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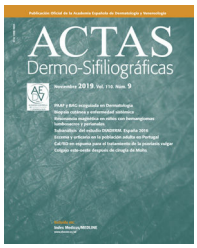

ORIGINAL

[Translated article] Four-year Epidemiological Surveillance of the Spanish Registry of Research in Contact Dermatitis and Cutaneous Allergy: Current Situation and Trends

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KEYWORDS
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Abstract

Background: The epidemiological surveillance of contact dermatitis is one of the objectives of the Spanish Registry of Research in Contact Dermatitis and Cutaneous Allergy. Knowing whether the prevalence of positive tests to the different allergens changes over time is important for this monitoring process.

Objectives: To describe the various temporary trends in allergen positivity in the GEIDAC standard series from 2018 through December 31, 2022.

Methods: This was a multicenter, observational trial of consecutive patients analyzed via patch tests as part of the study of possible allergic contact dermatitises collected prospectively within the Spanish Registry of Research in Contact Dermatitis and Cutaneous Allergy. The data was analyzed using 2 statistical tests: one homogeneity test (to describe the changes seen over time) and one trend test (to see whether the changes described followed a linear trend).

Results: A total of 11327 patients were included in the study. Overall, the allergens associated with a highest sensitization were nickel sulfate, methylisothiazolinone, cobalt chloride, methylchloroisothiazolinone/methylisothiazolinone, and fragrance mix I. A statistically significant decrease was found in the percentage of methylisothiazolinone positive tests across the study years with an orderly trend.

Conclusions: Although various changes were seen in the sensitizations trends to several allergens of the standard testing, it became obvious that a high sensitization to nickel, methylchloroisothiazolinone/methylisothiazolinone and fragrances mix I remained. Only a significant downward trend was seen for methylisothiazolinone.

PALABRAS CLAVE
Pruebas epicutáneas;
Metilisotiazolinona;
GEIDAC;
REIDAC;
Vigilancia epidemiológica;
Tendencias

Vigilancia epidemiológica en los últimos 4 años del Registro Español de Investigación en Dermatitis de Contacto y Alergia Cutánea: situación actual y tendencias

Resumen

Antecedentes: El Registro Español de Investigación en Dermatitis de Contacto y Alergia Cutánea tiene entre sus objetivos la vigilancia epidemiológica de la dermatitis de contacto. Para ello es importante conocer si se producen alteraciones en el tiempo de las prevalencias de las positividades a los distintos alérgenos.

Objetivos: Describir las variaciones en las tendencias temporales en positividades a alérgenos en la serie estándar del GEIDAC en el periodo comprendido entre 2018 y el 31 de diciembre de 2022.

Métodos: Estudio observacional multicéntrico de pacientes estudiados consecutivamente mediante pruebas epicutáneas dentro del estudio de un posible eczema alérgico de contacto recogidos de forma prospectiva en el seno del Registro Español de Investigación en Dermatitis de Contacto y Alergia Cutánea. Se analizaron los datos mediante 2 pruebas estadísticas: una de homogeneidad (para ver si hay cambios en los diferentes años) y otra de tendencia (para ver si los cambios siguen una tendencia lineal).

Resultados: Se incluyeron un total de 11.327 pacientes en el periodo de estudio. Los alérgenos en los que de forma global se detectó una sensibilización mayor fueron sulfato de níquel, metilisotiazolinona, cloruro de cobalto, metilcloroisotiazolinona/metilisotiazolinona y mezcla de fragancias I. Se detectó una disminución estadísticamente significativa en el porcentaje de positividades de metilisotiazolinona a lo largo de años de estudio con una tendencia ordenada.

Conclusiones: Si bien se pueden apreciar diferentes cambios en las tendencias a sensibilizaciones a varios de los alérgenos de la batería estándar, se observa que persiste una alta sensibilización al níquel, a la metilcloroisotiazolinona/metilisotiazolinona y a la mezcla de fragancias I. Solo se aprecia una tendencia a disminuir de forma significativa en el caso de la metilisotiazolinona.

Introduction

The Spanish Registry of Research in Contact Dermatitis and Cutaneous Allergy (REIDAC) has, among its objectives, the epidemiological surveillance of contact dermatitis. For this purpose, it is essential to know if there are any changes in the prevalences of sensitizations to different allergens over time.[1,2]

Patch tests constitute the fundamental method for detecting sensitization to contact allergens,[3,4] serving as an essential tool for diagnosing allergic contact dermatitis (ACD).[3,4] The evaluation of any patient with suspected ACD should include a standard national or international battery of patch tests and, optionally, one or more specific batteries, which may also include the patient's own products.[3,4]

The Spanish standard battery is a dynamic battery that is periodically updated by members of the Spanish Research Group on Contact Dermatitis and Skin Allergy (GEIDAC). To do this, various criteria are taken into consideration, such as the frequency of sensitization (> 0.5% to 1%), as well as other characteristics, such as whether there are emerging allergens in the dermatological medical literature available or neighboring countries, or whether they are of particular importance for a group of patients, or exposure environment.

