Received: 22 January 2020 | Revised: 22 February 2020 | Accepted: 24 February 2020

DOI: 10.1111/cod.13502

Check for updates

ORIGINAL ARTICLE

CONTACT DERMATITIS WILEY

Health education decreases incidence of hand eczema in metal work apprentices: Results of a controlled intervention study

Anna Reich[1,2,3] | Annika Wilke[2,3,4,5] | Günther Gediga[4] | Hansjörg Baurecht[6,7] | Elke Rodríguez[6] | Ivone Jakasa[8] | Johannes Geier[2,3,9] | Martin Mempel[1,2,3] | Timo Buhl[1,2,3] | Stephan Weidinger[6] | Sanja Kezic[10] | Swen M John[2,3,4,5] | Michael P Schön[1,2,3] | Richard Brans[2,3,4,5]

[1]Department of Dermatology, Venereology and Allergology, University Medical Center Göttingen, Göttingen, Germany

[2]Lower Saxony Institute of Occupational Dermatology, University Medical Center Göttingen, Göttingen, Germany

[3]Lower Saxony Institute of Occupational Dermatology, University of Osnabrück, Osnabrück, Germany

[4]Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrück, Osnabrück, Germany

[5]Institute for Interdisciplinary Dermatologic Prevention and Rehabilitation (iDerm), University of Osnabrück, Osnabrück, Germany

[6]Department of Dermatology, Allergology and Venereology, University Hospital Schleswig-Holstein, Kiel, Germany

[7]Department of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany

[8]Laboratory for Analytical Chemistry, Department of Chemistry and Biochemistry, Faculty of Food Technology and Biotechnology, University of Zagreb, Zagreb, Croatia

[9]Information Network of Department of Dermatology, Georg August University, Göttingen, Germany

[10]Coronel Institute of Occupational Health, Amsterdam University Medical Center, Amsterdam, The Netherlands

Correspondence
Dr Richard Brans, Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrück, Am Finkenhügel 7a, D-49076 Osnabrück, Germany.
Email: rbrans@uos.de

Funding information
Volkswagen Foundation, Grant/Award Number: ZN2778

Abstract

Background: Metal work apprentices (MWAs) frequently develop work-related hand eczema (HE).

Objectives: To evaluate the effect of health education on incidence of work-related HE in MWAs and to assess confounding factors.

Materials/methods: In a prospective controlled intervention study, 131 MWAs received educational training on prevention of HE, whereas 172 MWAs and 118 office work apprentices served as controls. At baseline and during three yearly follow-ups, questionnaires were completed and hands were examined. Saliva samples were collected for assessment of filaggrin (*FLG*) null mutations and an explorative genome-wide association study (GWAS), and levels of various cytokines were assessed from stratum corneum samples.

Results: The 2-year and 3-year incidence of HE in the metalwork control group was 20.9% and 32.6%, respectively, which was significantly higher than in the intervention group (odds ratio [OR] 2.63, 95% confidence interval [CI] 1.31 to 5.28, $P < .01$ and OR 3.47, 95% CI 1.88 to 6.40, $P < .0001$). The knowledge score was higher in unaffected MWAs ($P < .05$). Other factors significantly associated with developing

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
© 2020 The Authors. Contact Dermatitis published by John Wiley & Sons Ltd.

HE in MWAs were smoking cigarettes ($P < .01$) and *FLG* mutations ($P < .001$). No significant links were found regarding epidermal cytokine levels and GWAS.

Conclusions: Health education is effective in primary prevention of HE in MWAs. Individual factors should be considered in targeted counseling.

KEYWORDS

apprentices, hand eczema, health education, intervention, metal work, occupation, prevention, RRID:SCR_001905, work-related skin diseases

1 | INTRODUCTION

Hand eczema (HE) is the most common work-related skin disease.[1] Due to its often chronic course, it is associated with impaired health-related quality of life and a considerable socioeconomic burden related mainly to work absenteeism, loss-of-job, or retraining.[2-4] Metal workers have a particularly high share of work-related HE, with a lifetime prevalence of 30% to 63.1%.[5-7] In metal processing, this is due mainly to mechanical strain, wet work, and exposure to metalworking fluids with substantial irritant and allergenic potential. The onset of work-related HE occurs frequently already during apprenticeship.[7] However, data on the incidence of HE in metal work apprentices (MWAs) are scarce.[8-10] Considering the low adherence to skin protection recommendations among metalworkers,[5] raising awareness and health education on use of personal protective equipment is required. Although there is scant evidence for the effectiveness of health education in primary prevention of work-related HE due to a lack of standardized trials,[2,11] a few controlled prospective studies in apprentices of other professions suggest that health education effectively reduces the incidence of HE by improving skin protection behavior.[12-14] To our knowledge, with the exception of a single study assessing any skin changes in apprentices from various occupations including a small number of MWAs,[15] no such studies have been performed in MWAs.

Individual factors may modulate the risk of work-related HE and interfere with preventive measures.[16] Loss-of-function mutations in the filaggrin gene (*FLG*) cause skin barrier defects by reducing levels of epidermal filaggrin and its degradation products, which contribute to the natural moisturizing factor (NMF). *FLG* mutations are present in 8% to 10% of the general European population and have been linked to atopic dermatitis (AD).[17] Carriers have an increased risk of work-related irritant contact dermatitis, particularly when in combination with AD,[16,18-20] a more unfavorable course of the disease, and a lower probability of remaining in the workforce.[21] Genome-wide association studies (GWAS) may help to discover other genetic variants linked to work-related HE. They have already been applied in AD and identified susceptibility loci, mostly implicated in immune dysregulation.[22] Moreover, phenotypic variations in epidermal cytokine levels may explain individual predispositions toward skin inflammation and thus susceptibility to develop work-related HE.[23] Data on the association between tobacco smoking and prevalence of HE have been inconsistent, also in occupational settings.[24] However, recent studies suggest that work-related HE is more severe and persistent in smokers than in nonsmokers.[25,26]

Here, a controlled prospective health education intervention study was conducted in a large cohort of MWAs and control cohorts. The primary outcome was the effect of the intervention on the incidence of HE during apprenticeship. Secondary outcomes were the effect of the intervention on the disease-specific knowledge and protective behavior as well as associations between the incidence of HE and individual factors.

2 | MATERIAL AND METHODS

2.1 | Study population and study design

We conducted a controlled, prospective intervention study in MWAs from nine vocational schools (one in Osnabrück and eight in the city and catchment area of Göttingen, Germany) involving apprentices who were receiving training in a range of professions involving metal processing. An additional control cohort of office work apprentices from the same schools was recruited to assess the prevalence and incidence of HE in young adults of similar age, and ethnic and social background without exposure to major occupational skin hazards. The study protocol was independently approved by the ethics committees at the University of Osnabrück and the University Medical Center Göttingen. After obtaining permission from the regional school authorities and the vocational schools, the apprentices were recruited on a voluntary basis within the first weeks of apprenticeship in autumn of 2013 and 2014. All participating apprentices provided written informed consent. In minors (<18 years of age), informed written consent was given by their legal representatives. Assessments were carried out at baseline (T0) and at the end of the first (T1), the second (T2), and the third (T3) year of training (May/June of each respective year).

2.2 | Intervention

The MWAs from the vocational school in Osnabrück were assigned to the metalwork intervention group (MW-int). In the first weeks of apprenticeship, they received a structured 90-minute training on causes and prevention of work-related HE consisting of an oral, interactive, and dialogue-oriented presentation by an experienced health educator, combined with hands-on practical exercises on correct use

of protective gloves, barrier creams, and skin care products. This training was based on seminars regularly conducted by the University of Osnabrück for patients with work-related HE and previous studies[27,28] with adjustments for MWAs.[29] The maximum number of MWAs receiving the training at a time was 25. One year after enrollment (T1), a leaflet summarizing the key information of the training program and free samples of an unscented barrier cream and emollient were handed out to the participants in the MW-int. The MWAs from the other vocational schools were assigned to the metalwork control group (MW-ctrl) and did not receive training on prevention of HE by us, similar to the apprentices in the office work control group (OW-ctrl).

