

## ORIGINAL ARTICLE OPEN ACCESS

# Contact Sensitisation Trends in Slovenian Children and Adolescents: A Retrospective Single-Centre Study

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## ABSTRACT

**Background:** Existing data on contact sensitisation prevalence among children and adolescents is limited, especially regarding comparisons of specific allergens over extended timeframes. The objective of this study was to identify the most common allergens and to evaluate shifts in contact sensitisation trends.

**Methods:** We retrospectively evaluated patch test data of 1052 children and adolescents referred to a single tertiary medical centre. The analysis covered three periods: 2000–2004, 2010–2014, and 2020–2024. All patients were tested with the time-recommended baseline series of allergens.

**Results:** A significant decrease was reported for nickel prevalence, dropping from 12.6% to 4.0%. Although tested only in the latest period, textile dye mix (4.7%) and methylisothiazolinone (3.2%) emerged as important allergens. Children with atopic dermatitis (AD) showed a higher prevalence of contact sensitisation (27.7% vs. 22.7%). In contrast, among adolescents, rates were lower in those with AD (20.0% vs. 30.7%).

**Conclusions:** Our findings demonstrate a marked decline in nickel sensitisation, while dyes and preservatives are gaining importance. The clinical relevance of specific allergens is evolving in response to regulations and market trends. Continuous surveillance of contact sensitisation is also essential in the pediatric population to ensure that patch testing strategies and preventive measures remain current, targeted and effective.

## 1 | Introduction

Contact sensitisation (CS) is currently recognised as a common entity in children and adolescents, affecting around 16.5% of the paediatric population [1]. The most prevalent contact allergens identified in children are historically metals and fragrances [2]. The sources of exposure include personal care products, recreational activities, toys, jewellery, dyes, and temporary tattoos. Given the evolving nature of exposure sources, the profile of

common allergens is constantly changing [2, 3]. The association between CS and atopic dermatitis (AD) has been debated for a long time. Recent studies suggest that individuals with AD may exhibit similar or even heightened risk of CS compared to non-atopic individuals [3, 4].

The primary objective of this study was to analyse time trends in CS incidence and determine the most frequently observed allergens in the Slovenian paediatric population. Moreover, we

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assessed whether patients with atopic dermatitis, in whom a damaged skin barrier may facilitate the passage of the allergens through the skin, have an increased risk of CS.

## 2 | Methods

We conducted a retrospective study of children and adolescents, aged 18 years or younger, referred for patch testing to the Department of Dermatovenereology at the University Medical Centre Ljubljana, Slovenia. Data were retrieved from the patch testing unit database and included sociodemographic characteristics and patch test results. The study cohort comprised 1052 patients. Analyses were performed across three distinct time periods: 2000–2004, 2010–2014 and 2020–2024. In the latest period, additional data on personal history of AD, diagnosed according to the criteria of Hanifin and Rajka, were collected. The study was conducted in accordance with the Declaration of Helsinki. Approval was obtained from The National Medical Ethics Committee of the Republic of Slovenia (approval number: 0120-384/2024-2711-3). Due to the retrospective nature of the study and the use of anonymised clinical data, the requirement for informed consent was waived by the ethics committee.

Patch testing was performed using the European baseline series (EBS) of contact allergens recommended at the time. This series consisted of 23 allergens in the 2000–2004 period, 28 allergens in the 2010–2014 period and 30 allergens in the 2020–2024

period, with the latest corresponding to the 2015 version of the EBS. Patch test strips Curatest (St. Gallen, Switzerland) with allergens supplied by allergEAZE (SmartPractice, Canada) were applied to the patient's upper back for 48 h. Readings were performed on day (D) 2 and D3 after application. Reactions were graded according to the criteria established by the International Contact Dermatitis Research Group [5]. For the purposes of this study, a positive reaction was defined as one plus (+) or greater. Doubtful (?+) and irritant (IR) reactions were excluded from analysis. Patients were referred for patch testing due to suspected allergic contact dermatitis (ACD), other forms of dermatitis in which an allergic component needed to be ruled out, or in specific cases prior to the initiation of systemic therapy.