The objective of our work is to describe the variations in temporal trends in sensitizations to allergens in the standard series of GEIDAC from 2018 through December 31, 2022.

Materials and methods

REIDAC prospectively collects the results of all consecutively patched patients in the participant centers. The data are anonymized at the source, and the registry complies with all ethical standards on informed consent and data protection legislation. In addition to the present positivities and relevancies, the registry successively collects epidemiological, clinical, and allergic variables of patients who underwent patch tests at the participant centers across this period, including the data necessary to obtain the Male, Occupational dermatitis, Atopic dermatitis, Hand dermatitis, Leg dermatitis, Facial dermatitis, Age > 40 years (MOAHLFA) index. In this study, we used data from 2018 through December 31, 2022.[3]

Patch tests were performed following the recommendations of the European Society of Contact Dermatitis,[5] considering readings (+), (++), or (+++) as positive. Relevance was determined based on the patient's health record.

The latest update of the GEIDAC standard battery dates back to January 2022, including 4 new allergens (hydroxyethyl methacrylate, textile dye mix, linalool hydroperoxides, and limonene hydroperoxides), and removing 3 (ethylene diamine dihydrochloride, methyl dibromoglutaronitrile, and hydroxyisohexyl-3-cyclohexenecarboxaldehyde), which were not included in the current study.[3]

A descriptive analysis of the MOAHLFA index was performed, as well as the prevalence of each allergen, and its distribution over the years was compared. The results were graphically presented. Homogeneity comparisons were drawn using the chi-square test, and the linear trend analysis was performed using the linear trend tests for scores. For trend analysis, raw P values and MOAHLFA-adjusted values were obtained. The prevalence of each allergen in the standard battery was also presented by age and sex.

All statistical analyses were performed using the STATA v.17.0 software (Stata Corp. 2021. Stata Statistical Software: Release 17). P values < .0016 (adjusted with Bonferroni correction for multiple comparisons) were considered statistically significant.

REIDAC was approved by Hospitalario Universitario Insular-Materno Infantil Research Ethics Committee (2017/964) in full compliance with the Declaration of Helsinki. All patients signed a written informed consent form for participation purposes.

Results

The total number of patients included in REIDAC during the study period was 11327 participants. The distribution by years of this population, as well as the description of the MOAHLFA index by year, are included in Table 1.

Although there are statistically significant differences in some variables, conditioned by the large sample size, these are clinically less relevant, and when adjusting values for these differences, there are no changes in the trends reported.

Table 2 illustrates the total positives for different allergens in the standard series of GEIDAC in the patients studied over the study years in the overall population studied, differentiated by gender, and standardized by sex and age.

As can be seen, the allergens that showed a higher overall sensitization frequency across the study period were nickel sulfate, methylisothiazolinone, cobalt chloride, methylchloroisothiazolinone/methylisothiazolinone

Table 1 Variation of MOAHLFA index on a yearly basis.

MOAHLFA index per year											
	Year of consultation										
	2018		2019		2020		2021		2022		*P*
	N	%	N	%	N	%	N	%	N	%	
Total samples	1067	100	3.436	100	1701	100	2421	100	2.702	100	
Men (M)	322	30	1063	31	476	28	750	31	839	31	.1902
Occupational factors (O)	106	10	311	10	194	12	195	8	247	9	.0038**
Atopic dermatitis (A)	179	17	531	16	293	17	468	19	513	19	.0005***
Hands (H)	320	30	977	28	529	31	748	31	885	33	.0023**
Legs (L)	69	6	187	5	100	6	105	4	138	5	.0706
Face (F)	275	26	920	27	366	22	518	21	596	22	.0000***
Age > 40 years (A)	734	69	2463	72	1.132	67	1573	66	1790	67	.0000***
Any positive (P)	490	46	1595	46	769	45	1090	45	1196	44	0,5362

** $P < .01$.
*** $P < .001$.

(MCI/MI), and fragrance mix i. Some gender differences were seen while for women, the most frequently positive allergens were nickel sulfate, methylisothiazolinone, cobalt chloride, MCI/MI, fragrance mix i, and paraphenylenediamine (PPD), for men, they were nickel sulfate, MCI/MI, and potassium dichromate, with lower sensitization to PPD in men compared to in women (2.31 vs 3.31), and higher sensitization to potassium dichromate (4.7 vs 2.38), among other differences. The sensitization frequency to the allergens added in January 2022 in the studied patients was 4.44% for hydroxyethyl methacrylate, 2.58% for textile dye mix, 4.59% for linalool hydroperoxides, and 3.92% for limonene hydroperoxides.

Table 3 shows the percentage of positives for different allergens included in the standard GEIDAC series across different study years. The allergens recently included in the GEIDAC standard battery are included at the end of this table; since they were not systematically patched in the early years and, therefore, were studied in a much smaller number of patients, their data prior to their inclusion in 2022 are not included in the trend study.