2.3 | Questionnaires

At baseline, the participants filled out a paper-based questionnaire to provide basic sociodemographic data and information on preexisting skin disorders. This included questions if they ever had skin changes on their hands prior to the vocational training, or flexural eczema. At baseline and each follow-up, the apprentices completed another questionnaire with questions on occupational strain (eg, wet work, exposure to skin hazards) and individual skin protection behavior (eg, use of protective gloves, barrier creams, emollients). Moreover, the apprentices were regularly asked about skin changes on the hands in the previous year and, if so, about their morphology (redness, scaling, fissures, papules, vesicles), as well as their smoking behavior and if they felt they were being adequately informed about skin protection measures. A shortened version of the validated "Occupational Skin Diseases Knowledge Questionnaire (OSD-KQ-short)"[28,30] comprising 30 of the 65 original items, was used at baseline and each follow-up visit to assess knowledge on work-related skin diseases and their prevention.

2.4 | Clinical examination and atopy score

At each time point, a trained dermatologist used the validated Osnabrueck Hand Eczema Severity Index (OHSI)[31,32] to assess the apprentices' hands for presence of six morphological features (erythema, scaling, papules, vesicles, infiltration, and fissures) and the extent of the affected skin area. An Erlangen atopy score ≥10 at baseline was defined as atopic skin diathesis.[33]

2.5 | Genetic analyses

For genetic analyses, 2 mL of saliva per individual was collected with the OG-500 Oragene DNA Self-Collection Kit (DNA Genotek, Ottawa, Canada) following the manufacturer's instructions for sampling and storage. Automated purification of genomic DNA was performed on Autopure LS following the manufacturer's protocol (Qiagen, Hilden, Germany).

For genotyping of *FLG* mutations, the four most common *FLG* variants—R501X, 2282del4, R2447X, and S3247X—were analyzed with the TaqMan allelic discrimination method (Applied Biosystems, Carlsbad, California). TaqMan single nucleotide polymorphism (SNP) genotyping was carried out with 5 ng of dried genomic DNA in 384-well genotyping reactions and 5 μL reaction volumes following the standard procedures based on Applied Biosystems reagents. Probe detection was performed with the Applied Biosystems 7900HT Fast Real-Time PCR System.

For GWAS, all subjects were genotyped on the Infinium Global Screening Array v1.0 BeadChip (Illumina, San Diego, California). Genotype calling was carried out using the Illumina GenomeStudio 2.0.4 Data-Analysis software. Sample and marker quality control was performed with PLINK (v1.9, https://www.cog-genomics.org/plink/1.9).[34] Individuals with a person-wise call rate <92%, with excess of heterozygosity (inbreeding coefficient |F| > .1), duplicated and related samples (PI HAT > .1875), as well as outliers from principal component analysis were excluded. Variants with a call rate <95%, Hardy-Weinberg disequilibrium ($P < 10^{-8}$), minor allele frequency <1%, and a differential missingness between cases and controls ($P < 10^{-50}$) were also excluded. After quality control, 477 263 variants and 328 individuals were eligible for analysis.

2.6 | Sequential tape stripping of stratum corneum and analysis

Eight round adhesive tape discs (3.8 cm^2, D-Squame, CuDerm, Dallas, Texas) were consecutively attached to the skin at the flexural aspect of the lower arm.[35] Each tape was pressed on for 10 seconds with standardized force using a disc pressure applicator (CuDerm).

NMF was defined as the sum of the concentrations of histidine, 2-pyrrolidone-5-carboxylic acid, and *trans*- and *cis*- isomers of urocanic acid. NMF was extracted from tape strips number 6 and subsequently analyzed by high-performance liquid chromatography (HPLC) as published before.[35,36]

The samples for cytokine analyses were extracted from tape strips number 8 by 0.6 mL of phosphate-buffered saline (PBS) containing 0.05% Tween 20 and ultrasonificated for 15 min. The MESO QuickPlex SQ 120 assay (MSD, Rockville, Maryland) was used to analyze epidermal levels of the following cytokines: granulocyte-macrophage colony-stimulating factor (GM-CSF); interleukin (IL)-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8/CXCL8, IL-10, IL-12p40, IL-12p70, IL-13, IL-15, IL-16, and IL-17A, interferon (INF)-γ, tumor necrosis factor (TNF)-α, TNF-β, and vascular endothelial growth factor (VEGF).

2.7 | Data analysis

Statistical analyses were conducted with R (3.5.1) (www.r-project.org, RRID:SCR_001905) using the car and ez packages. Differences between groups for continuous variables were tested either by the Welch test or analysis of variance (ANOVA) with White adjustment. The Wilcoxon test was applied for categorical variables. In case of

comparison of repeated measures, the Wilcoxon signed-rank test for categorical variables, and for dichotomous variables the McNemar test was used. Odds were analyzed by logistic regression using the generalized linear model procedure. As specified in the text, variables such as age, gender, or smoking behavior were either included in the regression equation or were used to check the effect of confounding variables in the analysis for effect control. Differences were considered significant if the *P*-value obtained was less than .05. For GWAS, allele frequencies were compared between different groups (MWA-int, MWA-ctrl, OWA-ctrl) using logistic regression models with adjustment for sex and population stratification. All analyses were conducted with PLINK (v1.9, https://www.cog-genomics.org/plink/1.9).[34]

3 | RESULTS

3.1 | Demographic data

The 303 MWAs enrolled in this study received vocational training as industrial mechanic, cutting machine operator/precision mechanic, model builder/construction mechanic, toolmaker, or process mechanic (Table S1). While 131 MWAs were allocated to the intervention group (MW-int), the others (n = 172) were assigned to the metalwork control group (MW-ctrl). The office work control group (OW-ctrl) consisted of 118 apprentices in vocational programs for information technology or bank professions. The sociodemographic characteristics of the two groups of MWA did not differ in main aspects at baseline (Table 1). The apprentices in OW-ctrl had a slightly higher mean age of nearly 21 years, a higher share of females (14.4%), and on average a higher educational level than the MWAs in both groups. About one third of MWAs in both groups were self-reported tobacco smokers, with a significantly higher daily cigarette consumption in smokers of the MW-ctrl compared to the MW-int ($P < .01$).

3.2 | Follow-up

Figure 1 shows the number of participants who were unavailable at the respective follow-ups. Loss to follow-up in all three groups was up to 13.4% in 1 year (T1) and 19.8% at 2 years (T2) after inclusion into the study. The most common reasons for not participating in the respective follow-ups were illness on the day of the visit, or changing school or career for various reasons. The higher rate of drop-outs of up to 40.2% at the 3-year follow-up (T3) was mainly due to varying lengths of vocational training programs (some programs were only 2.5 years). Therefore, several apprentices who had finished their training early were not included in the final follow-up at T3. No drop-outs due to skin problems came to our attention. At T2, a significantly higher share of atopic skin diathesis ($P < .05$) was found among drop-outs. No other statistically significant differences in baseline characteristics between drop-outs and the other participants were detected.