Statistical analyses were performed using JASP software (JASP Team, version 0.19.3, Amsterdam, The Netherlands). Demographic characteristics and allergen prevalence were expressed as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test when expected frequencies were less than 5. Changes in allergen sensitisation over time were evaluated by comparing the first (2000–2004 or 2010–2014) and the latest (2020–2024) study period using the Chi-square test. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to determine the strength of association. A two-sided *p*-value of less than 0.05 was considered the threshold for statistical significance.

## 3 | Results

Demographic characteristics of the patients are presented in Table 1. Females represented the majority across all periods (56%–62%) and the median age ranged from 11 to 13 years. The 2010–2014 group differed slightly from the other periods, as children represented the largest age group (54%), whereas adolescents predominated in 2000–2004 (38%) and 2020–2024 (40%).

Positive patch test reaction rates (PPTRR), presented in Table 2, show that the overall rate of at least one positive reaction was stable in the first two periods (33.5% and 34.2%) but decreased in 2020–2024 (25.5%), despite the larger allergen panel. Females had overall higher PPTRR, however a decrease was observed in both sexes. The proportion of patients with more than one positive reaction ranged between 9.5% and 14.1%.

Sensitisation rates for individual allergens across the three study periods are presented in Table 3. A statistically

**TABLE 1** | Demographic data.

|                                         | 2000–2004   | 2010–2014   | 2020–2024   |
|-----------------------------------------|-------------|-------------|-------------|
| <i>N</i>                                | 239         | 433         | 380         |
| Females, <i>n</i> (%)                   | 149 (62.3%) | 244 (56.4%) | 225 (59.2%) |
| Males, <i>n</i> (%)                     | 90 (37.7%)  | 189 (43.7%) | 155 (40.8%) |
| Age, median (range)                     | 13 (4–18)   | 11 (3–18)   | 12 (3–18)   |
| Children (3–11 years), <i>n</i> (%)     | 90 (37.7%)  | 234 (54.0%) | 153 (40.3%) |
| Adolescents (12–18 years), <i>n</i> (%) | 149 (62.3%) | 199 (46.0%) | 227 (59.7%) |

**TABLE 2** | Patch test results data.

|                                    | 2000–2004  | 2010–2014   | 2020–2024  |
|------------------------------------|------------|-------------|------------|
| Number of allergens tested         | 23         | 28          | 30         |
| At least 1 positive, <i>n</i> (%)  | 80 (33.5%) | 148 (34.2%) | 97 (25.5%) |
| Females, <i>n</i> (%)              | 51 (34.2%) | 93 (38.1%)  | 63 (28.0%) |
| Males, <i>n</i> (%)                | 29 (32.2%) | 55 (29.1%)  | 34 (21.9%) |
| More than 1 positive, <i>n</i> (%) | 30 (12.6%) | 61 (14.1%)  | 36 (9.5%)  |
| Range of reactions per person      | 1–5        | 1–7         | 1–7        |

