

Fragrance allergy and quality of life – a case–control study

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Summary

Background. Fragrance ingredients can cause contact allergy, which may affect quality of life (QoL). However, few studies have investigated this topic.

Objectives. To investigate QoL life among subjects with a fragrance allergy as compared with other eczema patients.

Methods. A case–control survey was sent to subjects with a positive patch test reaction to a fragrance ingredient/marker ($n = 550$) and to a control group ($n = 1100$). It contained questions on eczema and the newly developed fragrance QoL index. Participants had been consecutively patch tested at Gentofte University Hospital (2000–2010). The response rate was 65.7%. Information on patch test data was retrieved from the National Contact Dermatitis Database.

Results. An increase in impairment of QoL was observed in women with fragrance allergy as compared with the control group ($p = 0.042$), which was not found among men. Several factors played a significant role in impairment of QoL in women: (i) number of fragrance allergies, (ii) severity of the patch test reaction, (iii) age combined with recent diagnosis; and (iv) allergy to specific fragrance ingredients/markers.

Conclusion. Fragrance-allergic subjects are just as affected in their QoL as other eczema patients. However, women, and in particular recently diagnosed young women, seem to be more impaired in their QoL than other eczema patients.

Key words: allergic contact dermatitis; eczema; fragrance; FQL index; quality of life; questionnaire

Fragrance ingredients constitute one of the most frequent causes of contact allergy; a prevalence of 16% was found in a European eczema population (1). It is a life-long condition, and symptoms may fluctuate or become chronic. Symptoms may be potentially avoidable if the person is not exposed to the allergen. However, avoidance can be difficult, because many different consumer products contain allergenic fragrances (2, 3), which may

require large changes in daily behaviour for those with fragrance allergy. This makes it of special interest to study quality of life (QoL) in subjects with fragrance allergy.

The main exposures are to cosmetic products comprising many different product categories: soaps, shampoos, cleansing wipes, deodorants, creams, sun protecting lotions, fine fragrances, aftershaves, etc. Other fragrance ingredients could be present in topical medicaments, toys, cleaning agents, and detergents.

We know that QoL in subjects with eczema is impaired (4–6), not only because of the disease activity, but also because of other factors (7). Little is known of the impairment of QoL in fragrance-allergic subjects, in spite of this being a frequent condition.

The aims of this study were: (i) to assess whether and how fragrance allergy affects QoL in fragrance-allergic subjects as compared with subjects without fragrance

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allergy, by use of the newly developed and validated instrument, the fragrance QoL index; (ii) to investigate whether certain fragrance ingredients affect QoL more than others; (iii) to assess whether the number of fragrance allergies affect QoL; and (iv) to assess whether the severity of the patch test reaction affects QoL.

Methods

Study design

The study was designed as a case–control study. A questionnaire was sent by post to all participants, and included a stamped, addressed, return envelope. The procedures involved in conducting the survey are described elsewhere (34).

Study population

All participants were aged 18–70 years, and had been consecutively patch tested at Gentofte University Hospital during 2000–2010. The study population consisted of a case group ($n = 550$) with at least one positive patch test reaction to a fragrance ingredient/marker, and a control group ($n = 1100$) of non-fragrance-positive individuals, which means they had no positive patch test reactions to fragrance markers/ingredients. Both the case group and the control group could have other allergies, skin diseases, and/or other diseases.

A control group was chosen with similar demographic characteristics, so that differences in QoL that might be observed could be ascribed to the fragrance allergy. The similarities that we could control for were as follows: (i) all participants had been patch tested and thus constituted a homogeneous eczema group; (ii) they had been consecutively patch tested at the same hospital, and thus came from the same geographical area; (iii) they were matched on age (± 1 year); (iv) they were matched on sex; and (v) they were matched on patch test year (± 1 year). A description of the study population is given in Table 1. We controlled for other conditions that showed significant differences (listed in Table 1) among the case and control groups in a logistic regression analyses.