3.3 | Hand eczema

HE was defined as the presence of (a) vesicles or (b) erythema in combination with at least one of the symptoms papules, scaling, or fissures on the hands, either observed during clinical examination (T0-T3) or self-reported for the time before baseline (T0) or within the year before the respective follow-up visits (T1-T3). Incident HE was defined as HE newly developed after recruitment, that is, in those without HE according to the above criteria during baseline examination and who denied having had HE prior to T0. Data of self-reported HE were included in the analysis. However, most HE was detected by clinical examination, in particular at T2 and T3 (data not shown). As shown in Figure 2, until the end of the first year, the incidence of HE was similar in all three groups (up to 7.6%). The 2-year and 3-year incidence of HE

TABLE 1 Demographic data at baseline (T0)

	MW-int	MW-ctrl	OW-ctrl
Mean age ± SD (y)[a,b]	18.37 ± 3.27	19.21 ± 3.34	20.58 ± 3.09
Females n/n $_{total}$ (%)	8/131 (6.1)	15/172 (8.7)	17/118 (14.4)
History of flexural eczema n/n $_{total}$ (%)	14/128 (11.4)	10/154 (6.5)	16/85 (18.8)
Atopic skin diathesis[c] n/n $_{total}$ (%)	4/128 (3.1)	2/172 (1.2)	3/118 (2.5)
Tobacco smokers n/n $_{total}$ (%)	41/127 (32.3)	60/169 (35.5)	34/118 (28.8)
Mean daily cigarette consumption in smokers ± SD[d]	9.71 ± 5.12	13.58 ± 7.03	11.81 ± 6.74
Highest educational level n/n $_{total}$ (%)[e]	n_{total} = 127	n_{total} = 169	n_{total} = 118
Lower secondary school certificate	18 (14.2)	27 (16.0)	1 (0.8)
Intermediate secondary school	91 (71.7)	111 (65.7)	38 (32.2)
Vocational baccalaureate diploma	8 (6.3)	15 (8.9)	29 (24.6)
A levels	10 (7.9)	16 (9.5)	50 (42.4)

Abbreviations: MW-int, metalwork intervention group; MW-ctrl, metalwork control group; OW-ctrl, office work control group; SD, standard deviation.
[a]MW-int vs MW-ctrl: $P < .05$.
[b]OW-ctrl vs MW-int/MW-ctrl: $P < .001$.
[c]Erlangen atopy score ≥10.
[d]MW-int vs MW-ctrl: $P < .01$.
[e]OW-ctrl vs MW-int/MW-ctrl: $P < .001$.

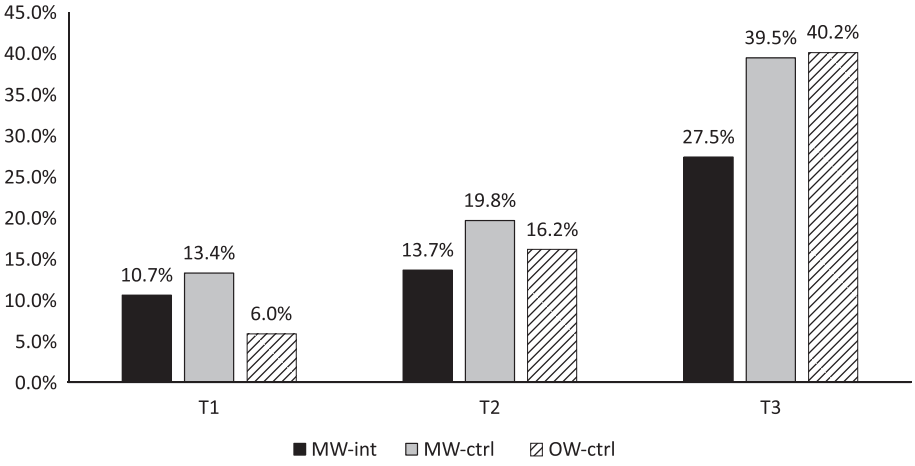


FIGURE 1 Loss to follow-up in metalwork intervention group (MW-int), metalwork control group (MW-ctrl), and office work control group (OW-ctrl) 1 year (T1), 2 years (T2), and 3 years (T3) after baseline

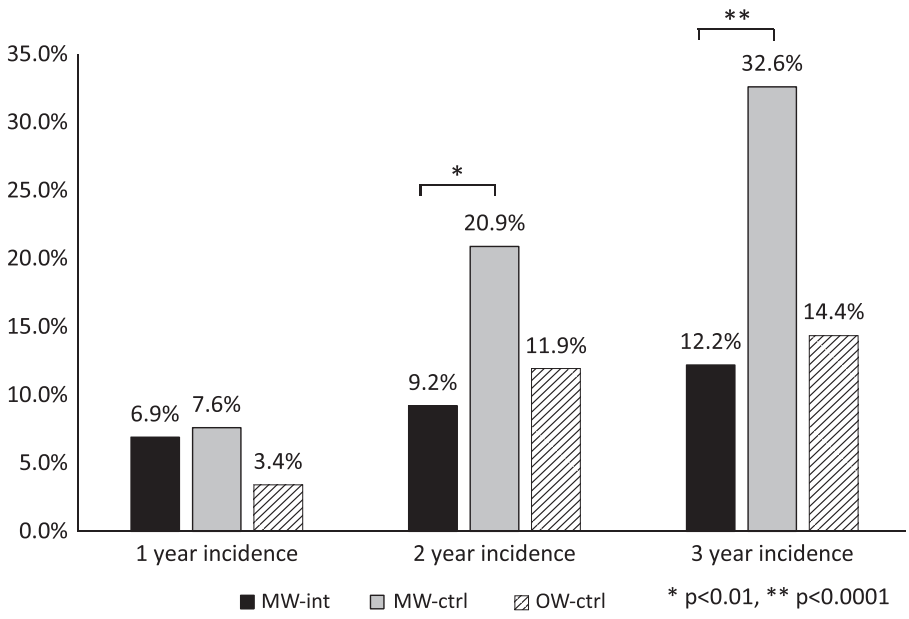


FIGURE 2 Incidence of hand eczema in available apprentices of the metalwork intervention group (MW-int), metalwork control group (MW-ctrl), and office work control group (OW-ctrl) at the respective follow-ups

in MW-ctrl was 20.9% and 32.6%, respectively, and thus, significantly higher than in MW-int (odds ratio [OR] 2.63, 95%CI [confidence interval]: 1.31-5.28, $P < .01$ and OR 3.47, 95%CI: 1.88-6.40, $P < .0001$). In MW-ctrl, the baseline prevalence of HE was 14.5% and increased to a 2-year and 3-year prevalence of 30.7% and 39.0%, respectively, which was significantly higher than in MW-int (OR 2.99, 95%CI: 1.63-5.46, $P < .001$ and OR 3.34, 95% CI: 1.92-5.84, $P < .001$) (Figure 3). There were no significant differences in the 1-year, 2-year or 3-year incidence or prevalence of HE between MW-int and OW- ctrl over the years.

3.4 | Exposure to skin hazards and skin protection behavior

The percentage of apprentices exposed to metalworking fluids and/or oil as well as the number of days per week in contact with metalworking fluids and/or oil was similar in the two groups of MWAs at baseline and at all follow-ups (Table S2). However, the number of individuals who reported wet work for at least 2 hours a day was higher in MW-ctrl at follow-up than in MW-int. This difference was significant at T3 (37.8% vs 19.1%, $P < .05$). The rate had increased significantly from T0 (19.6%) to T3 (37.8%) in MW-ctrl ($P = .004$) and was nearly unchanged in MW-int. Similarly, a daily hand washing frequency of ≥5 was more common in MW-ctrl than in MW-int at follow-ups, particularly pronounced at T3 (79.6% vs 68.1%), although not statistically significant. This is possibly related to a higher use of protective gloves in the MW-int compared to the MW- ctrl (T3: 93% vs 84%). In line with this, abrasive detergents were more often used in MW-ctrl than in MW-int (difference not significant). The self-reported use of skin barrier cream and emollients was similar in both groups at all time points and nearly unchanged over time.