**TABLE 3** | Time trends of individual contact allergens.

| Allergen                                                                            | 2000–2004<br>(N=239) | 2010–2014<br>(N=433) | 2020–2024<br>(N=380) | <i>p</i> | OR (95% CI)      |
|-------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|----------|------------------|
| Colophony 20.0% pet.                                                                | 4 (1.7%)             | 6 (1.4%)             | 9 (2.4%)             | 0.56     | 1.4 (0.43–4.7)   |
| Clioquinol 5.0% pet.                                                                | 0 (0.0%)             | 1 (0.2%)             | 1 (0.3%)             | 0.43     | 1.0 (0.08–46.6)  |
| Paraben mix 16.0% pet.                                                              | 1 (0.4%)             | 1 (0.2%)             | 1 (0.3%)             | 0.74     | 0.63 (0.04–10.1) |
| Potassium dichromate 0.5% pet.                                                      | 4 (1.7%)             | 7 (1.6%)             | 3 (0.8%)             | 0.31     | 0.47 (0.10–2.1)  |
| Nickel sulphate 5.0% pet.                                                           | 30 (12.6%)           | 45 (10.4%)           | 15 (4.0%)            | <0.001   | 0.29 (0.15–0.54) |
| Formaldehyde 2.0% aq.                                                               | 1 (0.4%)             | 2 (0.5%)             | 0 (0.0%)             | 0.21     | 0.21 (0.01–5.2)  |
| Paraphenylenediamine (PPD) 1.0% pet.                                                | 4 (1.7%)             | 21 (4.9%)            | 16 (4.2%)            | 0.082    | 2.6 (0.85–7.8)   |
| Cobalt chloride 1.0% pet.                                                           | 13 (5.4%)            | 32 (7.4%)            | 9 (2.4%)             | 0.045    | 0.42 (0.18–1.00) |
| Balsam of Peru 25.0% pet.                                                           | 8 (3.4%)             | 15 (3.5%)            | 12 (3.2%)            | 0.90     | 0.94 (0.38–2.3)  |
| Benzocaine 5.0% pet.                                                                | 4 (1.7%)             | 9 (2.1%)             | 5 (1.3%)             | 0.72     | 0.78 (0.21–3.0)  |
| Neomycin sulphate 20.0% pet.                                                        | 6 (2.5%)             | 16 (3.7%)            | 8 (2.1%)             | 0.74     | 0.83 (0.29–2.4)  |
| Mercaptobenzothiazole 2.0% pet.                                                     | 3 (1.3%)             | 9 (2.1%)             | 0 (0.0%)             | 0.029    | 0.09 (0.01–1.7)  |
| Mercapto mix 2.0% pet.                                                              | 6 (2.5%)             | 7 (1.6%)             | 0 (0.0%)             | 0.002    | 0.05 (0.00–0.84) |
| Thiuram Mix 1.0% pet.                                                               | 2 (0.8%)             | 6 (1.4%)             | 3 (0.8%)             | 0.95     | 0.94 (0.16–5.7)  |
| <i>N</i> -isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine (IPPD) 0.1% pet. | 2 (0.8%)             | 4 (0.9%)             | 3 (0.8%)             | 0.95     | 0.94 (0.16–5.7)  |
| Fragrance mix I 8.0% pet.                                                           | 17 (7.1%)            | 37 (8.6%)            | 16 (4.2%)            | 0.12     | 0.57 (0.28–1.2)  |
| Epoxy resin 1.0% pet.                                                               | 0 (0.0%)             | 0 (0.0%)             | 1 (0.3%)             | 0.43     | 1.9 (0.08–46.6)  |
| Lanolin alcohol 30.0% pet.                                                          | 11 (4.6%)            | 9 (2.1%)             | 3 (0.8%)             | 0.002    | 0.16 (0.05–0.56) |
| 4- <i>tert</i> -Butylphenol formaldehyde resin (PTBPT) 1.0% pet.                    | 5 (2.1%)             | 3 (0.7%)             | 2 (0.5%)             | 0.073    | 0.25 (0.05–1.3)  |
| Quaternium-15 1.0% pet.                                                             | 0 (0.0%)             | 2 (0.5%)             | 5 (1.3%)             | 0.075    | 7.0 (0.39–127.5) |
| MCI/MI 0.02% aq.                                                                    | 3 (1.3%)             | 6 (1.4%)             | 13 (3.4%)            | 0.098    | 2.8 (0.79–9.9)   |
| Sesquiterpene lactone mix 0.1% pet.                                                 | 0 (0.0%)             | 2 (0.5%)             | 0 (0.0%)             | /        | /                |
| Primoin 0.01% pet.                                                                  | 0 (0.0%)             | 0 (0.0%)             | 0 (0.0%)             | /        | /                |
| Tixocortol Pivalate 0.1% pet.                                                       | n.t. <sup>a</sup>    | 0 (0.0%)             | 0 (0.0%)             | /        | /                |
| Budesonide 0.01% pet.                                                               | n.t. <sup>a</sup>    | 0 (0.0%)             | 0 (0.0%)             | /        | /                |
| Fragrance Mix II 14.0% pet.                                                         | n.t. <sup>a</sup>    | 13 (3.0%)            | 6 (1.6%)             | 0.18     | 0.52 (0.19–1.4)  |
| Methyldiromo glutaronitrile (MDBGN) 0.5% pet.                                       | n.t. <sup>a</sup>    | 5 (1.2%)             | 7 (1.8%)             | 0.42     | 1.6 (0.51–5.1)   |
| Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) 5.0% pet.                       | n.t. <sup>a</sup>    | 1 (0.2%)             | 1 (0.3%)             | 0.93     | 1.1 (0.07–18)    |

