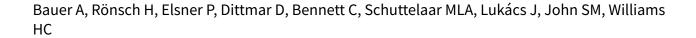**Cochrane** Database of Systematic Reviews

Interventions for preventing occupational irritant hand dermatitis (Review)

Bauer A, Rönsch H, Elsner P, Dittmar D, Bennett C, Schuttelaar MLA, Lukács J, John SM, Williams HC

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[Intervention Review]

Interventions for preventing occupational irritant hand dermatitis

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A B S T R A C T

Background

Occupational irritant hand dermatitis (OIHD) causes significant functional impairment, disruption of work, and discomfort in the working population. Different preventive measures such as protective gloves, barrier creams and moisturisers can be used, but it is not clear how effective these are. This is an update of a Cochrane review which was previously published in 2010.

Objectives

To assess the effects of primary preventive interventions and strategies (physical and behavioural) for preventing OIHD in healthy people (who have no hand dermatitis) who work in occupations where the skin is at risk of damage due to contact with water, detergents, chemicals or other irritants, or from wearing gloves.

Search methods

We updated our searches of the following databases to January 2018: the Cochrane Skin Specialised Register, CENTRAL, MEDLINE, and Embase. We also searched five trials registers and checked the bibliographies of included studies for further references to relevant trials. We handsearched two sets of conference proceedings.

Selection criteria

We included parallel and cross-over randomised controlled trials (RCTs) which examined the effectiveness of barrier creams, moisturisers, gloves, or educational interventions compared to no intervention for the primary prevention of OIHD under field conditions.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane. The primary outcomes were signs and symptoms of OIHD developed during the trials, and the frequency of treatment discontinuation due to adverse effects.

Main results

We included nine RCTs involving 2888 participants without occupational irritant hand dermatitis (OIHD) at baseline. Six studies, including 1533 participants, investigated the effects of barrier creams, moisturisers, or both. Three studies, including 1355 participants, assessed the effectiveness of skin protection education on the prevention of OIHD. No studies were eligible that investigated the effects of protective gloves. Among each type of intervention, there was heterogeneity concerning the criteria for assessing signs and symptoms of OIHD, the products, and the occupations. Selection bias, performance bias, and reporting bias were generally unclear across all studies. The risk of detection bias was low in five studies and high in one study. The risk of other biases was low in four studies and high in two studies.

The eligible trials involved a variety of participants, including: metal workers exposed to cutting fluids, dye and print factory workers, gut cleaners in swine slaughterhouses, cleaners and kitchen workers, nurse apprentices, hospital employees handling irritants, and hairdressing apprentices. All studies were undertaken at the respective work places. Study duration ranged from four weeks to three years. The participants' ages ranged from 16 to 67 years.

Meta-analyses for barrier creams, moisturisers, a combination of both barrier creams and moisturisers, or skin protection education showed imprecise effects favouring the intervention. Twenty-nine per cent of participants who applied barrier creams developed signs of OIHD, compared to 33% of the controls, so the risk may be slightly reduced with this measure (risk ratio (RR) 0.87, 95% confidence interval (CI) 0.72 to 1.06; 999 participants; 4 studies; low-quality evidence). However, this risk reduction may not be clinically important. There may be a clinically important protective effect with the use of moisturisers: in the intervention groups, 13% of participants developed symptoms of OIHD compared to 19% of the controls (RR 0.71, 95% CI 0.46 to 1.09; 507 participants; 3 studies; low-quality evidence). Likewise, there may be a clinically important protective effect from using a combination of barrier creams and moisturisers: 8% of participants in the intervention group developed signs of OIHD, compared to 13% of the controls (RR 0.68, 95% CI 0.33 to 1.42; 474 participants; 2 studies; low-quality evidence). We are uncertain whether skin protection education reduces the risk of developing signs of OIHD (RR 0.76, 95% CI 0.54 to 1.08; 1355 participants; 3 studies; very low-quality evidence). Twenty-one per cent of participants who received skin protection education developed signs of OIHD, compared to 28% of the controls.

None of the studies addressed the frequency of treatment discontinuation due to adverse effects of the products directly. However, in three studies of barrier creams, the reasons for withdrawal from the studies were unrelated to adverse effects. Likewise, in one study of moisturisers plus barrier creams, and in one study of skin protection education, reasons for dropout were unrelated to adverse effects. The remaining studies (one to two in each comparison) reported dropouts without stating how many of them may have been due to adverse reactions to the interventions. We judged the quality of this evidence as moderate, due to the indirectness of the results. The investigated interventions to prevent OIHD probably cause few or no serious adverse effects.

Authors' conclusions

Moisturisers used alone or in combination with barrier creams may result in a clinically important protective effect, either in the long- or short-term, for the primary prevention of OIHD. Barrier creams alone may have slight protective effect, but this does not appear to be clinically important. The results for all of these comparisons were imprecise, and the low quality of the evidence means that our confidence in the effect estimates is limited. For skin protection education, the results varied substantially across the trials, the effect was imprecise, and the pooled risk reduction was not large enough to be clinically important. The very low quality of the evidence means that we are unsure as to whether skin protection education reduces the risk of developing OIHD. The interventions probably cause few or no serious adverse effects.

We conclude that at present there is insufficient evidence to confidently assess the effectiveness of interventions used in the primary prevention of OIHD. This does not necessarily mean that current measures are ineffective. Even though the update of this review included larger studies of reasonable quality, there is still a need for trials which apply standardised measures for the detection of OIHD in order to determine the effectiveness of the different prevention strategies.

PLAIN LANGUAGE SUMMARY

Treatments to prevent hand skin irritation in the workplace

Review question

In this review, we set out to assess the available evidence on the effect of barrier creams, moisturisers, gloves, and educational programmes for employees who are at risk of developing irritation of the skin on the hands. We found nine studies. None of them investigated protective gloves. The evidence in this review is current to 17 January 2018.

Background

Occupational irritant hand dermatitis (OIHD) is a skin disease that occurs on the hands of employees in certain jobs. The first signs are red and scaly patches in the finger webs and on the knuckle area of the hands. Itchy blisters, painful cracks, and possibly infection are common, and eventually the skin becomes thickened.

Hand skin irritation can affect employees who regularly come into contact with water, detergents, chemicals, and other irritants, or who wear gloves during their working day. People at particular risk include hairdressers, nurses, cleaners, builders, and people who work in the dye, printing, metal, and food industries. The condition is relatively common and affects about 5 to 20 out of 10,000 full-time workers per year. Preventing OIHD from developing is important because it is difficult to clear once it starts.

Study characteristics

We included nine studies in this review, involving 2888 male and female workers aged between 16 and 67. The studies included several types of workers: metal workers, dye and print factory workers, gut cleaners in swine slaughterhouses, cleaners and kitchen workers, hospital employees, and hairdressing apprentices. We were unable to find out whether or not the preventive measures were equally effective in all these professions because there were too few trials. The studies lasted from four weeks up to three years.

Key results

Some of the preventive measures may reduce the risk of hand skin irritations. However, there were too few studies to be sure of this. The studies were too different from each other to combine in a meaningful way, and the results were too imprecise. Our results are therefore still debatable.

Various barrier creams, moisturisers, and skin protection education programs were investigated. It is possible that barrier creams may slightly reduce the risk of developing OIHD. This result was based on four studies. In these studies, 29% of people who applied barrier creams developed hand skin irritations. In the control group, who did not apply barrier creams, 33% developed hand skin irritations. The results of three studies showed that moisturisers may reduce the risk of developing OIHD by a useful amount. Thirteen per cent of the people who used moisturisers developed hand skin irritations, compared to 19% of those who did not use moisturisers. Two studies showed that using a combination of barrier creams and moisturisers may reduce the risk of developing OIHD by a useful amount. Eight per cent of the people who used moisturisers and barrier creams developed hand skin irritations, compared to 13% of the control group. Based on three studies, we are uncertain whether skin protection education reduces the risk of developing OIHD. In these studies, 21% of the people who received skin protection education developed hand skin irritations, compared to 28% of the people in the control group.

The safety and tolerability of these measures were not systematically addressed in these studies. However, no serious reactions to the treatments were reported. Mild reactions like itching or reddening of the skin were reported for only few people who applied the barrier creams or moisturisers. The measures to prevent hand skin irritations probably cause only few or no serious adverse effects.

Quality of the evidence

For barrier creams, moisturisers, or a combination of both, the quality of the evidence was low concerning the prevention of OIHD. There was not enough information and hand dermatitis was assessed differently across the studies.

For educational programmes, the quality of the evidence was very low concerning the prevention of hand skin irritation. There was not enough information, hand dermatitis was assessed differently across the studies, and the studies were poorly conducted in some important respects.

For the other key outcome, safety and tolerability of the treatments, the quality of the evidence was moderate because only indirect results were available.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.   Barrier creams compared to no treatment for preventing occupational irritant hand dermatitis

Barrier creams compared to no treatment for preventing occupational irritant hand dermatitis

Patient or population: workers at risk of occupational irritant hand dermatitis
Setting: metal or dye/print factories
Intervention: barrier creams
Comparison: no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with barrier creams**				
The proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant (proportion of OIHD) Follow up: range 6 months to 12 months	Study population		RR 0.87 (0.72 to 1.06)	999 (4 RCTs)	⊕⊕⊝⊝ LOW [1]	
	334 per 1000	291 per 1000 (241 to 354)				
Frequency of treatment discontinuation due to adverse effects Follow up: range 2 weeks to 12 months	All dropout reasons were unrelated to the treatment: the numbers of participants who dropped out of the individual trials ranged from 0% to 24%.			111 (3 RCTs)	⊕⊕⊕⊝ MODERATE[2]	Information only available from dropout analyses, which were not designed to detect adverse effects.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). The risk in the comparison group is based on mean proportion observed in the comparison groups.

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **OIHD**: occupational irritant hand dermatitis

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

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Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by two levels. Downgraded one level for imprecision because the confidence intervals were wide and included 1 as well as a clinically significant relative risk (0.75 or less). Downgraded one level for inconsistency because criteria for the diagnosis of OIHD varied across the included studies; signs and symptoms of OIHD were assessed by dermatologists, by study personnel, or by the participants.

[2] Downgraded by one level due to the indirectness of the results. None of the studies reported directly on treatment discontinuation due to adverse effects. Instead, the extracted results are based on dropout analyses, which did not focus on adverse effects. For the remaining two studies in this comparison the dropout analyses were not detailed enough to extract whether or not adverse effects were among the reasons. It cannot be fully excluded that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge.

Summary of findings 2.   Moisturisers compared to no treatment for preventing occupational irritant hand dermatitis

Moisturisers compared to no treatment for preventing occupational irritant hand dermatitis

Patient or population: workers at risk of occupational irritant hand dermatitis
Setting: metal factories
Intervention: moisturisers
Comparison: no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with moisturisers**				
The proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant (proportion of OIHD) Follow up: range 6 months to 12 months	Study population		RR 0.71 (0.46 to 1.09)	507 (3 RCTs)	⊕⊕⊝⊝ LOW [1]	
	187 per 1000	133 per 1000 (86 to 204)				
Frequency of treatment discontinuation due to adverse effects Follow up: range 2 weeks to 12 months	All dropout reasons were unrelated to the treatment: the numbers of participants who dropped out of the individual trials ranged from 0% to 37%			133 (2 RCTs)	⊕⊕⊕⊝ MODERATE[2]	Information only available from dropout analyses, which were not designed to detect adverse effects.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). The risk in the comparison group is based on mean proportion observed in the comparison groups.

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **OIHD:** occupational irritant hand dermatitis

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by two levels. Downgraded one level for imprecision because the confidence intervals were wide and included 1 as well as a clinically significant relative risk (0.75 or less). Downgraded one level for inconsistency because criteria for the diagnosis of OIHD varied across the included studies; signs and symptoms of OIHD were assessed by dermatologists, by study personnel, or by the participants.

[2] Downgraded by one level due to the indirectness of the results. None of the studies reported directly on treatment discontinuation due to adverse effects. Instead, the extracted results are based on dropout analyses, which did not focus on adverse effects. For the remaining two studies in this comparison the dropout analyses were not detailed enough to extract how often adverse effects were a reason. It cannot be fully excluded that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge.

Summary of findings 3.   Barrier creams and moisturisers compared to no treatment for preventing occupational irritant hand dermatitis

Barrier creams and moisturisers compared to no treatment for preventing occupational irritant hand dermatitis

Patient or population: workers at risk of occupational irritant hand dermatitis
Setting: metal factories
Intervention: barrier creams and moisturisers
Comparison: no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no treatment	**Risk with barrier creams and moisturisers**				
The proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant (proportion of OIHD) Follow up: median 12 months	Study population		RR 0.68 (0.33 to 1.42)	474 (2 RCTs)	⊕⊕⊖⊖ LOW [1]	
	126 per 1000	85 per 1000 (41 to 178)				

| Frequency of treatment discontinuation due to adverse effects

Follow up: range 2 weeks to 12 months | All dropout reasons were unrelated to the treatment: the numbers of participants who dropped out of the trial ranged from 8% to 24% | 100
(1 RCT) | ⊕⊕⊕⊝
MODERATE[2] | Information only available from dropout analyses, which were not designed to detect adverse effects. |

*The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). The risk in the comparison group is based on mean proportion observed in the comparison groups.

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **OIHD:** occupational irritant hand dermatitis

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded by two levels. Downgraded one level for imprecision because the confidence intervals were wide and included 1 as well as a clinically significant relative risk (0.75 or less). Downgraded one level for inconsistency because criteria for the diagnosis of OIHD varied across the included studies; signs and symptoms of OIHD were assessed by dermatologists, or by the participants.
[2] Downgraded by one level due to the indirectness of the results. None of the studies reported directly on treatment discontinuation due to adverse effects. Instead, the extracted results are based on dropout analyses, which did not focus on adverse effects. For the remaining study in this comparison no dropout analysis was performed. It cannot be fully excluded that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge.

Summary of findings 4.   Skin protection education compared to no or minimal intervention for preventing occupational irritant hand dermatitis

Skin protection education compared to no or minimal intervention for preventing occupational irritant hand dermatitis

Patient or population: workers at risk of occupational irritant hand dermatitis
Setting: slaughterhouses, nursing schools, and hospitals
Intervention: skin protection education
Comparison: no or minimal intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no or minimal intervention	**Risk with skin protection education**				

The proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant (proportion of OIHD) Follow up: range 1 years to 3 years	**Study population**		RR 0.76 (0.54 to 1.08)	1355[1] (3 RCTs)	⊕⊖⊖⊖ VERY LOW [2]	
	275 per 1000	209 per 1000 (148 to 297)				
Frequency of treatment discontinuation due to adverse effects Follow up: range 2 weeks to 12 months	All dropout reasons were unrelated to the treatment: the numbers of participants who dropped out of the trial ranged from 35% to 38%			250 (1 RCT)	⊕⊕⊕⊖ MODERATE[3]	Information only available from dropout analyses, which were not designed to detect adverse effects.

*The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). The risk in the comparison group is based on mean proportion observed in the comparison groups.

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **OIHD:** occupational irritant hand dermatitis

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] 'effective sample size' after correcting for cluster design in one study; number of natural participants: N = 1443

[2] Downgraded by three levels. Downgraded one level for risk of bias as the risk ratios may have been overestimated (due to detection bias and baseline imbalance) or underestimated (due to differential diagnostic criteria). Downgraded one level for imprecision because the confidence intervals were wide and included 1 as well as a clinically significant relative risk (0.75 or less). Downgraded one level for inconsistency because criteria for the diagnosis of OIHD varied across the included studies; signs and symptoms of OIHD were assessed by a physician, or by the participants.

