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## **Title: Occupational allergic contact dermatitis and major allergens in France: temporal trends for the period 2001-2010**

Running Title: Occupational allergic contact dermatitis trends in France, 2001-2010.

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#### **What's already known about this topic?**

- Occupational allergic contact dermatitis (OACD) is one of the major causes of work-related diseases.
- In France, little is known about the cause of OACD and no data have been available for estimating their temporal evolution.

#### **What does this study add?**

- The RNV3P has shown that notified OACD was temporally stable over the period 2001-2010.
- OACD due to isothiazolinones and fragrances, and to resins in the construction sector increase significantly. Conversely cases due to contact with cement decrease in the construction sector.
- An effort must be made to reduce skin sensitizers in the workplace by reinforcing prevention actions.

#### **ABSTRACT**

**Background:** Occupational Allergic Contact Dermatitis (OACD) is one of the most common occupational skin diseases in developed countries, but data about its temporal trends in incidence remains sparse.

**Objective:** The aim of this study is to describe OACD trends in terms of industrial activities and main causal agents in France over the period 2001-2010.

**Method:** Data were collected from the French National Network of Occupational Disease Vigilance and Prevention (RNV3P). All OACD considered probably or certainly associated with an occupational exposure were included in the study. Trends were examined (i) on annual crude numbers of OACD and (ii) on reported odds-ratios of OACD calculated using logistic regression models.

**Results:** Overall, 3738 cases of OACD were reported and the mean age of OACD cases was 35 years, 52% being women. The most frequent occupations were hairdressers, health care workers, cleaning staff and masons. The total number of OACD cases remained stable over the study period, but increases in OACD related to isothiazolinones ( $p=0.002$ ), epoxy resins ( $p=0.012$ ) and fragrances

( $p=0.005$ ) were observed. Conversely, decreases were noted for cement compounds ( $p=0.002$ ) and plant products ( $p=0.031$ ). These trends highlight specific sectors and exposures at risk of OACD.

Conclusion: Trends in OACD depend on the nature of exposure. Observed decreases were consistent with prevention measures taken during the study period, and the increases observed serve to highlight those areas where preventative efforts need to be made to reduce skin allergies in the workplace.

## INTRODUCTION

During the last decades an increase in allergic diseases has been observed in the general population<sup>1</sup>, but data on temporal trends of occupational allergies were sparse.

In developed countries, occupational skin disease (OSD) is one of the major causes of work-related diseases<sup>2-6,7-9</sup>, among them occupational contact dermatitis (OCD) accounts for 70% to 90% of all cases of OSD<sup>9</sup> reported. Although the true frequency is unknown, most studies estimate the incidence of OCD between 11 and 86 cases per 100,000 workers per year<sup>9</sup> depending on the country.<sup>2, 10-13</sup> Occupational allergic contact dermatitis (OACD) is one of the most common OCD after irritant disease.<sup>9</sup>

The most frequently reported agents and occupations related to OACD are well known<sup>9</sup> and most often documented from cross-sectional studies. Concerning temporal trends, recent studies based on continuous monitoring networks have identified the emergence or decline of some allergens in relation to preventative action.<sup>14</sup>

In France, data concerning contact allergies in workers are very limited. The only national statistics available on OCD comes from French National Health Insurance (CNAM-TS), where the estimated annual incidence of compensated OCD was 16 per 100,000 salaried workers between 2004 and 2007.<sup>15</sup> These data however are known to be incomplete, particularly as they do not take into account non-salaried workers.

The French Occupational and Environmental Disease Consultation Centres situated at 32 university hospitals make up the French National Network for Work-related Disease Vigilance and Prevention (RNV3P, Réseau National de Vigilance et de Prévention des Pathologies Professionnelles). RNV3P was established in 2000 and continuously monitors occupational diseases, including skin allergies. Overall organisation of RNV3P has been extensively described elsewhere.<sup>16</sup>

In this context, RNV3P offer the opportunity to describe general features and recent trends in notified OACD by activity sectors and main causal agents in France over the 2001-2010 period.

## **MATERIAL AND METHODS**

### **Study population**

The study population consisted of 69,779 work related diseases recorded in the RNV3P between 2001 and 2010, with completed data about occupational exposure (substances and occupation) and the potential association between occupational exposure and disease (Fig. 1).

### **Data collection**

Data were collected from the RNV3P network. This project received the approval of the National Board enforcing data protection legislation (CNIL).

Data collected from RNV3P concerned diseases (using ICD 10), exposures, occupations (ISCO-88, edited by ILO) and activity sectors (NAF93 edited by INSEE).<sup>16</sup> Substances recorded for exposure were coded according to their chemical identification and/or their common use according to a classification established by a group of five experts. Medical experts rate imputability, i.e. the evidence of association between the disease and each suspected causal exposure, on a four level-scale including null, possible, probable and certain. All data were coded and recorded by experienced occupational physicians. Patch tests (based on European baseline series and possibly completed with the screening series) were performed and read on day 2 and day 3 or day 4 according to guidelines of the International Contact Dermatitis research Group (ICDRG) in order to diagnose contact allergy.<sup>17</sup> Experts take patch testing results and their occupational relevance into consideration when determining the causal relation scale.

To improve standardisation of practices and quality reporting, all medical experts underwent quality training every 18 months. Automated procedures were performed to ensure reduction of input errors, missing data, duplicates and data capture inconsistencies in centres. Work-related diseases extracted from the database concerned complete data for diagnosis, exposure and imputability.<sup>16</sup>

For the present study, cases were defined as all new ACD (ICD-10 L23 and L23.0 to L23.9) notified from 2001 to 2010 that were considered to be probably or certainly associated with occupational exposure by the medical expert of each centre.

### **Data analysis**

Trend analyses were based on previously used statistical methods.<sup>18, 19</sup> Analysed data consisted of the number of new notified cases in the national database for a given year. The reporting odds ratio<sup>18</sup> (ROR) for OACD for a given year was defined as the ratio of the number of OACD cases to the number

of all other diseases in the given year. The ROR for OACD related to specific occupational exposure (namely a causal agent, an industrial sector, or both) for a given year was defined by the ratio of the number of OACD cases associated with this exposure to all other OACD cases in this year. The ROR for each year was calculated with reference to year 2005 (arbitrarily chosen as one of the two median years) using a logistic regression model which controlled for age and gender, the dependant dummy variable being OACD cases vs non OACD cases, or OACD related to a specific exposure vs other OACD cases. The main predictor - calendar time - was treated here as a categorical variable with each category parameter leading to an estimate of the corresponding year ROR.

An alternative method considering calendar time as a continuous variable with a scale of years in the logistic model was also used. In this model, the underlying hypothesis is that the trend would be a regular increase (or decrease) in the OACD number by a constant multiplicative factor.

Temporal trends were also tested by the non-parametric Kendall rank correlation test: (i) between calendar years 2001 to 2010 and the number of annual OACD cases, or annual OACD cases for specific occupational exposure or activity sectors, and (ii) between years and the ROR calculated for each year.

Statistical analyses were performed on R software (V.3.0.1). Statistical significance was defined as  $P < 0.05$ .

## **RESULTS**

### **Socio-demographic data**

In the 2001-2010 period, 3,738 cases of OACD were reported in the network, with a slight majority of women (1966, 52.6%), and with 2,792 (74.7%) considered as having a certain link between disease and exposure. The average age was 35.4 years (SD: 12.1), with women significantly younger than men: respectively 33.2 years (SD: 11.7) vs 37.7 years (SD: 12.2),  $p < 0.0001$  (Fig. 2).