3.5 | Knowledge on occupational skin diseases and skin protection measures

The mean score (number of correct answers) of the OSD-KQ-short is given in Table S2 (maximum possible score: 30). At all follow-ups, the mean score was significantly higher in MW-int than in MW-ctrl

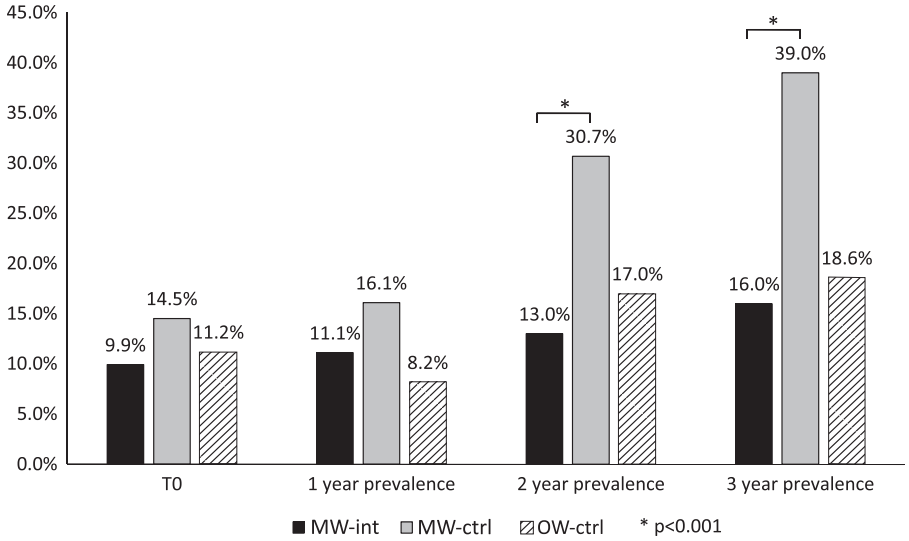


FIGURE 3 Prevalence of hand eczema in available apprentices of the metalwork intervention group (MW-int), metalwork control group (MW-ctrl), and office work control group (OW-ctrl) at baseline and the respective follow-ups

($P < .05$). The mean number of correct answers in MW-int increased substantially from T0 (14.20 ± 3.06) to T1 (17.64 ± 7.17) and reached the highest values at T2 (18.89 ± 5.05) and T3 (18.86 ± 4.56), whereas the number of correct answers in MW-ctrl increased steadily over time (T0: 12.69 ± 4.68, T1: 14.43 ± 4.64, T2: 15.81 ± 4.54, T3: 16.09 ± 4.31). The increase in correct answers from baseline values was significantly higher in MW-int than in MW-ctrl at T1 ($P < .01$) and T2 ($P < .05$) (data not shown). Accordingly, the self-estimated knowledge on skin protection measures was always higher in MW-int than in MW-ctrl.

3.6 | *FLG* mutation status

DNA was available from 328 apprentices, and all of them were successfully genotyped for *FLG* mutations. The call rates for all four mutations were >99% and genotype distributions were within the Hardy-Weinberg equilibrium. Eight apprentices from MW-int (8.0%), nine from the MW-ctrl (6.6%), and 10 from the OW-ctrl (10.9%) were heterozygous carriers of one of the four analyzed mutations. Homozygous or compound heterozygous carriers were not detected. Apprentices with a history of flexural eczema were more likely to have an *FLG* mutation than those without (12.5% vs 6.2%, n.s.). Epidermal levels of NMF were significantly lower in individuals with *FLG* mutation (n = 18, 0.583 ± 0.188 nmol/μg protein) than in those without (n = 287, 0.851 ± 0.268 nmol/μg protein, $P < .00001$).

3.7 | Factors associated with incident hand eczema

The number of apprentices with incident HE during vocational training (cases) was much higher in the MW-ctrl (n = 53) than in the MW-int (n = 16) and the OW-ctrl (n = 14). In a univariate analysis, MWAs with incident HE at any follow-up (n = 69) were compared with MWAs without incident HE (n = 234) (Table 2). Individuals with HE according to the above-mentioned criteria at baseline (preexisting HE) were part of the latter group. A lower age was significantly associated with incident HE. This was also true for *FLG* mutations (13.0% vs 3.4%, $P < .01$) and tobacco smoking (44.8% vs 31.0%, $P < .05$). The mean daily cigarette consumption in smokers was significantly higher in MWAs with incident HE than in those without (13.2 vs 11.1, $P < .05$), possibly related to the higher cigarette consumption in MW-ctrl. Notably, also in OW-ctrl, cigarette smoking was significantly associated with incident HE (42.9% vs 25.2%, $P < .05$) (Table S3). The average number of days with exposure to metalworking fluids was significantly lower in MWAs with incident HE only at T1 (Table 2). Otherwise, the differences between both groups regarding self-reported extent of exposure to metalworking fluids and oils, amount of wet work, a daily handwashing frequency ≥5, as well as use of protective gloves and abrasive detergents were not statistically significant. However, at T3, MWAs with incident HE reported more often daily wet work ≥2 hours (34.6% vs 26.9%), a daily handwashing frequency ≥ 5 (82.7% vs 69.2%), use of abrasive detergents (82.9% vs 78.6%), and a lower use of protective gloves (82.7% vs 90.3%). At T2, the percentage of MWAs reporting use of skin barrier creams was significantly lower in MWAs with incident HE than in those without (51.6% vs 68.5%, $P < .05$). Although not significantly, the self-reported use of skin care products was lower in MWAs with incident HE at all follow-ups. The self-estimated knowledge on skin protection measures was graded significantly lower by MWAs with incident HE at T1 and T2. The mean OSD-KQ-short score was always lower in MWAs with incident HE than in those without, with significant differences at T2 and T3 ($P < .05$). No significant association was found between other genetic variants and incident HE in the explorative GWAS (data not shown). Moreover, incident HE was not significantly associated with epidermal levels of NMF and the various cytokines (data not shown).

A logistic regression analysis covering all factors significantly associated with incident HE in the univariate analysis revealed that smoking cigarettes ($P < .01$) and *FLG* mutations ($P < .001$) were independent risk factors for development of HE in MWAs, both within MW-int and MW-ctrl. Only within MW-int and not within MW-ctrl, a

TABLE 2 Demographic data, exposure to skin hazards, skin protection measures, and knowledge in metalwork apprentices with and without incident hand eczema

	Case	Noncase
Mean age (T0) ± SD (y)	18.29 ± 2.11*	19.01 ± 3.59
Females (T0) n/n $_{total}$ (%)	3/69 (4.3)	20/234 (8.5)
History of flexural eczema (T0) n/n $_{total}$ (%)	4/65 (6.2)	20/213 (9.4)
Atopic skin diathesis (T0)[a] n/n $_{total}$ (%)	2/69 (2.9)	4/234 (1.7)
Tobacco smokers (T0) n/n $_{total}$ (%)	30/67 (44.8)*	71/229 (31.0)
Mean daily cigarette consumption in smokers (T0) ± SD	13.22 ± 8.10*	11.07 ± 6.44
Highest educational level (T0) n/n $_{total}$ (%)	n $_{total}$ = 67	n $_{total}$ = 229
Lower secondary school certificate	13 (19.4)	32 (12.0)
Intermediate secondary school certificate	44 (65.7)	158 (69.0)
Vocational baccalaureate diploma	5 (7.5)	18 (7.9)
A levels	5 (7.5)	21 (9.2)
FLG mutation carrier n/n total (%)	9/69 (13.0)**	8/234 (3.4)
Exposed to metalworking fluids n/n $_{total}$ (%)	T1: 58/68 (85.3)	T1: 171/198 (86.4)
	T2: 55/64 (85.9)	T2: 152/185 (82.2)
	T3: 40/52 (76.9)	T3: 129/145 (89.0)
Mean days per week with exposure to metalworking fluids ± SD	T1: 2.53 ± 1.12*	T1: 2.85 ± 0.96
	T2: 3.07 ± 1.18	T2: 3.23 ± 1.28
	T3: 3.29 ± 1.19	T3: 3.24 ± 1.24
Exposed to oil n/n $_{total}$ (%)	T1: 55/68 (80.9)	T1: 151/198 (76.3)
	T2: 48/64 (75.0)	T2: 145/185 (78.4)
	T3: 42/52 (80.8)	T3: 120/145 (82.8)
Mean days per week with exposure to oil ± SD	T1: 2.23 ± 1.27	T1: 2.45 ± 1.25
	T2: 2.91 ± 1.25	T2: 2.90 ± 1.38
	T3: 3.24 ± 1.21	T3: 3.07 ± 1.29
Amount of wet work n/n $_{total}$ (%)		
T1	n $_{total}$ = 68	n $_{total}$ = 196
No wet work	2 (2.9)	6 (3.1)
<0.5 h/d	16 (47.1)	72 (36.7)
≥0.5 h/d to <2 h/d	29 (42.6)	73 (37.2)
≥2 h/d	21 (30.9)	45 (23.0)
T2	n $_{total}$ = 63	n $_{total}$ = 185
No wet work	1 (1.6)	3 (1.6)
<0.5 h/d	17 (27.0)	74 (40.0)
≥0.5 h/d to <2 h/d	31 (49.2)	59 (31.9)
≥2 h/d	14 (22.2)	49 (26.5)
T3	n $_{total}$ = 52	n $_{total}$ = 145
No wet work	0 (0.0)	7 (4.8)
<0.5 h/d	18 (34.6)	49 (33.8)
≥0.5 h/d to <2 h/d	16 (30.8)	50 (34.5)
≥2 h/d	18 (34.6)	39 (26.9)
Hand washing frequency n/n $_{total}$ (%)		
T1: ≥ 5×/d	54/67 (79.4)	135/198 (68.2)
T2: ≥ 5×/d	45/64 (70.3)	130/185 (70.3)
T3: ≥ 5×/d	43/52 (82.7)	101/146 (69.2)