QoL measure

The fragrance QoL (FQL) index is a disease-specific instrument for investigating QoL in fragrance-allergic subjects. It consists of 13 items reflecting their subjective feelings at the time when they fill in the questionnaire. The items were answered on a visual analogue scale from 0 to 10. A summarized FQL score can be calculated,

with a maximum of 130 and a minimum of 0. The FQL index has recently been validated in a Danish eczema population (34) and translated into English with standardized methods (10, 11), but has yet to be validated in an English-speaking population.

It was developed in much in the same way as one of the most frequently used QoL instruments for dermatology patients, the Dermatology Life Quality Index by Finlay in 1994 (12). A content analysis based on written narratives from 68 fragrance-allergic subjects formed the basis for the 13 items in the FQL index. Several different validation analyses were performed. Overall, the FQL index was shown to be a good instrument for measuring QoL (34).

Database information

The National Contact Dermatitis Database is managed by the National Allergy Research Centre at the Department of Dermato-Allergy at Gentofte University Hospital. It contains information on patch test date, reactions, and demographic characteristics. All patch tests were performed according to international guidelines (13), with Finn Chambers[®] applied on the back with Scanpor[®] tape (Vitalfo Scandinavia, AB, Allerød, Denmark) for a period of 2 days. Readings were performed on D2, D3 or D4 and D7, according to the recommendation of the International Contact Dermatitis Research Group (14). Patch test reactions were read and classified into different categories. In this article, we will investigate the positive reactions, comprising +, ++ and +++ reactions, and the negative reactions, which were all of the other reactions (negative, doubtful and irritant reactions). During the 10-year study period (2000–2010), there were developments in the diagnosis of fragrance allergy. At Gentofte University Hospital, fragrance mix (FM) II and hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) were introduced in the baseline series in 2005 (15). From 2007, all patients investigated for allergy were additionally patch tested with our perfume series, which consists of the 26 fragrances that must be declared on cosmetic products according to the EU Cosmetics Directive (16). Furthermore, from January 2010, the oxidized forms of both limonene and linalool were also included as screening markers for fragrance allergy. However, by matching controls for the patch test year, a possible bias resulting from the changes in patch test materials over time will be minimized. Age groups were defined on the basis of percentiles, to ensure a representative number of fragrance-positive subjects in each group.

The two fragrance mixes [FM I and FM II] consist of several different fragrance ingredients (9, 17, 18), and some of the participants had also been tested with these

Table 1. Demographic and disease burden of the study population (n = 1084)

	Respondents									
	Women					Men				
	Fragrance-positive		Non-fragrance-positive			Fragrance-positive		Non-fragrance-positive		
	n	%	n	%	p	n	%	n	%	p
Participants	424	33.3	848	6.7	–	126	33.3	252	66.7	–
Responders	290	68.4	551	65.0	0.22	89	70.6	154	61.1	0.07
Eczema										
Point prevalence	160	56.7	271	50.0	0.07	42	47.7	81	52.6	0.41
Atopic dermatitis ^a	62	21.4	98	17.8	0.21	16	18.0	22	14.3	0.47
Occupational eczema	45	15.5	80	14.5	0.70	14	15.7	34	22.1	0.21
Other allergies ^b	183	63.1	222	40.3	0.001	44	49.4	54	35.1	0.03
Other skin diseases	118	40.7	214	38.5	0.52	24	27.0	38	24.7	0.60
Psoriasis	17	5.9	53	9.6	0.06	4	4.5	10	6.5	0.52
Acne	26	9.0	41	7.4	0.44	7	7.9	8	5.2	0.41
Urticaria	43	14.8	65	11.8	0.21	5	5.6	6	3.9	0.51
Skin diseases not mentioned above	52	17.9	89	16.2	0.51	11	12.4	19	12.3	0.97
Other disease ^c										
Rhinitis	94	34.3	159	30.6	0.28	34	41.5	35	24.1	0.006
Food allergy	70	25.5	104	20.2	0.08	12	14.6	22	15.4	0.89
Asthma	52	19.0	102	19.6	0.84	18	21.7	22	15.1	0.22
Depression	52	19.0	102	19.5	0.87	10	12.0	23	16.2	0.40
Diabetes	17	6.2	32	6.1	0.94	14	16.7	11	7.6	0.037
Anxiety	16	5.9	53	10.2	0.04	2	2.4	9	6.3	0.17
Heart disease	11	4.0	35	6.7	0.13	8	9.6	14	9.7	0.99
COPD	8	3.0	25	4.8	0.22	1	1.2	8	5.6	0.14
Stroke	4	1.5	18	3.4	0.11	5	6.0	10	7.0	0.79
Heart attack	2	0.7	9	1.7	0.27	6	7.1	7	4.9	0.49
MCS ^d	14	4.8	10	1.8	0.016	0	–	1	0.6	–

