributed to fragrances [■] (all occupations). The model included variables for calendar time (indicator variable for each year with 2015 as the reference year), reporter type (taking the value of '1' if core reporter, or '0' if sample reporter), season (indicator variables for each month with June as the reference month) and harvesting (taking the value '1' if it was the first month the reporter had reported, and '0' for all other months). Population offset is included in the model.

Buckley et al. found that healthcare workers had the highest number of reported cases of fragrance allergy (22.1%) (20). Data from the LFS for 2012–2013 showed that 31% of the population workforce were employed in health and social work, resulting in a lower calculated incidence per 100 000 employees (21). In one large study in healthcare workers, the prevalence of hand eczema was found to be double the prevalence in the general population (22). Hand hygiene is considered to be the most important factor for reducing the spread of healthcare-associated infections (23). Often, these preparations are perfumed. When hand washing with water was replaced by the use of a fragrance-free alcohol gel, surveillance at a large Swiss hospital of 3500 healthcare workers over a 10-year period showed no cases of ACD caused by alcohol-based hand hygiene products (24). Other hand hygiene products are necessary in particular scenarios, but fragrance is not essential for function, and so could be omitted from the formulation. A large study investigating OCD in nurses with data from the Information Networks of Departments of Dermatology between 2003 and 2012 highlighted that the spectrum of allergens has remained unchanged (25). The same network

looked at OCD in female geriatric nurses between 2005 and 2014. They found that the study group with OCD had a 5.7% higher rate of reactions to fragrance mix I than controls, a 4.2% higher rate of reactions to fragrance mix II, and a 3.3% higher rate of reactions to hydroxyisohexyl cyclohexene carboxaldehyde (HICC) (26).

Cleaners are exposed to many fragrances in industrial and household cleaning products. Some fragrances have other uses, including as solvents and degreasing agents, namely D-limonene. In an Italian study, limonene was one of the main declared allergens in 43.6% of household cleaning and washing products (20). A case series of OCD caused by D-limonene identified limonene-containing surface wipes and dish-washing liquids (27). As well as in cleaners, OCD caused by limonene has been reported in printers, mechanics, and maintenance, beauty and food workers (27).

Irritant dermatitis can contribute to the risk of developing contact allergy by reducing the barrier function of the skin, and allowing penetration and sensitization to fragrance (20, 28). In nurses, hairdressers, cosmetologists and bakers who develop OCD, the latency period between

the duration working in the occupation and the presentation of their dermatitis is shorter (median of 6 years) than in other occupational groups developing OCD (median of 15 years), that is, miners, agricultural labourers, and teachers (28). This may explain why our annual average incidence rates are higher in females aged < 24 years, as they are attracted to the beauty industry and nursing.

A study investigating trends in the incidence of occupational disease found a 3% decrease in OCD between 2000 and 2012 in the United Kingdom (29). In our 20-year study period, there was no significant change in the reported incidence of allergic OCD caused by fragrances. In contrast, a significant decrease in the incidence of ACD attributed to agents other than fragrances was observed for all groups (Fig. 2). It is therefore probable that fragrance allergy contributes to a greater proportion of OCD cases over time. Given that at least 2% of the general population are fragrance-allergic (1), employers need to be aware of the risk of fragrance allergy and implement appropriate preventive measures. Fragrance-free products should be used when perfume is not essential for function. Furthermore, when the presence of fragrance is necessary, the creation of products that are less likely to sensitize should be considered (30).

The nature of the reporting process means that reports specifically identifying individual causal agents within fragrances are limited [Unpublished observations from this dataset specified linalool (43), limonene (36), HICC (25), various cinnamates (24), and eugenol (14)]; 102 were more generally specified as essential oils/plant oils, and the rest were very generically categorized as perfumes or fragrances. Consequently, it is not yet possible to determine trends in the incidence of dermatitis caused by specific putative high-risk agents or to reliably identify novel causal agents. Therefore, more effort should be made to characterize and report the specific sensitizers. This will enable better advice to be given to the individual patient, as will help in product hazard or risk assessment and the prevention of emerging risks.

The explanation for the divergence between the number of cases reported to be attributable to all causes and those restricted to fragrances is potentially multifactorial. It is possible that, with time, improvements in the diagnosis of fragrance allergy might explain an increase, for example with the inclusion of fragrance mix II (31), and more recently limonene and linalool hydroperoxides, in the UK baseline series (32). However, trends were beginning to diverge before these changes were implemented, and have continued to do so since. Conversely, the explanation could be related to changes in exposure impacting on the development of allergic dermatitis, as has been seen with irritant dermatitis in healthcare

following the introduction of improved hand hygiene measures (33). Further studies would be needed to elucidate the varying contributory factors.

The current European cosmetic regulations on fragrances include a list of 26 fragrances that are recognized allergens, and these need to be present in ingredients lists when their concentrations exceed 0.001% in leave-on products and 0.01% in rinse-off products. The opinion of the Scientific Committee on Consumer Safety from 2012 highlighted many more fragrance sensitizers (34). Regulations for industrial products are set by the European Chemicals Agency, and vary greatly. The Classification, Labelling and Packaging Regulation states that substances only require labelling when they are classified as hazardous. Currently, the substance information for 'parfum' is undergoing the pre-registration process, and does not need to be listed (35).

A number of assumptions were made in the incidence rate calculations to adjust for cases not captured owing to non-participation of a dermatologist in EPIDERM and/or participation but for only 1 month a year (sample reporters) and/or non-response during their reporting month (6). This approach might overestimate rates, as it assumes that physicians who are not participating/responding would report (on average) at the same frequency as those who are. To compare incidence at the level of specific occupations (for which there may be increased uncertainty in the validity of making such assumptions), IRRs were calculated (although an adjustment for sample reporting was still made). The reference category was all occupations minus the occupation in question. This approach enables a comparison between ACD risk attributable to fragrances in an occupational setting as a whole but also in the specific occupations, but caution should be used when the IRRs of different occupations are compared/interpreted, owing to differences in the reference category. A further limitation of our study was that the multilevel model used to investigate the change in the incidence of ACD did not take into account the possible effects of reporter fatigue. However, if this were present, it would probably attenuate our results; that is, the observed increase for some occupations and fragrances would be even greater (36).

Conclusion

Although the incidence of occupational ACD overall has declined over the last 20 years, there has been no significant change in the incidence of fragrance allergy contributing to OCD. This implies that, currently, fragrance allergy accounts for a greater proportion of OCD than it did in the past. Occupational ACD attributed to fragrances was present in 4.2% of our patients, which is higher than

the 2% prevalence of fragrance allergy reported in the general population (1). Occupational ACD caused by fragrances was most often reported in the beauty, healthcare and food industries. Prevention should focus on the avoidance of fragrances when they are not essential for function, and the development of less sensitizing fragranced products when fragrances cannot be avoided.

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