(Continues)

TABLE 2 (Continued)

	Case	Noncase
Use of abrasive detergents n/n $_{total}$ (%)	T1: 40/50 (80.0)	T1: 165/214 (77.1)
	T2: 40/47 (85.1)	T2: 150/199 (75.4)
	T3: 29/35 (82.9)	T3: 125/159 (78.6)
Use of protective gloves n/n $_{total}$ (%)	T1: 51/68 (75.0)	T1: 151/198 (76.3)
	T2: 52/63 (82.5)	T2: 156/185 (84.3)
	T3: 43/52 (82.7)	T3: 131/145 (90.3)
Use of skin barrier cream n/n $_{total}$ (%)	T1: 44/68 (64.7)	T1: 123/198 (62.1)
	T2: 33/64 (51.6) *	T2: 126/184 (68.5)
	T3: 29/62 (46.8)	T3: 87/146 (59.7)
Mean daily application frequency of skin barrier cream ± SD	T1: 2.06 ± 1.45	T1: 2.29 ± 1.45
	T2: 2.44 ± 1.39	T2: 2.24 ± 1.55
	T3: 2.45 ± 2.10	T3: 2.20 ± 1.43
Use of emollient n/n $_{total}$ (%)	T1: 34/68 (50.0)	T1: 120/197 (60.9)
	T2: 35/64 (54.5)	T2: 109/184 (59.2)
	T3: 29/62 (46.8)	T3: 91/146 (62.3)
Mean daily application frequency of emollients ± SD	T1: 2.31 ± 1.66	T1: 1.71 ± 1.19
	T2: 2.36 ± 1.88	T2: 1.78 ± 1.17
	T3: 2.11 ± 1.51	T3: 1.63 ± 1.78
Self-estimated knowledge on skin protection (mean grade ± SD)[b]	T1: 2.87 ± 1.04 *	T1: 2.51 ± 0.97
	T2: 2.86 ± 0.96 *	T2: 2.52 ± 0.91
	T3: 2.79 ± 0.94	T3: 2.63 ± 0.97
Mean OSD-KQ-short score ± SD	T1: 15.47 ± 4.44	T1: 16.61 ± 5.80
	T2: 16.15 ± 5.30 *	T2: 17.88 ± 5.33
	T3: 16.10 ± 4.08 *	T3: 18.03 ± 4.60

Abbreviations: OSD-KQ, occupational skin diseases knowledge questionnaire; SD, standard deviation.
*P < .05.; **P < .01.; [a]Erlangen atopy score ≥10.
[b]According to the German school grading system (1 = very good, 2 = good, 3 = satisfactory, 4 = sufficient, 5 = poor, 6 = very poor).

low score in the knowledge test and not using skin barrier creams at T2 were additional risk factors for incident HE. A lower age, the self-reported amount of cigarettes smoked, and extent of exposure to metalworking fluids were not independent risk factors.

4 | DISCUSSION

To our knowledge, this is the first controlled prospective intervention study encompassing the entire period of apprenticeship that uses structured health education to prevent work-related HE in MWAs. The results indicate that the intervention effectively improved the disease-specific knowledge and reduced the incidence and prevalence of HE during apprenticeship. Factors significantly associated with developing HE in MWAs were smoking cigarettes and *FLG* mutations, irrespective of the intervention. Within the intervention group, not using skin barrier creams and lower knowledge scores were additionally associated with incident HE.

The incidence and prevalence of HE in the second and third years of apprenticeship in the metalwork intervention group (MW-int) were similar to the rates in the nonoccupationally exposed office work control group (OW-ctrl) and significantly lower than in the metalwork control group (MW-ctrl), indicating a positive effect of the intervention. Considering the high incidence rates of HE in the MW-ctrl compared to the other two groups and the exclusion of preexisting HE, it is likely that most of them were work-related. Berndt et al reported a 2.5-year incidence of 23% for HE in 201 MWAs,[8,9] whereas Funke et al found a 1-year and 3-year incidence of HE of 9.2% and 15.3%, respectively, among 1110 MWAs in the automobile industry.[10] Thus the incidence rates in our metalwork control group were similar to results of comparable cohorts of MWAs who did not receive special training in prevention of work-related HE. Differences are likely due to diverging definitions and assessment of HE and different exposures or extent of exposures to skin hazards at the various workplaces. As in other studies,[7,10,37] we used a symptom-based definition of HE to differentiate between minor, rather insignificant symptoms and presence of HE. However, there is no consensus on where "normal" skin ends and HE begins.[38] The 1-year prevalence of HE during the first year of apprenticeship in the MW-int and in the OW-ctrl groups was 11.1% and 8.2%, respectively, and thus similar to the 1-year

prevalence of about 10% reported for young people from the general population in Denmark and Sweden.[39,40] In contrast to the increasing prevalence of HE in the MW-ctrl group, this rate was nearly unchanged in the following years in the MW-int and in the OW-ctrl groups.

Our educational intervention led to improvements of knowledge regarding prevention of work-related HE as seen in other studies.[30,41] As expected, the knowledge gain was faster and higher in the intervention group than in the control group, in which most likely regular vocational training led to the observed slight increase of knowledge over time. Even though knowledge gain does not automatically translate into change of behavior, the significantly higher knowledge scores in those without incident HE, particularly in the intervention group, indicate that specific health education beyond the usual vocational training was effective in primary prevention of the disease. The increased knowledge may have changed attitudes and improved protective behavior and thus reduced levels of exposure to skin hazards as observed in other studies.[12-14] Wet work, particularly when exceeding 2 h/d, is a well-known risk factor for work-related HE.[2,42] In the present study, the percentage of MWA reporting wet work ≥2 h/d increased significantly from T0 to T3 in the control group, whereas this rate was nearly unchanged in the intervention group. Moreover, the number of those reporting wet work ≥2 h/d at T3 was significantly higher in MW-ctrl than in MW-int. This may indicate a positive effect of the intervention.

