

ORIGINAL ARTICLE

Temporal changes in chromium allergy in Denmark between 2002 and 2017

Farzad Alinaghi  | Claus Zachariae | Jacob P. Thyssen | Jeanne D. Johansen

National Allergy Research Centre, Department of Dermatology and Allergy, Copenhagen University Hospital Herlev-Gentofte, Hellerup, Denmark

Correspondence

Farzad Alinaghi, M.D, Department of Dermatology and Allergy, Herlev and Gentofte Hospital, Kildegårdsvej 28, 2900 Hellerup, Denmark.
Email: farzad.seyed-alinaghi.01@regionh.dk

Funding information

Lundbeck Foundation; National Board of Health's pool

Background: In 2012, Danish authorities submitted a proposal to the European Chemical Agency restricting the content of hexavalent chromium to a maximum of 3 ppm in leather goods. Following its adoption, this proposal was implemented in 2015 as a directive in the EU.

Objectives: To examine the temporal trend of chromium contact allergy in adult dermatitis patients patch tested between 2002 and 2017, and to determine clinical characteristics and causative exposures in these patients.

Methods: All adult dermatitis patients patch tested between 2002 and 2017 were included. Patch test data were reviewed retrospectively. Comparisons were performed with the χ^2 test and logistic regression analysis.

Results: A total of 13 379 adults aged 18 to 99 years were patch tested between 2002 and 2017. The overall prevalence of chromium allergy was 2.2%. An overall decreasing trend was found for the prevalence of chromium allergy ($P_{\text{trend}} = 0.00002$). Specifically, a significant difference was found for the study periods 2010 to 2013 ($P_{\text{trend}} = 0.002$) and 2014 to 2017 ($P_{\text{trend}} < 0.0001$) as compared with 2002 to 2005. Leather remained the most important single cause of allergic contact dermatitis caused by chromium. The proportion of clinically relevant leather exposures increased from 42.3% during 2002 to 2009 to 54.8% during 2010 to 2017 ($P = 0.04$).

Conclusions: The prevalence of chromium allergy is decreasing. The EU Directive restricting the use of hexavalent chromium in leather goods is thought to be playing a central role in this change.

KEYWORDS

chromium, contact allergy, hexavalent, leather, prevalence, regulation, trend

1 | INTRODUCTION

Chromium is a transition metal that is capable of causing severe allergic contact dermatitis (ACD). It has several oxidation states, of which only trivalent chromium and hexavalent chromium are sufficiently stable to act as haptens.¹ Historically, cement has been the most important source of exposure for the induction of chromium allergy, particularly among men.^{2,3} However, Zachariae et al⁴ reported that leather items had become the most frequent sources of chromium allergy in dermatitis patients patch tested during 1989 to 1994 in Gentofte, Denmark. In a cross-sectional follow-up study including >16 000 dermatitis patients, Thyssen et al⁵ found a significant increase in clinically relevant leather exposure when they compared 1989 to 1994 data and 1995 to 2007

data in Danish patients with suspected ACD, and a simultaneous significant increase in the prevalence of chromium allergy.

In a Danish market survey from 2009, it was found that nearly all of 60 randomly evaluated leather footwear items contained chromium, with a median content of 1.7%, emphasizing a significant source of chromium exposure.⁶ Notably, hexavalent chromium was released from 44% of 18 products evaluated with the ISO 17075 standard method, which has a detection limit of 3 ppm. To address the growing leather problem, the Danish government submitted a dossier in January 2012 to the European Chemical Agency elucidating the chromium problem. Subsequently, in May 2015, a legislative initiative was implemented by the EU prohibiting a content of more than 3 ppm of hexavalent chromium in leather products.⁷

In the present study, we provide an updated epidemiological analysis of the prevalence and exposure sources of chromium allergy in adult Danish patients with suspected ACD and who were patch tested at the Department of Dermatology and Allergy, Herlev-Gentofte Hospital over a 16-year period.