### **Activity sectors and occupations**

Significant gender differences were observed in the main industrial activities. For men the most common sectors were manufacturing and construction, whereas women were more often involved in health and social work (HSW), community, social and personal service activities (Table 1).

Significant gender differences were also observed for occupations with the most common occupations for men being masons and mechanics and for women, hairdressers, health care workers and cleaners (Table 1).

Agents or products most frequently involved were (Fig. 3): metals (n=718) (mainly nickel (n=403) and chromium (unspecified sources) (n=237)); hairdressing products (n=473) (including phenylenediamine=198 and bleaching products=93); biocidal products (n=460) (mainly quaternary ammonium compounds=130 and isothiazolinones=73); resins and glues (n=407) (mainly epoxy resins=209), rubber additives (n=388), cosmetics (n=226) (mainly ingredients of soaps=76 cutting oils and coolants (n=214) cleaning products (n=143) and cement (n=111).

### **Temporal trends**

Between 2001 and 2010, the overall number of reported OACD cases and calendar years did not show any significant correlations using the rank correlation method (Kendall's tau) whereas the ROR results suggest a decline of reported OACD cases relative to all other diseases (Table 2 and Fig. 4).

However, both crude numbers of reported OACD cases and ROR increased significantly over the period in personnel service activities (97% of cases concerned hairdressers and beauticians), in hotels and restaurants (more than 50% cases concerned cooks and waiters), in public administrations (42% concerned cleaners) and in other business activities including industrial cleaning (42% concerned cleaners) (Table 2). An increase was also suggested in the manufacturing of metals and fabricated metal products (only significant when based on annual change in ROR). We did not observe a significant decrease in any sectors.

Causal agent analyses (Table 3) showed a significant increase in both the crude numbers of notified cases and ROR for OACD related to isothiazolinones, epoxy resins, fragrances and cosmetic products, and a significant decrease in OACD related to cement compounds (i.e. chromium in cement) and plant products. An increase was observed for cases associated with biocides and with hair bleaching products relative to other agents, nearly significant using the Kendall rank correlation test and significant with the method based on annual change in ROR. Analyses restrained to OACD considered to be certainly associated with these agents showed identical results (data not shown).

Furthermore, trend results observed below were also confirmed in sectors where these agents are commonly used: the increase due to cosmetic products was also significant in personnel service activities and to an even higher extent in the health and social work sector; The increase due to resin products was focused in the construction sector; the increase due to hair bleaching products occurred especially in personnel service activities. Cases due to metals increased significantly only in other business activities (Table 4). Conversely, OACD resulting from contact with cement decreased in construction sectors (Table 4).

## DISCUSSION

For the first time in France, we have described OACD cases and trends in cases notified by the RNV3P network over the period 2001-2010. Whilst general stability was observed for all OACD compared to other diseases, trends differed depending on the causative agent, the sector, or the agent in a particular sector.

Most national registers combine all types of skin disease, but make no distinction regarding occupational contact dermatitis, and provide no information on the actual cause.<sup>20</sup> The strength of our surveillance scheme is based on occupational health reports that have a level of detail which distinguishes OACD from other skin disorders, and provides data on allergen contact in different occupations and industrial sectors.

However, before drawing any definitive conclusion from these, potential biases underlying the data need to be discussed.

Firstly, as frequently occurs in this type of population based-registry, we have to discuss a probable under-reporting of true OACD cases in our network.<sup>20</sup> However, it is likely that capture of OACD cases in occupational disease centres is far higher than the capture of work-related diseases as a whole. Indeed, standardised diagnostic procedures for determining OACD are performed by occupational medical experts and based on the rule of the best practice (based on patch testing).<sup>9, 21</sup> Experts in these centres are trained to look for and highlight specific work-related allergens. Furthermore these occupational disease centres serve as reference centres for workplace occupational physicians, general practitioners, and dermatologists for the diagnosis of OCD. The strength of our study is thus based on the diagnostic skills of trained occupational physicians, and probably provides the only reliable statistics on OACD in France. So far, the only other national statistics available for occupational diseases have come from compensated data, that underestimate the frequency of contact.<sup>15</sup>

With regard to temporal trends during the 2001-2010 period, increasing recognition of the links between OACD and allergens could have had an impact on results. This bias could compromise the consistency of diagnosis over time, an important criterion for valid estimation.<sup>22, 23</sup> However the method for diagnosing contact allergy is well-established as mentioned above, and has not significantly changed since the beginning of 2000s. Even if the nature of tested allergens varied with time, we can thus assume that progress in diagnostic procedures does not contribute to temporal trends in our study. Another known potential source of bias in surveillance programs is a reduction in reporting over the years due to reporter fatigue<sup>19, 22</sup>, and a tendency to under-report over time. We

are satisfied that any observed decrease in the number of ~~cases~~-inclusions was not due to such a bias because all cases were systematically and mandatorily reported in our scheme.<sup>19</sup> In addition, during the same period the total number of other reported diseases in the network increased significantly. Prevention campaigns or changes in the definition of OACD compensation could also have changed awareness of the problem in both patient and physicians, but there has been no such campaign or changes in compensation definition during the last ten years.

Lastly, a limiting factor in our temporal trends OACD study concerns the denominator, which is not based on the entire French occupational population, but on a specific subpopulation.<sup>16, 19</sup> However the study design, based on case-control studies, measures the disproportionality of specific OACD reports (cases) relative to all other OACD reports in the network (i.e. not-cases), thus enabling over-signals in reporting database to be detected over one year.<sup>18</sup> These signals have to be interpreted in comparison with the variation of reports other than those of interest. These data can thus provide valid information on time trends in subgroups without direct reference to the whole population.

Trends can be related to a specific activity or expertise in occupational and environmental disease centres, or to regional particularities. We tested the possible role of centres by using a multi-level regression model with centres as a random variable. Global trends were not modified (data not shown).

We are therefore confident that the RNV3P surveillance scheme provides reliable estimates of OACD trends in France.

Between 2001 and 2010, the overall number of OACD cases reported in the RNV3P did not show any significant increase or decrease, with a mean of roughly 370 cases per year, although there was a downward trend in OCD in some countries. Comparisons with occupational skin disease registries from other countries have to be treated with caution due to the fact that there are differences in the reporting and definition of skin diseases. Most of the time, these registries combine all subtypes of OSD and OCD.<sup>3, 22, 25</sup> In France, the annual number of compensated OCD has been relatively stable from year to year.<sup>15</sup>

Our results are consistent with previous studies that have found that contact dermatitis is higher in women than men, and occurs earlier in the life of women.<sup>3, 6, 25, 26</sup> In our surveillance scheme, apart from agriculture, which is poorly represented in RNV3P<sup>16</sup>, these are the same sectors typically highlighted in the literature<sup>20</sup>, even if the terminology of sectors is somewhat different.<sup>25</sup> Besides, the occupations most frequently reported are known to be at high risk of developing OACD.<sup>9</sup>

The predominant agents causing OACD reported in our scheme are well-known sensitizers that cause OACD.<sup>27</sup> It should be noted that the role of quaternary ammonium compounds is probably overestimated because they are irritants which often give false positive skin tests. Most of the cases concerned health care workers and could be due exposure to benzalkonium chloride found in disinfectants and antiseptics widely used in this sector.<sup>28</sup> Cases due to quaternium-15 allergy, a formaldehyde releaser, could have been mis-classified into this category instead of formaldehyde category, and results should be considered cautiously.