COPD, chronic obstructive pulmonary disease.

Fragrance-positive group (case group): respondents with at least one positive patch test reaction to a fragrance ingredient (could also have other allergies, skin conditions, and/or other diseases).

Non-fragrance-positive group (control group): respondents with no positive patch test reaction to a fragrance ingredient (could have other allergies, skin conditions, and/or other diseases).

%; Crude percentages. If respondents had not answered the item, they were counted as missing in the analysis.

Logistic regression accounting for the matching; *p*-values of < 0.05 are considered to be statistically significant. Fisher's exact test was performed with small samples, but no statistically significant differences were found.

^a Atopic dermatitis, UK criteria (8).

^b A positive patch test reaction to a marker of the baseline series other than a fragrance marker/ingredient.

^c The diagnosis was established by the question 'Has your doctor ever told you that you have/have had ...?'

^d MCS, multiple chemical sensitivity syndrome; La Cour's criteria (9).

individual fragrance ingredients. Thus, we counted the number of fragrance allergies in the following way: as one allergy when a subject had a positive patch test reaction to an individual fragrance ingredient or to a mix when they had not been tested with the individual fragrances, or had been negative to them; as one allergy when a subject had a positive patch test reaction to one of the mixes and one of its constituents; and as two allergies if a subject had a positive patch test reaction to a mix and two of its constituents, etc.

Statistics and data management. Statistical analyses were performed with SPSS (SPSS, Chicago, IL, USA) for

Windows version 19. Standard methods were used for the descriptive statistics, crude percentages, mean, and standard deviation. The analyses for differences between the case group and the control group were performed, accounting for the matching, in: (i) a conditional logistic regression model, which is a model designed for analysing responses in a case–control setting where one or several controls are matched to one case; and (ii) univariate analyses accounting for the matching. Several logistic regression analyses and Mann–Whitney tests were performed, stratified by case group and control group to test for differences and confounding factors within each group. The binary logistic regression analyses were

checked with the Hosmer–Lemeshow goodness of fit test. In all of the statistical analyses, a p -value of < 0.05 was considered to be significant.

Results

Demographics and disease burden of the study population

The questionnaire was sent to 1650 participants, and 1084 (65.7%) responded. No difference was found in response rates between fragrance-positive women and non-fragrance-positive women ($p = 0.22$), and likewise for the men ($p = 0.07$). No age difference was found in the response rates between fragrance-positive and non-fragrance-positive control groups. There was no difference in the point prevalence of having eczema between women with a fragrance allergy and their controls ($p = 0.07$), and likewise for the men ($p = 0.41$) (Table 1). Several conditions were unevenly distributed between the fragrance-positive group and the non-fragrance-positive group (Table 1), and were used in the analyses of QoL in a regression analysis accounting for them as confounding factors.

QoL and fragrance allergy stratified by sex

QoL measured with the FQL index showed impairment of QoL in both the fragrance-positive group and the non-fragrance-positive group. The impairment was statistically significantly greater in the fragrance-positive case group than in the non-fragrance-positive control group ($p = 0.042$). However, this difference was seen only among women, where significant QoL impairment was observed ($p = 0.014$); no significant difference was observed among men ($p = 0.732$). Regression analyses were performed separately for women and men, including the parameters showing statistically significant differences in disease burden/conditions (Table 1). We found that QoL impairment was still significantly associated with having a positive patch test reaction to a fragrance ingredient for women ($p = 0.042$). For men and their controls, we again found no significant association between QoL and fragrance allergy ($p = 0.163$).