2 | METHODS

This study was performed in accordance with the “strengthening the reporting of observational studies in epidemiology” (STROBE) statement.⁸ Data were extracted from the National Database for Contact Allergy in Denmark. All adult patients (≥ 18 years) with suspected ACD who were patch tested during 2002 to 2017 at the Department of Dermatology and Allergy, Herlev-Gentofte Hospital were included. Through a retrospective review of patient data regarding patch testing (test year, reading day, and test results, ie, the presence or absence of chromium allergy), the clinical relevance of chromium allergy (current, past, or unknown), the MOAHLFA index (male, occupational dermatitis, history of atopic dermatitis [AD], hand eczema, leg dermatitis, facial dermatitis, and age > 40 years),⁹ the presence of foot eczema and sources of exposure were retrieved. Permission was obtained from the Danish data Protection Agency.

2.1 | Definitions

The clinical relevance of positive patch test reactions to chromium was assessed by the consulting physician: “current relevance” was registered when a patient presented with a dermatitis reaction in combination with a history of current skin exposure to a source of chromium; “past relevance” was registered when a patient had a positive patch test reaction to chromium in combination with a history of a past dermatitis reaction caused by skin exposure to a source of chromium; and “unknown relevance” or “missing” was registered when patients had dermatitis and chromium allergy, and no relationship with current or past chromium exposure could be assessed, or no evaluation had been performed by the physician. Relevant causative exposures were based on the physician’s notes in medical charts.

2.2 | Patch testing

Patch testing was performed with the European baseline series by the use of Trolab allergens (Hermal, Reinbek, Germany) and Allergeaze allergens from April 2016 with Finn Chambers (8 mm; Epitest, Tuusula, Finland) on Scanpor tape (Epitest). Dosing of the chamber was performed with 20 mg of the test preparation. Potassium dichromate 0.5% pet. was used for testing. Patch test readings were performed according to ESCD recommendations,¹⁰ with an exposure time of 48 hours and readings on day (D) 2, D3 or D4, and D7. Patch test reactions designated as +, ++ or +++ were interpreted as positive reactions. Irritant responses and doubtful (?) or negative readings were interpreted as negative responses.

2.3 | Statistical analysis

Data analysis was performed with SPSS for Windows (release 22.0). The χ^2 test of independence was used to test for associations between categorical variables, including age groups (18–40, 41–60 and > 60 years), patch test year (2002–2005, 2006–2009, 2010–2013, and 2014–2017), MOAHLFA index, clinical relevance of positive reactions, and relevant sources of exposure (leather shoes, leather gloves, “other leather” exposure, chemicals, and tools). Fisher’s exact test was applied when the expected value in any of the cells of the contingency table was < 5 . As the registration of foot dermatitis first began in 2004, we were not able to estimate its prevalence during the initial study period of 2002 to 2005. Linear-to-linear association tests and χ^2 trend tests were used for trend analysis across test years.

Furthermore, a logistic regression model was applied with “chromium allergy” as the dependent dichotomous categorical variable, and with sex, patch test year, age group, AD, foot dermatitis, hand eczema and face dermatitis as independent categorical variables. Interactions between the main covariates were evaluated with the Wald test. All results were expressed as adjusted odds ratios (ORs). A significance level of 5% was applied, and 95% confidence intervals (CIs) were constructed.