[3] Downgraded by one level due to the indirectness of the results. None of the studies reported directly on treatment discontinuation due to adverse effects. Instead, the extracted results are based on dropout analyses, which did not focus on adverse effects. For the remaining two studies in this comparison no dropout reasons were reported. It cannot be fully excluded that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge.

BACKGROUND

Description of the condition

Definition and epidemiology

Occupational hand dermatitis is the most frequent work-related skin disease in many Western countries (Diepgen 2003). The two major subgroups are occupational irritant hand dermatitis (OIHD) and occupational allergic hand dermatitis (OAHD) (Johansen 2011). This review focuses on OIHD and especially on the primary prevention of OIHD in healthy individuals, because preventing the development of dermatitis may help to reduce the development of severe and chronic dermatitis, and possibly related outcomes such as loss of employment (Brans 2016; Wulfhorst 2011). Studies of interventions which treat existing OIHD with the aim of preventing worsening of symptoms or repeat episodes of OIHD or those studies which focus on improving existing symptoms do exist, but are outside the scope of this review.

Occupational irritant hand dermatitis (OIHD) is an inflammatory response of the skin on the hands after contact with various irritant factors, such as water, detergents, soaps, solvents, gloves, food, and oils which cause direct damage to the skin (Lodi 2000; Skoet 2004). Clinically, OIHD shows a wide range of symptoms from acute, to subacute and chronic. Morphologically the clinical features in acute cases range from redness, oedema, and vesiculation, to thickening of the skin, hyperkeratosis, desquamation, and fissuring in chronic cases. Itching, burning sensations, and cracks are the most common complaints, sometimes leading to pain and infection (Johansen 2011; McFadden 2001). Mild dermatitis typically starts in the finger webs and the knuckle areas of the hands. In moderate cases the area enlarges to the back of the hands and the fingers. In severe cases the entire hands and the wrists can be affected, and there may also be pain or infection.

Occupational allergic hand dermatitis (OAHD) is caused by sensitisation to contact allergens, e.g. metals, fragrance and fragrance-related allergens, rubber ingredients, and preservatives. Skin lesions usually appear between 24 and 48 hours after direct skin contact with the allergens, at the contact point. Signs and symptoms resemble that of OIHD. In chronic cases, this can lead to diagnostic difficulties. Diagnostic patch testing with a standard series of allergens can help rule out a contact allergy as a contributing factor (Johansen 2011).

Epidemiological data on the incidence of occupational hand dermatitis in Europe and the USA are available from occupational skin disease registers from Ministries of Labour and insurance organisations. Other sources are case series and cross-sectional studies in occupations that are at high risk of occupational hand dermatitis. Despite differences in definitions and ways of registration, the pattern of occupational skin diseases is similar in Europe and the USA. In most Western countries occupational hand dermatitis has been the most frequent, or at least the second most frequent, occupational disease in recent years, accounting for approximately 30% of the total occupational disease burden (Burnett 1998; Cherry 2000; Diepgen 2003; DGUV 2008; Karjalainen 1998). On the basis of different data sources, Diepgen and Coenraads calculated an incidence rate of registered occupational hand dermatitis of about 5 to 20 cases per 10,000 full-time workers per year (Diepgen 1999). In reality the figures are probably considerably higher than this due to the well known phenomenon of under-diagnosis and under-reporting of occupational diseases for fear of job loss (Diepgen 2002; Meding 1987; Smit 1993).

Causes

Occupational irritant hand dermatitis (OIHD) occurs mainly in employees who perform a high amount of 'wet work' in their occupational life, e.g. hairdressers, health professionals, food industry workers, metal workers, and brick layers who have to frequently expose their hands to wet working conditions as part of their job. Additionally, in outdoor occupations winter weather might negatively influence the skin condition. OIHD results from continued, unprotected, low-grade exposure to mild irritants such as detergents, soaps, solvents, water, food ingredients, and cutting oils or fluids but also from the frequent wearing of gloves, and develops when the regenerative capacities of the skin are exhausted and contact with the irritants continues (Diepgen 1996; Johansen 2011; Malten 1981).

In addition to external factors, other endogenous factors have been identified as risk factors for the development of OIHD. Patients with a proven tendency for atopic dermatitis were shown to be at higher risk of developing OIHD of the hands when working in occupations where the skin is at risk of damage (Bauer 1997; Bauer 1998; Bauer 2001; Coenraads 1998; Dickel 2003; Smit 1994; Uter 1998a; Uter 1999). The role of other attributes, such as age, sex, genetics, and ethnic differences, in predisposing people to OIHD are still unclear (Diepgen 1999; Kezic 2009).

Impact

Occupational irritant hand dermatitis (OIHD) is not a life-threatening disease and mild forms do not usually interfere with daily life to a large extent, but in more severe cases the impact of OIHD on all aspects of an individual's quality of life can be considerable (Jowett 1985; Boehm 2012). It may cause long-term illness with uncertain prognosis, social isolation, and eventually unemployment or change of occupation (Cvetkovski 2005; Lerbaek 2008; Meding 2005). This can be devastating in times of high unemployment and limited government social support (Meding 1990). The costs of OIHD for the individual and social security systems are likely to be significant (Diepgen 2013; Mathias 1985; Politiek 2016; Saetterstrøm 2014).

Assessment

Signs, symptoms, and severity of OIHD can vary from redness and dryness of the skin to chronic dermatitis with thickening and fissuring. Assessments of the severity of OIHD can be reported in a number of ways using different scores, which include qualitative and quantitative measures of signs and symptoms (erythema, oedema, vesiculation, dryness, scaling, hyperkeratosis, fissuring, itching, burning) and the area of hands involved. Recently several validated scoring systems for assessing the severity of hand dermatitis have been established, such as the hand eczema severity index (HECSI) by Held 2005, and the Osnabrück Hand Eczema Severity Index (OHSI) and Manuscore by Dulon 2009. The impact of the condition on employees is also reflected in the numbers staying or leaving the occupation due to OIHD.

Bioengineering methods can measure changes in the skin's barrier function or hydration even before visible changes appear. One such bioengineering method is tewametry, a technique that measures the amount of water that is lost through the outside layer of the

skin (known as TEWL, transepidermal water loss). TEWL values are reported as g/m²h (amount of water lost from skin measured in gram per square metre per hour). Very often, inflamed skin does not hold water very well, and as a result the water in the body is lost more easily through the disrupted outer layer of the skin. An increase in TEWL has been demonstrated in cases of diseased or damaged skin, reflecting the impairment of the barrier function (Pinnagoda 1989). TEWL is typically used as an objective measure in clinical evaluation (Pinnagoda 1990).

Corneometry, another bioengineering method, is a tool used to measure the levels of skin hydration in healthy and diseased skin, i.e. how much water the skin holds. It is widely used to assess the efficacy of skin care and protection ointments in hydrating the stratum corneum. The stratum corneum, which is made of dead skin cells, is the outer layer of the skin and has an important barrier function (Fischer 1998; Leveque 1983).

Description of the intervention

The principles and methods of prevention strategies in occupations at high risk of OIHD are well defined. First line prevention strategies are based on technical-organisational hazard control, e.g. automation of processes, replacing the need of workers to expose their skin to irritants, the replacement of dangerous substances by less toxic, less irritative, or less allergenic ones. Examples of additional strategies include changing the environment by substitution of wet work and encouraging changes in worker behaviour such as frequency of hand washing. Since these first options are more fundamental than personal protection, they are usually given priority over the other measures, but if these strategies cannot be put into action, individual protective measures, e.g. protective gloves, barrier creams, and moisturisers, are recommended.

Barrier creams/skin protection creams

A barrier cream, also called skin protection cream, is a topical preparation that is applied to the skin to provide a barrier, helping to reduce the effect of skin contact with contaminants. Barrier creams are used to protect employees against work-related skin hazards. Ideally they are specially designed for and adapted to the profile of the workplace. Barrier creams are recommended for use before work, and two to three times during work time when necessary.

Under experimental conditions there is evidence that barrier creams show protective effects against the acute irritation caused by solvents (Mahmoud 1984; Mahmoud 1985). Different skin protection products have been shown to prevent or significantly reduce detergent-induced irritation (Frosch 1994; Patterson 1999; Schliemann 2014; Zhai 1996). The effects of barrier creams on improvement of OIHD in hairdressers has been reported (Bock 2001). However, an international survey revealed that the majority of international experts are sceptical about the specific properties of barrier creams (Hogan 1990).

Moisturisers/emollients/skin care creams

Moisturisers, also called emollients or skin care creams, are used for regenerative skin care during and after work, and should be applied regularly during work time after hand washing, and after work at home to support the regenerative capacities of the skin (Halkier-Sørensen 1993; Mathias 1990; Wigger-Alberti 1997).

Protective gloves

Protective gloves are meant to be used when contact with toxic or irritant substances, allergens, or infectious material should be avoided. Although it is widely accepted that gloves protect against irritants, allergens, and microbial agents, there are concerns that occlusive gloves themselves are a substantial factor in the promotion of OIHD and OAHD if not used properly (Ramsing 1996; Rose 2009; Wrangsjö 1994).

Complex interventions using barrier creams, moisturisers, and protective gloves

Barrier creams and gloves combined with adequate moisturisers are widely recommended as the most important means of personal protection in professions where the skin is at risk. Various in vivo and in vitro methods have investigated their efficacy (Boman 1989; Fluhr 2007; Frosch 1994; Gabard 1995; Henry 1994; Mellström 1994; Treffel 1994; Wahlberg 1996).

Skin protection education

Most studies reveal a considerable lack of knowledge of exposed workers regarding the essential aspects of skin protection (Wulfhorst 2011). Skin protection education may address varying aspects of preventing OIHD. This includes advice on how to apply barrier creams, moisturiser, and gloves. Also, workers can be advised to reduce the extent of hand washing and wet work or avoid wearing jewellery at work. Practical training can be included as part of educational interventions for exposed workers. Behavioural interventions supported by health psychological approaches are used to promote the dissemination of knowledge concerning skin protection. Apart from practical training, these may include role models, working groups, and reminders. The programmes will be described individually for the included studies.

How the intervention might work

Barrier creams/skin protection creams

Barrier creams are meant to provide a thin layer on the skin and thereby help to reduce contact to irritants. The layer is thought to facilitate the removal of contaminants, thereby reducing the irritations of intensive hand washing (Kütting 2008; Mathias 1990). Barrier creams can also contain active ingredients which may trap or transform irritants (Frosch 1994; Lachapelle 1996; Zhai 2006). It is however controversial if there exists an essential difference between barrier creams and moisturisers or if this is only a matter of timing (before versus after exposure).

Moisturisers/emollients/skin care creams

Moisturisers are topical preparations that use a variety of agents designed to increase the hydration of the outer layers of the skin by reducing water loss from the skin. Moisturisers have been shown under experimental and real-life conditions to have significant preventive and therapeutic effects. They prevent irritant skin reactions induced by detergents and have been shown to accelerate the regeneration of a disrupted barrier in irritated skin (De Paepe 2000; Loden 1997; Ramsing 1997; Williams 2010; Zhai 1998).

Protective gloves

Gloves are worn in order to reduce contact to irritants.

Skin protection education

Providing knowledge about skin protection can help workers at risk of OIHD to adopt an adequate preventive behaviour. The potential benefit of skin protection education is indirect because it also depends on the effectiveness of the advised measures. As knowledge alone does not guarantee the uptake of preventive behaviour it may be reasonable to include behavioural and psychological elements which aim to overcome impediments and promote the workers' motivation to protect their skin.

Why it is important to do this review

Occupational irritant hand dermatitis (OIHD) may cause serious problems for the individuals affected and their families. Even with social security systems in place, long-term illness, unemployment or the necessity of occupational change can affect families to a large extent, especially in times of high unemployment, and uncertain prospects for future employment, even after retraining.

There are many indications that protective measures may be effective in the prevention of OIHD. However, the actual benefit of each measure, when used singly or in combination, under real-world conditions in the work place is still unclear. In particular, it is important to establish whether individual protection measures are really beneficial, or whether they are potentially hazardous for employees under certain circumstances (Hogan 1990; Wigger-Alberti 1998).

This review is an update of 'Interventions for preventing occupational irritant hand dermatitis' (Bauer 2010).

OBJECTIVES

To assess the effects of primary preventive interventions and strategies (physical and behavioural) for preventing occupational irritant hand dermatitis (OIHD) in healthy people (who have no hand dermatitis) who work in occupations where the skin is at risk of damage due to contact with water, detergents, chemicals or other irritants, or from wearing gloves.

METHODS

Criteria for considering studies for this review

Types of studies

We considered randomised controlled trials (RCTs) for inclusion, which investigated the efficacy of interventions in the primary prevention of occupational irritant hand dermatitis (OIHD), and were conducted under normal working conditions in the work place. We included parallel, split-body, or cross-over trials. We did not include controlled clinical trials (CCTs) because they provide a lower level of evidence.

Types of participants

We considered any employee in 'wet work' occupations for inclusion, where there is a risk of developing OIHD (incident cases), e.g. nurses, hairdressers, employees in the food processing industry, cleaners, metal workers, printers, bricklayers, etc. We included only primary prevention studies and not studies where participants had existing hand dermatitis, unless the participant population was mixed and disaggregated data were available for those participants who were healthy with no hand dermatitis at the start of the study. Whether or not hand dermatitis was present at baseline was decided based on the baseline data reported by the study investigators. The diagnostic criteria were not evaluated in this regard.

Types of interventions

We included studies of interventions for the primary prevention of OIHD, in working populations. This did not include experimental studies.

Examples of primary prevention interventions include:

- barrier creams;
- moisturisers;
- protective gloves;
- complex interventions using combinations of interventions e.g. barrier creams, moisturisers, and protective gloves;
- skin protection education.

We included studies in which interventions were compared with another intervention or compared with no intervention.

Types of outcome measures

We included studies that measured the following outcomes, at any follow-up time.

Primary outcomes

- The proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) and/or hand dermatitis scores (e.g. HECSI, Manuscore) as rated by the investigator (physician/nurse) or the participant.
- Frequency of treatment discontinuation due to adverse effects. We did not perform a separate search for adverse effects of the target intervention. However, we did examine data on adverse effects from the included studies we identified.

Secondary outcomes

- Severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores, e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant.
- Proportion of participants with significant changes (difference in average score or difference from baseline, or both) in barrier function or hydration, measured using TEWL (skin barrier), and corneometry (skin hydration).
- Change of occupation because of OIHD versus staying in the occupation.
- Proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products).
- Other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies).

Search methods for identification of studies

We aimed to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

For this update, we revised all the search strategies in line with current Cochrane Skin practices. Details of the previous search strategies are available in Bauer 2010.

We searched the following databases up to 17 January 2018:

- the Cochrane Skin Specialised Register, using the search strategy in Appendix 1;
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 12) in the Cochrane Library, using the strategy in Appendix 2;
- MEDLINE via Ovid (from 1946), using the strategy in Appendix 3; and
- Embase via Ovid (from 1974), using the strategy in Appendix 4.