<sup>a</sup>n.t. = not tested.

significant decrease in sensitisation was observed for nickel sulphate (12.6%–4.0%;  $p < 0.001$ ), lanolin alcohol (4.6%–0.8%;  $p = 0.002$ ), and mercapto mix (2.5%–0%;  $p = 0.002$ ). Although not reaching statistical significance, several allergens appeared to show a declining trend in sensitisation prevalence over time, including cobalt chloride, fragrance mix I (FMI), and fragrance mix II (FMII). In contrast, colophony, paraphenylenediamine (PPD), methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), and quaternium-15 appeared

to show an increasing trend; however, once again, these changes did not reach statistical significance. For illustrative purposes, temporal trends in sensitisation to selected contact allergens are presented in Figure 1.

Two new allergens were introduced to the panel in the latest period, and their high prevalence requires specific mention. The most frequent allergen in this period was textile dye mix (TDM) 6.6% pet., with 18 patients testing positive (4.7%).

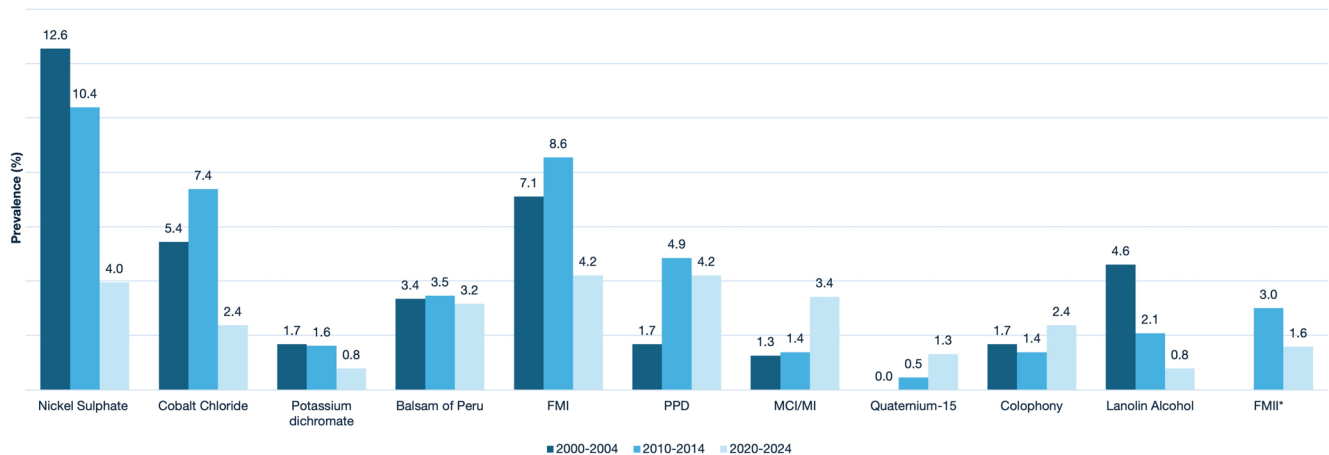
Methylisothiazolinone (MI) 0.2% aq., additionally showed an important prevalence, with 12 patients testing positive (3.2%).