At T3, MWAs with incident HE reported a higher amount of wet work, handwashing frequency, and use of abrasive detergents and a lower use of protective gloves. Although these differences were not statistically significant, it is possible that the intervention optimized selection and correct handling of protective gloves, which may have reduced wet work and soiling and thus, the need for excessive handwashing and use of abrasive detergents. The self-reported use of skin barrier creams and/or skin care products (around 60%) and their application frequency did not differ significantly between both groups of MWAs at baseline and follow-ups and did not change over time, indicating that their use did not increase by the intervention. Possibly, these products were not sufficiently provided at all workplaces. The self-reported use of skin barrier creams and/or skin care products, however, was lower in those with incident HE, with a significant difference for barrier creams at T2, primarily within the intervention group, which may indicate a positive effect of its use. In line with this, a prospective intervention study by Kütting et al demonstrated that skin conditions in metalworkers improved most when using both skin care products and barrier creams, followed by using barrier creams alone.[37] However, there is an ongoing discussion whether barrier creams are truly effective in prevention of HE.[43]

The lack of association between a history of flexural eczema as indicator for AD and incident HE in MWAs is in contrast to the study by Berndt et al[9] and might be related to a low share of apprentices in the MW-ctrl, affirming a history of flexural eczema at baseline (6.5%). Instead, a strong association was detected between incident HE in MWAs and *FLG* mutations, which are associated with skin barrier deficiency. This is in accordance with other studies reporting an increased risk of developing work-related irritant contact dermatitis in *FLG* mutation carriers.[16,18,20] Even though *FLG* mutations are linked to AD,[17] up to 40% of *FLG* mutation carriers do not develop AD.[44] This may explain the missing association with flexural eczema despite the link to *FLG* mutations in the present study. As shown before,[45,46] *FLG* mutation carriers had significantly lower epidermal levels of NMF. However, epidermal levels of NMF and various cytokines were not significantly associated with incident HE. Similarly, no significant genetic susceptibility loci were detected by an explorative GWAS. This was probably due to the comparatively small study size. Another possible explanation is that exposure-related factors have outweighed endogenous effects.

Around 30% of the MWA were self-reported tobacco smokers. This is in line with current data demonstrating that among the 18- to 25-year-old young adults in Germany, 22.5% of women and 29.4% of men are self-reported smokers.[47] Apart from male gender, blue-collar work and a lower level of education are associated with a higher prevalence of tobacco smoking.[48] Accordingly, the rate of self-reported tobacco smokers was higher among MWAs than among office work apprentices, who had on average a higher educational level and a higher share of females. Data on associations between tobacco smoking and work-related HE are contradictory.[24] In contrast to Berndt et al,[8] we found a significant association between tobacco smoking and incident HE in MWAs and similarly in office work apprentices. This effect was independent from the daily number of cigarettes smoked. From previous studies we know that work-related HE is more severe and persistent in smokers than in nonsmokers and that tobacco smoking is associated with work absenteeism and leaving the workforce.[25,26] Tobacco smoking is considered to induce proinflammatory mechanisms and tissue damage in the skin,[49] which may have an impact on development and course of HE. However, it is unclear if tobacco smoking itself confers the detrimental effects or whether it is a proxy for other unfavorable factors associated with smoking. To refrain from or stop smoking may still be an important target in prevention and management of HE.

Although this is a prospective, controlled intervention study in a real-world setting with regular follow-ups covering the whole apprenticeship, a limitation of this study was the randomization on school level and the lack of blinding for practical reasons. However, the two groups of MWAs were considered appropriate for comparison, as they did not differ significantly with respect to basic demographic data at baseline and occupational exposure to skin hazards, such as metalworking fluids. Occurrence of HE was detected mainly by clinical examination, but was also assessed by self-administered questionnaires. Self-reporting may be less accurate, but it allowed retrieval of information on the presence of HE before recruitment and in-between school visits.

In conclusion, the intervention based on health education was effective in primary prevention of HE in MWAs, suggesting that its implementation in regular vocational training may reduce the burden of the disease. Moreover, tobacco smoking and *FLG* mutations should be considered as individual risk factors and addressed in more-targeted approaches.

ACKNOWLEDGEMENTS

We would like to thank the teachers and participating apprentices from the following vocational schools (berufsbildende schulen): Hannoversch Münden, Alfeld, Northeim (I and II), Goslar-Bassgeige, Osterode (II), Göttingen (II), Einbeck, and Osnabrück (Brinkstrasse).

CONFLICTS OF INTEREST

There are no conflicts of interest.

AUTHOR CONTRIBUTIONS

AR, RB, AW, MPS, and SMJ designed the study. AR and RB performed the clinical examinations and collected the data. AW developed and conducted the educational intervention. GG and RB analyzed the data. Genotyping and genome-wide association studies were done by HB, ER, and SW. Protein analyses were performed by IJ and SK. RB and AR drafted the manuscript. All authors critically reviewed and revised the manuscript.

ORCID

Annika Wilke https://orcid.org/0000-0002-6903-0449
Johannes Geier https://orcid.org/0000-0002-5047-8948
Timo Buhl https://orcid.org/0000-0002-3139-129X
Richard Brans https://orcid.org/0000-0002-1245-024X