3 | RESULTS

The baseline characteristics of the included dermatitis patients are shown in Table 1. A total of 13 379 (9013 women) adults aged 18 to 99 years were patch tested in 2002 to 2017. The mean age at diagnosis was 48.7 ± 16.8 years. Chromium allergy was found in 296 (2.2%) of all patients: in 96 (2.2%) men and in 200 (2.2%) women. In crude analyses, patients with chromium allergy were frequently aged > 40 years (78.7% vs 67.6%, $P = 0.00005$), and were more frequently affected by foot eczema (31.8% vs 5.0%, $P < 0.00001$) and hand eczema (62.8% vs 37.6%, $P < 0.00001$). Face dermatitis was more common in dermatitis patients without chromium allergy (16.6% vs 24.0%, $P = 0.003$). Furthermore, adjusted regression analysis showed significant associations between chromium allergy and, respectively, foot eczema (OR = 7.4, 95%CI: 5.7–9.8), hand eczema (OR = 2.3, 95%CI: 1.8–3.0), and AD (OR = 1.5, 95%CI: 1.1–2.1). However, the significant association with AD disappeared (OR = 1.4, 95%CI: 0.8–2.4) when an interaction term was inserted between AD and test year ($P = 0.02$). Specifically, AD was more prevalent in chromium-allergic patients during the study period 2010 to 2013. Patients from the lowest age group, that is, 18 to 40 years, were less likely to have chromium allergy (OR = 0.5, 95%CI: 0.3–0.7) than patients in the age group > 60 years. Furthermore, dermatitis patients from the study period 2002 to 2005 were more likely to have chromium allergy than those from the study period 2014 to 2017 (OR = 2.2, 95%CI: 1.6–3.1). No significant association was found with sex or face dermatitis in regression analysis. We found no interaction between test year and foot eczema ($P = 0.08$) or sex ($P = 0.8$).

Table 2 shows the prevalence of chromium allergy in both sexes stratified by age group and test year. The prevalence was similar in men and women aged 41 to 60 years (2.7% vs 2.6%, $P = 0.7$), in men

TABLE 1 Baseline characteristics of included dermatitis patients (n = 13 379) during 2002 to 2017 at Gentofte, Denmark

Characteristics	Total	Patients with chromium allergy	Patients without chromium allergy	P-value*
All patients, % (n)	100 (13 379)	2.2 (296)	97.8 (13 083)	-
Age $\pm$ SD (years)	48.7 $\pm$ 16.8	52.8 $\pm$ 15.1	48.8 $\pm$ 16.9	-
Male, % (n)	32.6 (4366)	32.4 (96)	32.6 (4270)	-
Female, % (n)	67.4 (9013)	67.6 (200)	67.4 (8813)	-
Age > 40 y, % (n)	67.8 (9072)	78.7 (233)	67.6 (8839)	0.00005
Foot eczema, % (n)	5.6 (743)	31.8 (94)	5.0 (649)	<0.00001
Hand eczema, % (n)	38.2 (5111)	62.8 (186)	37.6 (4925)	<0.00001
Atopic dermatitis, % (n)	17.6 (2361)	20.9 (62)	17.6 (2299)	0.1
Facial dermatitis, % (n)	23.8 (3184)	16.6 (49)	24.0 (3135)	0.003
Occupational dermatitis, % (n)	18.7 (2496)	17.9 (53)	18.7 (2443)	0.7

The bold values represent the level of significance is 0.05 (5%).

* χ^2 test comparing dermatitis patients with and without chromium allergy.

TABLE 2 The prevalence of chromium allergy among 13 379 adult dermatitis patients stratified by age group and patch test year

Characteristic ^a	Total, % (n)	Men, % (n)	Women, % (n)
All patients	100 (13379)	32.6 (4366)	67.4 (9013)
Chromium allergy	2.2 (296)	2.2 (96)	2.2 (200)
Age group (years)			
18-40	1.5 (66/4456)	1.1 (15/1325)	1.6 (51/3131)
41-60	2.6 (142/5442)	2.7 (49/1801)	2.6 (93/3641)
>60	2.5 (88/3481)	2.6 (32/1240)	2.5 (56/2241)
Year of patch test			
2002-2005	3.2 (99/3136)	2.9 (32/1112)	3.3 (67/2024)
2006-2009	2.3 (62/2671)	2.7 (24/903)	2.1 (38/1768)
2010-2013	1.9 (68/3665)	1.7 (19/1103)	1.9 (49/2562)
2014-2017	1.7 (67/3907)	1.7 (21/1248)	1.7 (46/2659)