We investigated the association between sex and patch test positivity. Nickel sulphate showed sex-specific differences in favour of girls in the 2000–2004 (16.1% vs. 6.7%,  $p=0.033$ , OR (95% CI): 2.69 (1.05–6.86)) and 2010–2014 (13.5% vs. 6.3%,  $p=0.015$ , OR (95% CI): 2.31 (1.16–4.60)). This significance was lost in 2020–2024 (4.9% vs. 2.6%,  $p=0.256$ , OR (95% CI): 1.94 (0.61–6.21)). Conversely, PPD (6.7% vs. 0.7%,  $p=0.004$ , OR (95% CI): 11.00 (1.44–83.33)) and TDM (7.6% vs. 0.7%,  $p=0.002$ , OR (95% CI): 12.66 (1.66–100.00)) showed a significant female predominance in the 2020–2024 period. The other allergens showed no specific sex-related differences.

The co-reactivity patterns of the most common allergens are shown in Table 4. Co-reactivity between nickel and cobalt showed changes across time. In 2000–2004, co-sensitisation was observed in 13.2% of cases. This proportion increased to 24.2%

in 2010–2014, however in 2020–2024, co-sensitisation declined markedly to 9.1%. On the other hand, single cases of cobalt sensitisation increased from 21.0% to 31.8%. For Balsam of Peru and FMI, co-reactivity progressively decreased over time, from 19.0% to 7.7%, while single cases of Balsam of Peru sensitisation increased from 19.0% to 38.5%. In 2020–2024, co-reactivity between MCI/MI and MI was observed in 38.9% of cases. A notably high rate of co-reactivity was identified for TDM and PPD in 2020–2024, with 78.9% of patients showing concomitant sensitisation. This represents the highest co-sensitisation proportion among all allergen pairs analysed.

We evaluated the association between CS and AD in 380 patients assessed in the 2020–2024 period, data comparing sex and age is presented in Table 5. Individual allergens did not statistically significantly differ by AD status, although prevalence differences existed. Among AD patients, FMI was the most common (5.5%), followed by nickel (4.8%), MCI/MI (3.0%), MI (3.0%) and cobalt (2.4%). In patients without AD, TDM had the highest rate



**FIGURE 1** | Trends in the prevalence of contact allergens over three decades. The bar chart illustrates the percentage prevalence of eight specific contact allergens across three time intervals: 2000–2004 (green), 2010–2014 (purple) and 2020–2024 (blue). Abbreviations: FMI, fragrance mix I; FMII, fragrance mix II (\*introduced in 2010); MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; PPD, paraphenylenediamine.

**TABLE 4** | Co-reactivity patterns for selected contact allergens.

| Allergen pair (A and B) | Only A positive | Only B positive | Co-sensitised |
|-------------------------|-----------------|-----------------|---------------|
| <b>2000–2004</b>        |                 |                 |               |
| Nickel and Cobalt       | 25 (65.8%)      | 8 (21.0%)       | 5 (13.2%)     |
| Balsam of Peru and FMI  | 4 (19.0%)       | 13 (62.0%)      | 4 (19.0%)     |
| <b>2010–2014</b>        |                 |                 |               |
| Nickel and Cobalt       | 30 (48.4%)      | 17 (27.4%)      | 15 (24.2%)    |
| Balsam of Peru and FMI  | 11 (22.9%)      | 33 (68.8%)      | 4 (8.3%)      |
| <b>2020–2024</b>        |                 |                 |               |
| Nickel and Cobalt       | 13 (59.1%)      | 7 (31.8%)       | 2 (9.1%)      |
| Balsam of Peru and FMI  | 10 (38.5%)      | 14 (53.8%)      | 2 (7.7%)      |
| MCI/MI and MI           | 6 (33.3%)       | 5 (27.8%)       | 7 (38.9%)     |
| TDM and PPD             | 3 (15.8%)       | 1 (5.3%)        | 15 (78.9%)    |