REFERENCES

1. Keegel T, Moyle M, Dharmage S, Frowen K, Nixon R. The epidemiology of occupational contact dermatitis (1990-2007): a systematic review. *Int J Dermatol*. 2009;48(6):571-578.
2. Diepgen TL, Andersen KE, Chosidow O, et al. Guidelines for diagnosis, prevention and treatment of hand eczema. *J Dtsch Dermatol Ges*. 2015;13(1):e1-e22.
3. Diepgen TL, Scheidt R, Weisshaar E, John SM, Hieke K. Cost of illness from occupational hand eczema in Germany. *Contact Dermatitis*. 2013;69(2):99-106.
4. Diepgen TL. Occupational skin diseases. *J Dtsch Dermatol Ges*. 2012;10(5):297-313; quiz 314-295.
5. Kütting B, Weistenhöfer W, Baumeister T, Uter W, Drexler H. Current acceptance and implementation of preventive strategies for occupational hand eczema in 1355 metalworkers in Germany. *Br J Dermatol*. 2009;161(2):390-396.
6. Gruvberger B, Isaksson M, Frick M, Pontén A, Bruze M. Occupational dermatoses in a metalworking plant. *Contact Dermatitis*. 2003;48(2):80-86.
7. Apfelbacher CJ, Radulescu M, Diepgen TL, Funke U. Occurrence and prognosis of hand eczema in the car industry: results from the PACO follow-up study (PACO II). *Contact Dermatitis*. 2008;58(6):322-329.
8. Berndt U, Hinnen U, Iliev D, Elsner P. Hand eczema in metalworker trainees – an analysis of risk factors. *Contact Dermatitis*. 2000;43(6):327-332.
9. Berndt U, Hinnen U, Iliev D, Elsner P. Role of the atopy score and of single atopic features as risk factors for the development of hand eczema in trainee metal workers. *Br J Dermatol*. 1999;140(5):922-924.
10. Funke U, Fartasch M, Diepgen TL. Incidence of work-related hand eczema during apprenticeship: first results of a prospective cohort study in the car industry. *Contact Dermatitis*. 2001;44(3):166-172.
11. Bauer A, Rönsch H, Elsner P, et al. Interventions for preventing occupational irritant hand dermatitis. *Cochrane Database Syst Rev*. 2018;4:CD004414. https://doi.org/10.1002/14651858.CD004414.pub3.
12. Bauer A, Kelterer D, Bartsch R, et al. Skin protection in bakers' apprentices. *Contact Dermatitis*. 2002;46(2):81-85.
13. Bregnhoj A, Menné T, Johansen JD, Søsted H. Prevention of hand eczema among Danish hairdressing apprentices: an intervention study. *Occup Environ Med*. 2012;69(5):310-316.
14. Held E, Wolff C, Gyntelberg F, Agner T. Prevention of work-related skin problems in student auxiliary nurses: an intervention study. *Contact Dermatitis*. 2001;44(5):297-303.
15. Wilke A, Brans R, Nordheider K, et al. Skin protection seminars to prevent occupational skin diseases: results of a prospective longitudinal study in apprentices of high-risk professions. *Saf Health Work*. 2018;9(4):398-407.
16. Kezic S, Visser MJ, Verberk MM. Individual susceptibility to occupational contact dermatitis. *Ind Health*. 2009;47(5):469-478.
17. Irvine AD, McLean WH, Leung DY. Filaggrin mutations associated with skin and allergic diseases. *N Engl J Med*. 2011;365(14):1315-1327.
18. Visser MJ, Landeck L, Campbell LE, et al. Impact of atopic dermatitis and loss-of-function mutations in the filaggrin gene on the development of occupational irritant contact dermatitis. *Br J Dermatol*. 2013;168(2):326-332.
19. Visser MJ, Verberk MM, Campbell LE, et al. Filaggrin loss-of-function mutations and atopic dermatitis as risk factors for hand eczema in apprentice nurses: part II of a prospective cohort study. *Contact Dermatitis*. 2014;70(3):139-150.
20. Timmerman JG, Heederik D, Spee T, et al. Contact dermatitis in the construction industry: the role of filaggrin loss-of-function mutations. *Br J Dermatol*. 2016;174(2):348-355.
21. Landeck L, Visser M, Skudlik C, Brans R, Kezic S, John SM. Clinical course of occupational irritant contact dermatitis of the hands in relation to filaggrin genotype status and atopy. *Br J Dermatol*. 2012;167(6):1302-1309.
22. Bin L, Leung DY. Genetic and epigenetic studies of atopic dermatitis. *Allergy Asthma Clin Immunol*. 2016;12(52):1-14.
23. de Jongh CM, Verberk MM, Withagen CE, Jacobs JJ, Rustemeyer T, Kezic S. Stratum corneum cytokines and skin irritation response to sodium lauryl sulfate. *Contact Dermatitis*. 2006;54(6):325-333.
24. Sørensen JA, Clemmensen KK, Nixon RL, Diepgen TL, Agner T. Tobacco smoking and hand eczema - is there an association? *Contact Dermatitis*. 2015;73(6):326-335.
25. Sørensen JA, Fisker MH, Agner T, Clemmensen KK, Ebbehøj NE. Associations between lifestyle factors and hand eczema severity: are tobacco smoking, obesity and stress significantly linked to eczema severity? *Contact Dermatitis*. 2016;76(3):138-145.
26. Brans R, Skudlik C, Weisshaar E, et al. Association between tobacco smoking and prognosis of occupational hand eczema: a prospective cohort study. *Br J Dermatol*. 2014;171(5):1108-1115.
27. Wilke A, Gediga G, Schlesinger T, John SM, Wulfhorst B. Sustainability of interdisciplinary secondary prevention in patients with occupational hand eczema: a 5-year follow-up survey. *Contact Dermatitis*. 2012;67(4):208-216.
28. Wilke A, Brans R, Nordheider K, et al. Skin protection seminars to prevent occupational skin diseases: results of a prospective longitudinal study in apprentices of high-risk professions. *Safety and Health at Work*. 2018;9(4):398-407.
29. Wilke A, Gediga G, Goergens A, et al. Interdisciplinary and multiprofessional outpatient secondary individual prevention of work-related skin diseases in the metalworking industry: 1-year follow-up of a patient cohort. *BMC Dermatol*. 2018;18(1):12.
30. Wilke A, Gediga K, John SM, Wulfhorst B. Evaluation of structured patient education in occupational skin diseases: a systematic assessment of the disease-specific knowledge. *Int Arch Occup Environ Health*. 2014;87(8):861-869.
31. Skudlik C, Dulon M, Pohrt U, Appl KC, John SM, Nienhaus A. Osnabrueck hand eczema severity index – a study of the

interobserver reliability of a scoring system assessing skin diseases of the hands. *Contact Dermatitis*. 2006;55(1):42-47.
32. Dulon M, Skudlik C, Nubling M, John SM, Nienhaus A. Validity and responsiveness of the Osnabruck Hand Eczema Severity Index (OHSI): a methodological study. *Br J Dermatol*. 2009;160(1):137-142.
33. Diepgen TL, Sauerbrei W, Fartasch M. Development and validation of diagnostic scores for atopic dermatitis incorporating criteria of data quality and practical usefulness. *J Clin Epidemiol*. 1996;49(9):1031-1038.
34. Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: rising to the challenge of larger and richer datasets. *Gigascience*. 2015;4(7):1-6. https://doi.org/10.1186/s13742-015-0047-8.
35. Kezic S, Kammeyer A, Calkoen F, Fluhr JW, Bos JD. Natural moisturizing factor components in the stratum corneum as biomarkers of filaggrin genotype: evaluation of minimally invasive methods. *Br J Dermatol*. 2009;161(5):1098-1104.
36. Dapic I, Jakasa I, Yau N, Kezic S, Kammeyer A. Evaluation of an HPLC method for the determination of natural moisturizing factors in the human stratum corneum. *Anal Lett*. 2013;46(14):2133-2144.
37. Kütting B, Baumeister T, Weistenhöfer W, Pfahlberg A, Uter W, Drexler H. Effectiveness of skin protection measures in prevention of occupational hand eczema: results of a prospective randomized controlled trial over a follow-up period of 1 year. *Br J Dermatol*. 2010;162(2):362-370.
38. Baumeister T, Uter W, Weistenhöfer W, Drexler H, Kütting B. On the lookout for precursor lesions: where does dry skin end and slight hand eczema begin? *Contact Dermatitis*. 2011;66(2):63-71.
39. Yngveson M, Svensson A, Johannisson A, Isacsson A. Hand dermatosis in upper secondary school pupils: 2-year comparison and follow-up. *Br J Dermatol*. 2000;142(3):485-489.
40. Bregnhoj A, Søsted H, Menné T, Johansen JD. Healthy worker effect in hairdressing apprentices. *Contact Dermatitis*. 2011;64(2):80-84.
41. Held E, Mygind K, Wolff C, Gyntelberg F, Agner T. Prevention of work related skin problems: an intervention study in wet work employees. *Occup Environ Med*. 2002;59(8):556-561.
42. Carøe TK, Ebbehøj NE, Bonde JPE, Flachs EM, Agner T. Hand eczema and wet work: dose-response relationship and effect of leaving the profession. *Contact Dermatitis*. 2018;78(5):341-347.
43. Fartasch M, Diepgen TL, Drexler H, Elsner P, John SM, Schliemann S. S1 guideline on occupational skin products: protective creams, skin cleansers, skin care products (ICD 10: L23, L24) – short version. *J Dtsch Dermatol Ges*. 2015;13(6):594-606.
44. O'Regan GM, Irvine AD. The role of filaggrin in the atopic diathesis. *Clin Exp Allergy*. 2010;40(7):965-972.
45. Kezic S, Kemperman PM, Koster ES, et al. Loss-of-function mutations in the filaggrin gene lead to reduced level of natural moisturizing factor in the stratum corneum. *J Invest Dermatol*. 2008;128(8):2117-2119.
46. Kezic S, O'Regan GM, Yau N, et al. Levels of filaggrin degradation products are influenced by both filaggrin genotype and atopic dermatitis severity. *Allergy*. 2011;66(7):934-940.
47. Orth B, Merkel C. The decline of cigarette smoking among adolescents and young adults in Germany and the rising relevance of waterpipes, ecigarettes and ehookahs. *Bundesgesundheitsbl*. 2018;61(11):1377-1387.
48. Dorner TE, Stronegger WJ, Hoffmann K, Stein KV, Niederkrotenthaler T. Socio-economic determinants of health behaviours across age groups: results of a cross-sectional survey. *Wien Klin Wochenschr*. 2013;125(9–10):261-269.
49. Ortiz A, Grando SA. Smoking and the skin. *Int J Dermatol*. 2012;51(3):250-262.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Reich A, Wilke A, Gediga G, et al. Health education decreases incidence of hand eczema in metal work apprentices: Results of a controlled intervention study. *Contact Dermatitis*. 2020;1–11. https://doi.org/10.1111/cod.13502

Online Supplemental Table 1: Professions in which metal work apprentices in the intervention group (MW-int) and the control group (MW-ctrl) received vocational training at baseline (T0)