We can see how the percentage of positives for methylisothiazolinone decreases over time, with an orderly trend.

The figures below represent the variation in the percentage of positives for different allergens across the study years, both globally and differentiated by gender.

Figure 1 includes allergens with sensitization rates > 4% (nickel sulfate, methylisothiazolinone, cobalt chloride, MCI/MI, and fragrance mix I).

The allergens that showed sensitization frequencys ranging from 1% to 4% during the study period were PPD, fragrance mix II, balsam of Peru, potassium dichromate, formaldehyde, carbamate mix, thiuram mix, p-tert-butylphenol-formaldehyde resin, and rosin, as shown in Figure 2.

Figure 3 illustrates the variation in the percentage of positive results over the years for the remaining allergens, each of which had an overall sensitization frequency < 1%.

Discussion

Epidemiological surveillance in contact dermatitis is key to understand the variations in sensitizations to different allergens over the years, thereby enabling the implementation of proper measures for their prevention at both individual and community levels. In Spain, such surveillance is one of the objectives of REIDAC

In 1977, the first national epidemiological study of this kind was published, including 2806 patients studied through patch tests.[2] The most frequently positive allergens at that time were nickel, potassium dichromate, tetramethylthiuram disulfide, PPD, a mixture of mercaptans, and wood tar extracts. Since then, various changes in exposure have led to modifications in the allergens studied (with several changes made to the GEIDAC standard series),[3,4] and differences in sensitization frequencies. However, some of the allergens that were already common in those years continue to be so today. In 2011, another publication of 1161 patients from 5 national centers[1] claimed that the most frequently positive allergens were nickel sulfate (25.88%), potassium dichromate (5.31%), cobalt (5.10%), a mixture of fragrances (4.64%), and balsam of Peru (4.44%). Also, there is a recent publication from our region on a specific population from Gran Canaria, Canary Islands, Spain which identified nickel sulfate, MCI/MI, methylisothiazolinone, PPD, and potassium dichromate as the most frequent allergens, even at higher frequencies than those reported at national level.[6]

In the international scientific medical literature available, there are other publications that attempt to capture changes in the percentage of sensitization to different allergens over the years in a similar way. In most of these series, the changes seen across years are not systematically recorded, and they are not always collected prospectively. Some series pertain to other populations,[7] some of which, despite spanning across many more years, include fewer patients.[8] Additionally, there are several European publications[9–15] that either focus on data from years prior to ours or, in addition to that, focus on specific groups

Table 2 Positivity rates to the different allergens included in the standard GEIDAC series in all the studied patients differentiated by sex.