Cases due to nickel do not decline during the study period suggesting that the EU Nickel directive, implemented in 2000 to protect European citizens from nickel allergy, was probably insufficient to prevent OACD.<sup>29</sup>

Regardless of sector in RNV3P, OACD due to isothiazolinones increased over the study period. Isothiazolinones, are well-known for causing skin allergy. These preservatives/biocides, include methylchloroisothiazolinone (MCI), and methylisothiazolinone (MI), widely used in occupational, household and cosmetic products, and benzisothiazolinone used in paints, varnishes and adhesives.<sup>30</sup> An epidemic of contact allergy to mixture MCI/MI was observed in the mid-1990s but significantly decreased after European Cosmetics regulation.<sup>31, 32</sup> Since the early 2000s MI which was considered to be a weaker sensitizer was included alone, without restriction, in industrial products. From 2005 it was also allowed in cosmetics products. Subsequently an increase in incidence of contact allergy to MI alone was observed,<sup>31</sup> with some authors suggesting that was probably due to increased consumer and worker exposure.<sup>33–35</sup> Our results are may be partly related to MI exposure at workplace, and emphasise the need for the EU to further restrict methylisothiazolinone content in industrial products.<sup>31, 36</sup>

OACD caused by synthetic resins, in particular epoxy resin compounds (which are strong skin sensitizers), increased among construction workers in our network. Recently, Geier<sup>37</sup> observed the same increase in the building trade. Resins are widely used in this sector as injection resins to repair cracks in concrete, and are also used in parking floor covering.

Cosmetics and ~~particularly~~ fragrances from a variety of sources are widely used in the workplace, mainly in perfumed soaps and moistures. For the purposes of coding we treated as cosmetics fragrances which could have been contained in detergents or cleaning products. The increase of OACD associated with cosmetics and probably fragrances in personnel service activities (composed almost exclusively of hairdressers) and in HSW is consistent with an increase in the use of fragranced products such as detergents which may not be under the control of the 1976 EU Cosmetics directive.<sup>30</sup> This directive is mainly written for the protection of consumers but different types of use

of these products not covered by the regulation may occur in the workplace. Therefore, the prevalence of contact allergy to fragrances might show a significant decrease in the general European population but not in the work population.<sup>36</sup>

The rise of OACD due to hair bleaching products on personnel service activities, i.e. hairdressers, concerned ammonium persulfate, a major sensitizer in hairdressing.<sup>38, 39</sup> In Germany, Uter<sup>38</sup> observed no reduction of sensitisations to ammonium persulfate among hairdressers (unlike to other allergens), and an increase was observed by Valks in Spain<sup>40</sup> underlining that this allergen is still a problem in the workplace.

Allergy to cement is well known, especially in the construction industry, and the observed decrease in this sector may be related to a decrease of exposure to chromium, the main sensitizer in the cement, following the 2005 regulation on hexavalent chromium content in cement. Studies conducted on construction workers strongly indicate that this regulation has contributed to the decreasing prevalence of chromium allergy and chromium dermatitis.<sup>36, 37, 41, 42</sup> The absence of trend in chromium allergy (from unspecified sources) might be due to occupational sources other than cement, such as leather products, paint, galvanized sheeting or welding.<sup>36</sup>

## CONCLUSION

RNV3P is a sufficiently stable surveillance scheme that can provide valid information on temporal trends, helping identify persisting or emerging skin allergies (in certain occupational subgroups). This can then lead to better prevention for specific sectors and agents. Such preventative measures can then be evaluated by trend analysis. RNV3P can play a real role in helping government authorities make decisions to reduce work-related contact dermatitis, and to monitor the efficacy of preventative measures.

## REFERENCES

- 1 Ring J, Krämer U, Schäfer T, *et al.* Why are allergies increasing? *Curr Opin Immunol* 2001;**13**:701–8.
- 2 Halkier-Sørensen L. Occupational skin diseases. *Contact Derm* 1996;**35**:1–120.
- 3 Cherry N, Meyer JD, Adisesh A, *et al.* Surveillance of occupational skin disease: EPIDERM and OPRA. *Br J Dermatol* 2000;**142**:1128–34.
- 4 Lushniak BD. The importance of occupational skin diseases in the United States. *Int Arch Occup Environ Health* 2003;**76**:325–30.
- 5 Nicholson PJ, Llewellyn D, English JS. Evidence-based guidelines for the prevention, identification and management of occupational contact dermatitis and urticaria. *Contact Derm* 2010;**63**:177–86.
- 6 Diepgen TL. Occupational skin diseases. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft* 2012;**10**:297–315.
- 7 Kogevinas M, Zock J-P, Jarvis D, *et al.* Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet* 2007;**370**:336–41.
- 8 Karjalainen A, Kurppa K, Martikainen R, *et al.* Work is related to a substantial portion of adult-onset asthma incidence in the Finnish population. *Am J Respir Crit Care Med* 2001;**164**:565–8.
- 9 Nicholson PJ, Llewellyn D, English JS. Evidence-based guidelines for the prevention, identification and management of occupational contact dermatitis and urticaria. *Contact Derm* 2010;**63**:177–86.
- 10 Meyer JD, Chen Y, Holt DL, *et al.* Occupational contact dermatitis in the UK: a surveillance report from EPIDERM and OPRA. *Occup Med (Lond)* 2000;**50**:265–73.
- 11 Diepgen TL. Occupational skin-disease data in Europe. *Int Arch Occup Environ Health* 2003;**76**:331–8.
- 12 McDonald JC, Beck MH, Chen Y, *et al.* Incidence by occupation and industry of work-related skin diseases in the United Kingdom, 1996-2001. *Occup Med (Lond)* 2006;**56**:398–405.
- 13 Turner S, Carder M, van Tongeren M, *et al.* The incidence of occupational skin disease as reported to The Health and Occupation Reporting (THOR) network between 2002 and 2005. *Br J Dermatol* 2007;**157**:713–22.
- 14 Schnuch A, Geier J, Lessmann H, *et al.* Surveillance of contact allergies: methods and results of the Information Network of Departments of Dermatology (IVDK). *Allergy* 2012;**67**:847–57.
- 15 Halioua B, Bensefa-Colas L, Bouquiaux B, *et al.* Occupational Contact Dermatitis in 10,582 French Patients Reported between 2004 and 2007: A Descriptive Study. *Dermatology (Basel)* 2013;**354**–63.