Trials registers

We searched the following trials databases up to 22nd January 2018:

- the ISRCTN registry (www.isrctn.com), using the search terms: (Occupational OR contact OR irritant OR prevention) AND ("hand dermatitis" OR "hand eczema") OR OIHD;
- ClinicalTrials.gov (www.clinicaltrials.gov), using the search terms: (Occupational OR contact OR irritant OR prevention) AND ("hand dermatitis" OR "hand eczema") OR OIHD;
- the Australian New Zealand Clinical Trials Registry (www.anzctr.org.au), using the search terms: (Occupational OR contact OR irritant OR prevention) AND (hand dermatitis OR hand eczema) OR OIHD;
- the World Health Organization International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/), using the search terms: occupational AND hand dermatitis OR contact AND hand dermatitis OR irritant AND hand dermatitis OR occupational AND hand eczema OR contact AND hand eczema OR irritant AND hand eczema OR OIHD OR hand eczema AND primary prevention; and
- the EU Clinical Trials Register (www.clinicaltrialsregister.eu), using the search terms: hand eczema OR hand dermatitis.

Searching other resources

Searching reference lists

We checked the bibliographies of included studies for further references to relevant trials.

Unpublished literature

One review author (AB) searched the following dermatology conference proceeding abstracts from 1999 up to January 2018:

- Arbeitsgemeinschaft Berufs und Umweltdermatologie; and
- American Contact Dermatitis Society.

Data collection and analysis

Selection of studies

For the first published review version (Bauer 2010), one review author (AB) checked titles and abstracts identified from the searches. Two review authors, AB and Jochen Schmitt (co-author of the first published review version), independently assessed the full-text versions of all possibly relevant studies. Two review authors (AB, JSch) decided which studies met the inclusion criteria, and recorded their methodological quality. The review authors (AB, JSch) resolved any disagreement by discussion. One review author (AB) attempted to obtain missing information from the trial reports by contacting the study investigators.

For the update, four review authors (HR, PE, AB, HCW) checked titles and abstracts identified in the updated searches. Two review authors (HR, PE) independently assessed the full-text versions of all possibly relevant studies and three review authors (AB, PE, HR) decided which studies met the inclusion criteria. Any disagreement was resolved in discussion. One review author (HR) attempted to obtain missing information from the trial reports by contacting the study investigators.

Data extraction and management

For the first published review version, two review authors (AB, JSch) performed the data extraction and a third (HCW) resolved discrepancies (Bauer 2010). We slightly modified and then pilot-tested the Cochrane Skin data collection form for intervention reviews (Version 3, April 2014) for the extractions.

Two review authors (HR, JL) independently extracted data from studies which were added during the update and reviewed by three authors (DD, MLS, AB). We resolved all discrepancies through discussion (HR, AB, JL, DD, MLS) and a consensus was reached.

We entered data into Cochrane Review Manager 5.3 software for data management and analysis (RevMan 2014).

Assessment of risk of bias in included studies

In the quality assessment we evaluated the components listed below for each included study, since there is some evidence that these are associated with biased estimates of treatment effect (Juni 2001). Two authors (AB, JSchm) independently assessed the risk of bias in the four studies included in the first published version of the review, according to the guidelines in the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.0.0 (Higgins 2008). For this update, one author (HR) re-assessed these as described in the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.1.0 (chapter 8) (Higgins 2011). Two review authors (HR, DD) independently assessed the four newly included studies. One newly included trial was independently assessed by two authors (HR, AB) (Brüning 2008). We used the criteria listed below and categorised the studies' risk of bias as 'low', 'high', or 'unclear' for each domain.

- Random sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of participants and personnel (performance bias): lack of blinding possibly influences the proportion of OIHD or the other outcomes, but there is insufficient information to judge whether this is likely. The bias risk of studies which did not blind participants or key personnel was therefore judged as 'unclear' for all outcomes.

- Blinding of outcome assessment (detection bias): lack of blinding is considered to introduce:
  * a low risk of detection bias for the objectively measured secondary outcome 2 (TEWL and/or corneometry)
  * a high risk of detection bias for all other outcomes, which were subjectively assessed.
- Incomplete outcome data (attrition bias) was assessed separately for the following outcome groups. (When attrition was low or reasons for loss to follow-up were unlikely to be related to the outcome, we judged the risk as 'low'; when attrition was considerable and reasons for loss to follow-up were likely to be related to the outcome, we judged the risk as 'high'; when in doubt whether or not reasons for missing were likely to be related to the outcome, we judged the risk as 'unclear'.)
  * Outcomes related to signs and symptoms of hand eczema (primary outcome 1 and 2, secondary outcomes 1, 2, 3, and 5)
  * Secondary outcome 4 (proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products))
- Selective reporting (reporting bias): we judged the risk as 'low' only if a protocol or other convincing text was available.

We resolved all discrepancies through discussion (HR, DD, MLS, AB; with advice from CB) and reached consensus.

Measures of treatment effect

For measuring of treatment effect we used risk ratios (RRs) and corresponding 95% confidence intervals (CIs). Where possible we calculated RR (95% CI) from the information given in the trial papers. The risk ratio can easily be interpreted as the risk of developing OIHD in the intervention group compared to the control group. For continuous outcomes, we planned to calculate mean difference (MD and 95% CI). Where we were unable to perform meta-analyses, we reported the results from the individual trials.

Unit of analysis issues

When no correction for cluster randomisation was performed by the study investigators, we tried to retrieve the necessary data and calculated the intraclass correlation coefficients (ICCs) and corresponding design effects. We divided numbers from such trials (number of participants, number of events) by the design effect before including them in the meta-analysis. When study investigators neither performed corrections for cluster randomisation nor provide the requested data, we searched the literature for appropriate ICC estimates and performed a Sensitivity analysis.

Studies with split-body or cross-over designs may only report their data as if they were derived from a parallel design (Higgins 2011 section 16.4.5 and 9.3.8). This can introduce unit-of-analysis issues because confidence intervals for such trials are likely to be too wide and the studies receive too little weight in meta-analyses. It is controversial how serious these issues are (Higgins 2011 section 16.4.5). When the data required to include a paired analysis in a meta-analysis were not given, we included them as if they were not paired and conducted a Sensitivity analysis that excluded these trials.

Dealing with missing data

We did not perform any intention-to-treat (ITT) calculations and missing data were dealt with descriptively (see Characteristics of included studies: attrition bias).

Concerning studies that did not report primary intervention data or other crucial information, two review authors (AB, HR) obtained missing data from the study investigators where possible.

Assessment of heterogeneity

We assessed statistical heterogeneity in the studies' results concerning OIHD using the I² statistic (Higgins 2011).

We commented on clinical and methodological diversity — including diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD), scoring system for the severity of OIHD, and quality of bioengineering methods — in the appropriate sections (Included studies; Effects of interventions; Discussion; Characteristics of included studies) (Pinnagoda 1990).

Assessment of reporting biases

The Cochrane Handbook for Systematic Reviews of Interventions states that 'reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results' (Higgins 2011). We tried to minimise reporting bias by extensive searching of online databases, etc. (see Search methods for identification of studies).

We could not use funnel plots due to the small number of the included studies, varying interventions and varying methods to determine the main review outcome OIHD across studies (Higgins 2011 chapter 10.4.3.1). Funnel plot assessment of reporting bias will only be used in future if the number of included studies increases at subsequent updates of this review.

Data synthesis

We always used outcome data from the last follow-up time point. When meta-analysis was possible, we assessed risk ratio (RR) and corresponding 95% confidence interval (95% CI) applying the Mantel-Haenszel method in a random-effects model for dichotomous outcomes. For continuous outcomes we had planned to calculate the standardised mean difference.

Due to the small number of studies, we pooled trials without accounting for their risk of bias; the risk was addressed in the risk of bias tables (Risk of bias in included studies) and in the results section (Characteristics of included studies).

In studies with more than two arms, we used the control groups for several comparisons but never double-counted within one comparison of interventions.

Whenever we had identified insufficient comparable trials to perform meta-analyses, we described these outcomes by a narrative approach.

Subgroup analysis and investigation of heterogeneity

We were not able to conduct the subgroup analyses that we had planned (subgrouping according to less than, and greater than 30 years of age; sex; atopy; and occupation). See Differences between protocol and review for more details.

Sensitivity analysis

We excluded each trial with potential Unit of analysis issues (uncorrected cluster design, no paired analysis of data from cross-over or split-body designs) for the sensitivity analyses in order to assess whether or not the findings were robust to these issues. For cases where an uncorrected cluster-randomised trial had an impact on whether or not significance was reached, we planned to calculate a critical design effect and corresponding ICC, above which overall significance would be reached. Correcting for cluster-randomisation reduces a study's effective sample size in a meta-analysis (Higgins 2011 chapter 16.3.4). The assessment of a critical ICC is based on the assumption that with rising ICC (and therefore reduced sample size), a study's impact on the meta-analysis will drop. The relation is to a minor degree subject to rounding errors.

Another issue was the measurement of the first primary outcome (proportion of participants developing any signs and symptoms of OIHD). We excluded all trials that reported signs of hand eczema instead of manifest hand eczema in the sensitivity analyses in order to evaluate whether this was influential on the overall results.

'Summary of findings' tables

We chose two key outcomes (signs and symptoms of OIHD, treatment discontinuation due to adverse effects) as important for decision making, and presented them in our 'Summary of findings' tables. We assessed the quality of the evidence for these outcomes using GRADEproGDT software (GRADEpro GDT 2015). In the GRADE system, evidence derived from RCTs, as in this review, receives a high quality of evidence rating, but the quality can be downgraded due to weaknesses in the following domains: risk of bias, indirectness of evidence, inconsistency of evidence, imprecision of the estimated effect, or publication bias (Schünemann 2013). We described the rationale for downgrading in the footnotes of the respective tables.

R E S U L T S

Description of studies

Results of the search

We combined the results of the searches for this update with those from the searches for the last published version of this review.

We identified a total of 1845 records through the database searches (after removing duplicates). We identified six additional records through other sources (including reference lists), giving a total of 1851 results. We excluded 1798 records based on titles and abstracts.
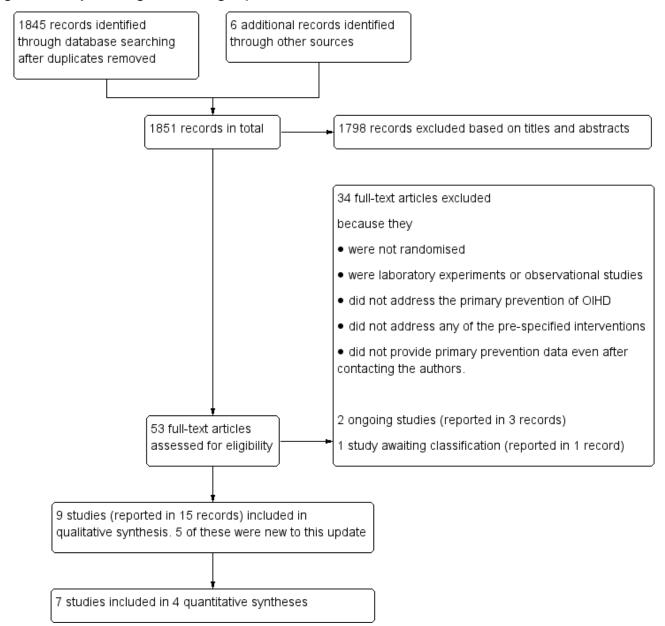
We assessed 53 records in full text. Of these, we excluded 34 (see Characteristics of excluded studies). We categorised two further studies (reported in three references) as ongoing (see Characteristics of ongoing studies) and one study is awaiting classification (reported in one reference) (see Characteristics of studies awaiting classification).

Nine studies (described in 15 records), met the review inclusion criteria and were included (see Characteristics of included studies). Five of these were new to this update. We included a total of seven studies in the meta-analyses.

For a full description of the screening process see our study flow diagram (Figure 1).

Figure 1.   Study flow diagram including all previous searches.

Figure 1. Study flow diagram including all previous searches.

[1845 records identified through database searching after duplicates removed] [6 additional records identified through other sources] → [1851 records in total] → [1798 records excluded based on titles and abstracts]; [53 full-text articles assessed for eligibility] → [34 full-text articles excluded because they • were not randomised • were laboratory experiments or observational studies • did not address the primary prevention of OIHD • did not address any of the pre-specified interventions • did not provide primary prevention data even after contacting the authors. 2 ongoing studies (reported in 3 records) 1 study awaiting classification (reported in 1 record)]; [9 studies (reported in 15 records) included in qualitative synthesis. 5 of these were new to this update] → [7 studies included in 4 quantitative syntheses]

Included studies

Our searches of electronic databases identified nine randomised controlled trials (RCTs), with a total of 2888 initially healthy participants, which met the inclusion criteria (Brüning 2008; Duca 1994; Flyvholm 2005; Goh 1994; Halkier-Sørensen 1993; Kütting 2010; Löffler 2006; Meer 2015; Perrenoud 2001a). Please see Characteristics of included studies for more details of the trial conditions and 'Risk of bias' assessments for each study. Five studies were funded by official funding sources: German metal cooperative union (Vereinigung der Metall-Berufsgenossenschaften VMBG); Danish Ministry of Health; Danish Insurance Association, Copenhagen, L. P. Hansen's fund, Odense, and Danfoss A/S, Nordborg, Denmark; German Statutory Accident Insurance (DGUV) and the Franz-Koelsch-Stiftung e.V.; Netherlands Organization for Health Research and Development (ZONMW). One

study was funded by industry (Asche Chiesi GmbH, Hamburg, Germany) and three studies did not report any funding sources.

Design

All of the nine included studies were randomised controlled trials. With the exception of two cross-over studies (Halkier-Sørensen 1993; Perrenoud 2001a), the studies had a parallel design. Four parallel studies were cluster-randomised (Flyvholm 2005; Kütting 2010; Löffler 2006; Meer 2015). All of these were analysed by the study investigators on the individual level without accounting for the clustering and without reporting intraclass correlation coefficients (ICCs). This introduces over-precise results with standard errors and P values which are too small (Higgins 2011). The comparability of such studies to individually randomised studies is compromised (Brüning 2008; Duca 1994; Goh 1994; Halkier-Sørensen 1993; Perrenoud 2001a). For the data from Meer

2015, we calculated an ICC of 0.005 and a corresponding design effect of 1.0989, based on data provided by the study investigators.

Additionally to the individual randomisation to two parallel study groups, one study randomised the participants' hands to the interventions in a second step, thus creating four study arms (Brüning 2008). This design introduces a minor unit of analysis issue and possibly also contamination effects.

Most of the included studies had two arms, while one was a three-armed trial (Goh 1994), and two had four arms (Brüning 2008; Kütting 2010).

We could not include the two cross-over studies, Perrenoud 2001a and Halkier-Sørensen 1993, in the meta-analyses of the first primary outcome because they did not report evaluable quantitative data. One reported only scores and no dichotomised data (Perrenoud 2001a), while the other reported the required data only for the no-treatment period (Halkier-Sørensen 1993).

Sample sizes

A total of 2888 participants were evaluable for this review (healthy at the beginning of the study, not lost to follow-up). Most studies reported some attrition and some studies also recruited participants with existing occupational irritant hand dermatitis (OIHD). The numbers of participants who were excluded or lost to follow-up are given in the Characteristics of included studies tables.The sample sizes varied from 16 to 893 participants in the individual trials.

The sample sizes reported throughout the review text do not necessarily refer to the actual number of participants that were eligible for evaluation. In order to correct for cluster design in the meta-analyses, a reduced 'effective sample size' (Higgins 2011, sections 16.3.4 and 16.3.5) was estimated for the respective studies. The sample sizes of natural participants are reported in the Characteristics of included studies tables.