	All			Women			Men		
	Result			Result			Result		
		Positivity (+/++/+++)			Positivity (+/++/+++)			Positivity (+/++/+++)	
	N	N (%)	Statistics (95%CI)	N	N (%)	Statistics (95%CI)	N	N (%)	Statistics (95%CI)
1. Nickel sulfate	1 1258	2604 (23.13)	17.01 (16.31-17.71)	7836	2266 (28.92)	22.96 (22.03-23.91)	3420	338 (9.88)	8.08 (7.17-9.03)
2. Lanolin alcohols	11 241	66 (0.59)	0.46 (0.35-0.61)	7820	43 (0.55)	0.46 (0.32-0.64)	3419	23 (0.67)	0.46 (0.27-0.76)
3. Neomycin sulfate	11 241	99 (0.88)	0.95 (0.78-1.14)	7820	69 (0.88)	0.84 (0.65-1.06)	3419	30 (0.88)	1.11 (0.79-1.53)
4. Potassium dichromate	11 255	347 (3.08)	3.09 (2.78-3.42)	7831	186 (2.38)	2.48 (2.14-2.85)	3422	161 (4.7)	4 (3.35-4.7)
5. Cain mix	7322	69 (0.94)	1.11 (0.88-1.38)	5141	47 (0.91)	0.84 (0.61-1.13)	2179	22 (1.01)	1.5 (1.05-2.13)
6. Fragrance mix I	11 243	465 (4.14)	3.63 (3.29-3.99)	7821	334 (4.27)	3.77 (3.36-4.22)	3420	131 (3.83)	3.42 (2.85-4.1)
7. Colophony	11 247	153 (1.36)	1.43 (1.23-1.68)	7825	105 (1.34)	1.5 (1.24-1.8)	3420	48 (1.4)	1.33 (0.96-1.76)
8. Paraben mix	11 250	46 (0.41)	0.49 (0.37-0.64)	7826	22 (0.28)	0.29 (0.18-0.43)	3422	24 (0.7)	0.8 (0.52-1.15)
10. Peru balsam	11 245	362 (3.22)	3.37 (3.04-3.72)	7824	226 (2.89)	2.93 (2.56-3.33)	3419	136 (3.98)	4.03 (3.38-4.73)
12. Cobalt chloride	11 257	536 (4.76)	4.12 (3.76-4.51)	7833	402 (5.13)	4.56 (4.11-5.05)	3422	134 (3.92)	3.45 (2.87-4.13)
13. P-tert-Butylphenol formaldehyde resin	11 244	173 (1.54)	1.37 (1.16-1.6)	7822	132 (1.69)	1.68 (1.41-1.99)	3420	41 (1.2)	0.9 (0.62-1.29)
14. Epoxy resin	11 243	102 (0.91)	0.72 (0.57-0.89)	7822	54 (0.69)	0.53 (0.38-0.71)	3419	48 (1.4)	1 (0.69-1.39)
15. Carbamix mix	11 201	187 (1.67)	1.66 (1.43-1.91)	7792	98 (1.26)	1.1 (0.89-1.37)	3407	89 (2.61)	2.49 (2-3.08)
16. Black rubber mix/IPPD	11 243	100 (0.89)	1.18 (0.99-1.4)	7822	68 (0.87)	1.11 (0.88-1.36)	3419	32 (0.94)	1.3 (0.94-1.73)
17. Methylchloroisothiazolinone/methylisothiazolinone	9358	420 (4.49)	4.02 (3.62-4.43)	6520	284 (4.36)	4.07 (3.6-4.58)	2836	136 (4.8)	3.93 (3.24-4.71)
18. Quaternium-15	11 255	94 (0.84)	0.91 (0.74-1.1)	7830	73 (0.93)	0.99 (0.78-1.23)	3423	21 (0.61)	0.78 (0.52-1.15)
20. Paraphenylenediamine	11 243	416 (3.7)	3.25 (2.92-3.59)	7821	337 (4.31)	3.67 (3.27-4.12)	3420	79 (2.31)	2.6 (2.1-3.2)
21. Formaldehyde	9777	254 (2.6)	2.6 (2.29-2.93)	6799	181 (2.66)	2.91 (2.52-3.34)	2976	73 (2.45)	2.14 (1.64-2.71)
22. Mercaptan mix	11 241	42 (0.37)	0.41 (0.29-0.54)	7820	22 (0.28)	0.25 (0.15-0.38)	3419	20 (0.58)	0.65 (0.4-0.98)
24. Thiuram mix	11 240	177 (1.57)	1.34 (1.14-1.57)	7819	111 (1.42)	1.08 (0.86-1.33)	3419	65 (1.9)	1.74 (1.32-2.23)
25. Diazolidinyl urea	11 258	49 (0.44)	0.67 (0.53-0.84)	7831	32 (0.41)	0.61 (0.44-0.8)	3425	17 (0.5)	0.75 (0.5-1.11)
27. Tixocortol pivalate	11 245	41 (0.36)	0.45 (0.34-0.6)	7821	32 (0.41)	0.56 (0.4-0.74)	3422	9 (0.26)	0.3 (0.14-0.54)
29. Imidazolidinyl urea	11 259	44 (0.39)	0.4 (0.29-0.53)	7832	30 (0.38)	0.37 (0.25-0.53)	3425	14 (0.41)	0.43 (0.25-0.72)
30. Budesonide	11 247	84 (0.75)	0.79 (0.64-0.98)	7823	44 (0.56)	0.64 (0.48-0.85)	3422	40 (1.17)	1.03 (0.72-1.42)
32. Mercaptobenzothiazole	11 241	40 (0.36)	0.41 (0.3-0.55)	7820	18 (0.23)	0.31 (0.2-0.46)	3419	22 (0.64)	0.56 (0.34-0.87)
33. Methylisotiazolinone	10 295	729 (7.08)	6.84 (6.36-7.34)	7154	470 (6.57)	6.42 (5.86-7.01)	3139	259 (8.25)	7.47 (6.58-8.45)
35. Fragrance mix II	10 293	351 (3.41)	3.35 (3.01-3.71)	7150	232 (3.24)	3.03 (2.65-3.46)	3141	119 (3.79)	3.81 (3.16-4.53)
38. 2-HEMA	6245	277 (4.44)	3.19 (2.77-3.66)	4358	265 (6.08)	5.02 (4.38-5.7)	1885	12 (0.64)	0.44 (0.18-0.84)
39. Textile dye mix	6211	202 (3.25)	2.98 (2.57-3.43)	4290	137 (3.19)	2.92 (2.45-3.48)	1919	65 (3.39)	3.08 (2.36-3.96)
40. Linalool hydroperoxides	6507	361 (5.55)	6.01 (5.45-6.62)	4538	265 (5.84)	6.11 (5.42-6.84)	1967	96 (4.88)	5.87 (4.87-7)
41. Limonene hydroperoxides	6532	284 (4.35)	4.36 (3.87-4.88)	4546	216 (4.75)	4.5 (3.91-5.14)	1984	68 (3.43)	4.15 (3.31-5.13)

IPPD, N-isopropyl-n-phenyl-phenylenediamine; 2-HEMA, hydroxyethyl methacrylate; Statistics (95%CI): age and sex standardized percentage (95% confidence interval)

Table 3 Percentage of positivity for various allergens included in the standard GEIDAC series across the study years.