^a No significant difference was found by sex.

and women aged >60 years (2.6% vs 2.5%, $P = 0.9$), and in the youngest age group of 18 to 40 years (1.1% vs 1.6%, $P = 0.2$, respectively). The overall prevalence of chromium allergy decreased from 2002 to 2017 ($P_{\text{trend}} = 0.00002$) (Figure 1). Specifically, a decreasing trend was seen from 3.2% in 2002 to 2005 to 1.7% in 2014 to 2017 ($P_{\text{trend}} < 0.0001$), and a decreasing trend was also observed from 2002 to 2005 to 2010 to 2013 ($P_{\text{trend}} = 0.002$). Table 3 shows the different clinical variables stratified by test year in dermatitis patients with chromium allergy. The prevalence of foot dermatitis decreased after a peak during 2006 to 2009 (2014-2017 vs 2006-2009, $P_{\text{trend}} = 0.01$). Regarding AD, an increasing trend was found during 2010 to 2013 as compared with 2002 to 2005 ($P_{\text{trend}} = 0.003$) and 2006 to 2009 ($P_{\text{trend}} = 0.005$). After this, the prevalence of AD remained stable. Regarding present or past clinical relevance, an increasing trend was noted for 2010 to 2013 as compared with 2002 to 2005 ($P_{\text{trend}} = 0.005$).

Table 4 shows the characteristics of all patients with chromium allergy. Whereas occupational dermatitis more frequently occurred in men with chromium allergy (29.2% vs 12.5%, $P = 0.0005$), AD was significantly more common in women with chromium allergy than in men (25.5% vs 11.5%, $P = 0.005$). Dermatitis was most often localized on the hands (62.8%), the feet (32.4%), and the face (16.6%). The clinical relevance of positive patch reactions to chromium was generally high,

as current or past relevance was registered in 56.1% and 32.4% of patients, respectively. There was no significant difference between men and women regarding the clinical relevance of positive chromium test reactions. Leather was the most common relevant source of exposure in our patients (47.6%); leather shoes (36.8%), leather gloves (12.8%), and "other leather" items (7.4%), including furniture, watch straps, car wheels, and clothing. Leather gloves were more common sources of exposure in men than in women (24.1% vs 5.4%, $P < 0.00001$). Table 5 shows the sources of chromium exposure in dermatitis patients from 2002 to 2009 as compared with those from 2010 to 2017. The relative proportion of leather exposures as the cause of chromium allergy increased significantly from 42.3% during 2000 to 2009 to 54.8% during 2010 to 2017 ($P = 0.04$); leather shoe exposures increased from 27.8% to 40.0% ($P = 0.02$), leather glove exposures increased from 9.3% to 15.6% ($P = 0.1$), and "other leather" exposures increased from 2.5% to 13.3% ($P = 0.00008$). The proportion of unknown exposure sources decreased significantly from 57.1% to 44.4% ($P = 0.03$).

4 | DISCUSSION

This cross-sectional study showed that the overall prevalence of chromium allergy decreased for adult male and female dermatitis patients