Participants and setting

Exclusively healthy participants were recruited for five studies (Brüning 2008; Goh 1994; Halkier-Sørensen 1993; Kütting 2010; Perrenoud 2001a). Four studies (Duca 1994; Flyvholm 2005; Löffler 2006; Meer 2015) also recruited workers who were suffering from OIHD at the beginning of the study, but data for initially healthy participants was available.

Three studies (Goh 1994; Löffler 2006; Perrenoud 2001a) included only apprentices or newly employed workers. The mean age of participants in these trials ranged from 18 to 22 years. In the remaining studies (Brüning 2008; Duca 1994; Flyvholm 2005; Halkier-Sørensen 1993; Kütting 2010; Meer 2015) the mean age ranged from 32 to 41 years.

Two trials included exclusively male workers (Brüning 2008; Kütting 2010). In three trials the majority of participants was male (65% to 92%) (Duca 1994; Flyvholm 2005; Goh 1994), and in the remaining trials the majority was female (78% to 99%) (Halkier-Sørensen 1993; Löffler 2006; Meer 2015; Perrenoud 2001a).

All nine included studies were field studies in occupations prone to OIHD. The studies dealt with different occupations and different stages of experience:

- metal workers (Brüning 2008; Goh 1994: newly employed; Kütting 2010);
- dye and print industry workers (Duca 1994);
- gut cleaners in swine slaughterhouses (Flyvholm 2005);
- cleaners and kitchen assistants (Halkier-Sørensen 1993);
- hospital employees (Löffler 2006: 1st year nurse apprentices; Meer 2015);
- apprentice hairdressers (Perrenoud 2001a).

Eight trials were performed in the following European countries: Denmark (Halkier-Sørensen 1993; Flyvholm 2005); Germany (Brüning 2008; Kütting 2010; Löffler 2006); Italy (Duca 1994); Netherlands (Meer 2015); Switzerland (Perrenoud 2001a). One trial was performed in Singapore (Goh 1994).

Interventions

The duration of the interventions was between four weeks and three years. The participants of five studies received barrier creams, also called skin protection creams (Brüning 2008; Duca 1994; Goh 1994; Kütting 2010; Perrenoud 2001a).

- In Duca 1994, the barrier creams were provided by the employer, were applied twice per day for 12 months, and fell into two main groups: silicone or hydrocarbon containing barrier creams.
- In Brüning 2008, the participants received skin protection (Travabon or Stoko Protect), skin care (Estolan), both, or no product for 12 months. The products were applied to one hand while using a glove for the other hand. Further requirements for the application were not described.
- In Goh 1994, 54 healthy, newly employed metal workers exposed to cutting fluids were randomised to apply a barrier cream, to apply a moisturiser, or to the control group for six months. The barrier cream (Arretil) was used on the hands before work and after each meal break. The moisturiser (Keri Lotion) was used daily as an after-work emollient.
- In Kütting 2010, the volunteers received skin protection, skin care, both, or no recommendation for 12 months. All participants used the skin care and protection products that were provided by the employer. Barrier creams were used before or during working hours. Skin care products were applied solely after work.
- In Perrenoud 2001a, the participants started either with a barrier cream (Excipial protect) or with its vehicle. Excipial protect contains aluminium hydroxychloride and glycerine; the vehicle was designed specifically for skin care for occupational users. The first cream was applied five days per week for two weeks with a washout period of two days followed by another two-week treatment period with the second cream and vice versa.

In four studies, the participants received moisturiser, also called skin care creams or emollients. Three of them are described above because they also investigated the effects of barrier creams (Brüning 2008; Goh 1994; Kütting 2010).

- In Halkier-Sørensen 1993, the participants were randomly allocated to two cross-over groups for two lots of two weeks. One group started with a moisturiser (Locobase); the other group started with no treatment. Application requirements were not described.

Three studies implemented skin protection education programmes (Flyvholm 2005; Löffler 2006; Meer 2015), which could include providing products (Löffler 2006; Meer 2015). All three educational programmes advised the participants to substitute hand washing with alcohol-based hand disinfection when there is no visible contamination, to wear gloves appropriately, and to apply skin care creams.

- In Flyvholm 2005, a prevention programme (skin protection education) was evaluated for 12 months. The prevention strategy consisted of a two-part concept, with an evidence-based prevention programme giving recommendations for prevention of work-related skin problems in wet work occupations, and a documented method for implementation. The recommendations were aimed at the management and at the employees. The local project group included two to five gut cleaners who acted as role models.
- In Löffler 2006, the intervention group received skin protection education (educational lecture with practical parts), and skin care cream (Asche Basis Creme). The cream was also given to participants in of the control group. The lectures took place three times in the first year, and twice in the second and third year.
- In Meer 2015, a multifaceted implementation strategy (skin protection education) was evaluated for 12 months. The intervention included participatory working groups, role modes, an educational programme including reminders, and a leaflet, while the comparison group received only the leaflet.

Comparisons

The included trials fell in four categories of interventions:

- barrier creams versus no intervention (Brüning 2008; Duca 1994; Goh 1994; Kütting 2010);
- moisturisers versus no intervention (Brüning 2008; Goh 1994; Kütting 2010);
- combination of barrier creams and moisturisers versus no intervention (Brüning 2008; Kütting 2010);
- skin protection education versus no or minimal intervention (Flyvholm 2005; Löffler 2006; Meer 2015).

We identified no trials which used the remaining predefined types of interventions (protective gloves; complex interventions using barrier creams, moisturisers, and protective gloves).

Outcomes

This section describes how the review outcomes were reported in the included studies. For results, see Effects of interventions.

Primary outcome 1: the proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) and/or hand dermatitis scores (e.g. HECSI, Manuscore) as rated by the investigator (physician/nurse) or the participant

None of the included studies used the term OIHD. We decided that the following outcomes were eligible as primary review outcome 1:

- hand eczema (Flyvholm 2005; Halkier-Sørensen 1993; Kütting 2010; Meer 2015);
- abnormal morphology (Brüning 2008: 'klinischer Hautbefund'; Duca 1994: 'esame obiettivo positivo per uno o più dei segni'; Löffler 2006: 'Morphologie auffällig');

- cutting fluid dermatitis (Goh 1994).

One study applied scores for measuring skin damage and did not dichotomise their data (Perrenoud 2001a), so that no proportion could be extracted.

The outcome was assessed by the study personnel except for three studies (Flyvholm 2005; Kütting 2010; Meer 2015), in which the participants reported hand eczema in standardised interviews.

The proportion was reported as point prevalence at last follow-up (Brüning 2008; Halkier-Sørensen 1993), period prevalence of the last three or six months (Flyvholm 2005; Kütting 2010; Meer 2015), or as proportion of participants with signs of OIHD at either follow-up (Duca 1994; Goh 1994; Löffler 2006).

Primary outcome 2: frequency of treatment discontinuation due to adverse effects

In one cross-over study (Halkier-Sørensen 1993), this outcome was addressed to some extent, while in some others it was evident from the dropout analyses that no participant was lost to follow-up because of adverse effects (Brüning 2008; Goh 1994; Löffler 2006).

Secondary outcome 1: severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant

Some studies applied scores (Halkier-Sørensen 1993; Kütting 2010; Meer 2015; Perrenoud 2001a), but they were not reported separately for incident cases of OIHD.

Secondary outcome 2: proportion of participants with significant changes (difference in average score or difference from baseline, or both) in barrier function or hydration, measured using transepidermal water loss (TEWL), and corneometry (skin hydration)

TEWL was reported in three studies (Brüning 2008; Goh 1994; Halkier-Sørensen 1993), but in Brüning 2008, quartiles were given instead of mean and standard deviation. Only figures were provided in Halkier-Sørensen 1993.

Skin hydration was assessed in two studies (Brüning 2008; Halkier-Sørensen 1993). One study assessed TEWL, corneometry, and chromometry (measurement of colour), but did not report their results (Perrenoud 2001a).

Secondary outcome 4: proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products)

Two studies addressed the participants' opinion on the products (Halkier-Sørensen 1993; Perrenoud 2001a).

Secondary outcome 5: other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies)

Two studies described this outcome (Halkier-Sørensen 1993; Perrenoud 2001a).

Excluded studies

We excluded 20 studies that may have been expected to be included. Of these, 11 were RCTs, eight were controlled clinical trials (CCTs), and one was a qualitative study.

Reasons for excluding the RCTs are as follows.

- We excluded three studies because they violated the inclusion criteria by exclusively including workers suffering from OIHD and therefore dealing with secondary prevention not with primary prevention of OIHD (Arbogast 2004; Berndt 2000; McCormick 2000).

- We excluded Held 2002, because some workers who already had hand dermatitis at baseline ('skin problems': 25% to 30%) participated. The study investigators responded that providing the required data for initially healthy participants would be too difficult because the study was conducted almost 15 years ago. The study investigators of another trial, Winker 2009, replied that they would not provide the requested data because they feared the power would be too low if participants with OIHD at baseline were removed from the sample size. We were unable to contact the study investigators of Frosch 2003, which did not provide sufficient information about hand dermatitis at baseline. Furthermore, the design of this trial showed weaknesses: only five laboratories were randomised to four products; and it used only a partial cross-over-design (two out of four products were tested in the same laboratory). In this update we were able to include two studies which had previously been excluded, after the study investigators provided the requested data (Flyvholm 2005; Löffler 2006).

- We excluded Perrenoud 2001b, which investigated protective cream versus no intervention, because only preliminary data (no quantitative data) were available on OIHD and it was unclear if participants with existing OIHD were included. One study did not address the prevention of OIHD and did not report data on OIHD or any other review outcome (Mody 2003). We excluded another study, Winnefeld 2000, because its interventions (non-medicated soap versus an alcohol-based hand rinse) were not defined as interventions to prevent OIHD according to this review. Furthermore, the trial only took eight days and the incidence of OIHD was not assessed. We excluded another study, Dobson 1979, because it examined the effect of industrial hand cleansers, an intervention that was not considered in this review, and there was no data on OIHD. Their only outcome was TEWL. The only study concerning protective glove use was excluded because it was performed in an experimental setting (Davis 2005).

We excluded seven controlled clinical trials because they were not randomised (Amphoux 1975; Bauer 2002; Bolam 1971; Bregnhøj 2012; Held 2001; Schwanitz 2003; Sell 2005). We also excluded Glantz 1976, because it was probably not randomised and no relevant outcome data was assessed.

We excluded one study, Brown 2007, because for the most part it was a qualitative study (intervention implementation research) and it did not provide sufficient data on OIHD for the different interventions.

Risk of bias in included studies

A summary of the 'Risk of bias' assessments, which we carried out for each included study, can be seen in Figure 2 and Figure 3. Details can be found in the Characteristics of included studies tables.
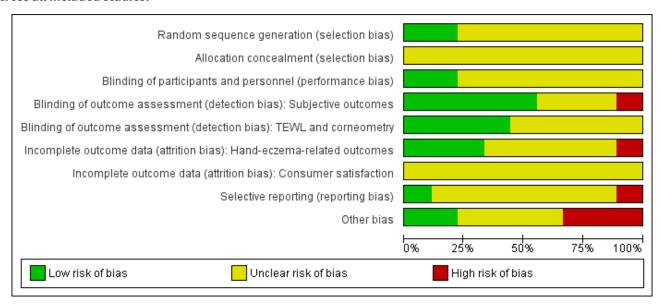
Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Figure 3. 'Risk of bias' graph: review authors' judgements about each 'Risk of bias' item presented as percentages across all included studies.

Allocation

Most studies did not provide any information on allocation except that it was at random, and we judged the risk of bias as unclear in these cases. Allocation concealment was not mentioned in any study; we therefore judged the risk of bias for this domain as unclear, except for in Kütting 2010. The risk of bias in this trial was high because potential confounders were significantly unbalanced at baseline.

Blinding

We judged the risk of performance bias as unclear for all four studies which did not blind the workers, and for four studies with unclear blinding. Only two studies reported blinding their participants (Meer 2015; Perrenoud 2001a).

In five studies, the outcome assessors were blinded, so we judged them as having a low risk of detection bias (Brüning 2008; Duca 1994; Löffler 2006; Meer 2015; Perrenoud 2001a). For one study, we judged the risk of bias as high because the outcome assessors were not blinded (Flyvholm 2005). Three studies probably did not blind the outcome assessors and so we judged them as having an unclear risk of bias for this domain (Goh 1994; Halkier-Sørensen 1993; Kütting 2010).

Incomplete outcome data

Three trials had a low risk of attrition bias (Brüning 2008; Goh 1994; Löffler 2006). The risk of attrition bias was high in one study (Halkier-Sørensen 1993). For five studies, the risk of bias was unclear because there was there was no dropout analysis or the analysis did not provide the information required for the risk of bias assessment (Duca 1994; Flyvholm 2005; Kütting 2010; Meer 2015; Perrenoud 2001a).

Selective reporting

We assessed most trials as having an unclear risk of reporting bias, because the study protocols were not available. One study,

Meer 2015, reported the predefined outcomes so we assessed this study as having a low risk of reporting bias. Another study, Halkier-Sørensen 1993, did not report their results according to the original randomisation, but according to the ability of the participants to complete the study period. Thus, the results were not reported in a way appropriate for an RCT, so we assigned a judgement of high risk of bias. They did not provide any data on OIHD that may have been used in the meta-analysis.

Other potential sources of bias

In three of the four cluster-randomised trials, no correction for the design effect was applied (Flyvholm 2005; Kütting 2010; Löffler 2006). They were analysed on the individual level without accounting for the clustering. This does not lead to a biased estimate of effect but it introduces over-precise results with too small standard errors and P values (Higgins 2011). The comparability to individually randomised studies is therefore compromised. Data from one trial, Kütting 2010, was used in the meta-analyses of the effect of barrier creams or moisturisers (or both) on OIHD (comparisons 1, 2, 3). All three studies included in the meta-analysis of educational programmes (comparison 4) were cluster-randomised trials.

Baseline imbalances introduced a high risk of bias to two studies (Flyvholm 2005; Halkier-Sørensen 1993). They introduced an unclear risk of bias in three studies (Duca 1994: insufficient information; Goh 1994; Perrenoud 2001a: insufficient information). One study reported a possible, unclear bias introduced through differential diagnostic activity across study groups (Meer 2015). Apart from these exceptions, there was a low risk of bias concerning design, baseline imbalances, funding sources, and blocked randomisation. For three remaining studies, all these possible risks of bias were low (Brüning 2008; Kütting 2010; Löffler 2006).

Effects of interventions

See: **Summary of findings for the main comparison** Barrier creams compared to no treatment for preventing occupational irritant hand dermatitis; **Summary of findings 2** Moisturisers compared to no treatment for preventing occupational irritant hand dermatitis; **Summary of findings 3** Barrier creams and moisturisers compared to no treatment for preventing occupational irritant hand dermatitis; **Summary of findings 4** Skin protection education compared to no or minimal intervention for preventing occupational irritant hand dermatitis

We performed four meta-analyses for the main outcome, proportion of participants developing signs or symptoms of occupational irritant hand dermatitis (OIHD), with up to four trials for each type of intervention.

For details on clinical and methodological diversity of the pooled studies, see Characteristics of included studies.

Studies relevant to this review fall into four comparisons. In total there were nine relevant randomised studies.