All	Percentage of pos. per year of consultation					Corrected *P* value	.0016	
	2018	2019	2020	2021	2022	*P* value homogeneity	*P* value trend	*P* value adjusted trend
1. Nickel sulfate	24.93	23.23	23.65	22.87	22.20	.4592	.1031	.2061
2. Lanolin alcohols	0.75	0.44	0.65	0.67	0.60	.7052	.7065	.6004
3. Neomycin sulfate	1.03	1.14	0.77	0.83	0.60	.2239	.0331	.0445
4. Potassium dichromate	3.10	3.66	3.19	2.54	2.76	.1255	.0397	.0212
5. Cain mix	0.44	0.84	1.31	0.74	1.14	.2882	.1862	.3812
6. Fragrance mix I	3.95	4.57	3.67	4.29	3.82	.4853	.3973	.5267
7. Colophony	1.41	1.67	1.30	1.17	1.16	.4114	.1016	.0513
8. Paraben mix	0.47	0.56	0.41	0.25	0.34	.4428	.1242	.9651
9. Peru balsam	3.01	3.19	3.08	3.04	3.59	.7880	.4008	.3678
10. Cobalt chloride	4.05	4.59	4.91	4.87	5.07	.7139	.1870	.8976
11. P-tert-Butylphenol formaldehyde resin	1.98	1.76	1.30	1.17	1.57	.2624	.1736	.6070
12. Epoxy resin	0.75	1.00	1.18	0.58	0.97	.2943	.7691	.4718
13. Carbamix mix	2.45	1.43	1.72	1.60	1.70	.2699	.6302	.6766
14. Black rubber mix/IPPD	1.60	1.00	0.47	0.58	1.01	.0121	.1440	.8857
15. Methylchloroisothiazolinone/methylisothiazolinone	5.08	4.30	5.34	5.07	3.57	.0488	.1470	.6301
16. Quaternium-15	0.66	1.11	0.77	0.67	0.75	.3200	.2687	.1568
17. Paraphenylenediamine	4.33	3.78	3.66	3.92	3.18	.4711	.1544	.4577
18. Formaldehyde	2.58	2.93	2.55	2.52	2.33	.7384	.2623	.1630
19. Mercaptan mix	0.56	0.35	0.41	0.33	0.34	.8510	.4745	.5352
20. Thiuram mix	1.79	1.46	2.13	1.46	1.39	.3130	.4415	.5161
21. Diazolidinyl urea	0.38	0.50	0.30	0.46	0.45	.8810	.9628	.4792
22. Tixocortol pivalate	0.85	0.29	0.35	0.33	0.30	.1045	.1622	.3815
23. Imidazolidinyl urea	0.00	0.44	0.30	0.50	0.45	.2207	.1631	.3252
24. Budesonide	0.75	0.88	0.77	0.92	0.41	.2176	.1340	.1648
25. Mercaptobenzothiazole	0.66	0.29	0.65	0.29	0.19	.0458	.0806	.4879
26. Methylisotiazolinone	8.55	8.00	7.82	6.79	5.21	**.0002**	**.0000**	.0232
27. Fragrance mix II	2.62	4.08	2.83	3.46	3.20	.0957	.5608	.9768
28. 2-HEMA					4.73			
29. Textile dye mix					2.58			
30. Linalool hydroperoxides					4.59			
31. Limonene hydroperoxides					3.92			

IPPD, N-isopropyl-n-phenyl-phenylenediamine; 2-HEMA, hydroxyethyl methacrylate; Pos.: positivity
Data with statistically significant differences highlighted in bold.