- 16 Bonneterre V, Faisandier L, Bicout D, *et al.* Programmed health surveillance and detection of emerging diseases in occupational health: contribution of the French national occupational disease surveillance and prevention network (RNV3P). *Occup Environ Med* 2010;**67**:178–86.
- 17 Lindberg M, Matura M. Patch Testing. In: Johansen JD, Frosch PJ, Lepoittevin J-P, eds. *Contact Dermatitis*. Berlin, Heidelberg: : Springer Berlin Heidelberg 2011. 439–64.
- 18 Rothman KJ, Lanes S, Sacks ST. The reporting odds ratio and its advantages over the proportional reporting ratio. *Pharmacoepidemiol Drug Saf* 2004;**13**:519–23.
- 19 Paris C, Ngatchou-Wandji J, Luc A, *et al.* Work-related asthma in France: recent trends for the period 2001-2009. *Occupational and environmental medicine* 2012;**69**:391–7.
- 20 Diepgen T, Coenraads PJ. Occupational contact dermatitis. In: *Kanerva's Occupational Dermatology*. 2012. 51–8.
- 21 Lindberg M, Matura M, Mihaly. Patch testing. In: *Contact dermatitis*. Springer-Verlag, Berlin Heidelberg 2011.
- 22 McNamee R, Carder M, Chen Y, *et al.* Measurement of trends in incidence of work-related skin and respiratory diseases, UK 1996-2005. *Occup Environ Med* 2008;**65**:808–14.
- 23 Shapiro-Mendoza CK, Tomashek KM, Anderson RN, *et al.* Recent National Trends in Sudden, Unexpected Infant Deaths: More Evidence Supporting a Change in Classification or Reporting. *Am J Epidemiol* 2006;**163**:762–9.
- 24 Uter W. Surveillance in Occupational Contact Dermatitis. In: Rustemeyer T, Elsner P, John S-M, *et al.*, eds. *Kanerva's Occupational Dermatology*. Berlin, Heidelberg: : Springer Berlin Heidelberg 2012. 59–63.
- 25 Pal TM, de Wilde NS, van Beurden MM, *et al.* Notification of occupational skin diseases by dermatologists in The Netherlands. *Occup Med (Lond)* 2009;**59**:38–43.
- 26 Skoet R, Olsen J, Mathiesen B, *et al.* A survey of occupational hand eczema in Denmark. *Contact Derm* 2004;**51**:159–66.
- 27 *Textbook of Kanerva's occupational skin diseases*. New York: : Springer 2012.
- 28 Suneja T, Belsito DV. Occupational dermatoses in health care workers evaluated for suspected allergic contact dermatitis. *Contact Derm* 2008;**58**:285–90.
- 29 Lidén C. Nickel. In: Rustemeyer T, Elsner P, John S-M, *et al.*, eds. *Kanerva's Occupational Dermatology*. Berlin, Heidelberg: : Springer Berlin Heidelberg 2012. 485–94.
- 30 Thyssen JP, Giménez-Arnau E, Lepoittevin J-P, *et al.* The critical review of methodologies and approaches to assess the inherent skin sensitization potential (skin allergies) of chemicals. Part II. *Contact Derm* 2012;**66 Suppl 1**:25–52.
- 31 Gonçalo M, Goossens A. Whilst Rome burns: the epidemic of contact allergy to methylisothiazolinone. *Contact Derm* 2013;**68**:257–8.
- 32 Thyssen JP, Johansen JD, Menné T. Contact allergy epidemics and their controls. *Contact Derm* 2007;**56**:185–95.

- 33 Geier J, Lessmann H, Schnuch A, *et al.* Recent increase in allergic reactions to methylchloroisothiazolinone/methylisothiazolinone: is methylisothiazolinone the culprit? *Contact Dermatitis* 2012;**67**:334–41.
- 34 Uter W, Gefeller O, Geier J, *et al.* Methylchloroisothiazolinone/methylisothiazolinone contact sensitization: diverging trends in subgroups of IVDK patients in a period of 19 years. *Contact Dermatitis* 2012;**67**:125–9.
- 35 Lundov MD, Opstrup MS, Johansen JD. Methylisothiazolinone contact allergy – a growing epidemic. *Contact Dermatitis* 2013;**69**:271–5.
- 36 Thyssen JP, Giménez-Arnau E, Lepoittevin J-P, *et al.* The critical review of methodologies and approaches to assess the inherent skin sensitization potential (skin allergies) of chemicals. Part III. *Contact Derm* 2012;**66 Suppl 1**:53–70.
- 37 Geier J, Krautheim A, Uter W, *et al.* Occupational contact allergy in the building trade in Germany: influence of preventive measures and changing exposure. *Int Arch Occup Environ Health* 2011;**84**:403–11.
- 38 Uter W, Lessmann H, Geier J, *et al.* Contact allergy to hairdressing allergens in female hairdressers and clients--current data from the IVDK, 2003-2006. *J Dtsch Dermatol Ges* 2007;**5**:993–1001.
- 39 Stenveld H. Hairdressers. In: Rustemeyer T, Elsner P, John S-M, *et al.*, eds. *Kanerva's Occupational Dermatology*. Berlin, Heidelberg: : Springer Berlin Heidelberg 2012. 1507–18.
- 40 Valks R, Conde-Salazar L, Malfeito J, *et al.* Contact dermatitis in hairdressers, 10 years later: patch-test results in 300 hairdressers (1994 to 2003) and comparison with previous study. *Dermatitis* 2005;**16**:28–31.
- 41 Halioua B, Bensefa-Colas L, Crepy M-N, *et al.* [Has application of the decree banning the use of cement with a high chromium VI content led to a reduction in occupational cement dermatitis in salaried workers in the construction industries?]. *Presse Med* Published Online First: 22 October 2012. doi:10.1016/j.lpm.2012.04.030
- 42 Stocks SJ, McNamee R, Turner S, *et al.* Has European Union legislation to reduce exposure to chromate in cement been effective in reducing the incidence of allergic contact dermatitis attributed to chromate in the UK? *Occup Environ Med* 2012;**69**:150–2.

### List of figure legends

Figure 1: Flow chart of study population: work related diseases recorded in the RNV3P network between 2001 and 2010.

Figure 2: Distribution of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) by age group and gender (n=3736), p<0.0001.

Figure 3: Distribution of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) by agents (n=3738).

Figure 4: Annual reporting odds ratio of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) relative to all other diseases (n=3738).

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Table 1. Activity sectors and occupations of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) (n=3738).

|                                                                                                            | <i>Men<br/>n (%)</i> | <i>Women<br/>n (%)</i> | <i>P- value</i> |
|------------------------------------------------------------------------------------------------------------|----------------------|------------------------|-----------------|
| <b>Activity Sectors, n (%)*</b>                                                                            |                      |                        | <0.0001         |
| A. Agriculture, hunting and forestry                                                                       | 27 (1.65)            | 26 (1.42)              |                 |
| B. Fishing, aquiculture                                                                                    | 3 (0.18)             | 2 (0.11)               |                 |
| C. Mining and quarrying                                                                                    | 4 (0.24)             | 0 (0.00)               |                 |
| D. Manufacturing                                                                                           | <b>634 (38.82)</b>   | 207 (11.29)            |                 |
| E. Electricity, gas and water supply                                                                       | 8 (0.49)             | 0 (0.00)               |                 |
| F. Construction                                                                                            | <b>338 (20.70)</b>   | 8 (0.44)               |                 |
| G. Wholesale and retail trade ; repair of motor vehicles, motorcycles and personal and household goods     | 205 (12.55)          | 116 (6.33)             |                 |
| H. Hotels and restaurants                                                                                  | 68 (4.16)            | 60 (3.27)              |                 |
| I. Transport, storage and communication                                                                    | 34 (2.08)            | 8 (0.44)               |                 |
| J. Financial activities                                                                                    | 1 (0.06)             | 5 (0.27)               |                 |
| K. Real estate, renting and business activities                                                            | 80 (4.90)            | 86 (4.69)              |                 |
| L. Public administrations and defence; compulsory social activities                                        | 46 (2.82)            | 84 (4.58)              |                 |
| M. Education                                                                                               | 20 (1.22)            | 34 (1.85)              |                 |
| N. Health and social work activities                                                                       | 82 (5.02)            | <b>644 (35.13)</b>     |                 |
| O. Community, social and personnel service activities                                                      | 74 (4.53)            | <b>534 (29.13)</b>     |                 |
| P. Private households employing staff and undifferentiated production activities of households for own use | 4 (0.24)             | 18 (0.98)              |                 |
| Q. Extra-territorial organisations and bodies                                                              | 5 (0.31)             | 1 (0.05)               |                 |
| <b>Total</b>                                                                                               | <b>1633 (100)</b>    | <b>1833 (100)</b>      |                 |
| <b>Occupations, n (%)</b>                                                                                  |                      |                        | <0.0001         |
| 5141 Hairdressers, barbers, beauticians and related workers                                                | 58 (3.27)            | 581 (29.55)            |                 |
| 9132 Helpers and cleaners in offices, hotels and other establishments                                      | 48 (2.71)            | 174 (8.85)             |                 |
| 3231 Nursing associated professionals                                                                      | 12 (0.68)            | 196 (9.97)             |                 |
| 5132 Institution-based personal care workers                                                               | 15 (0.85)            | 180 (9.16)             |                 |
| 7122 Bricklayers and stonemasons                                                                           | 159 (8.97)           | 1 (0.05)               |                 |
| 9131 Domestic helpers and cleaners                                                                         | 16 (0.90)            | 133 (6.77)             |                 |
| 7231 Motor vehicle mechanics and fitters                                                                   | 127 (7.17)           | 4 (0.20)               |                 |
| 7223 Machine-tool setters and setter-operators                                                             | 77 (4.35)            | 8 (0.41)               |                 |
| 7412 Bakers, pastry-cooks and confectionery makers                                                         | 71 (4.01)            | 9 (0.46)               |                 |
| 5122 Cooks                                                                                                 | 55 (3.10)            | 24 (1.22)              |                 |
| 2230 Nursing and midwifery professionals                                                                   | 1 (0.06)             | 67 (3.41)              |                 |
| 7141 Painters and related workers                                                                          | 58 (3.27)            | 4 (0.20)               |                 |
| 8211 Machine-tool operators                                                                                | 49 (2.77)            | 11 (0.56)              |                 |
| 5220 Shop salespersons and demonstrators                                                                   | 4 (0.23)             | 54 (2.75)              |                 |