Fragrance-positive women showed a significant difference from non-fragrance-positive women in how much they worried about being exposed to things that could provoke their rash; they also felt that people should be more considerate of their illness, and they felt greater impairment of physical contact than their control group. Some sex similarities were observed, as both men and women with a fragrance allergy felt that they more

frequently had to take special measures to avoid situations that could provoke their rash; they all missed smelling nice, and felt that they had a better understanding of what provoked their rash than the control groups (Table 2).

Sex differences were quite apparent in many aspects regarding QoL and fragrance allergy.

Overall, men were not as affected by fragrance allergy in their QoL. Thus, results for men are shown in the tables and figures, but not mentioned in the text.

QoL in women in different age groups and stratified by patch test year

Impairment of QoL for women with fragrance allergy was not significantly correlated with age (Pearson's test; $p = 0.24$). However, for the non-fragrance-positive women, a significant inverse correlation was observed, as they were less affected in their QoL with higher age (Pearson's test; $p = 0.02$). Impairment of QoL for each of the age groups stratified by time of patch test showed a significant difference in the youngest age group. This difference is shown in Fig. 1, and illustrates the QoL impairment for different age groups over time. Thus, the more recently women in the youngest age group had been diagnosed with a fragrance allergy, the greater the QoL impairment (trend test; $p = 0.03$). This increased QoL impairment in the youngest age group most recently diagnosed with a fragrance allergy was also significant as compared with the older age groups (QoL in the youngest age group of women diagnosed in 2009 and 2010 as compared with the older age groups; univariate analysis; $p = 0.016$).

QoL in women and allergy to specific fragrance markers

Allergies to some fragrance ingredients/markers affected QoL more than others among women. In our study population, the prevalence of having a positive patch test reaction to a fragrance marker was highest for FM I ($n = 174$), followed by *Myroxylon pereirae* ($n = 94$) and FM II ($n = 54$). The top 10 fragrance markers for allergy among those who responded to the questionnaire survey are shown in Table 3, together with their QoL impairment. Significantly greater QoL impairment was detected among women with an allergy to FM I, FM II, HICC, and *M. pereirae*. The strongest significance was seen for HICC, which also showed the greatest QoL impairment of all the individual fragrance markers among women.

QoL in women and multiple allergies

In women, a gradual but significant increase in impairment of QoL in relation to number of positive

Table 2. Quality of life (QoL) measured with the fragrance QoL (FQL) index

QoL instruments	Respondents													
	Women and men							Men						
	Women							Men						
	Fragrance-positive n = 379			Univariate analysis accounting for the matching				Non-fragrance-positive n = 290			Univariate analysis accounting for the matching			
FQL index	Mean	SD	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p	Mean	SD
Item 1. Eczema and QoL	4.1	3.2	3.9	3.2	4.3	3.3	0.156	4.3	3.3	3.8	3.3	0.059	3.7	2.9
Item 2. Avoid situations	5.2	3.6	4.0	3.7	5.3	3.6	< 0.001	5.3	3.6	4.2	3.8	< 0.001	4.5	3.4
Item 3. Fissures and cracks	4.7	3.5	4.7	3.7	4.8	3.5	0.862	4.8	3.5	4.6	3.7	0.446	4.4	3.6
Item 4. Itching	5.6	3.4	5.3	3.6	5.6	3.4	0.218	5.6	3.4	5.2	3.6	0.128	5.4	3.3
Item 5. Pain and smarting	4.1	3.4	4.1	3.6	4.2	3.4	0.774	4.2	3.4	4.0	3.7	0.444	3.8	3.2
Item 6. Work and school	3.4	4.0	3.2	4.0	3.6	4.1	0.371	3.6	4.1	3.2	4.0	0.175	2.7	3.9
Item 7. Impaired physical contact	0.9	2.1	0.5	1.5	1.0	2.3	0.001	1.0	2.3	0.5	1.5	< 0.001	0.5	1.2
Item 8. Irritation and stress	2.8	3.0	2.7	3.1	2.8	3.1	0.627	2.8	3.1	2.7	3.2	0.468	2.5	2.8
Item 9. Worried	3.3	3.2	2.5	3.1	3.5	3.4	< 0.001	3.5	3.4	2.5	3.1	< 0.001	2.6	2.6
Item 10. Less attractive	2.6	3.2	2.6	3.3	2.8	3.4	0.861	2.8	3.4	2.7	3.4	0.636	1.8	2.5
Item 11. Miss smelling nice	3.7	3.6	1.9	3.1	4.1	3.7	< 0.001	4.1	3.7	2.0	3.1	< 0.001	2.6	3.1
Item 12. Understand triggers	7.2	3.1	5.3	3.8	7.3	3.0	< 0.001	7.3	3.0	5.5	3.8	< 0.001	6.6	3.3
Item 13. Consideration from people	2.0	2.9	1.4	2.4	2.2	3.0	< 0.001	2.2	3.0	1.5	2.5	0.001	1.4	2.3
FQL score	44.0	27.3	40.4	27.0	45.7	28.2	0.042	45.7	28.2	40.5	27.5	0.014	38.4	23.6
													39.6	25.0