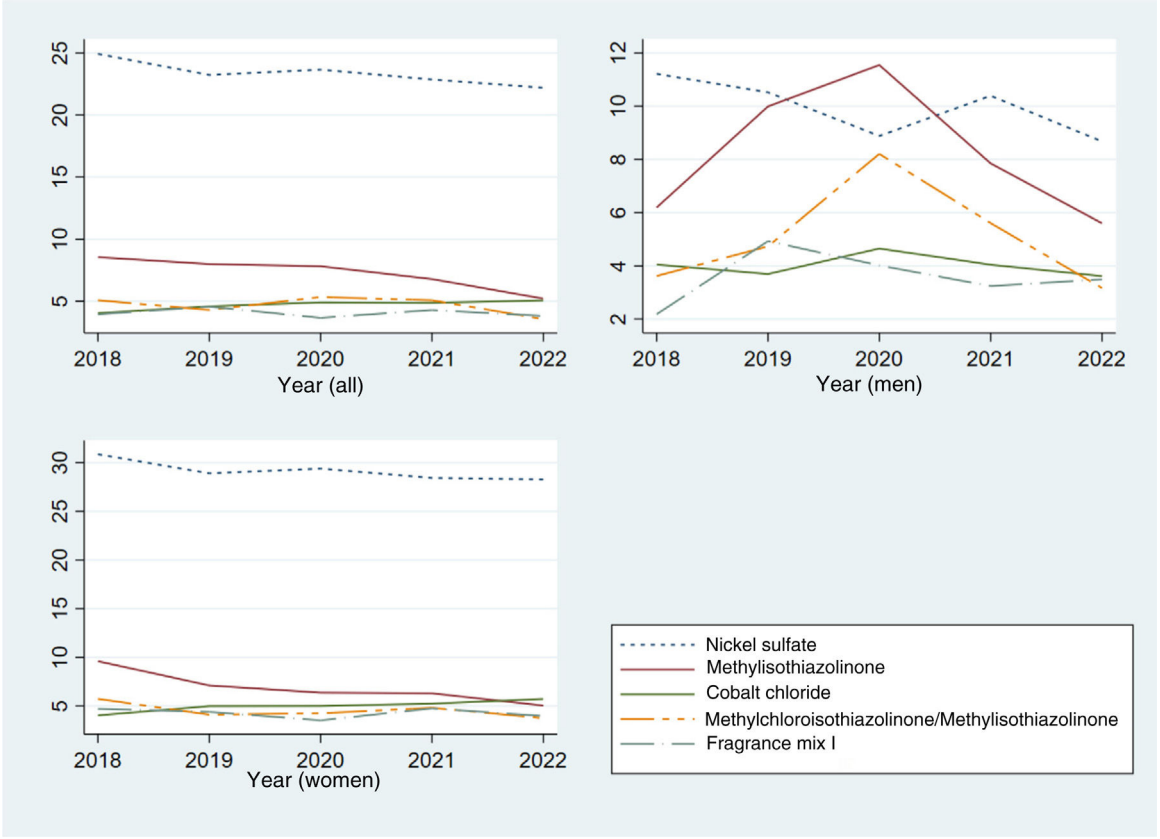

Figure 1 Variation across time for allergens with overall sensitization rates in the study years > 4%, both for the ovefrall population and broken down by gender.

of allergic contact eczemas, such as those associated with occupational exposure,[14] or due to specific allergens.[15]

With the current technology, a real-time approach to the most common allergens in Spain is possible.[16]

Among the results obtained, the persistence of high sensitization to nickel sulfate stands out, as mentioned earlier. In fact, it was already documented the early studies conducted in Spain (25.88),[12] as well as in other European studies (23.98%).[17] Nickel is a metal found in alloys, being nickel salts responsible for dermatitis, promoting their release and penetration into the skin primarily facilitated by sweating. In 1994, European regulations were passed to control the release of nickel in jewelry, but they did not become effective until 2021. Despite the ongoing high sensitization, many of the positive cases detected today do not seem to be relevant today.

PPD continues to exhibit high sensitization in our environment, especially among women, as mentioned earlier. In a recent publication on PPD sensitization across various Spanish centers,[18] it remained fairly stable at nearly 4% of all patch-tested patients from 2004 through 2014, and no significant changes reported despite the regulation implemented in 2009 regarding hair dyes (reducing its maximum concentration from 6% down to 2%). Several hypotheses have been proposed for the persistence of this sensitization, such as the maintenance of the habit of getting temporary henna tattoos, which are often adulterated with PPD, whose concentration has not yet been regulated,[19] or lifestyle changes leading to more and more patients using cosmetics containing PPD at younger ages.

In our study, sensitization to fragrance mix I also persists at a high level, despite regulatory changes introduced in the mandatory labeling of certain fragrances. Also, it remains at levels similar to those reported in previous national series (4.99%),1 and recent European studies (3.4%).[17]

High sensitization to isothiazolinones, both MCI/MI (which remains high throughout across the study years) and methylisothiazolinone should also be mentioned here. In the case of the latter, although sensitization remains high, there is a drop in sensitization frequency across the years, both in raw values and when adjusted for sex and age being the only allergen with statistically significant changes reported.

Methylisothiazolinone is a derivative of isothiazolinones, and is widely used as a preservative in rinse-off cosmetics, household detergents, water-based paints, and industrial products. Sensitization to it occurs both in the domestic environment—mainly due to exposure to cosmetics and household detergents—and in the workplace, especially among cleaning workers.