|                                                                  |                   |                   |
|------------------------------------------------------------------|-------------------|-------------------|
| 7132 Floor layers and tile setters                               | 48 (2.71)         | 3 (0.15)          |
| 8232 Plastic-products machine operators                          | 30 (1.69)         | 18 (0.92)         |
| 7142 Varnishers and related painters                             | 43 (2.43)         | 3 (0.15)          |
| 9333 Freight handlers                                            | 23 (1.30)         | 18 (0.92)         |
| 7213 Sheet metal workers                                         | 38 (2.14)         | 2 (0.10)          |
| 6113 Gardeners, horticultural and nursery growers                | 18 (1.02)         | 21 (1.07)         |
| 7212 Welders and flame cutters                                   | 30 (1.69)         | 6 (0.31)          |
| 5123 Waiters, waitresses and bartenders                          | 14 (0.79)         | 21 (1.07)         |
| 7233 Agricultural- or industrial-machinery mechanics and fitters | 32 (1.81)         | 1 (0.05)          |
| 7222 Tool-makers and related workers                             | 31 (1.75)         | 1 (0.05)          |
| 8284 Metal-, rubber- and plastic-products assemblers             | 14 (0.79)         | 17 (0.86)         |
| Other                                                            | 562 (39.56)       | 276 (20.80)       |
| <b>Total</b>                                                     | <b>1772 (100)</b> | <b>1966 (100)</b> |

\*Missing data: 272

Table 2: Annual distribution of OACD reported in RNV3P network (between 2001-2010) by selected activity sectors according to observed trends. [ROR= Reporting odd ratio; 95% CI =95% confidence interval].

| ACD cases (n)                                          | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | Kendall Tau (P-value) | Kendall Tau (P-value) | ROR (year j vs j-1): [95% CI] | P value      |
|--------------------------------------------------------|------|------|------|------|------|------|------|------|------|------|-----------------------|-----------------------|-------------------------------|--------------|
| All diseases                                           | 4565 | 4676 | 4778 | 5411 | 5252 | 5366 | 5542 | 6271 | 6467 | 6621 | 0.911 (<0.001)        | -                     | -                             | -            |
| All cases                                              | 410  | 351  | 340  | 365  | 350  | 356  | 384  | 391  | 423  | 368  | 0.333 (0.18)          | -0.36 (0.151)         | 0.978 [0.966;0.99]            | <0.001       |
| <b>Sectors with significant rises</b>                  |      |      |      |      |      |      |      |      |      |      |                       |                       |                               |              |
| D-27. 28. Metallurgy and manufacture of metal products | 17   | 17   | 20   | 26   | 24   | 28   | 19   | 29   | 37   | 19   | 0.477 (0.058)         | 0.422 (0.089)         | <b>1.052 [1.004;1.103]</b>    | <b>0.034</b> |
| K-74. Other business activities                        | 8    | 9    | 14   | 12   | 15   | 19   | 21   | 15   | 11   | 25   | <b>0.584 (0.02)</b>   | <b>0.494 (0.048)</b>  | <b>1.082 [1.022;1.147]</b>    | <b>0.007</b> |
| H. Hotels and restaurants                              | 8    | 11   | 8    | 12   | 12   | 15   | 18   | 15   | 17   | 12   | <b>0.613 (0.017)</b>  | <b>0.584 (0.02)</b>   | 1.062 [0.999;1.131]           | 0.057        |
| L. Public administrations                              | 10   | 7    | 9    | 15   | 10   | 11   | 18   | 21   | 16   | 13   | <b>0.539 (0.031)</b>  | <b>0.556 (0.025)</b>  | <b>1.07 [1.007;1.138]</b>     | <b>0.031</b> |
| O-93. Personnel service activities                     | 43   | 45   | 59   | 49   | 40   | 70   | 66   | 64   | 70   | 69   | <b>0.539 (0.031)</b>  | <b>0.6 (0.016)</b>    | <b>1.064 [1.026;1.104]</b>    | <b>0.001</b> |
| <b>Sectors with no significant trends</b>              |      |      |      |      |      |      |      |      |      |      |                       |                       |                               |              |
| A. Agriculture, hunting and forestry                   | 8    | 5    | 4    | 1    | 5    | 4    | 8    | 6    | 5    | 7    | 0.141 (0.583)         | 0.022 (0.929)         | 1.014 [0.924;1.114]           | 0.771        |
| D-15. Food Manufacture                                 | 13   | 2    | 13   | 11   | 8    | 9    | 11   | 12   | 14   | 13   | 0.303 (0.236)         | 0.315 (0.209)         | 1.045 [0.977;1.119]           | 0.199        |
| D-24. Manufacture of Chemicals and Chemical            | 6    | 6    | 0    | 5    | 10   | 2    | 4    | 3    | 10   | 10   | 0.163 (0.523)         | 0.2 (0.421)           | 1.081 [0.986;1.18]            | 0.1          |

| Products                                         |    |    |    |    |    |    |    |    |    |    | 9]                |                   |                        |       |
|--------------------------------------------------|----|----|----|----|----|----|----|----|----|----|-------------------|-------------------|------------------------|-------|
| D-25. Manufacture of Rubber and Plastic Products | 10 | 14 | 6  | 7  | 9  | 12 | 4  | 8  | 11 | 2  | -0.244<br>(0.325) | -0.2<br>(0.421)   | 0.93<br>[0.862;1.003]  | 0.06  |
| D-35. Manufacture of other transport equipment   | 5  | 4  | 8  | 11 | 6  | 5  | 11 | 8  | 3  | 4  | -0.116<br>(0.649) | -0.111<br>(0.655) | 0.984<br>[0.904;1.071] | 0.708 |
| D.29-33. Manufacture of machinery and equipment  | 9  | 9  | 12 | 16 | 6  | 7  | 12 | 16 | 13 | 11 | 0.23<br>(0.365)   | 0.156<br>(0.531)  | 1.027<br>[0.962;1.097] | 0.427 |
| D. Other Manufactures                            | 9  | 11 | 9  | 13 | 6  | 3  | 10 | 3  | 7  | 11 | -0.138<br>(0.587) | -0.156<br>(0.531) | 0.958<br>[0.887;1.033] | 0.262 |
| F. Construction                                  | 48 | 35 | 37 | 32 | 26 | 27 | 35 | 34 | 36 | 36 | -0.068<br>(0.787) | -0.18<br>(0.473)  | 0.983<br>[0.944;1.024] | 0.41  |
| G-50. Trade and repair of motor vehicles         | 17 | 7  | 10 | 18 | 27 | 18 | 17 | 11 | 10 | 11 | -0.07<br>(0.785)  | -0.045<br>(0.858) | 0.986<br>[0.93;1.045]  | 0.629 |
| G-52. Retail trade and repair of household goods | 21 | 16 | 13 | 10 | 22 | 10 | 12 | 10 | 14 | 14 | -0.21<br>(0.412)  | -0.333<br>(0.18)  | 0.947<br>[0.893;1.003] | 0.066 |
| M. Education                                     | 5  | 2  | 6  | 8  | 2  | 3  | 9  | 11 | 6  | 2  | 0.163<br>(0.523)  | 0.111<br>(0.655)  | 1.023<br>[0.933;1.123] | 0.635 |
| N. Health and social work activities             | 78 | 77 | 61 | 76 | 62 | 64 | 73 | 83 | 89 | 63 | 0.067<br>(0.788)  | -0.09<br>(0.719)  | 0.985<br>[0.955;1.015] | 0.319 |