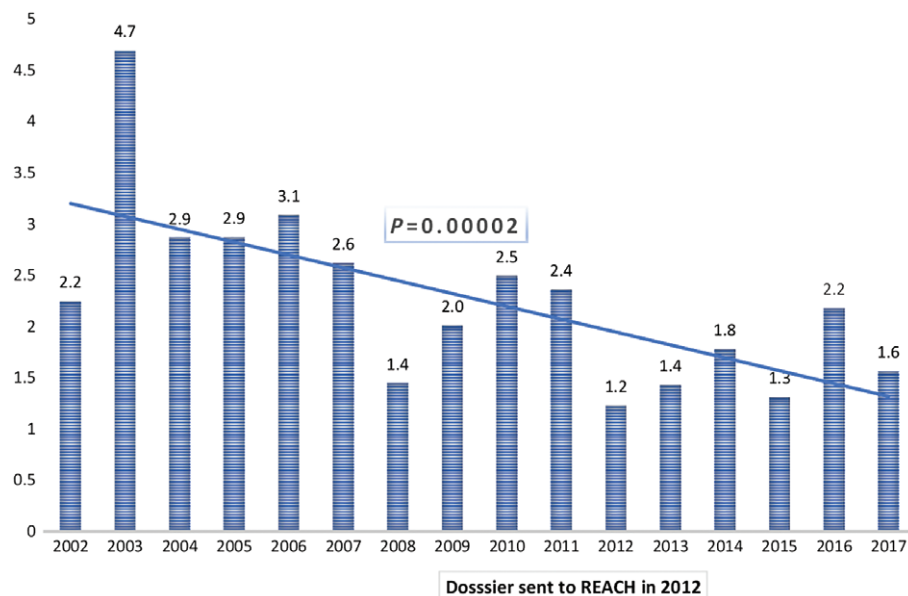


FIGURE 1 Prevalence of chromium allergy in dermatitis patients during 2002 to 2017. Decreasing trends were found for the study periods 2010 to 2013 vs 2002 to 2005 ($P_{\text{trend}} = 0.002$) and 2014 to 2017 vs 2002 to 2005 ($P_{\text{trend}} < 0.0001$)

TABLE 3 Profile of dermatitis patients with chromium allergy stratified by patch test year ($n = 296$)

Characteristics	2002-2005, % (n)	2006-2009, % (n)	2010-2013, % (n)	2014-2017, % (n)	P_{trend}^a
Age group (years)					
18-40	22.2 (22/99)	19.4 (12/62)	29.4 (20/68)	17.9 (12/67)	0.9
41-60	44.4 (44/99)	54.8 (34/62)	44.1 (30/68)	50.7 (34/67)	0.6
>60	33.3 (33/99)	25.8 (16/62)	26.5 (18/68)	31.3 (21/67)	0.7
Men	32.3 (32/99)	38.7 (24/62)	27.9 (19/68)	31.3 (21/67)	0.6
Women	67.7 (67/99)	61.3 (38/62)	72.1 (49/68)	68.7 (46/67)	0.6
Hand eczema	54.5 (54/99)	74.2 (46/62)	69.1 (47/68)	58.2 (39/67)	0.5
Foot dermatitis ^b	-	51.6 (32/62)	41.2 (28/68)	29.9 (20/67)	0.01
Facial dermatitis	14.1 (14/99)	12.9 (8/62)	16.2 (11/68)	23.9 (16/67)	0.1
Atopic dermatitis	14.1 (14/99)	12.9 (8/62)	33.8 (23/68)	25.4 (17/67)	0.009
Occupational dermatitis	12.1 (12/99)	24.2 (15/62)	22.1 (15/68)	16.4 (11/67)	0.4
Clinical relevance ^c	58.6 (58/99)	71.0 (44/62)	79.4 (54/68)	73.1 (49/67)	0.01

The bold values represent the level of significance is 0.05 (5%).

^a Across the entire study period.

^b The registration of foot dermatitis started in 2004.

^c Present or past relevance.

during 2002 to 2017 (Table 2). Notably, a decreasing trend was observed for foot dermatitis during the most recent years (2014-2017), indicating that the frequency of clinical disease has also been reduced (Table 4). In the remaining cases of chromium allergy, relevance increased and leather was still the single most important cause of ACD.