SD, standard deviation.

Fragrance-positive: at least one positive patch test reaction to a screening marker/ingredient of fragrance allergy.

Non-fragrance-positive: no positive patch test reaction to a screening marker/ingredient of fragrance allergy.

Mean: The items were answered on a visual analogue scale (0–10). The higher the score, the more affected the respondents.

p-Values < 0.05 are considered statistically significant.

Table 3. The prevalence of positive patch test reactions to the top 10 fragrance markers/ingredients and quality of life (QoL) in subjects tested with these fragrance ingredients/markers

Patch test markers of fragrance allergy	Positive patch test reactions				FQL index score					
	Women		Men		Women		p-value	Men		p-value
	Numbers positive/tested	%	Numbers positive/tested	%	Fragrance-positive Mean (SD)	Non-fragrance-positive Mean (SD)		Fragrance-positive Mean (SD)	Non-fragrance-positive Mean (SD)	
Fragrance mix I	174/825	21.1	51/239	21.3	46.0 (28.0)	41.4 (27.7)	0.03	39.2 (23.2)	39.1 (25.0)	0.89
<i>Myroxylon pereirae</i>	94/838	11.2	22/241	9.1	48.2 (28.0)	41.7 (27.8)	0.02	30.8 (20.7)	40.1 (24.8)	0.13
Fragrance mix II	54/524	10.3	17/160	10.6	50.8 (27.3)	43.0 (28.2)	0.04	36.9 (26.3)	42.1 (25.4)	0.49
Oxidized linalool	7/68	10.3	1/23	4.3	53.6 (32.7)	49.5 (25.8)	0.39	54.0 (–)	43.0 (30.1)	0.81
Oxidized limonene	6/67	9.0	3/22	13.6	53.5 (41.4)	49.3 (25.0)	0.38	47.3 (22.8)	42.9 (31.1)	0.99
<i>Evernia furfuracea</i>	25/281	8.9	10/90	11.1	48.6 (22.3)	45.9 (28.7)	0.44	39.1 (23.9)	45.8 (25.9)	0.53
Hydroxycitronellal	49/669	7.3	7/193	3.6	34.8 (26.5)	43.6 (27.8)	0.18	29.5 (20.6)	40.5 (24.9)	0.27
<i>Evernia prunastri</i>	48/760	6.3	20/219	9.3	48.4 (24.8)	42.4 (27.9)	0.07	37.4 (18.1)	39.6 (24.9)	0.64
HICC	32/671	4.8	14/194	7.2	56.6 (26.3)	42.2 (27.6)	0.002	29.5 (23.6)	41.2 (24.9)	0.13
Isoeugenol	25/670	3.0	6/193	3.1	45.1 (30.0)	42.9 (27.7)	0.41	47.4 (30.7)	39.9 (24.6)	0.61

FQL, fragrance QoL; HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; SD, standard deviation.