Table 3: Annual distribution of OACD reported in RNV3P network (between 2001-2010) by selected causal agents according to observed trends. [ROR= Reporting odd ratio; 95% CI=95% confidence interval].

| ACD Cases (n)              | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | Kendall's Tau (P-value) | Kendall's Tau (P-value) | ROR(year j vs j-1): [95% CI] | P-value          |
|----------------------------|------|------|------|------|------|------|------|------|------|------|-------------------------|-------------------------|------------------------------|------------------|
| <b>Product categories:</b> |      |      |      |      |      |      |      |      |      |      |                         |                         |                              |                  |
| Biocides                   | 51   | 29   | 34   | 38   | 37   | 42   | 46   | 72   | 66   | 45   | <b>0.467 (0.06)</b>     | 0.449 (0.072)           | <b>1.053 [1.018;1.09]</b>    | <b>0.003</b>     |
| Cosmetics                  | 16   | 16   | 11   | 16   | 18   | 27   | 32   | 35   | 33   | 22   | <b>0.644 (0.011)</b>    | <b>0.6 (0.016)</b>      | <b>1.092 [1.041;1.15]</b>    | <b>&lt;0.001</b> |
| Resins/Glue                | 41   | 29   | 37   | 39   | 40   | 47   | 37   | 45   | 46   | 46   | 0.477 (0.058)           | 0.449 (0.072)           | 1.031 [0.995;1.07]           | 0.093            |
| Hairdressing products      | 64   | 44   | 48   | 41   | 32   | 49   | 52   | 40   | 47   | 56   | 0.022 (0.929)           | 0.048 (0.881)           | 0.974 [0.938;1.01]           | 0.169            |
| Cement                     | 17   | 18   | 12   | 14   | 9    | 9    | 10   | 9    | 7    | 6    | <b>-0.782 (0.002)</b>   | <b>-0.689 (0.006)</b>   | <b>0.892 [0.832;0.95]</b>    | <b>0.001</b>     |
| Plant products             | 11   | 7    | 5    | 5    | 6    | 6    | 4    | 5    | 4    | 5    | <b>-0.564 (0.031)</b>   | <b>-0.6 (0.016)</b>     | <b>0.909 [0.829;0.99]</b>    | <b>0.039</b>     |
| Metals                     | 73   | 88   | 69   | 67   | 69   | 53   | 66   | 62   | 93   | 78   | -0.135 (0.59)           | -0.135 (0.59)           | 0.996 [0.968;1.02]           | 0.765            |
| Rubber additives           | 39   | 32   | 36   | 48   | 50   | 33   | 34   | 37   | 37   | 42   | 0.18 (0.473)            | -0.135 (0.59)           | 0.994 [0.957;1.0]            | 0.667            |

|                                     |    |    |    |    |    |    |    |    |    |    |                   |                   |                       |        |
|-------------------------------------|----|----|----|----|----|----|----|----|----|----|-------------------|-------------------|-----------------------|--------|
|                                     |    |    |    |    |    |    |    |    |    |    | )                 | 3]                |                       |        |
| Cutting oils and coolants           | 20 | 24 | 23 | 31 | 14 | 18 | 16 | 32 | 23 | 13 | -0.18<br>(0.473)  | -0.156<br>(0.531) | 0.979<br>[0.932;1.03] | 0.398  |
| Dyes/Inks                           | 6  | 1  | 7  | 9  | 10 | 9  | 5  | 2  | 4  | 7  | -0.023<br>(0.928) | -0.022<br>(0.929) | 0.986<br>[0.903;1.08] | 0.743  |
| Family of substances:               |    |    |    |    |    |    |    |    |    |    |                   |                   |                       |        |
| Quaternary ammonium                 | 12 | 8  | 10 | 9  | 3  | 18 | 11 | 22 | 21 | 16 | 0.378<br>(0.128)  | 0.333<br>(0.18)   | 1.089<br>[1.024;1.16] | 0.007  |
| Isothiazolones                      | 1  | 2  | 1  | 6  | 2  | 5  | 6  | 17 | 16 | 19 | 0.782<br>(0.002)  | 0.733<br>(0.003)  | 1.389<br>[1.259;1.54] | <0.001 |
| Aldehydes                           | 23 | 6  | 7  | 10 | 14 | 5  | 15 | 12 | 10 | 5  | -0.159<br>(0.528) | -0.225<br>(0.369) | 0.933<br>[0.872;1]    | 0.041  |
| Fragrances                          | 3  | 3  | 3  | 6  | 4  | 7  | 9  | 13 | 10 | 7  | 0.722<br>(0.005)  | 0.733<br>(0.003)  | 1.139<br>[1.044;1.25] | 0.004  |
| Epoxy resins                        | 17 | 11 | 15 | 20 | 22 | 29 | 26 | 28 | 20 | 30 | 0.629<br>(0.012)  | 0.644<br>(0.009)  | 1.087<br>[1.035;1.14] | 0.001  |
| Acrylic resins                      | 5  | 8  | 11 | 9  | 8  | 8  | 5  | 9  | 15 | 10 | 0.33<br>(0.2)     | 0.333<br>(0.18)   | 1.042<br>[0.969;1.12] | 0.270  |
| Hair bleaching products             | 8  | 6  | 2  | 2  | 8  | 15 | 13 | 13 | 13 | 13 | 0.466<br>(0.076)  | 0.422<br>(0.089)  | 1.125<br>[1.042;1.22] | 0.003  |
| PPD and other para-amino compounds* | 29 | 23 | 25 | 24 | 17 | 23 | 17 | 21 | 23 | 21 | -0.471<br>(0.067) | -0.629<br>(0.012) | 0.958<br>[0.913;1.01] | 0.081  |
| Nickel                              | 38 | 53 | 37 | 47 | 30 | 24 | 35 | 39 | 54 | 46 | 0.067<br>(0.788)  | -0.022<br>(0.929) | 0.994<br>[0.959;1.03] | 0.754  |
| Chromium (unspecified sources)      | 26 | 25 | 25 | 15 | 29 | 25 | 21 | 17 | 27 | 27 | 0.023<br>(0.927)  | 0.156<br>(0.531)  | 1.003<br>[0.958;1.05] | 0.891  |