**TABLE 5** | Demographic and patch test results of patients with AD and without AD.

|                                | AD          | No AD       | <i>p</i> | OR (95% CI)     |
|--------------------------------|-------------|-------------|----------|-----------------|
| <i>N</i>                       | 165 (43.4%) | 215 (56.6%) |          |                 |
| Males                          | 62 (40.0%)  | 93 (60.0%)  |          |                 |
| Females                        | 103 (45.8%) | 122 (54.2%) |          |                 |
| At least 1 positive patch test | 38 (23.0%)  | 59 (27.4%)  | 0.33     | 0.79 (0.49–1.3) |
| Males                          | 15 (24.2%)  | 19 (20.4%)  | 0.58     | 1.2 (0.58–2.7)  |
| Females                        | 23 (22.3%)  | 40 (32.8%)  | 0.082    | 0.59 (0.32–1.1) |
| Children (0–11 years)          | 18 (27.7%)  | 20 (22.7%)  | 0.48     | 1.3 (0.62–2.7)  |
| Adolescents (11–18 years)      | 20 (20.0%)  | 39 (30.7%)  | 0.068    | 0.56 (0.30–1.1) |

(6.5%) followed by PPD (6.0%), Balsam of Peru (4.2%), MCI/MI (3.7%) and nickel (3.3%).

#### 4 | Discussion

Temporal analysis of our cohort revealed a downward trend in overall CS prevalence in children and adolescents. The percentage of patients having at least one positive patch test reaction dropped from 33.5% to 25.5% despite the larger allergen panel. While diminished referrals during the COVID-19 pandemic could have played a part, the primary cause appears to be changes in sensitisation to key allergens.

A significant finding was the sharp decline in nickel sensitisation prevalence, which decreased from 12.6% to 4.0%. While metals, particularly nickel, are typically the most common contact allergens [1–4, 6–8], our latest findings suggest that nickel has been overtaken as the leading sensitiser. The observed reduction aligns with declining prevalence across other EU countries, especially among younger patients, and it can be largely attributed to effective regulatory measures limiting nickel release from consumer goods [7–9]. Additional contributing factors include improved piercing practices, reinforced public awareness, and increased use of nickel-free materials [10]. Despite nickel sensitisation being more common in females, this decline has begun to equalise the historical gender difference [11]. In our study, nickel sensitisation was statistically more common in females in the earlier time periods, but this difference was lost in the latest period, in which 4.9% of females and 2.6% of males tested positive, supporting the finding that the gender gap is narrowing. Despite the observed decline, it is important to mention that a substantial proportion of consumer products intended for piercing still exceeds regulatory limits [9]. Moreover, cultural and geographical differences can also influence exposure patterns [7]. Therefore, continued vigilance and effective preventive strategies remain warranted.

Nickel and cobalt co-sensitisation is already well reported in literature [8]. We observed a temporal reduction in nickel and cobalt co-sensitisation, consistent with reports of decreasing concomitant reactions. Since nickel and cobalt often coexist in the same alloys, this suggests a shift in exposure sources.

Conversely, isolated cobalt allergy rates increased, and in the literature, dental alloys have been reported as a potential source of the increasing sensitisation rates [8]. Potassium dichromate was less common in our cohort, decreasing from 1.7% to 0.8%. We attribute this decline to the inclusion of leather goods in chromium EU legislation, as potassium dichromate is frequently implicated in foot dermatitis caused by leather shoes [12].