Mean: mean of the FQL index score; a high score indicates greater QoL impairment.

The screening for fragrance allergy comprises 32 markers/ingredients: the 10 listed above and the following 22 ingredients methyl 2-octynoate, cinnamal, citral, eugenol, cinnamyl alcohol, α -hexyl cinnamal, butylphenyl methylpropional, amyl cinnamal, geraniol, benzyl salicylate, coumarin, amyl cinnamyl alcohol, trimethylbenzenepropanol (majantol), citronellol, non-oxidized limonene, non-oxidized linalool, benzyl cinnamate, benzyl alcohol, farnesol, benzyl benzoate, α -isomethyl ionone, and anis alcohol. Not all participants had been tested with all of the screening markers of fragrance allergy, owing to changes in the screening methods. Also, not all respondents were included in each analysis, as some had been patch tested prior to the study period, and the results of that patch test reaction were unobtainable or uncertain.

Positive patch test reactions comprise all positive reactions (+, ++, +++). Negative reactions comprise all irritant, doubtful and negative reactions.

A statistically significant difference ($p < 0.05$) between subjects with a positive patch test reaction to the individual fragrance marker and subjects with no positive reaction, univariate analysis accounting for the matching.

patch test reactions to fragrance ingredients/markers ($p = 0.001$) was seen (Fig. 2).

QoL in women and severity of the patch test reaction

The severity of patch test reactions varied; the stronger the reaction, the higher the score (+, ++, +++). A + reaction was observed in 200 subjects, a ++ reaction was observed in 171 subjects, and a +++ reaction was observed in 8 subjects. As only 8 subjects had a +++ reaction, we combined these subjects with those who had a ++ reaction, in order to give a better description of the population (Fig. 3). Women showed a significant linear increase in QoL impairment in relation to severity of the patch test reaction (correlation analysis; $p = 0.008$).

Discussion

The results of this matched case–control study show that subjects with a fragrance allergy are affected in their QoL. Sex differences in QoL were apparent throughout the results, as fragrance allergy in general seems to affect women more than men. Thus, women with a fragrance allergy showed significantly greater QoL impairment than

their control group. It is well known that sex differences exist in contact allergy, and it is well documented that more women than men are affected (19, 20), most likely because of their different exposure patterns (19). Women and men have different obligations in their daily lives, both at work and at home (21), which can affect their disease and thus affect their QoL, which our study also indicates. The sex differences that we observed in relation to QoL may be explained by the fact that women in general are more exposed to fragrance ingredients than are men, and therefore women have to make a greater effort and more changes in their behaviour to avoid fragrance ingredients. In addition, it is a significant sacrifice for them to avoid fragrances in their daily lives. We particularly found that young women who had been diagnosed for fragrance allergy recently showed significantly greater QoL impairment. It could be argued that this tendency was seen because it is more difficult to live with fragrance allergy now than it was 10 years ago, because of different exposure patterns. However, we would expect to see this impact on QoL in all of the age groups recently diagnosed, which we did not. Thus, this is more likely an illustration of how young women in particular find it very difficult