Comparison 1: barrier creams versus no treatment or vehicle

Four trials compared barrier creams against no treatment (Brüning 2008; Duca 1994; Goh 1994; Kütting 2010), while one study compared a protection cream against its vehicle (Perrenoud 2001a).

1.1 Primary outcome 1: the proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant

We identified four studies relevant to this outcome (total number of participants (N) = 999). The trials investigated metal workers exposed to cutting fluids (almost exclusively male) or dye/print factory workers. The duration was between six and 12 months. Except for Brüning 2008, all trials showed a slightly reduced risk of developing OIHD when applying barrier creams. In the intervention groups, 29% of participants developed symptoms of OIHD, compared to 33% in the control groups. However, when these data were pooled, the wide confidence intervals were consistent with either a reduced risk or no effect (risk ratio (RR) 0.87, 95% confidence interval (CI) 0.72 to 1.06; P = 0.18), and the quality of the evidence was low (Summary of findings for the main comparison). Across the individual studies, the RR ranged from 0.51 to 1.29, but the I^2 measure showed no substantial heterogeneity (I^2 = 9%) (Analysis 1.1).

Sensitivity analysis

The results of the sensitivity analyses are shown in Table 1. When we removed Kütting 2010, a cluster-randomised trial, from the meta-analysis, the confidence intervals were still wide and included no effect. We deduced that correcting for cluster randomisation in this study would still yield no significant results.

There was another unit-of-analysis issue since one study, Brüning 2008, had a partial split-body design. The hands that were randomised to the barrier cream belonged to the same individuals as the hands randomised to the control arm. When we excluded this study from the analysis, the relative risk was marginally lower, and the confidence intervals only just included no effect. Apart from the

unit-of-analysis issue, contamination between the two study arms may have obliterated the preventive effect in this study.

Including only studies with the outcome hand eczema or hand dermatitis showed a greater effect, but the confidence intervals were still wide and included no effect.

Overall the sensitivity analyses revealed that the findings were quite robust concerning unit-of-analysis and measures-of-effect issues.

Other data

One study could not be pooled with other trials (Perrenoud 2001a). It found that the barrier cream (Excipial protect) and its vehicle, used for five days a week for two weeks, were similarly protective. Most participants developed no or mild symptoms. We could not estimate RR or score values because no quantitative data were reported by the study investigators.

1.2 Primary outcome 2: frequency of treatment discontinuation due to adverse effects

In two studies, it was evident from the dropout analyses that no participant was lost to follow-up because of adverse effects from the barrier creams (Brüning 2008; Goh 1994). In one further study, dropout reasons were unrelated to the trial (Perrenoud 2001a). However, we cannot fully exclude the possibility that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge. In two studies, dropout analyses were not performed or not detailed enough to extract whether or not adverse effects were among the reasons for dropout (Kütting 2010; Duca 1994). The numbers of participants who dropped out of the individual trials ranged from 0% to 24% and are given in the Characteristics of included studies tables.

1.3 Secondary outcome 1: severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both) as rated by the investigator (physician/nurse) or the participant

Two studies applied scores (Kütting 2010; Perrenoud 2001a), but they were not reported separately for incident cases of OIHD. One study reported the follow-up proportions of OIHD in participants with OIHD at baseline, but they did not report any scores (Duca 1994). Two studies did not address this outcome (Brüning 2008; Goh 1994).

1.4 Secondary outcome 2: proportion of participants with significant changes (difference in average score or difference from baseline, or both) in barrier function or hydration, measured using trans epidermal water loss (TEWL) (skin barrier) and corneometry (skin hydration)

TEWL

Tewl, a measure of skin barrier function, was reported in three studies (Brüning 2008; Goh 1994; Perrenoud 2001a), but one study gave quartiles instead of mean and standard deviation (Brüning 2008), and another only gave figures and P values (Perrenoud 2001a). One study, Goh 1994, reported TEWL only for one time point but did not clarify for which. We were therefore unable to pool the data. The TEWL differences in the barrier cream groups compared to their respective controls were neither clinically important nor statistically significant in any of the three trials.

In Brüning 2008, the metal workers' median TEWL after one year was lower than at baseline in all study arms, including the control, but the changes were not significant (Table 2). TEWL in the barrier cream group was somewhat lower at the last follow-up compared to control (not significant).

In Goh 1994, it remains unclear for which time point basal TEWL was reported. The values showed no significant differences between the groups. Results for TEWL analysis were as follows: in the control group the mean basal TEWL was 16.7 g/m²h while in the barrier cream group it was 15.5 g/m²h; the mean TEWL difference between groups was 1.2 g/m²h (not clinically important nor statistically significant). Concerning the three trial groups (barrier cream, moisturiser, control), the trial investigators found that changes of the metal workers' TEWL, 'throughout the six-month study period, were almost identical'.

In Perrenoud 2001a, no important changes in TEWL values were observed. TEWL increased during barrier cream treatment without reaching statistical significance (Table 3).

Skin hydration

This outcome was assessed in two studies (Brüning 2008; Perrenoud 2001a), but figures and P values were only provided in Perrenoud 2001a.

In Brüning 2008, median skin hydration was higher in the barrier cream group at last follow-up compared to baseline (P = 0.0491, Table 2). Skin hydration at baseline and after one year in the intervention group was almost equal to the controls.

In Perrenoud 2001a, skin hydration of apprentice hairdressers measured by corneometry was significantly higher during the two weeks of vehicle use (P < 0.01, Table 3) than for the barrier cream. However, skin hydration was already visibly lower at the beginning of the verum period compared to the vehicle.

The details of these bioengineering methods are given in the Characteristics of included studies tables.

1.5 Secondary outcome 3: change of occupation because of OIHD versus staying in the occupation

None of the trials reported this outcome.

1.6 Secondary outcome 4: proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products)

Only one study addressed this outcome (Perrenoud 2001a). The satisfaction with the products was generally high. No difference was noted between the creams except with regard to texture. The vehicle was regarded as too oily by 11 out of 16 participants, while four considered the barrier cream to be too oily. Five participants did not plan to use the vehicle, two would not use the barrier cream, and one would not use either again.

1.7 Secondary outcome 5: other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies)

Only one study addressed this outcome. Mild adverse events like transient reddening and itching (no values reported) after use of Excipial protect or its vehicle were reported in Perrenoud 2001a.

Comparison 2: moisturisers versus no treatment

Four trials compared moisturisers against no treatment (Brüning 2008; Goh 1994; Halkier-Sørensen 1993; Kütting 2010).

2.1 Primary outcome 1: the proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant

We identified three studies relevant to this outcome (N = 507). The trials investigated metal workers (almost exclusively male) exposed to cutting fluids. The duration was between six and 12 months. All trials showed a reduced risk of developing OIHD when applying moisturisers. In two individual trials as well as in the pooled analysis, the risk reduction was clinically important (0.75 or less). In the intervention groups, 13% of participants developed symptoms of OIHD compared to 19% in the control groups. However, when these data were pooled, the wide confidence intervals were consistent with either an important effect or no effect (RR 0.71, 95% CI 0.46 to 1.09; P = 0.11) and the quality of evidence was low (Summary of findings 2). Across the individual studies, RR ranged from 0.63 to 0.99. The heterogeneity was not substantial (I² = 10%) (Analysis 2.1).

Sensitivity analysis

The results of the sensitivity analysis are shown in Table 4. Despite low heterogeneity, data from the remaining two studies showed a reduced risk of developing OIHD when moisturisers were applied after removing Brüning 2008. In this comparison, the study by Brüning and colleagues was the only study which did not define hand eczema or hand dermatitis as their outcome (it used abnormal morphology instead). Another limitation of this study was the partial split-body design, which may have introduced contamination.

When removing Kütting 2010, the confidence intervals were still very wide and included no effect. We deduced that correcting for cluster randomisation in this study would still not yield significant results.

The sensitivity analysis revealed that the findings were robust concerning uncorrected cluster design (Kütting 2010), but the preventive effect of moisturisers appeared much clearer without data from Brüning 2008.

Other data

We could not pool one cross-over study with other trials because no dichotomised data were available for the treatment period (Halkier-Sørensen 1993). The study found that cleaners and kitchen workers often developed signs of OIHD during the two weeks of the control period: nineteen participants (20.4%) developed dry eczema, another 15 (16.1%) developed dryness and scaling, and 38 (40.9%) developed dryness only (N = 93 workers who completed both periods (group one), or ceased from the control period prematurely (group two)). For the two-week treatment period with a moisturiser (Locobase), no such data were reported. However, a score which summarised severity ratings for several symptoms of OIHD was significantly reduced after the treatment period compared to the control period (Wilcoxon test, P < 0.001).

2.2 Primary outcome 2: frequency of treatment discontinuation due to adverse effects

In two studies it was evident from the dropout analyses that no participant was lost to follow-up because of adverse effects from the moisturisers (Brüning 2008; Goh 1994). However, we cannot fully exclude the possibility that some of the participants who completed these studies may have stopped applying the products without the researchers' knowledge.

In one cross-over study (Halkier-Sørensen 1993), 12 participants violated the protocol or declined to continue the study because they developed or feared to develop hand dermatitis during the no-treatment period. Six participants turned up only once, did not find Locobase acceptable, or went on vacation. It remains unclear if some of these discontinued the treatment phase due to adverse effects. Severe dryness of the skin caused 23 participants (20.7%) to drop out during the no-treatment phase.

No dropout analyses were performed in Kütting 2010.

The numbers of participants who dropped out of the individual trials ranged from 0% to 37% and are given in the Characteristics of included studies tables.

2.3 Secondary outcome 1: severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both) as rated by the investigator (physician/nurse) or the participant

None of the included studies addressed this outcome. Some studies applied scores (Halkier-Sørensen 1993; Kütting 2010), but they were not reported separately for incident cases of OIHD.

2.4 Secondary outcome 2: proportion of participants with significant changes (difference in average score or difference from baseline, or both) in barrier function or hydration, measured using TEWL (skin barrier) and corneometry (skin hydration)

TEWL

TEWL was reported in three studies (Brüning 2008; Goh 1994; Halkier-Sørensen 1993), but one study gave quartiles instead of mean and standard deviation (Brüning 2008), and another only gave figures and P values (Halkier-Sørensen 1993). One study reported TEWL only for one time point but did not clarify for which (Goh 1994). The TEWL differences in the barrier cream groups compared to their respective controls were neither clinically relevant nor statistically significant in any of the three trials.

In Brüning 2008, the metal workers' median TEWL after one year was lower than at baseline in all study arms, including the control, but the authors reported that the changes were not significant (Table 2). There was no important difference between moisturiser and control at both points in time. For metal workers exposed to cutting fluids, the application of a moisturiser over one year had no significant effects on TEWL.

In Goh 1994, it remains unclear for which time point basal TEWL was reported. The values showed no significant differences between the groups. Results for TEWL analysis were as follows: In the control group, the mean basal TEWL was 16.7 g/m^{2}h. In the moisturiser group, the mean basal TEWL was 15.4 g/m^{2}h (not statistically significant). Concerning the three trial groups (barrier cream,

moisturiser, control), the study investigators found that changes of the metal workers' TEWL, 'throughout the six-month study period, were almost identical'.

In Halkier-Sørensen 1993, TEWL after the moisturisers period in was marginally higher compared to the control period (not significant, Table 5).

Skin hydration

This outcome was assessed in two studies (Brüning 2008; Halkier-Sørensen 1993), but only one of these gave figures and P values (Halkier-Sørensen 1993).

In both moisturiser group and controls of Brüning 2008, median skin hydration was higher at last follow-up compared to baseline (not significant, Table 2). Skin hydration was marginally lower in the moisturisers group at baseline and after one year compared to controls (not significant).

In Halkier-Sørensen 1993, after the no-treatment period, the cleaners' and kitchen workers' skin hydration was considerably lower compared to the period when they used a moisturiser (P < 0.001, Table 5).

The details of these bioengineering methods are given in the Characteristics of included studies tables.

2.5 Secondary outcome 3: change of occupation because of OIHD versus staying in the occupation

None of the trials reported this outcome.

2.6 Secondary outcome 4: proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products)

Only one study addressed this outcome. In Halkier-Sørensen 1993, 80% of the participants rated the quality of the moisturiser as good or very good. Thirteen per cent stated that it had no effect. Two participants did not find Locobase cosmetically acceptable. No data on adherence were given in that study.

2.7 Secondary outcome 5: other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies)

Only one study addressed this outcome. Itching, stinging, and dry skin after application of Locobase were reported in 7% of the participants of the study of Halkier-Sørensen 1993.

Comparison 3: barrier creams and moisturisers versus no treatment

Four trials compared a combination of barrier creams and moisturisers against no treatment (Brüning 2008; Goh 1994; Halkier-Sørensen 1993; Kütting 2010).

3.1 Primary outcome 1: the proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant

We identified two studies relevant to this outcome (N = 474). Two studies of male German metal workers were pooled for the meta-

analysis of barrier creams and moisturisers versus no intervention. The duration was 12 months. Both trials showed a reduced risk of developing OIHD when applying barrier creams and moisturisers. The risk reduction was clinically important (less than 0.75) in one individual trial and in the pooled analysis. In the intervention groups, 8% of participants developed symptoms of OIHD compared to 13% in the control groups, but when the data were pooled the very wide confidence intervals were consistent with either an important effect or no effect (RR 0.68, 95% CI 0.33 to 1.42; P = 0.30) and the quality of evidence was low (Summary of findings 3). RR ranged from 0.43 to 0.92. This outcome had moderate levels of heterogeneity (Chi^2 = 1.84; df = 1.0; P = 0.17; I^2 = 46%) (Analysis 3.1).

Sensitivity analysis

The results of the sensitivity analysis are shown in Table 6. When we excluded the trial Brüning 2008, which addressed abnormal morphology instead of hand eczema and had a partial split-body design, the remaining study showed a considerable effect but this did not reach significance.

When we removed Kütting 2010, the effect estimate was still very imprecise. We deduced that correcting for cluster randomisation in this study would still yield no significant results.

Because only two trials with moderate statistical heterogeneity were included in this comparison, the sensitivity analysis showed a considerable change in RR but not in statistical significance when either study was removed.

3.2 Primary outcome 2: frequency of treatment discontinuation due to adverse effects

In one study it was evident from the dropout analyses that no participant was lost to follow-up because of adverse effects from the moisturisers (Brüning 2008). However, we cannot fully exclude the possibility that some of the participants who completed this study may have stopped applying the products without the researchers' knowledge.

No dropout analyses were performed in Kütting 2010.

The numbers of participants who dropped out of the individual trials ranged from 8% to 24% and are given in the Characteristics of included studies tables.

3.3 Secondary outcome 1: severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both) as rated by the investigator (physician/nurse) or the participant

None of the included studies addressed this outcome. One study applied scores (Kütting 2010), but they were not reported separately for incident cases of OIHD.

3.4 Secondary outcome 2: proportion of participants with significant changes (difference in average score and/or difference from baseline) in barrier function or hydration, measured using TEWL (skin barrier) and corneometry (skin hydration)

TEWL

TEWL was reported in one study (Brüning 2008). The study investigators gave quartiles instead of mean and standard deviation. The metal workers' median TEWL after one year was lower than at baseline in all study arms, including the control, but the changes were small and not significant (Table 2). There was no clinically important difference between barrier creams plus moisturiser and control at the last follow-up.