The decreasing trend of chromium allergy is noteworthy, as it probably reflects the effect of the regulatory initiatives restricting the content of hexavalent chromium to a maximum of 3 ppm in leather articles and articles containing leather parts used by consumers or workers. Historically, allergic chromium dermatitis mainly affected the hands of construction workers because of cement exposure, resulting in a high degree of occupational disability.¹¹ However, prompted by a highly effective regulatory intervention in 2005 by the EU,¹² preceded

by Denmark in 1983¹³ and Sweden in 1989, the addition of ferrous sulfate to cement became compulsory to reduce the amount of water-soluble hexavalent chromium to no more than 2 ppm. We found significantly decreasing trends in the prevalence of chromium allergy for the study periods 2010 to 2013 and 2014 to 2017 in our patients as compared with previous years. The decreasing trend during the last period is likely to be a consequence of the adoption and enforcement of the new EU regulatory directive against leather during 2014 to 2015. The EU regulation on leather is expected to be 80%⁷ effective in reducing the incidence of hexavalent chromium ACD, according to the regulatory text. However, an allergic response may be elicited at lower concentrations than the present limit of 3 ppm in already sensitized individuals.¹⁴ This highlights the need for sustained efforts to reach the ultimate goal of complete removal of hexavalent

TABLE 4 Characteristics of 296 adults with chromium allergy during 2002 to 2017 stratified by sex

Variable	Total, % (n)	Men, % (n)	Women, % (n)	P-value*
Clinical profile				
Males	32.4 (96)	-	-	-
Occupational dermatitis	17.9 (53)	29.2 (28)	12.5 (25)	0.0005
Atopic dermatitis	20.9 (62)	11.5 (11)	25.5 (51)	0.005
Hand dermatitis	62.8 (186)	65.6 (63)	61.5 (123)	0.5
Leg dermatitis	6.1 (18)	5.2 (5)	6.5 (13)	0.7
Facial dermatitis	16.6 (49)	13.5 (13)	18.0 (36)	0.3
Age > 40 years	78.7 (233)	85.4 (82)	75.5 (151)	0.05
Foot dermatitis	32.4 (96)	33.3 (32)	32.0 (64)	0.8
Relevance of positive patch test reactions				
Current relevance	56.1 (166)	61.5 (59)	53.5 (107)	0.2
Past relevance	32.4 (96)	30.2 (29)	33.5 (67)	0.6
Unknown relevance	30.7 (91)	36.6 (59)	23.7 (32)	0.02
Relevant exposures				
Leather shoes	36.8 (109)	32.3 (31)	39.0 (78)	0.3
Leather gloves	12.8 (38)	26.0 (25)	6.5 (13)	<0.00001
Other leather exposure ^a	7.4 (22)	7.3 (7)	7.5 (15)	0.9
Chemicals	1.4 (4)	3.1 (3)	0.5 (1)	0.1

The bold values represent the level of significance is 0.05 (5%).

* χ^2 test comparing men and women.

^aFurniture, watch straps, car wheels, and clothing.

TABLE 5 Sources of chromium exposure in dermatitis patients with chromium allergy during 2002 to 2009 and 2010 to 2017 at Gentofte Hospital, Denmark

Exposure sources	2002-2009 (N = 161), % (n)	2010-2017 (N = 135), % (n)	P-value ^a
Leather shoes	34.8 (56)	37.8 (51)	0.6
Leather gloves	9.3 (15)	15.6 (21)	0.1
Other leather sources ^a	2.5 (4)	13.3 (18)	0.0004
Leather (total)	42.3 (69)	54.8 (74)	0.04
Other sources of chromium	1.9 (3)	4.4 (6)	0.3
Unknown	57.1 (92)	44.4 (60)	0.03

The bold values represent the level of significance is 0.05 (5%).

*P-value of χ^2 test comparing 2000 to 2009 and 2010 to 2017.