The epidemic of sensitization to methylisothiazolinone at the beginning of the 21st century is well known.[20–22] As a result, after recognizing the problem, the use of methylisothiazolinone was ill-advised in rinse-off cosmetics by the European cosmetic industry at the end of 2013. At the same time, the Scientific Committee on Consumer Safety reevaluated the risk, which lead to the recommen-

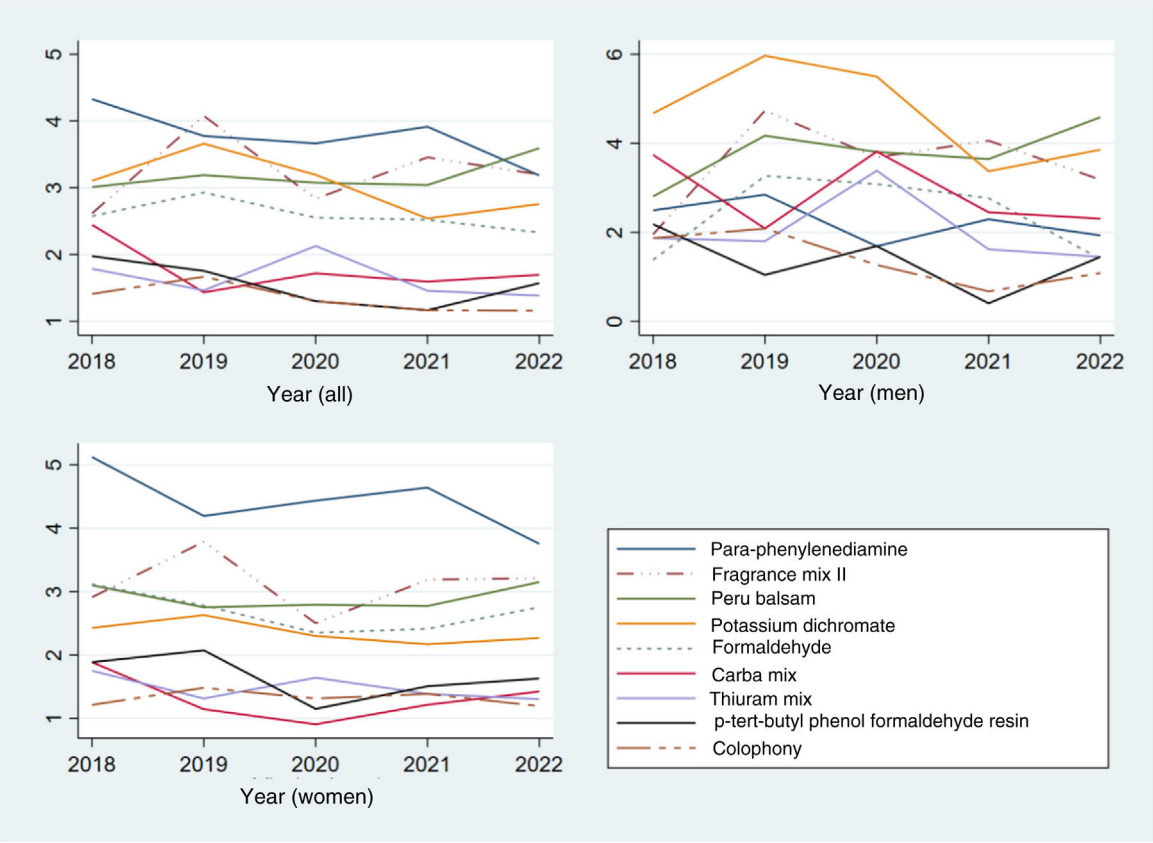

Figure 2 Variation across time for allergens with overall sensitization rates in the study years from 1% to 4%, both for the overall population and broken down by gender.

dation to ban the use of methylisothiazolinone in rinse-off cosmetics and keep the maximum allowable level to 15 ppm in leave-on cosmetics. Although it took time for this recommendation to translate into an actual regulation, and the regulation again allowed for transition periods, a change in sensitization trends could be expected as confirmed by our most recent data.

In the United States, according to the most recent data from the North American Contact Dermatitis Group, the highest prevalence of sensitization to isothiazolinones occurred later than it did in Europe.[23] While in Europe, sensitization to MCI/MI from 2013 through 2014 reached levels of 5.4% to 7.6%, before dropping in 2017-2018 down to 3.2%-4.4%,[24,25] in the United States, positivity to MCI/MI increased from 2.5% in 2009-2010 up to 10.8% in 2017-2018. The same thing happened for methylisothiazolinone, where reactions decreased in Europe down to 3.4%-5.5% compared to 15% in the North American Contact Dermatitis Group during 2017-2018. This is likely due to the lack of regulations on the use of isothiazolinones in cosmetics across the United States.

According to recent data published by REIDAC,[22] sensitization to both MI and MCI/MI is associated with being an active worker, hand dermatitis, the use of detergents, and being older than 40 years.

Some other changes in sensitization trends can be seen, but none of them are significant. For example, in the case of neomycin, there is a downward trend since data collection began, although it is not significant, possibly indicating reduced use of topical drugs including combinations of antibiotics and other agents (corticosteroids, antifungals, etc.). In Spain, prescriptions for topical products combining corticosteroids and antibiotics have not been funded for years.