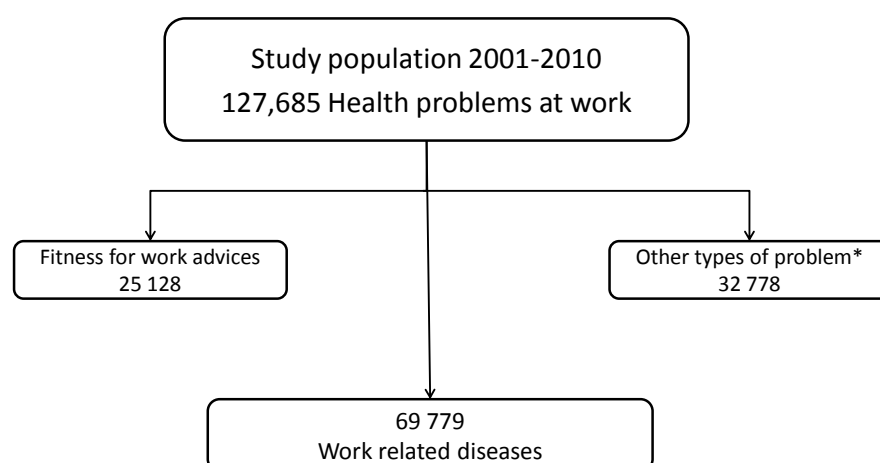
\*: PPD = p-phenylenediamine

Table 4: Annual distribution of OACD by selected agents reported in RNV3P network (between 2001-2010) and by selected activity sectors according to observed trends. [ROR= Reporting odd ratio; 95% CI=95% confidence interval].

| ACD cases (n)                                                      | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | Kendall Tau (P-value) | Kendall Tau (P-value) | ROR(year j vs j-1): [95% CI] | P-value |
|--------------------------------------------------------------------|------|------|------|------|------|------|------|------|------|------|-----------------------|-----------------------|------------------------------|---------|
| <b>Agents with significant rises in industrial activities</b>      |      |      |      |      |      |      |      |      |      |      |                       |                       |                              |         |
| F. Construction/Resins/Glues                                       | 5    | 4    | 4    | 7    | 3    | 7    | 10   | 11   | 9    | 11   | 0.598 (0.019)         | 0.689 (0.006)         | 1.137 [1.045;1.241]          | 0.003   |
| N. Health and social work /Cosmetics                               | 3    | 5    | 3    | 5    | 5    | 7    | 8    | 12   | 14   | 7    | 0.754 (0.003)         | 0.778 (0.002)         | 1.134 [1.041;1.24]           | 0.005   |
| O-93. Personnel service activities / Cosmetics                     | 1    | 1    | 2    | 1    | 2    | 11   | 8    | 7    | 3    | 5    | 0.489 (0.056)         | 0.539 (0.031)         | 1.161 [1.037;1.308]          | 0.012   |
| K-74. Other business activities /Metals                            | 0    | 1    | 2    | 2    | 5    | 5    | 6    | 1    | 2    | 6    | 0.549 (0.034)         | 0.467 (0.06)          | 1.143 [1.006;1.309]          | 0.046   |
| F. Construction/ Epoxy resins                                      | 4    | 3    | 4    | 7    | 3    | 6    | 10   | 9    | 6    | 11   | 0.552 (0.03)          | 0.511 (0.04)          | 1.134 [1.037;1.24]           | 0.007   |
| O-93. Personnel service activities / Hair bleaching products       | 5    | 4    | 2    | 2    | 8    | 14   | 11   | 12   | 11   | 12   | 0.506 (0.046)         | 0.2 (0.421)           | 1.155 [1.063;1.26]           | 0.001   |
| <b>Agents with significant declines by industrial activities</b>   |      |      |      |      |      |      |      |      |      |      |                       |                       |                              |         |
| F. Construction/Cement                                             | 14   | 14   | 9    | 10   | 7    | 4    | 8    | 8    | 5    | 4    | -0.69 (0.007)         | -0.644 (0.009)        | 0.882 [0.814;0.954]          | 0.002   |
| <b>Agents with no significant trends by industrial activities</b>  |      |      |      |      |      |      |      |      |      |      |                       |                       |                              |         |
| D-27. 28. Metallurgy and manufacture of metal products / Metals    | 4    | 1    | 6    | 6    | 7    | 6    | 3    | 4    | 10   | 4    | 0.167 (0.519)         | 0.244 (0.325)         | 1.048 [0.953;1.156]          | 0.335   |
| D-27. 28. Metallurgy and manufacture of metal products / Oils/Fats | 8    | 10   | 7    | 13   | 6    | 11   | 7    | 18   | 15   | 6    | 0.068 (0.787)         | 0.067 (0.788)         | 1.034 [0.965;1.109]          | 0.339   |
| F. Construction/ Metals                                            | 17   | 10   | 15   | 5    | 11   | 10   | 5    | 7    | 12   | 15   | -0.092 (0.717)        | -0.023 (0.927)        | 0.98 [0.915;1.048]           | 0.552   |
| N. Health and social work /Biocides                                | 29   | 16   | 21   | 20   | 15   | 22   | 19   | 40   | 24   | 12   | -0.067 (0.788)        | -0.18 (0.473)         | 0.983 [0.936;1.031]          | 0.475   |
| N. Health and social work /Synthetic Rubber additives              | 10   | 11   | 9    | 15   | 18   | 16   | 10   | 9    | 13   | 15   | 0.138 (0.587)         | 0.067 (0.788)         | 1.006 [0.945;1.07]           | 0.855   |
| N. Health and social work / Metals                                 | 12   | 20   | 8    | 21   | 11   | 10   | 15   | 10   | 21   | 18   | 0.114 (0.652)         | 0.067 (0.788)         | 1.009 [0.952;1.07]           | 0.757   |
| O-93. Personnel service activities / Hairdressing products         | 34   | 27   | 40   | 34   | 25   | 42   | 44   | 36   | 40   | 48   | 0.477 (0.058)         | 0.405 (0.106)         | 1.035 [0.992;1.08]           | 0.112   |
| O-93. Personnel service activities / Metals                        | 4    | 6    | 5    | 4    | 4    | 5    | 7    | 10   | 10   | 5    | 0.435 (0.096)         | 0.333 (0.18)          | 1.058 [0.967;1.16]           | 0.223   |
| O-93. Personnel service activities / Resins/Glues                  | 1    | 3    | 6    | 2    | 4    | 2    | 5    | 5    | 7    | 2    | 0.303 (0.236)         | 0.156 (0.531)         | 1.047 [0.935;1.176]          | 0.430   |
| D-25. Manufacture of Rubber and Plastic /                          | 5    | 4    | 3    | 3    | 5    | 7    | 1    | 5    | 1    | 0    | -0.377 (0.143)        | 0.6 (0.016)           | 1.064 [1.026;1.104]          | 0.001   |

|                                                   |    |   |    |   |    |   |   |   |    |    |                  |                  |                       |           |
|---------------------------------------------------|----|---|----|---|----|---|---|---|----|----|------------------|------------------|-----------------------|-----------|
| Resins/Glues                                      |    |   |    |   |    |   |   |   |    |    |                  | )                | ]                     |           |
| F. Construction/Chromium<br>(unspecified sources) | 13 | 7 | 13 | 4 | 10 | 9 | 5 | 5 | 11 | 14 | 0.023<br>(0.928) | 0.067<br>(0.788) | 1.005<br>[0.935;1.08] | 0.88<br>6 |

Figure 1. Flow chart of study population: work related diseases recorded in the RNV3P network between 2001 and 2010.



\*: Environmental diseases, diseases with no association with exposure, opinions on clinical files...

Figure 2 : Distribution of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) by age group and gender (n=3736),  $p<0.0001$ .