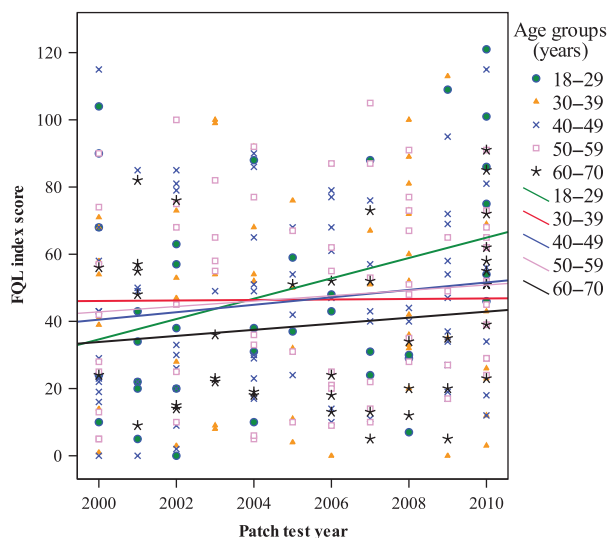


Fig. 1. Quality of life (QoL) in women with fragrance allergy in different age groups stratified by patch test year. A scatter plot is shown with trend lines for QoL measured with the disease-specific QoL instrument for fragrance allergy [fragrance QoL (FQL) index] in women in different age groups stratified by patch test year. Each line represents the linear association between QoL and age group during different patch test years. Green line: 18–29 years; trend test, $p = 0.03$. Orange line: 30–39 years; $p = 0.95$. Blue line: 40–49 years; $p = 0.20$. Pink line: 50–59 years; $p = 0.39$. Black line: 60–70 years; $p = 0.32$.

when initially diagnosed, but then learn to live with their fragrance allergy and manage it. Previous studies have shown that being patch tested has a positive impact on QoL (22), the improvement in QoL being more marked in those with a positive patch test reaction (6).

A factor that may influence why men with a fragrance allergy did not show the effect on QoL that was seen among women could be the presence of confounders. For example, the prevalence of occupational eczema was higher among non-fragrance-positive men (22.1%) than among fragrance-positive men (15.7%), and occupational eczema has been linked to increased QoL impairment (23, 24). Although this difference was not statistically significant, it indicates that the study population is not completely homogeneous, and other factors could exist and have contributed to the fact that only minor differences were observed in QoL among fragrance-positive men and their control group, as compared with that observed for women.

Allergy to some fragrance ingredients/markers clearly plays a larger role than allergy to others in QoL in women. Allergy to HICC, in particular, is associated with greater QoL impairment in women. This may be because of its widespread use in consumer products (25,

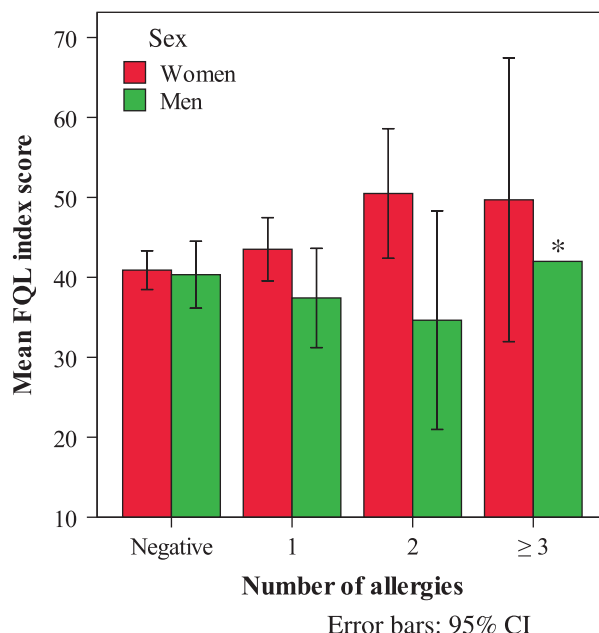


Fig. 2. Quality of life (QoL) in relation to number of patch test reactions to fragrance ingredients/markers. A bar chart with 95% confidence intervals (CIs) is shown, illustrating QoL measured with the disease-specific QoL instrument [fragrance QoL (FQL) index] for men (green) and women (red) in relation to the number of patch test reactions. The higher the score, the more impaired the QoL. Numbers of allergies are determined by the number of positive patch test reactions (+, ++, +++) to any of the fragrance ingredients/markers tested. However, if a subject has a reaction to one of the mixes and to one of its constituents, it is counted as one allergy. If a person has reacted to one of the mixes and two different individual constituents, it is counted as two allergies, etc. Correlation analyses: $p_{\text{women}} = 0.01$; $p_{\text{men}} = 0.33$. *The last error bar (≥ 3) is not shown in the chart as the calculations yielded infinite results.

26), which makes the fragrance ingredient difficult to avoid. Furthermore, the allowed concentration of HICC in cosmetic products has been too high for many years (27–29), and exposure to products containing HICC could therefore lead to sensitization and elicitation of contact allergy. Thus, industry must take steps to lower the doses of fragrance ingredients in products to below elicitation doses, as otherwise subjects with a fragrance allergy will be at risk of having a reaction, which also affects their QoL.