Similarly, we can see also non-significant downward trend in sensitization to potassium dichromate. The most common sources of exposure to potassium dichromate are wet cement and chromium-tanned leather products. Since 2005, the use of cements with > 2 ppm of hexavalent chromium has been restricted, and a decrease in sensitization has been detected based on historical data and in certain regions.[6,26] The decrease in sensitization is likely related to this regulation, and with the improved preventive measures implemented by construction workers. Additionally, a probable decrease in the use of leather footwear in recent years may have also contributed to its decline, although there is not enough data to confirm this hypothesis to date.

Our study included data on allergens that have been more recently added to the standard GEIDAC panel, and a high overall level of sensitization to all of them can be observed (hydroxyethyl methacrylate, textile dye mix, linalool hydroperoxides, and limonene hydroperoxides).

For a specific population, changes in sensitization to different allergens often depend on the chemical characteristics of these allergens (which, overall, do not change), and the degree of exposure to them. Therefore, assuming that the characteristics of our population have remained fairly

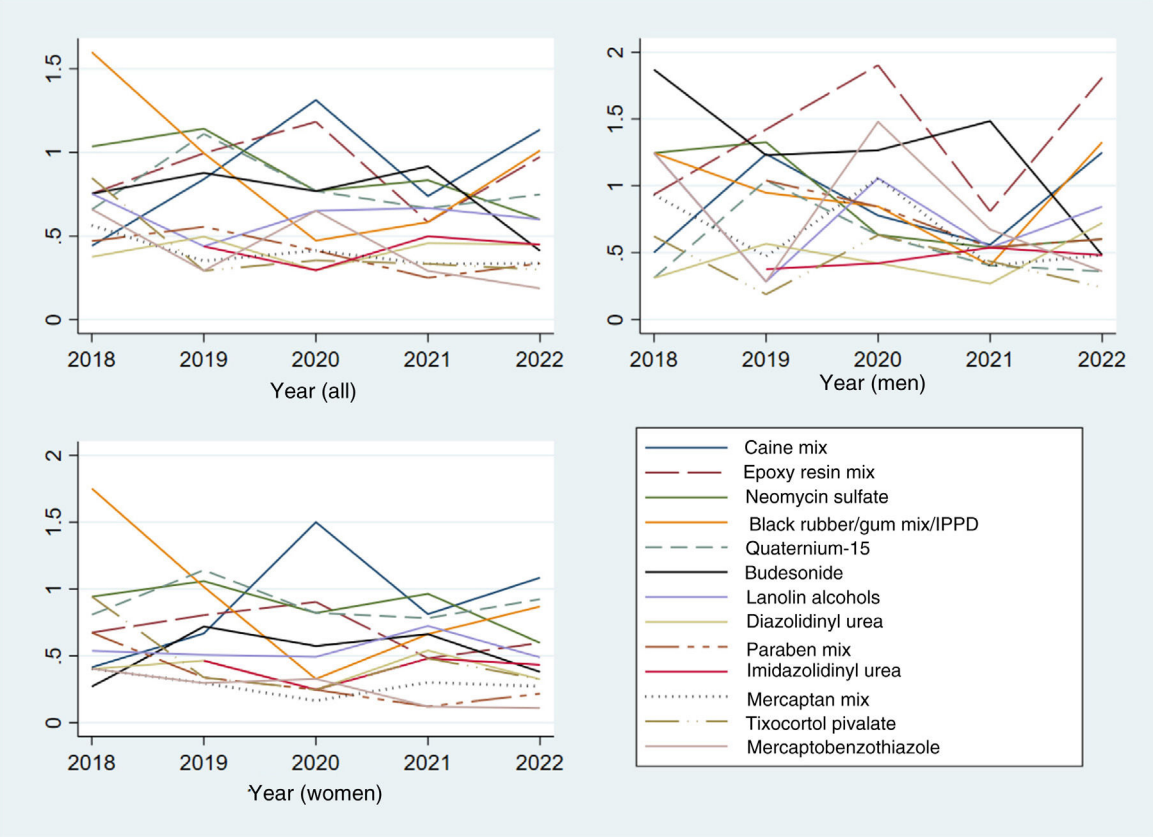

Figure 3 Variation across time for allergens with overall sensitization rates in the study years < 1%, both for the overall population and broken down by gender.

consistent across the years (no significant differences in the MOAHLFA data across the years can be seen, as shown in Table 1, except perhaps for the face, where a decrease was seen in the 2020-2022 compared to previous years, possibly influenced by the use of masks during the COVID pandemic years), the differences detected in sensitization should be attributed to changes in various exposures.

Conclusions

According to the data obtained in our study, the persistence of high sensitization to allergens such as nickel, MCI/MI, and fragrance mix I is noteworthy. Only a significant downward trend for methylisothiazolinone was found.

We want to emphasize the importance of multicenter registries, which allow us to gather data on a large scale and thereby detect trends. This enables us to observe potential increases in sensitization to certain allergens, prompting us to consider the need for measures to reduce this. Additionally, as is the case with methylisothiazolinone, it helps us verify the effectiveness of the measures taken to reduce sensitization.

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Conflicts of interest

None declared.

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