Skin hydration

This outcome was assessed in one study (Brüning 2008). The study investigators gave quartiles instead of mean and standard deviation. For barrier creams plus moisturiser, median skin hydration was somewhat higher at last follow-up compared to baseline (P = 0.0402). Without reaching significance or clinical importance, skin hydration was lower in this group at baseline and after one year.

The details of these bioengineering methods are given in the Characteristics of included studies tables.

3.5 Secondary outcome 3: change of occupation because of OIHD versus staying in the occupation

None of the trials reported this outcome.

3.6 Secondary outcome 4: proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products)

None of the trials reported this outcome.

3.7 Secondary outcome 5: other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies)

None of the trials reported this outcome.

Comparison 4: skin protection education versus no or minimal intervention

We identified three studies for this comparison.

4.1 Primary outcome 1: the proportion of participants developing any signs and symptoms of OIHD (incident cases) measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both, as rated by the investigator (physician/nurse) or the participant

For this outcome we found three relevant studies. A total number of 1443 gut cleaners, nurse apprentices, or hospital employees were included. In order to account for the cluster design in Meer 2015, the effective sample size needed to be corrected to a total of 1355 participants. The duration was between one and three years. With a skin protection education, the risk of developing OIHD was reduced in two studies (Flyvholm 2005; Löffler 2006). In these two studies, the risk reduction was clinically important (less than 0.75). One study showed an non-significant but clinically important increased risk compared to the minimal implementation group (leaflet only) (Meer 2015). When we pooled these data, the wide confidence intervals were consistent with either a reduced risk or no effect (RR 0.76, 95% CI 0.54 to 1.08; P = 0.12) and the GRADE quality of evidence was very low (Summary of findings 4). In the intervention groups 21% of participants developed symptoms of OIHD, compared to 28% in the control groups. RR ranged from 0.69 to 1.26. We observed high levels of statistical heterogeneity (Chi^2 = 4.44; df = 2.0; P = 0.11; I^2 = 55%) (Analysis 4.1).

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Sensitivity analysis

The results of the sensitivity analysis are shown in Table 7. All three trials were cluster-randomised and only the authors of one study provided the data required for the correction of the design effect (Meer 2015). After removing Flyvholm 2005, the effect was still very imprecise and the CI included 1. The same was true for removing Löffler 2006, or both trials, from the meta-analysis. We deduced that correcting for cluster randomisation in these two studies would still yield no significant results. Only one study in this comparison did not measure hand eczema or hand dermatitis, but instead measured morphological changes (Löffler 2006).

The risk reduction appeared considerably smaller when either or both studies with uncorrected cluster design were removed. One partial reason for this is that uncorrected cluster designs often show an artificially greater effect. Another reason is that the only study without unit-of-analysis issues showed a negative effect of skin protection education. The study authors speculate that this was the case because the participants of their intervention group were more aware of hand dermatitis due to the education and may have reported it more often only due to this awareness.

4.2 Primary outcome 2: frequency of treatment discontinuation due to adverse effects

In one study it was evident from the dropout analyses that no participant was lost to follow-up because of adverse effects (Löffler 2006). However, we cannot fully exclude the possibility that some of the participants who completed the study may have stopped applying the products without the researchers' knowledge.

Two studies did not report any dropout reasons (Flyvholm 2005; Meer 2015).

The numbers of participants who dropped out of the individual trials ranged from 35% to 38% and are given in the Characteristics of included studies tables.

4.3 Secondary outcome 1: severity of clinical signs and symptoms in incident cases of OIHD (measured by clinical scores (IGA) or hand dermatitis scores (e.g. HECSI, Manuscore), or both) as rated by the investigator (physician/nurse) or the participant

None of the included studies addressed this outcome. One study applied scores (Meer 2015), but they were not reported separately for incident cases of OIHD

4.4 Secondary outcome 2: proportion of participants with significant changes (difference in average score or difference from baseline, or both) in barrier function or hydration, measured using TEWL (skin barrier) and corneometry (skin hydration)

None of the trials in this comparison reported these outcomes.

4.5 Secondary outcome 3: change of occupation because of OIHD versus staying in the occupation

None of the trials in this comparison reported these outcomes.

4.6 Secondary outcome 4: proportion of participants satisfied with the products given (cosmetic, preventive, therapeutic properties of the products)

None of the trials in this comparison reported these outcomes.

4.7 Secondary outcome 5: other adverse outcomes: those that are not severe enough to warrant participants to leave the study (e.g. mild irritation or other complaints about products applied in the studies)

None of the trials in this comparison reported these outcomes.

DISCUSSION

Summary of main results

We included nine randomised controlled trials (RCTs) involving 2888 initially randomised participants without occupational irritant hand dermatitis (OIHD) from different occupations. The primary outcomes were signs and symptoms of OIHD developed during the trials, and the frequency of treatment discontinuation due to adverse effects. Six studies including 1533 participants investigated the effects of barrier creams, moisturisers, or both, compared to no intervention. Three studies including 1355 participants assessed the effectiveness of skin protection education on the prevention of OIHD compared to no intervention. Among these four types of intervention, the comparability of the studies was limited since the criteria for assessing signs and symptoms of OIHD, the products, and the occupations varied.

The trials involved metal workers exposed to cutting fluids, dye and print factory workers, gut cleaners in swine slaughterhouses, cleaners and kitchen workers, nurse apprentices, hospital employees handling irritants, and hairdressing apprentices. All studies were undertaken at the respective work places. Study duration ranged from four weeks up to three years. The participants' ages ranged from 16 to 67 years.

We performed four meta-analyses, each comprising a maximum of four trials, for the primary outcome of signs and symptoms of OIHD. The meta-analyses for barrier creams, moisturisers, a combination of both barrier creams and moisturisers, or skin protection education showed imprecise effects favouring the intervention. Barrier creams alone were investigated for metal workers, print and dye industry workers and may have a limited protective effect in these occupations compared to no intervention (Analysis 1.1; low-quality evidence according to GRADE criteria). Moisturisers alone were investigated for metal workers and may have a clinically important protective effect in these occupations compared to no intervention (Analysis 2.1; low-quality evidence). Likewise, there may be a clinically important reduced risk of developing OIHD in participants using a combination of barrier creams and moisturisers (Analysis 3.1; low-quality evidence). We are uncertain whether skin protection education has a protective effect in gut cleaners and nurse apprentices (Analysis 4.1; very-low quality evidence).

Sensitivity analyses showed that the findings concerning barrier creams were robust (Table 1), but the findings concerning the other interventions were not, as the magnitude of the protective effects varied depending on which trials were included (Table 4; Table 6; Table 7).

When we excluded Brüning 2008, the meta-analyses revealed slightly stronger preventive effects of barrier creams (Table 1), and considerably stronger effects of moisturisers (Table 4), or both (Table 6). In this study there might have been some contamination due to the partial split-body design.

No major harmful or other adverse effects were identified. None of the studies addressed the frequency of treatment discontinuation due to adverse effects of the products directly. However, in four studies the dropout reasons were unrelated to adverse effects. The investigated interventions to prevent OIHD probably cause few or no serious adverse effects. The quality of evidence was moderate, according to GRADE criteria.

Although the findings of this review were generally positive, the results were imprecise and the GRADE quality of evidence concerning effectiveness was rated as low or very low. We concluded that there is insufficient evidence, at present, for the effectiveness of most of the interventions identified for preventing new cases of OIHD in the workplace.

Overall completeness and applicability of evidence

There are a number of potential limitations to the applicability of the findings of this review. We identified only a limited number of randomised controlled trials investigating the effectiveness of measures to prevent OIHD under field study settings in different occupations. The lack of studies may be due to the high costs and effort involved in conducting field studies rather than ineffectiveness of primary prevention measures. Also, such studies are not required in order to sell barrier creams and moisturisers as they are classed as cosmetics.

In occupational settings, chronic OIHD is caused by a summation of subclinical exposures. Two of the nine studies we identified were short-term studies (28 and 29 days) providing only limited information on long-term effectiveness. Occupational irritant hand dermatitis is most prevalent in workers who have been exposed to high cumulative irritant damage (Malten 1981). Quite a long observation period is necessary when the effect of protective measures in a field study setting should be evaluated (Bauer 1997; Bauer 1998; Smit 1994; Uter 1998a). Moreover, interindividual differences in susceptibility and regenerative capacities play a major role, indicating an individual threshold for irritation (Agner 1991; Fartasch 1995; Pinnagoda 1989; Rietschel 1997; Tupker 1989a; Tupker 1989b; Kezic 2009).

No RCTs on the use of gloves for preventing OIHD were identified. We speculate that this is mainly because in many occupations it would be unethical to assign participants to a control group without glove use. In practice, guidelines and recommendations on glove use are mainly based on rules and regulations as well as on expert opinion (Mellström 1994).

Apart from OIHD, the review outcomes (including adverse effects) were usually addressed in very few studies, allowing only a narrative description of the findings.

Despite the limited body of evidence, our results do provide information on the effectiveness of barrier creams and moisturisers in primary prevention. However, there is insufficient evidence to make recommendations about their use. The data suggest that protection creams, moisturisers may reduce the risk of developing signs of OIHD to some extent. From the observed confidence intervals, we consider it unlikely for any intervention to reduce the risk to 50% or less. Policy makers, providers and users of primary prevention strategies for OIHD may find this information useful.

Quality of the evidence

For barrier creams, moisturisers, or both, we assessed the quality of evidence (according to GRADE criteria) as low concerning outcome 1 (the proportion of participants developing OIHD). We downgraded our quality assessments for these comparisons by two levels because the results were imprecise and included inconsistent outcomes, as described below (Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3). For skin protection education, we assessed the quality of evidence as very low, according to GRADE criteria (Summary of findings 4). We downgraded our quality assessment for this comparison by three levels because the results were imprecise, included inconsistent outcomes, and were subject to a high risk of bias (the risk ratio may have been underestimated or overestimated). Since only few studies could be included in each comparison and the upper limits of the confidence intervals only barely included 1 (except for barrier creams and moisturisers combined), it is very likely that future research will have an important impact on deciding whether or not the investigated interventions do reduce the risk of developing signs and symptoms of OIHD.

We assessed the quality of evidence for primary outcome 2 (safety) as moderate for all comparisons because the only available data were indirect.

We did not apply the GRADE criteria to the secondary review outcomes because they are not among our key outcomes. Very few data were reported for these outcomes and meta-analyses were not possible.

A variety of scores were assessed and are described in the Characteristics of included studies tables (Brüning 2008; Halkier-Sørensen 1993; Kütting 2010; Meer 2015; Perrenoud 2001a). They either consisted of three categories or were quantitative. In most cases, the scores were apparently developed by the study investigators and not validated. The two exceptions were Kütting 2010, with good to excellent inter- and intra-observer reliability, and Meer 2015, which applied a participant-reported rating which belongs to a validated questionnaire (NOSQ 2002).

TEWL or corneometry (or both) were measured in four studies (Brüning 2008; Goh 1994; Halkier-Sørensen 1993; Perrenoud 2001a). The methods were generally well-described and adequate, but it was not always ensured that the measurements were taken from the exact same skin areas (Brüning 2008; Perrenoud 2001a).

Skin signs and symptoms of OIHD occur after repetitive contact with various irritant factors (known as consecutive subclinical irritation). OIHD develops over an extended period of time (weeks up to months). Therefore extended study periods are necessary. The study period was adequate in the majority of studies: three years (Löffler 2006), one year (Duca 1994; Brüning 2008; Flyvholm 2005; Kütting 2010; Meer 2015), and six months (Goh 1994). However the study period was too short to investigate a long-term protective effect in two studies: 28 days in Halkier-Sørensen 1993, and 29 days in Perrenoud 2001a.

Study limitations (design and risk of bias)

In each of the three comparisons of barrier creams and/or moisturisers, one trial was cluster-randomised without correction (Kütting 2010). For educational programmes two out of three trials lacked appropriate correction for the design effect. We did not

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downgrade our GRADE quality assessments in any of these cases because sensitivity analyses showed that correcting for any value of design effect would not change the conclusion that the preventive effects were not significant.

Across all domains and trials the risk of bias was predominantly unclear. We decided not to downgrade our GRADE quality assessments for the comparisons of barrier creams and/or moisturisers. Biases generally result in more positive effect estimates whereas the observed effects were often small and mostly not significant in the included trials. There was no evidence to lower our confidence in the estimated RRs concerning risk of bias.

For skin protection education, the risk of bias was mainly unclear but was high for some domains. The relative risk may be higher than estimated due to lack of blinding of outcome assessors and baseline imbalances in Flyvholm 2005. On the other hand, RR may be lower than estimated due to an overestimation of OIHD in the intervention group in Meer 2015. We downgraded the quality of evidence of the primary review outcome 1 by one level for this comparison.

Inconsistency of results

Concerning methodological consistency, the diagnostic criteria for the diagnosis of OIHD varied across the included studies. Signs and symptoms of OIHD were assessed by dermatologists (Brüning 2008), by study personnel (Duca 1994; Goh 1994; Halkier-Sørensen 1993; Löffler 2006; Perrenoud 2001a), or by the participants (with a standardised interview, as in Kütting 2010, or with the validated questionnaire NOSQ 2002, as in Flyvholm 2005; Meer 2015). None of the trials was designed to exclude endogenous/atopic hand eczema or allergic contact dermatitis of the hands. Non-occupational hand eczema could not be excluded, either.

The limited number of eligible studies and the even smaller number of studies reporting manifest hand eczema made it necessary to define the key review outcome very broadly and investigate any signs and symptoms of OIHD. Accordingly, the majority of the studies showed methodological weaknesses. A variety of non-standardised semi-quantitative methods were used to assess the key review outcome signs and symptoms of OIHD. In two studies the criteria were not described; four studies reported any irritant skin changes; and three studies had the presence of OIHD assessed by the participant.

Therefore, we downgraded our GRADE assessments of the primary review outcome 1 by one level for all comparisons. This limitation will be an issue until further studies, with more consistently defined outcomes concerning OIHD, are available for subsequent updates of the review.

Another methodological inconsistency concerns the study populations. Occupations varied across trials evaluating barrier creams, and skin protection education, respectively. Moreover, the workers were employed in their respective occupations for varying and often unreported durations. While it is hard to tell whether this introduced a bias, it does lower our confidence in the results. Still, since we already downgraded for methodological inconsistency, we judged that no further downgrade was necessary.

Concerning statistical consistency of the results, two studies showed less positive or even negative effects of their respective interventions, possibly due to their study designs (Brüning 2008; Meer 2015). However, we decided not to downgrade our GRADE ratings of these comparisons further because the inconsistencies were not significant and 95% confidence intervals did overlap. Also, the main problem introduced by statistical inconsistency was the wide confidence intervals. This issue was already considered when we downgraded by one level due to imprecision.

Indirectness of evidence

For signs and symptoms of OIHD, no comparison was downgraded for indirectness of the evidence because the populations, interventions, comparisons, and outcome measures were reported as predefined for the review.

We downgraded the primary review outcome 2 by one level due to the indirectness of the results throughout all comparisons. None of the studies reported directly on treatment discontinuation due to adverse effects. Instead, the extracted results are based on dropout analyses, which did not focus on adverse effects of the interventions. No study reported whether or not treatment was discontinued by participants who did not drop out. For several studies, dropout analyses were not performed or not detailed enough to extract whether or not adverse effects were among the reasons.

Imprecision

None of the comparisons yielded significant results. However, the confidence intervals included 1 as well as clinically relevant RRs of 0.75 or less and were therefore too wide to be certain that the interventions had no impact.