Our data suggest a decline in sensitisation to fragrance mixes, with rates of FMI dropping to 4.2% and FMII to 1.6%. These results strengthen established data that CS rates to fragrances, despite decreasing, still remain high due to their widespread use in personal care products [13, 14]. However, recent studies suggest that this decline may represent a shift in sensitisation rather than an overall reduction in fragrance allergy. Linalool and limonene hydroperoxide are now reported to be the major common culprit fragrance allergens, but they are not yet included in existing fragrance mixes [11, 15]. This underscores the necessity of a third standardised fragrance mix. In our cohort, sensitisation rates to Balsam of Peru remained stable, ranging from 3.2% to 3.5%. Its low co-reactivity with FMI indicates a separate sensitisation potential, supporting findings that it must be tested to avoid missing relevant fragrance allergies [16].

MCI/MI prevalence appears to be increasing, with rates rising from 1.3% to 3.4%. Furthermore, MI, tested only in the latest period, yielded a prevalence of 3.2%. Co-sensitisation between MCI/MI and MI is high; however, 27.8% of MI allergy cases would have been missed if only MCI/MI was tested. The observed surge in sensitisation to isothiazolinones is well reported in the literature, with rates peaking during the 2010s [6, 17]. Following the introduction of EU regulatory restrictions on MCI/MI and MI concentrations in personal care products, sensitisation rates began to stabilise or even decline [17, 18]. Our observation of an increasing trend in MCI/MI sensitisation contrasts with these reports. This discrepancy may be explained by increasing exposure from non-cosmetic sources, such as glues, paints, detergents, and adhesives, which are exempt from current restrictions and mandatory labelling [4, 17–20]. Moreover, recent data from a Spanish study demonstrate that isothiazolinones still remain among the most common allergens in children, with reported sensitisation rates of approximately 7.6%

for MI, 3.3% for MCI/MI, and 2.6% for benzisothiazolinone (BIT) [21]. Of particular concern is the rising prevalence of BIT sensitisation, which likely reflects its widespread presence in household products and indicates a shift rather than a true reduction in isothiazolinone exposure [18, 19, 22]. Overall, our findings support the notion that, despite regulatory efforts, isothiazolinone sensitisation persists, underscoring the need for continued surveillance and suggesting that further expansion of regulatory measures to include non-cosmetic products should be considered.

Recent research points to a new popular consumer trend among children called homemade slime. This activity involves mixing various household products, including glues and shaving creams, which may contain sensitisers, such as isothiazolinones and quaternium-15 [23]. The widespread popularity of slime offers a plausible explanation for the unexpected increase in quaternium-15 sensitisation rates in our cohort, which reached 1.3% in the 2020–2024 period. Another possible explanation for the increasing rates to these substances, that are banned in cosmetics, could be globalisation. Regulations in many non-EU markets are less restrictive [13, 24]. Global online shopping platforms allow consumers within the EU to easily purchase imported foreign products, including cosmetics and personal care items, that might contain banned preservatives or allowed preservatives in much higher concentrations [13].

Sensitisation to PPD appears to be increasing, with rates rising from 1.7% to 4.2%. Although the increase might not be statistically significant, its sustained prevalence is clinically relevant. Concurrently, TDM has emerged as the most common allergen in the latest period, achieving a 4.7% sensitisation rate. Both PPD and TDM display major sex-related differences, with females achieving dramatically higher rates compared to males. Furthermore, a high association exists between the two allergens, as 78.9% of positive patch test to dyes were co-reactive to both. The EU limits the use of PPD in hair dyes and prohibits its use in henna tattoos, yet the use of such products is increasing in younger ages [13, 25]. Textile dye allergy is getting recognised as common, with higher rates in countries where the use of synthetic textiles is higher and the weather is more humid [26]. Fast fashion products and black henna seem to be easily accessible online at very low prices through various online shopping retailers that may bypass EU regulations. Our findings indicate that sensitisation to dyes remains a persistent and potentially increasing concern in our population. This highlights the need for ongoing monitoring of exposure trends and regulatory compliance.