Severity of the patch test reaction was significantly associated with increased impairment of QoL, and this could be interpreted as follows: the more severe the patch test reaction, the lower the elicitation threshold in the individual, and the more likely it will be to provoke an allergic response (27, 30), leading to greater QoL impairment. The number of fragrance allergies that a subject has was also shown to have a significant

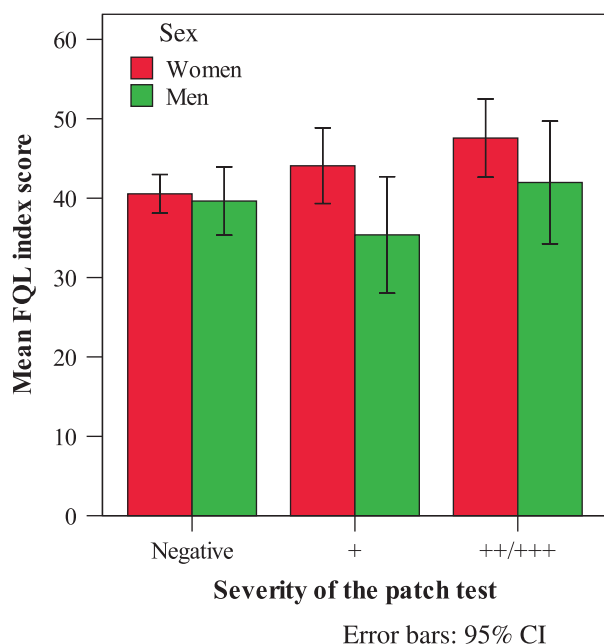


Fig. 3. Quality of life (QoL) in relation to severity of the patch test reaction to a fragrance ingredient/marker (negative, +, ++/+++) in women and in men. A bar chart with 95% confidence intervals (CIs) is shown, illustrating the difference in QoL measured with the disease-specific QoL instrument for fragrance-allergic subjects [fragrance QoL (FQL) index] in relation to intensity of a patch test reaction to a fragrance marker/ingredient in women (red) and men (green). Negative reactions comprise all negative, doubtful and irritant reactions. A + reaction was observed in 200 subjects, a ++ reaction in 171 subjects, and a +++ reaction in 8 subjects. The 8 subjects with a +++ reaction were combined with the subjects with a ++ reaction to give a better description of the population. Correlation analyses: $p_{\text{women}} = 0.008$; $p_{\text{men}} = 0.877$.

association with QoL impairment. Again, this could be an indication that the more allergies a person has, the more exposures have to be avoided, and perhaps, because of synergistic effects, the more likely there is to be elicitation

of the contact allergy (31, 32), which influences QoL.

Overall, the control group seems to be a good match for subjects with a fragrance allergy. However, it is difficult to find an appropriate control group. We chose other eczema patients, as we expected they would have a similar disease burden of eczema, and thus the differences that we observed could be attributed to the fragrance allergy. We did find that some other diseases/conditions had significantly different prevalence rates among the fragrance-positive women and men and their controls (Table 1). However, after adjustment for these significant differences in a multiple logistic regression analysis, no difference was observed; thus, women still had significantly greater QoL impairment, whereas men did not show any significant effect on QoL. To further eliminate bias, the control group was chosen from subjects examined at the same hospital, allowing the elimination of referral bias. The controls were matched on sex and age to minimize these as confounding effects. Furthermore, controls were matched for time of patch test to minimize any confounding effect of examination procedures in particular (33, 8), but also differences in referral and exposure patterns.

In conclusion, we found that QoL is affected by having a fragrance allergy. Women, and in particular young women, with a recent diagnosis of fragrance allergy were most affected. The number of fragrance allergies and severity of the allergy influenced the impact on QoL. Also, having an allergy to FM I, FM II, *M. pereirae* and, especially, HICC was associated with significantly greater QoL impairment.

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