For all comparisons, we downgraded our quality assessments of the evidence for primary review outcome 1 by one level due to imprecision.

Publication bias

An assessment of the reporting bias was not possible (Assessment of reporting biases). We did not downgrade any comparison due to publication bias.

Potential biases in the review process

We did not impose any language restriction and searched the grey literature, proceedings of relevant conferences, and contacted experts of the field. However, we might have missed trials on primary prevention of OIHD, especially those not published because of null or negative findings (publication bias). Therefore potential biases in the review process cannot be excluded.

In this review, we interpreted prevention as meaning interventions applied to healthy people. We chose to investigate the effectiveness of primary preventive measures applied to people who were assessed by the study investigators as not having any signs or symptoms of OIHD. In reality there will be some participants with some level of disease especially when it is very prevalent like dermatitis, or there will be those who have not (yet) asked for medical help because they are not aware that they have a medical problem. We acknowledge that exclusion of studies that were not primary prevention studies, i.e. where some participants had existing OIHD (unless the participant population was mixed and disaggregated data was available for those participants who were healthy with no OIHD at the start of the study), may not

be directly applicable to field conditions. Interventions to prevent worsening or improve existing OIHD are available, but analysis of their effectiveness was outside the scope of this review and should be addressed in a separate systematic review.

Most included studies assessed the proportion of hand eczema. However, other dichotomised data were chosen for the primary outcome 1. Also, the time point varied across studies as we always used data from the last follow-up. The weighting of trials in the meta-analyses led to an over-representation of studies that focused on minor irritant skin changes. The alternative would have been to weight all studies equally. We discarded this option because the primary outcome was any signs and symptoms of OIHD, and because only five of the nine trials assessed hand eczema or hand dermatitis. A related problem was that the confidence intervals of the risk ratios depend on the numbers of cases. This means that confidence intervals tended to be broader in studies which observed OIHD and narrower in studies which observed any irritant skin changes. The results of the meta-analyses must be considered as preliminary.

Subjectivity occurred while judging the risk of performance bias and conducting GRADE quality assessments. One could judge that not blinding the participants introduces only a low risk of performance bias concerning the outcome OIHD (instead of an unclear bias). The risk of attrition bias might as well be judged as high in some cases, but we decided to judge the risk as unclear when the dropout reasons were not distinctly connected to the outcome OIHD. Other researchers might have further downgraded the quality of evidence based on the unclear risk of bias in most trials and domains.

Agreements and disagreements with other studies or reviews

We compared our findings to other reviews in this field of investigation. Individual studies were outside the scope of this overview.

The principles and measures of technical-organisational hazard control and individual protective measures in workplaces where the skin is at risk are well-defined (Halkier-Sørensen 1993; Mathias 1990; Wigger-Alberti 1997). In the available literature, barrier creams and gloves combined with adequate moisturisers are recommended widely as the most important means of personal protective equipment in professions with skin hazards.

In their 2003 review of skin protection creams (barrier creams) for the prevention of occupational dermatitis, Kütting and Drexler identify most of the studies included in our review which were available by that time (Duca 1994; Goh 1994; Perrenoud 2001a, but not Halkier-Sørensen 1993) (Kütting 2003). Moreover, they discuss experimental trials, primary prevention trials, and trials which were not randomised. They argue that it is unclear whether experimental settings are suitable to simulate real workplace conditions. Most clinical trials they identify were too short, did not have a non-intervention control, or were only suited to evaluate therapeutic effects. Similar to our findings, they conclude that they could not answer the question whether or not barrier creams and gloves can prevent or provoke contact dermatitis based on the available data. Concerning the protection of barrier creams against resorption of dangerous substances at the workplace, they conclude that the data was controversial. This question was beyond the scope of our

review. Kütting and Drexler summarised that further studies under workplace conditions were needed in order to give evidence-based recommendations about skin protection measures.

Saary and colleagues systematically reviewed the literature on the treatment and prevention of contact dermatitis (Saary 2005). Their focus is on occupational dermatitis, but experiments and studies involving other populations are included. They found good-quality evidence that certain barrier creams can prevent irritant contact dermatitis. There is also good-quality evidence for the preventive effects of moisturisers, especially with high lipid content. Saary and colleagues could not identify any good-quality studies on educational programmes and found little evidence of their preventive effects. One fair-quality study shows evidence that the use of cotton glove liners prevents from signs of irritant contact dermatitis that originates from wearing occlusive gloves.

Kampf and colleagues reviewed the prevention of irritant dermatitis among health care workers concerning hand hygiene practices (Kampf 2007). They report that there exists category IA (CDC/HICPAC guidelines) evidence concerning the recommendations of hand wash with soap and hand disinfection. The review concludes that healthcare workers should wash their hands with soap and water only as a rare exception, when there is visible soiling. Instead, they recommend to apply alcohol-based hand rubs routinely when the hands have been contaminated. While this question was beyond the predefined comparisons of our review (except as part of an educational programme), the recommendations are highly relevant for the prevention of OIHD in health care workers.

Kütting and Drexler reviewed the efficacy of the three-step programme of skin protection for primary prevention as opposed to secondary prevention (Kütting 2008). While the review focuses on occupational dermatitis, trials involving other populations are not excluded. Kütting and Drexler encourage the avoidance or substitution of hand cleansing, but the evidence they present is very scarce. Based on three studies, Perrenoud 2001a, Berndt 2000, and McCormick 2000, they report no significant benefit of barrier creams compared to vehicles or an oil-containing lotion. They found very weak but undisputed evidence that barrier creams may help in removing contaminations more gently (Mathias 1990). Morevover, they point to adverse effects of barrier creams (increased susceptibility to irritants or allergens), which are reported in four studies. Three studies, which were excluded from our review, also report an increased susceptibility after the use of skin care creams (moisturisers). However, Kütting and Drexler argue that skin care can be used after work without the risk of an increased resorption of working substances. They report that after-work skin care can prevent OIHD in subclinically damaged skin, based on five trials which were not included in our review. They also present four studies which show benefits of educational programmes (excluded from our review). Nevertheless, they conclude that a primary prevention benefit of barrier creams and skin care creams is not yet based on evidence.

With reference to Saary 2005, and some individual studies, Nicholson reports mixed evidence for the protective effects of pre-work (barrier) creams (Nicholson 2010). This paper concludes that some creams may have protective effects, but that pre-work creams are not generally effective in the prevention of OIHD; only scarce information on protective gloves is presented. They found evidence that educational programmes help to reduce the incidence of

occupational hand dermatitis. Only one of the three referenced studies matched our inclusion criteria (Flyvholm 2005). Referring to Saary 2005, and the trial Arbogast 2004, Nicholson et al report that regular application of emollients helps to prevent occupational contact dermatitis.

One systematic review looks at RCTs and controlled clinical trials (CCTs) on primary and secondary prevention strategies of patients who are at risk of hand dermatitis or have signs and symptoms, i.e. their review is not limited to occupational irritant dermatitis (Van Gils 2011). They include only two of the trials that are also included in our review. Their results are hard to compare to those of our review because the outcomes were categorised as 'occurrence' of hand dermatitis, 'adherence to preventive measures', 'clinical outcomes and skin condition' (including signs of hand dermatitis), and 'self-reported outcomes' (including self-reported hand dermatitis). Moreover, the varying preventive strategies were not presented separately. Van Gils et al conclude that there is evidence that preventive strategies are effective for workers at risk for or with hand dermatitis. Our meta-analyses provide only limited support for this assessment.

In Holness 2013, the evidence on occupational dermatitis prevention is briefly reviewed. She identifies systematic reviews and summarises that their results found moderate evidence for the effectiveness of prevention programmes (Saary 2005; Bauer 2010; Nicholson 2010; Van Gils 2011). She also argues that protective creams, while shown to be effective in experimental studies, may be applied in too small amounts in real workplace environments.

Based on the findings of Saary 2005, one paper reports that barrier creams show varying effects in interventional trials (Hines 2017). Referring to Kütting 2008, and Zhai 2006, they judge that recent research does demonstrate the effectiveness of barrier creams. Kütting and Drexler however indicate that only minimal evidence is available for the effectiveness of barrier creams whereas Zhai et al report that there is good evidence from experimental studies. Hines and colleagues also point to the significant benefit reported by Kütting 2010, referring to the outcome 'skin score', whereas the efficacy of barrier creams in this study is substantial but not significant for our primary outcome. Concerning skin care creams (moisturisers), Hines and colleagues consider four studies of primary research. Half of these studies are also included in our review (Goh 1994; Kütting 2010), while the other two are excluded because they are not primary prevention trials (Arbogast 2004; Winker 2009). Hines and colleagues adopt the study investigators' conclusions that skin care creams are beneficial, but they do not report or discuss how the effectiveness is measured.

AUTHORS' CONCLUSIONS

Implications for practice

Low-quality evidence suggests that moisturisers alone or combined with barrier creams may achieve a clinically important protective effect, either in the long- or short-term, for primarily preventing occupational hand dermatitis (OIHD).

Low-quality evidence indicates that barrier creams alone may have a slight protective effect on OIHD, but this does not appear to be clinically important. We are unsure whether the result for educational interventions can be generalised for practical application because of the very low quality of the evidence.

The interventions probably cause few or no serious adverse effects.

There is a complete absence of evidence to support or refute the use of protective gloves in the prevention of OIHD. However, protective gloves are indispensable for personal protection against chemical, biologic and physical hazards in many occupations.

We conclude that at present there is insufficient evidence to confidently assess the effectiveness of interventions used in the primary prevention of OIHD in the workplace. This does not necessarily mean that current measures are ineffective. There is still a need for trials which apply standardised measures for the detection of OIHD in order to determine the effectiveness of the different prevention strategies.

Implications for research

The absence of substantial evidence of efficacy to support specific or complex interventions that are in use for the primary prevention of OIHD does not necessarily imply that they are not effective. Our results indicate that further large randomised controlled trials (RCTs) over extended time periods (six months up to one year) are needed to determine whether complex or single interventions for preventing OIHD in skin risk occupations are working. There is not enough evidence available at present to comment on whether moisturisers, barrier creams, gloves, and other skin protection measures work in real-world wet work settings. Further trials, which are pragmatic (in real-life conditions, to determine if an intervention works or not) and explanatory (in experimental conditions, to determine why and how an intervention might work), could explore the effectiveness of gloves, barrier creams, and moisturisers in different occupational settings with different irritant profiles. Such studies need to include new cases and examine primary prevention strategies in different work places.

In particular, we noticed a lack of RCTs concerning the effectiveness of gloves. While it may often be unethical to prohibit control group participants from using gloves, future studies can evaluate the effectiveness of different gloves, the use of cotton liners, or compare the promoted use of gloves to usual practice.

The agreement on diagnostic criteria of established OIHD are quite clear, but research should be directed to further develop and validate hand dermatitis scoring systems for a better and standardised discrimination of irritant skin changes from irritant contact dermatitis. A standard core outcome set is necessary in order to allow more direct comparisons across studies.

Researchers conducting cluster-randomised trials need to apply a correction for the design effect to their evaluations as well as to their sample size calculations. Published intraclass correlation coefficients (ICCs) are lacking in the context of OIHD. Reporting ICCs would not only improve an individual study's quality, but also provide comparable estimates for planning and evaluating other studies. Even publishing ICCs for trials which are already concluded will be a valuable contribution. Currently, the only available ICC estimate in this context is low (Meer 2015; ICC = 0.005) but may be considerably higher in other studies. Sample sizes for future trials must be inflated accordingly.

Future researchers should be aware that having OIHD assessed by the participants has its strengths and weaknesses. On the one hand, it may be more convenient and it makes it possible to detect OIHD not only at a specific time point, but over a larger range (e.g.

three or six months), which produces more cases and therefore yields higher power. On the other hand, participants are harder to blind in comparison to study personnel. Also, participants of the intervention groups may be more sensitised to spotting OIHD compared to the controls.

In order to facilitate subgroup analyses, researchers should additionally present their data stratified by sex, age (more or less than 30 years), history of atopy and hand dermatitis.

Various in vivo and in vitro methods are in place to investigate the efficacy of skin protective measures under experimental conditions (Boman 1989; Frosch 1994; Gabard 1995; Henry 1994; Mellström 1994; Treffel 1994; Wahlberg 1996; Zimmerli 1996). The results of those experimental studies are not sufficient to forecast the effectiveness of the products under real-life conditions. In skin risk occupations, the controlled conditions of an experimental setting never exist and a variety of irritants and allergens as well as mechanical factors may repetitively impair the skin at the same time or follow each other. Field studies therefore seem to be the best way to ensure that recommendations given are substantiated by evidence. However, field studies incur specific problems like the possible contamination of the groups after randomisation, difficulties with blinding, the necessity of large sample sizes, and changes in compliance because of the presence of the investigator (Coenraads 2003).

In addition, it is challenging to conduct RCTs in the workplace environment. While high-quality evidence is still lacking, it may be helpful to conduct another systematic review with broader inclusion criteria (e.g. experimental trials, non-randomised controlled trials) in order to provide a complete overview of the available evidence. However, data from experimental settings is hardly meaningful to forecast efficacy at workplaces, and the inclusion of controlled clinical trials would lead to an even lower evidence level.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Brüning 2008

Methods	Individually randomised controlled trial
	Combination of parallel and split-body design, 2x2 arms

Brüning 2008 *(Continued)*

Duration: 12 months

3 follow-ups at 3, 6, and 12 months

Participants	**Final number evaluable after 12 months:** N = 96 healthy metal workers exposed to cutting fluids • Group 1 (N = 46): skin protection/no product on randomly allocated hand • Group 2 (N = 50): skin protection + skin care/skin care only on randomly allocated hand **Number of participants randomised:** N = 100 (group 1: N = 50; group 2: N = 50) **Lost to follow-up:** 4 in group 1 **Mean age in years (participants evaluable after 12 months)**: group 1: 35.5 (range 17 to 59); group 2: 41.5 (range 17 to 59) **Sex:** male **Inclusion criteria** • Male • 17-65 years • Exposure to cutting fluids • Forced to mostly work without hand gloves • Written consent **Exclusion criteria** • Female • Fitzpatrick skin type IV, V , VI • Hand eczema during recruitment • Local therapy of the hands • Intake of cortisone or immunosuppressives 3 weeks before recruitment • Absence from factory for 3 months or more **Setting**: one medium-sized German factory
Interventions	Comparison of the effectiveness of skin protection, skin care, or both, versus no intervention (4 study arms, all relevant to the review). The metal workers' hands were randomised to: • Travabon or Stoko Protect (skin protection / barrier cream); • Estolan (skin care/moisturiser); • both; • no intervention. No details on application described, but participants received a flyer and the product. One-sided application using a glove for the other hand. Participants were randomised to use product on either left or right hand.
Outcomes	1. Proportion of OIHD: after 12 months, abnormal morphology ('klinischer Hautbefund') was assessed by study physician. Conspicuous and minor conspicuous findings were extracted as signs and symptoms of OIHD. 2. Treatment discontinuation due to adverse effects: all 4 withdrawals were due to personal reasons. We deduce that there were no cases of treatment discontinuation due to adverse effects. 3. TEWL and skin hydration were extracted (only quartiles, no mean or SD given) 4. Microtopographic parameters (not extracted for this review) All outcomes were measured at baseline, after 3, 6, and 12 months. For the visits at 3 and 6 months, abnormal morphology was not reported while the other outcomes were reported in diagrams of the medians only.