Colophony rates appear to be slightly increasing, from 1.7% to 2.4%. A higher prevalence of colophony sensitisation was found in schoolers, as it can be present in rubber, glue and adhesives, that are frequently used in schooling activities [27]. There have also been increasing cases of ACD in children to the adhesive parts of insulin pumps and glucose sensors, with colophony being among the culprit allergens [28].

In our cohort, overall CS rates did not significantly differ by AD status. However, among children, CS was more common in those with AD (27.7%) than those without (22.7%), compared to adolescents, where CS was less common in those with AD

(20.0%) than those without (30.7%). While individual allergens did not show statistical differences, common allergens in AD patients included FMI, nickel and isothiazolinones. Literature on this topic is inconsistent, however most studies agree that CS in children with AD is as common as in those without [3, 6]. In younger children, as in our findings, CS appears to be even more common in patients with AD [4, 11]. These patients are often sensitised to ingredients of their own products. This is likely because of the constant use of emollients, and it was proved that even products sold as ‘hypoallergenic’ might contain sensitisers, such as fragrances and preservatives [11, 29]. Reports on specific allergens in AD patients vary, however most report lanolin alcohol and fragrances as more common in this population [3, 13]. We registered an important decline in lanolin allergy, with rates dropping from 4.6% to only 0.8%, aligning with a recent Italian study, which links the decline to the improved purity of modern lanolin [30]. However, in other countries lanolin is still relevant, and Amerchol L-101 was reported to improve the chances of detecting lanolin allergy [3]. Even with the marked decline in prevalence, lanolin allergy should not be overlooked and requires continued monitoring, especially among patients with AD.

This study's strengths include a robust sample size of patients spanning an observation period of 25 years. However, limitations include low statistical power for specific subgroups, as reflected by wide confidence intervals, and potential selection bias, as patients were not only referred for suspicion of ACD but also when the diagnosis was unclear or prior to introducing systemic therapy. Furthermore, due to its retrospective design and single-centre setting, the findings have limited generalisability. Another limitation involves the periodic updates to the baseline patch test series over time. While testing followed the standardised recommendations, minor variations in allergen concentration or vehicle composition may have influenced the results and should be considered when interpreting them. Another limitation of this study is the absence of the MOAHFLA-index, which was not routinely collected during the study period. Given the retrospective design, AD severity was not assessed, and this may have influenced the observed sensitisation patterns. Despite these limitations, this study provides a strong foundation for future research in this field. Larger, multicentre studies with greater sample sizes are needed to confirm and validate our findings.

These findings emphasise the need for both dermatologists and paediatricians to remain aware of evolving allergen patterns and common exposure sources to support timely diagnosis and preventive guidance.

In conclusion, our findings suggest that sensitisation to key allergens may be decreasing. In particular, we observed a marked decline in nickel sensitisation, while textile dyes and isothiazolinones pose new risks. These observations are consistent with a positive impact of current regulations; however, as reported in the literature, allergy cases to regulated substances can still occur from alternative sources or with products non-compliant with EU regulations. CS in children and adolescents is already prevalent; a further increase, driven by regulatory gaps, would likely result in a significant public health burden and escalating healthcare expenditures. Monitoring of trends in CS and stricter regulatory oversight is therefore essential.

## Author Contributions

**Mateja Starbek Zorko:** conceptualization, supervision, writing – review and editing, data curation, methodology. **Thomas Peric:** data curation, writing – original draft, software, conceptualization, visualization, formal analysis, writing – review and editing, project administration. **Tomaž Lunder:** supervision, conceptualization, writing – review and editing, data curation, methodology.

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The authors have nothing to report.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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