^aFurniture, watch straps, car wheels, and clothing.

chromium from leather. Interestingly, no effect of regulatory interventions on leather was noted in the latest report by the European Surveillance System on Contact Allergies during the study period 2013 to 2014, including 31 689 patients from 12 European countries,¹⁵ as a largely stable prevalence of chromium allergy (3.2%) was found as compared with a similar analysis in 2004. However, the sample of participating European departments was only partly identical with that used in the 2004 analysis. The decreasing trend observed in our patients already began during 2010 to 2013, more specifically in 2012, and could be explained by proactive producers and independent national initiatives against chromium before the collective implementation by the EU during 2014 to 2015. In line with this, the Federal Institute for Risk Assessment in Germany already proposed restricting the content of hexavalent chromium in leather to a maximum of 3 ppm in 2007 (<http://www.bfr.bund.de/cd/9575>, last accessed

August 18, 2018). Such initiatives might already have affected both domestic and foreign markets years before the EU regulation, favouring the use of chromium-free tanning and other available techniques to considerably reduce or even completely remove hexavalent chromium from leather. Interestingly, the North American Contact Dermatitis Group (NACDG) reported a decrease in the prevalence of chromium allergy from 4.8% during 2005 to 2006 to 1.6% and 2.2% during 2011 to 2012 and 2013 to 2014, respectively.¹⁶ The participating departments in the NACDG were only partly identical over the years, introducing a potential bias. However, this decrease has been partially ascribed to secondary effects of chromium regulation in other countries, as no regulation on chromium salts in leather yet exists in North America. Nevertheless, the prevalence of chromium allergy remains high in countries in which no regulation regarding this metal yet exists.¹⁷⁻¹⁹

We observed no cases of chromium allergy resulting from cement exposure during the study period; instead, we found a relative increase in leather exposures as a cause of chromium allergy, from 42.3% to 54.8%, during the study periods 2002 to 2009 and 2010 to 2017, respectively ($P = 0.04$) (Table 5). This increase seemed to be explained by a marked increase in exposures from "other leather" items ($P = 0.0004$). The latter finding might also explain the significant proportional decrease in "unknown sources of exposure" between these two study periods (57.1% vs 44.4%, $P = 0.03$). Furthermore, the overall proportion of "unknown sources of exposure" during 2002 to 2017 was high (51.4%), emphasizing the need for continued registration and search for potentially new sources of exposure causing chromium allergy.

In an extensive systematic review and meta-analysis regarding the association between AD and contact allergy, Hamann et al²⁰ reported a significant association between chromium allergy and AD

(OR = 1.3, 95%CI: 1.0-1.6). In our regression model, interaction analysis showed that AD was more prevalent in chromium-allergic patients than in those without chromium allergy only during 2010 to 2013. We have no explanation for this, and it might be a chance finding.

Concerning strengths and limitations, the relative increase in leather as a source of exposure might have been partially biased by an increased focus on leather as the main source among our physicians. We were unable to estimate the prevalence of foot dermatitis in chromium-allergic patients during 2002 to 2005, as its registration in the database began in 2004. Strengths of this study include the standardized and similar reading techniques for patch test reactions throughout the entire study period. Other strengths include the large number of dermatitis patients included, the unchanged patch test methods over the years, the wide timespan, facilitating trend analysis, and the fact that clinical disease was diagnosed by physicians.

5 | CONCLUSION

This study shows that the overall prevalence of chromium allergy, and of foot dermatitis, among chromium-allergic individuals has decreased significantly in recent years. This sudden change strongly suggests a positive effect of the regulatory discussion and initiatives against hexavalent chromium in leather goods. Future studies, both nationally and internationally, are required to continuously monitor the effect of regulatory directives.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

ACKNOWLEDGEMENTS

This study was supported by a grant from the National Board of Health's pool for projects promoting health and prevention of disease. J. P. Thyssen is supported by an unrestricted grant from the Lundbeck Foundation.