Profession n (%)	MW-int $n_{total} = 131$	MW-ctrl $n_{total} = 172$
Industrial mechanic	39 (29.8)	66 (38.4)
Cutting machine operator/precision mechanic	40 (30.5)	30 (17.4)
Model builder/construction mechanic	20 (15.3)	33 (19.2)
Tool maker	18 (13.7)	23 (13.4)
Process mechanic	14 (10.7)	20 (11.6)

Online Supplemental Table 2: Exposure to skin hazards, skin protection measures and knowledge in apprentices of the metalwork intervention group (MW-int) and metalwork control group (MW-ctrl)

	MW-int	**MW-**ctrl
Exposed to metalworking fluids n/n $_{total}$ (%)	T0: 80/128 (62.5) T1: 97/117 (82.9) T2: 86/112 (76.8) T3: 79/ 95 (83.2)	T0: 133/171 (77.8) T1: 132/149 (88.6) T2: 121/137 (88.3) T3: 90/102 (88.2)
Mean days per week with exposure to metalworking fluids ± SD	T0: 2.42 ± 1.15 T1: 2.98 ± 1.08 T2: 2.99 ± 1.42 T3: 3.07 ± 1.30	T0: 2.70 ± 0.69 T1: 2.54 ± 1.03 T2: 3.29 ± 1.19 T3: 3.41 ± 1.08
Exposed to oil n/n $_{total}$ (%)	T0: 70/128 (54.7) T1: 88/117 (75.2) T2: 83/112 (74.1) T3: 78/ 95 (82.1)	T0: 117/171 (68.4) T1: 118/149 (79.2) T2: 110/137 (80.3) T3: 84/102 (82.4)
Mean days per week with exposure to oil ± SD	T0: 2.43 ± 1.02 T1: 2.66 ± 1.28 T2: 2.88 ± 1.38 T3: 3.04 ± 1.28	T0: 2.43 ± 0.94 T1: 2.15 ± 1.21 T2: 2.92 ± 1.36 T3: 3.22 ± 1.19
Amount of wet work n/n $_{total}$ (%) T0 No wet work < 0.5h/d ≥ 0.5h/d to < 2h/d ≥ 2h/d T1 No wet work < 0.5h/d ≥ 0.5h/d to < 2h/d ≥ 2h/d T2 No wet work < 0.5h/d ≥ 0.5h/d to < 2h/d ≥ 2h/d T3 No wet work < 0.5h/d ≥ 0.5h/d to < 2h/d ≥ 2h/d	 n $_{total}$ = 128 12 (9.4) 65 (50.8) 27 (21.1) 24 (18.7) n $_{total}$ = 116 3 (2.6) 41 (35.3) 48 (41.4) 24 (20.7) n $_{total}$ = 112 3 (2.7) 49 (43.8) 34 (30.4) 26 (23.2) n $_{total}$ = 94 6 (6.4) 34 (36.2) 36 (38.3) 18 (19.1) *	 n $_{total}$ = 168 9 (5.4) 75 (44.6) 51 (30.4) 33 (19.6) n $_{total}$ = 148 5 (3.4) 47 (31.8) 54 (36.5) 42 (28.4) n $_{total}$ = 136 1 (0.7) 42 (30.9) 56 (41.2) 37 (27.2) n $_{total}$ = 103 1 (1.0) 33 (32.0) 30 (29.1) 39 (37.8)
Hand washing frequency (≥ 5x/d) n/n total (%)	T0: 83/126 (65.9) T1: 78/117 (66.7) T2: 75/112 (67.0) T3: 55/ 91 (68.1)	T0: 116/170 (68.3) T1: 115/149 (77.0) T2: 101/137 (73.7) T3: 82/103 (79.6)
Use of abrasive detergents n/n total (%)	T0: 90/125 (72.0)	T0: 131/166 (78.9)

	MW-int	**MW-**ctrl
	T1: 85/115 (73.9) T2: 82/110 (74.5) T3: 23/ 92 (75.0)	T1: 120/149 (80.5) T2: 108/136 (79.4) T3: 85/102 (83.3)
Use of protective gloves n/n $_{total}$ (%)	T0: 64/128 (50.0) T1: 92/117 (78.6) T2: 100/112 (89.3) T3: 87/ 94 (92.6)	T0: 112/167 (67.1) T1: 110/149 (73.8) T2: 108/136 (79.4) T3: 87/103 (84.5)
Use of skin barrier cream n/n $_{total}$ (%)	T0: 62/99 (62.6) T1: 71/117 (60.7) T2: 71/111 (64.0) T3: 55/95 (57.9)	T0: 80/166 (48.2) T1: 96/149 (64.4) T2: 88/137 (64.2) T3: 61/103 (59.2)
Mean daily application frequency of skin barrier cream ± SD	T0: 2.31 ± 0.94 T1: 2.17 ± 1.12 T2: 2.18 ± 1.56 T3: 2.15 ± 1.78	T0: 2.18 ± 1.47 T1: 1.71 ± 1.59 T2: 2.19 ± 1.59 T3: 2.35 ± 1.61
Use of emollient n/n total (%)	T0: 59/99 (59.6) T1: 68/117 (58.1) T2: 63/111 (56.8) T3: 54/95 (56.8)	T0: 67/167 (40.1) T1: 86/148 (58.1) T2: 81/137 (59.1) T3: 90/153 (58.8)
Mean daily application frequency of emollients ± SD	T0: 1.76 ± 0.85 T1: 1.67 ± 0.70 T2: 2.19 ± 1.55 T3: 2.35 ± 1.61	T0: 1.71 ± 1.17 T1: 1.52 ± 1.50 T2: 2.15 ± 1.78 T3: 2.16 ± 1.33
Self-estimated knowledge on skin protection (mean grade ± SD) †	T0: 2.18 ± 0.85 T1: 2.31 ± 1.14 T2: 2.40 ± 1.00 T3: 2.41 ± 1.11	T0: 3.26 ± 1.06 T1: 2.83 ± 1.05 T2: 2.78 ± 0.98 T3: 2.92 ± 1.00
Mean OSD-KQ-short score ± SD	T0: 14.20 ± 3.06 T1: 17.64 ± 7.17 * T2: 18.89 ± 5.05 * T3: 18.86 ± 4.56 *	T0: 12.69 ± 4.68 T1: 14.43 ± 4.64 T2: 15.81 ± 4.54 T3: 16.09 ± 4.31

MW-int: metalwork intervention group; MW-ctrl: metalwork control group; SD: standard deviation; OSD-KQ: occupational skin diseases knowledge questionnaire

† According to the German school grading system (1=very good, 2=good, 3=satisfactory, 4=sufficient, 5=poor, 6=very poor)

* $P<.05$

Online Supplemental Table 3: Demographic data of office work apprentices with and without incident hand eczema

	Case	**Non-Case**
Mean age (T0) ± SD (years)	21.14 ± 3.39	20.46 ± 3.02
Females (T0) n/n $_{total}$ (%)	1/14 (7.1)	16/103 (15.5)
History of flexural eczema (T0) n/n $_{total}$ (%)	2/10 (20.0)	14/ 74 (18.9)
Atopic skin diathesis (T0)† n/n $_{total}$ (%)	0/12 (0.0)	3/102 (3.0)
Tobacco smokers (T0) n/n $_{total}$ (%)	6/14 (42.9) *	26/103 (25.2)
Mean daily cigarette consumption in smokers (T0) ± SD	11.38 ± 8.94	10.58 ± 6.87
Highest educational level (T0) n/n $_{total}$ (%) Lower secondary school certificate Intermediate secondary school certificate Vocational baccalaureate diploma A levels	n=14 0 (0.0) 5 (35.7) 4 (28.6) 5 (35.7)	n=107 1 (1.0) 33 (32.0) 25 (24.3) 44 (42.7)
FLG mutation carrier n/n total (%)	0/14 (0.0)	10/103 (9.7)

SD: standard deviation; † Erlangen atopy score ≥ 10

* $P<.05$