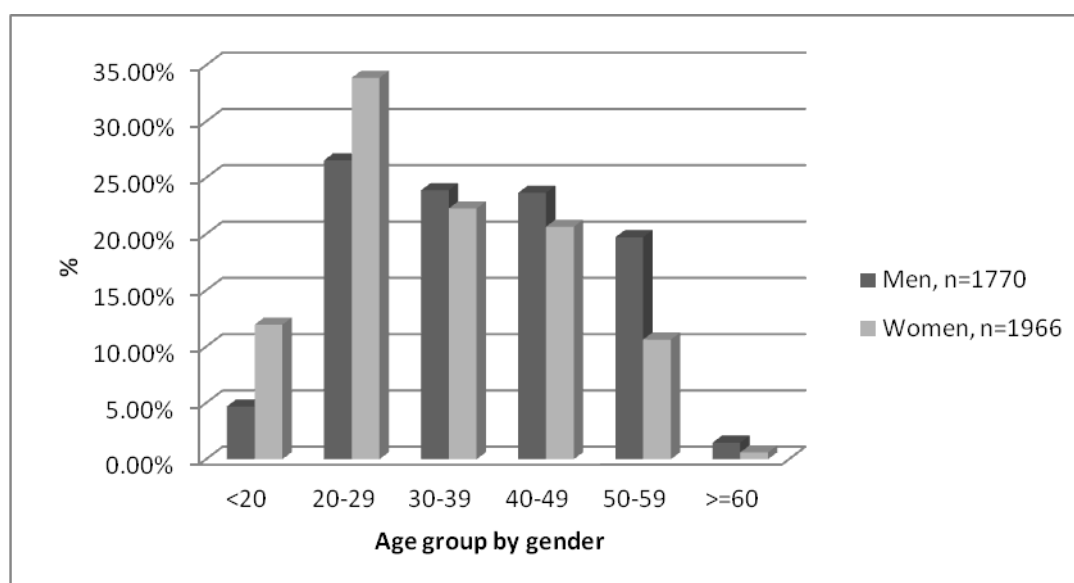


Figure 3. Distribution of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) by agents (n=3738).

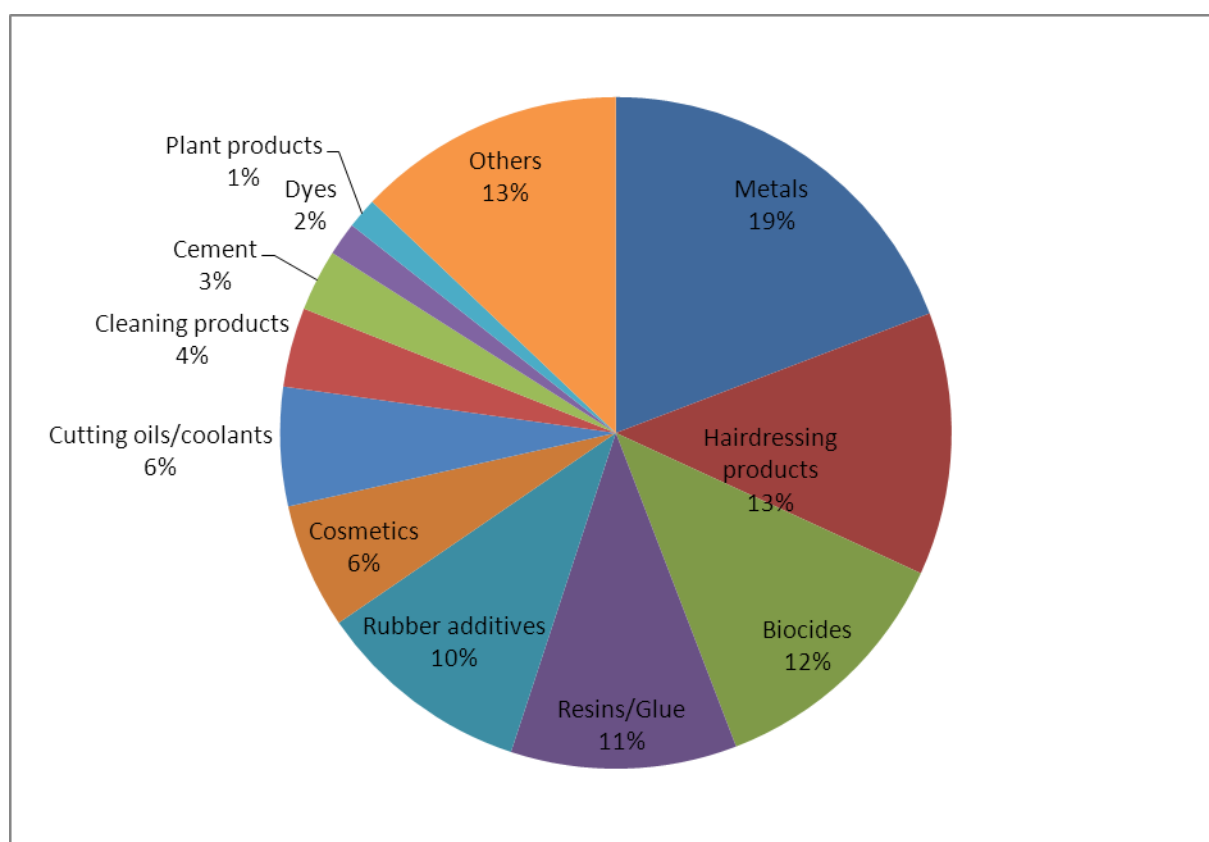
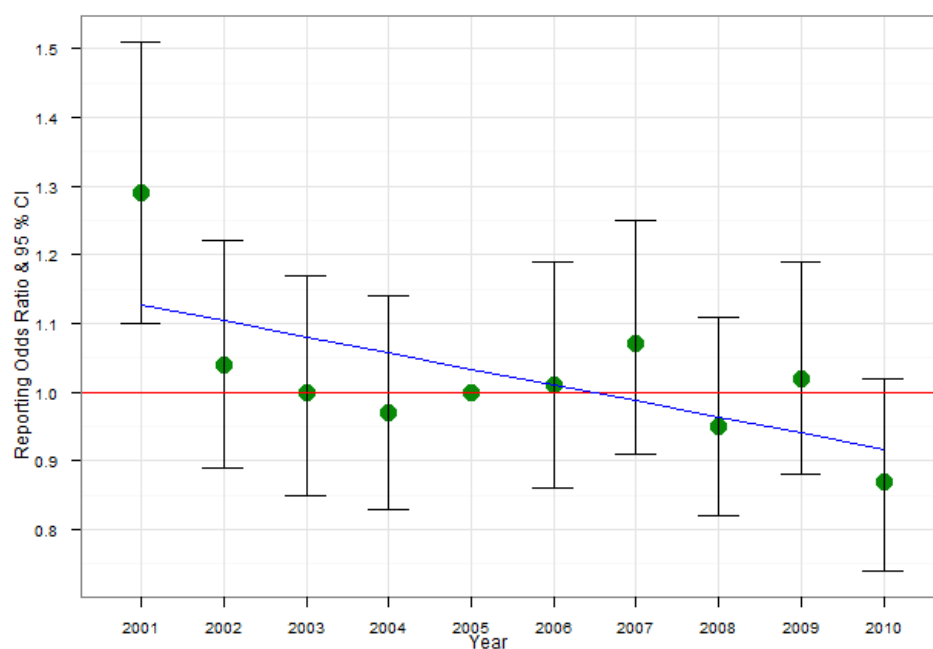


Figure 4. Annual reporting odds ratio of occupational allergic contact dermatitis cases reported in RNV3P network (between 2001-2010) relative to all other diseases (n=3738) \*



\*Kendall tau on ROR= -0.36 (P-value=0.151)