ORCID

Farzad Alinaghi  <https://orcid.org/0000-0003-1527-4242>

REFERENCES

- Buters J, Biedermann T. Chromium(VI) contact dermatitis: getting closer to understanding the underlying mechanisms of toxicity and sensitization! *J Invest Dermatol*. 2017;137:274-277.
- Thyssen JP, Johansen JD, Menné T. Contact allergy epidemics and their controls. *Contact Dermatitis*. 2007;56:185-195.
- Jager H, Pelloni E. Test épicutanés aux bichromates, positifs dans l'eczéma au ciment. *Dermatologica*. 1950;100:207-215.
- Zachariae CO, Agner T, Menné T. Chromium allergy in consecutive patients in a country where ferrous sulfate has been added to cement since 1981. *Contact Dermatitis*. 1996;35:83-85.
- Thyssen JP, Jensen P, Carlsen BC, Engkilde K, Menné T, Johansen JD. The prevalence of chromium allergy in Denmark is currently increasing as a result of leather exposure. *Br J Dermatol*. 2009;161:1288-1293.
- Thyssen JP, Strandesen M, Poulsen PB, Menné T, Johansen JD. Chromium in leather footwear—risk assessment of chromium allergy and dermatitis. *Contact Dermatitis*. 2012;66:279-285.
- European Union, Commission Regulation (EU) No. 301/2014 of 25 March 2014 amending Annex XVII to Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards chromium VI compounds Text with EEA relevance.
- von Elm E, Altman DG, Egger M, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008; 61:344-349.
- Schnuch A, Geier J, Uter W, et al. National rates and regional differences in sensitization to allergens of the standard series. Population-adjusted frequencies of sensitization (PAFS) in 40,000 patients from a multicenter study (IVDK). *Contact Dermatitis*. 1997;37:200-209.
- Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing—recommendations on best practice. *Contact Dermatitis*. 2015;73: 195-221.
- Menné T, Bachmann E. Permanent disability from skin diseases. A study of 564 patients registered over a six year period. *Derm Beruf Umwelt*. 1979;27:37-42.
- European Union. Directive 2003/53/EC of the European Parliament and of the Council of 18 June 2003 amending for the 26th time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (nonylphenol, nonylphenol ethoxylate and cement). *Off J Eur Union*. 2003;178: 24-27.
- Arbejdstilsynets bekendtgørelse nr 661 af 28. November 1983.
- Basketter D, Horev L, Slodovnik D, Merimes S, Trattner A, Ingber A. Investigation of the threshold for allergic reactivity to chromium. *Contact Dermatitis*. 2001;44:70-74.
- Uter W, Amario-Hita JC, Balato A, et al. European Surveillance System on Contact Allergies (ESSCA): results with the European baseline series, 2013/14. *J Eur Acad Dermatol Venereol*. 2017;31:1516-1525.
- DeKoven JG, Warshaw EM, Belsito DV, et al. North American Contact Dermatitis Group patch test results 2013-2014. *Dermatitis*. 2017;28: 33-46.
- Morrone A, Bordignon V, Barnabas GA, et al. Clinical-epidemiological features of contact dermatitis in rural and urban communities in northern Ethiopia: correlation with environmental or occupational exposure. *Int J Dermatol*. 2014;53:975-980.
- Khatami A, Nassiri-Kashani M, Gorouhi F, et al. Allergic contact dermatitis to metal allergens in Iran. *Int J Dermatol*. 2013;52:1513-1518.
- Sabatini N, Cabrera R, Bascuñán C, et al. [Reactivity and evolution of 4022 patch tests in Chilean patients with contact dermatitis]. *Rev Med Chil*. 2015;143:751-758.
- Hamann CR, Hamann D, Egeberg A, Johansen JD, Silverberg J, Thyssen JP. Association between atopic dermatitis and contact sensitization: a systematic review and meta-analysis. *J Am Acad Dermatol*. 2017;77:70-78.

How to cite this article: Alinaghi F, Zachariae C, Thyssen JP, Johansen JD. Temporal changes in chromium allergy in Denmark between 2002 and 2017. *Contact Dermatitis*. 2019;80: 156–161. <https://doi.org/10.1111/cod.13181>