Brüning 2008 *(Continued)*

Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD)

Strengths

- Clinical examination by dermatologists was performed. Good method to assess prevalence of hand eczema.

Limitations

- No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed)
- No exclusion of non-occupational hand eczema

Comparability

- Broad outcome definition -> comparatively many cases expected;
- Time frame: point prevalence

Scoring system for the severity of OIHD: the study investigators applied a score which consisted of 3 categories: *'unauffällige klinische Befundung'* (inconspicuous findings), *'geringfügig auffällige klinische Befundung'* (minor conspicuous findings) and *'auffällige klinische Befundung'* (conspicuous findings).

Strengths

- Blinded: the dermatologist did not know which group the participant belonged to
- Double assessment: a second dermatologist independently assessed a photograph of the skin
- Already minor symptoms were noted

Limitations

- Score not validated for inter- or intra-observer reliability
- Not based on different symptoms or extent of affected area (objective parameters)
- Very subjective

Quality of bioengineering methods (Pinnagoda 1990): the measurements were performed on four defined skin areas (back of the left and right hand, distal part of the volar site of the lower left and right arm) after a 20-minute adjustment phase at a standardised temperature (20°C) and relative humidity (50%). The participants were asked not to take a shower, eat or drink anything and to refrain from smoking within the hour before the measurement. TEWL was measured according to international recommendations (Pinnagoda 1990, Rogiers 2001). For the corneometry, electrical measurements of conductibility (κ), impedance (Ω) and capacity (F) were performed.

Strengths

- Information on the test room is given (temperatures, relative humidity)
- Measurements were taken in a standardized environment (temperature, relative humidity)
- Potentially interfering factors were excluded (shower, food, drinks, smoking)
- An adjustment phase of 20 minutes was allowed before measurements
- Method is well-described

Limitations

- No information is given on the instruments
- Measurements were taken on the back of the hand and the distal part of the volar site of the lower arm. Rather vague information. Does not ensure that measurements were performed always in the exact same area.

Notes	The left/right hand design may have led to failures when applying the products.
	Study funding sources: Vereinigung der Metall-Berufsgenossenschaften (VMBG) (financial, content-related and organisational support)

Brüning 2008 *(Continued)*

Possible conflicts of interest not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described. Quote: 'Während der Erstuntersuchung wurden die Probanden zufällig in zwei Gruppen aufgeteilt. Danach erfolgte in jeder Probandengruppe die zufällige Aufteilung der Probanden in jeweils zwei Interventionsarme (jeweils einer pro Hand).' (p. 7) [At baseline, probands were randomly assigned to two groups. Subsequently in each group of probands, the probands were randomly assigned to two intervention arms each (one for each hand).]
Allocation concealment (selection bias)	Unclear risk	Block randomisation was performed, no details given. Unclear selection bias.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding of participants, participants could have influenced performance by intentionally applying products to the wrong hand. Possible influence on proportion of OIHD.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Physician was blinded.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Low risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Low risk	Only 4 withdrawals, due to personal reasons, in group 1 (control/skin protection).
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes mentioned in the report were reported at least for first and last examination.
Other bias	Unclear risk	**Design:** more than one intervention arm. This was accounted for in meta-analysis. The control group was not double-counted within one meta-analysis. The split-body design may have introduced contamination, especially concerning the control arm. (unclear risk) **Baseline imbalances** • Median age 35.5 in group 1 (skin protection, control) vs 41.5 in group 2 (skin protection + care, skin care) • 2.2% left-handed in group 1 vs 10% in group 2 • Slightly more smokers in group 2 • 13% with known HE in group 1 vs 24% in group 2 **Blocked randomisation in unblinded trials:** block randomisation was performed, no details given. Unclear selection bias.

Brüning 2008 *(Continued)*

> **Differential diagnostic activity:** no different diagnostic activities across study arms.

Duca 1994

Methods	Individually randomised controlled trial Parallel groups, 2 arms **Duration**: 1 year 3 follow-ups at 4, 8, and 12 months
Participants	**Final number evaluable after 12 months**: N = 497 initially healthy dye and print factory workers (intervention: N = 248; control: N = 249) **Number of participants randomised:** N = 868 (intervention: N = 428; control: N = 440) **Lost to follow-up:** N = 211 (intervention: N = 102; control: N = 109) **Excluded from review due to OIHD at beginning of study:** N = 160 (intervention: N = 78; control: N = 82) **Mean age in years (all included participants):** intervention: 32.6; control group: 32.1 **Sex:** 91% male, balanced between groups **Mean duration of employment (all 868 participants)**: barrier cream and control group, 7.9 years **Inclusion criteria**: dye and print industry workers **Exclusion criteria**: other dermatological disease on the hands **Setting**: field study in 13 dye and print factories, North Italy
Interventions	Comparison of the effectiveness of: • barrier creams 2 x/day (silicone or hydrocarbon containing formulations) versus; • no intervention. The workers were randomised to receive either the barrier creams (silicone or hydrocarbon containing barrier creams), which they used twice a day for 1 year, or no intervention.
Outcomes	1. Proportion of OIHD: positive objective exam for at least one follow-up. Presence of the following skin changes: erythema, edema, exudation, vesicles, blisters, desquamation, hyperkeratosis, rhagades, dryness, atrophy, lichenisation. ('Positività all'esame obiettivo in almeno un controlo.' p. 235; 'In particolare l'esame obiettivo consisteva nel rilevare la presenza di lesioni dermatologiche a mani e avambracci distinguendo: eritema, edema, essudazione, vescicole, bolle, desquamazione, ipercheratosi, ragadi, secchezza, atrofia, lichenificazione.' p. 233) Assessments took place after 4, 8, and 12 months. **Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD):** objective skin lesions assessed by study personnel (erythema, edema, exudation, vesicles, blisters, desquamation, hyperkeratosis, rhagades, dryness, atrophy, lichenisation) Strengths • Clinical examination by physicians who were trained by a dermatologist was performed. Good method to assess prevalence of hand eczema. Limitations

Duca 1994 *(Continued)*

- No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed)
- No exclusion of non-occupational hand eczema

Broad outcome definition -> comparatively many cases expected

Time frame: combined incidence at 4, 8, or 12 months

Scoring system for the severity of OIHD: no score assessed
Quality of bioengineering methods (Pinnagoda 1990): not relevant

| Notes | **Study funding sources**: Not described. |
| | **Possible conflicts of interest:** Not described. |

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: 'La procedura di randomizzazione.....base di una sequenza di numeri casuali' (p. 233) [The randomisation procedure ... based on a sequence of random numbers] Matched pairs were used in order to achieve balanced groups.
Allocation concealment (selection bias)	Unclear risk	Inadequate concealment of the allocation sequence may have resulted from pairwise assigning the first person of the pair to group A if the random number was even, to group B if odd. The second person of the pair was assigned to the alternative group. Efforts to conceal the allocation were not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants remains unclear.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Quote: 'Controllo clinici periodici ....all`oscuro del gruppo' [Periodical clinical examination ... blinded to group] - Outcome assessors were blinded.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Low risk	TEWL and corneometry were not measured.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Unclear risk	12 months follow-up: 102 missing from the barrier cream group, 109 missing from the control group due to dropout and unavailability at the examination time points. The study investigators did mention ITT analysis but this merely meant that compliance was ignored. Missing values were not estimated. Dropout was due to the long duration of recruitment and due to workers leaving the factories, but there was no detailed analysis.
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	Insufficient information.
Other bias	Low risk	**Design:** no sources of bias were identified.

Duca 1994 *(Continued)*

Baseline imbalances: demographic data of participants were only available for the entire study population (N = 868). It remains unclear whether the demographic characteristics of the initially healthy workers from intervention and control group (N = 708) differed significantly in this study (low risk)

Blocked randomisation in unblinded trials: not enough information was given to decide whether or not allocation concealment was broken by the pairwise allocation. (unclear allocation concealment bias)

Differential diagnostic activity: no different diagnostic activities across study arms.

Flyvholm 2005

Methods	Cluster-randomised controlled trial; 18 clusters (departments)
	Parallel design, 2 arms
	Duration: 1 year
	1 follow-up at 1 year
Participants	**Final number evaluable after 12 months:** N = 212 initially healthy Danish gut cleaners (intervention: N = 59; control: N = 153)
	Number of participants randomised: N = 644 baseline responders (intervention: N = 205; control: N = 439)
	Lost to follow-up: N = 228 were lost to follow-up or stopped working as gut cleaners (intervention: N = 69; control: N = 159)
	Excluded from review due to OIHD at beginning of study: N = 204 (intervention: N = 77; control: N = 127)
	Mean age in years (all follow-up respondents including those with OIHD at baseline and those not available at baseline): intervention: 36.1 (range 17-62 years); control: 37.8 (range 17-66)
	Sex: 66.3% male (intervention), 64.1% male (control)
	Inclusion criteria: not described
	Exclusion criteria: not described
	Setting: field study in 18 swine slaughterhouses in different Danish cities, all departments belonging to one company
Interventions	Comparison of the effectiveness of a:
	• prevention programme, versus
	• comparison group (probably no intervention).
	The prevention strategy consisted of a two part concept, with an evidence based prevention programme giving recommendations for prevention of work related skin problems in wet work occupations, and a documented method for implementation. The recommendations were aimed at the management and at the employees.
	• Avoid or reduce wet and dirty manual working procedures.
	• Use protective gloves for wet and dirty working procedures, if possible.
	• Protective gloves must be intact, clean, and dry inside and must be worn on clean, dry, and well cared for skin.
	• Use fabric gloves, e.g. cotton gloves underneath the protective gloves.

Flyvholm 2005 *(Continued)*

- Use a skin care product when needed during the working day and always after work.
- Use a skin care product before wet and dirty working procedures if you do not use protective gloves.
- The skin care product should have a high content of petrolatum and a low content of water.
- Do not wear finger rings, jewellery, or wristwatch on hands or forearms during work.
- Wash your hands in cool water, rinse off the soap thoroughly, and dry your hands carefully with a soft material afterwards.
- When there is no visible contamination of the hands, hand washing can with advantage be substituted by an alcohol based hand disinfectant.
- Protective gloves, hand soaps, skin care products, and hand disinfectants should be without known irritant and allergic substances or with lowest possible content of them (p. 643).

The local project group included 2-5 gut cleaners who acted as role models.

Outcomes	1. Proportion of OIHD (hand eczema): The case definition for eczema was: eczema on hands or forearms within the past three months based on questions D1, D2, and D5 of NOSQ 2002 (telephone interview). Assessed at 12 months. 2. Use of gloves, use of cotton gloves underneath plastic/rubber gloves, and use of skin care products were not extracted for this review. **Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD)** Strengths - The questions used to assess the prevalence of hand eczema belong to a validated questionnaire (NOSQ 2002). Limitations - Self-reporting of hand eczema underestimates the true prevalence of hand eczema. Especially mild changes are often not reported. - No differentiation between hand eczema and eczema on the forearms - No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed) - No exclusion of non-occupational hand eczema Comparability - relatively narrow outcome definition - time frame: period prevalence: last 3 months -> comparatively many cases expected **Scoring system for the severity of OIHD:** no score assessed **Quality of bioengineering methods** (Pinnagoda 1990): not relevant
Notes	79 participants had stopped working as gut cleaners and were analysed as a separate group in the report regardless of the intervention. For this review, they were not considered and treated as dropouts. Demographic data were only available for participants who were not lost to follow-up, including those with OIHD at baseline. There was a mistake in the paper concerning primary outcome 1, which MA Flyvholm corrected in an email (05/052015): 'For the intervention group (corrected: comparison group), 67% of those with eczema at baseline reported eczema at follow up and 33% no eczema; 37% with no eczema at baseline reported eczema at follow up.' (p. 646) **Study funding sources**: 'The project was financially supported by an appropriation for prevention of asthma and allergy, administered by the Danish Ministry of Health.' (p. 648) **Possible conflicts of interest:** none declared.

Risk of bias

Flyvholm 2005 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described ('randomly allocated' p. 643).
Allocation concealment (selection bias)	Unclear risk	Method not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding, possible influence on proportion of OIHD.
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	No blinding likely to influence reporting of OIHD.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Unclear risk	TEWL and corneometry were not measured.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Unclear risk	149 participants (23,1%) lost to follow-up, an unspecified number of which (max. 51) dropped out without stating reasons.
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	Insufficient information.
Other bias	High risk	**Design:** no correction for cluster randomisation -> no bias, but over-precise results and limited comparability.
		Baseline imbalances
		• Significantly less OIHD (eczema on hands/forearms in the previous 3 months) in comparison group, study investigators explain this with the more frequent use of gloves in one comparison department -> high risk
		• Those who stopped as gut cleaners had worked as such for a shorter time -> probably no bias
		Blocked randomisation in unblinded trials: no block randomisation reported.
		Differential diagnostic activity: no different diagnostic activities across study arms.

Goh 1994

Methods	Individually randomised controlled trial
	Parallel groups, 3 arms
	Duration: 6 months (also reported as 30 weeks) for each participant, 3 years altogether

Goh 1994 *(Continued)*

	3-weekly follow-ups
Participants	**Final number evaluable after 6 months:** N = 54 initially healthy, newly employed metal workers exposed to cutting fluids (barrier cream: N = 17; moisturiser: N = 14; control: N = 23)
	Number of participants randomised: N = 54
	Lost to follow-up: N = 0
	Mean age in years: barrier cream group: 22 (range 16 to 37); moisturiser group: 22 (range 16 to 36); control: 22 (range 17 to 35)
	Sex: 50 out of 54 male
	Exclusion criteria: 'Only machinists who had not handled cutting fluids previously were included in the study. Machinists who had already worked for more than I week were excluded.' (p. 177)
	Setting: field study in the grinding and turning sections of one large ball-bearing manufacturing factory, Singapore
Interventions	Comparison of the effectiveness of: • a barrier cream Arretil (Stockhausen, Germany); 3 to 4 x /day, and • an after work moisturiser Keri Lotion (Westwood Pharmaceuticals, USA); 1 x after work, versus • no intervention. The participants were randomised to receive either a barrier cream (60 g tube every 6 weeks used on the hands before work and after each meal break), or a moisturiser used daily as an after work emollient, or no intervention. Arretil is a water-soluble, non-oily, silicone-free barrier cream. Keri lotion is a liquid paraffin lotion (16%) and contains lanolin oil. The participants were followed up every 3 weeks for 6 months.
Outcomes	1. Proportion of OIHD (as defined by the study investigators): 'All cases of cutting fluid dermatitis were diagnosed clinically as irritant contact dermatitis' (p. 178). Dermatitis was assessed 'arbitrarily' (p. 177) and 'cutting fluid dermatitis was diagnosed on the history and clinical findings' (p. 177) (which probably meant the arbitrary assessment of dermatitis). The study investigators probably counted a subject as a case when irritant contact dermatitis was diagnosed at any of the 3-weekly follow-ups (combined point prevalence): 'Machinists who developed cutting fluid dermatitis (cases) and those who did not (non-cases)' (p. 178). This was measured from week 1 to 12 and subsequent 18 weeks and extracted only for the last 18 weeks. 2. The secondary outcome measures was the amount of skin barrier impairment (TEWL) in the groups (mean and SD). 3. Frequency of treatment discontinuation due to adverse effects: No dropouts reported. **Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD):** classification of dermatitis severity: mild = less than 25% of the total surface area of either hand involved (up to wrist line), moderate = more than 25% of the total surface area of either hand involved (up to wrist line). Strengths • Clinical examination was performed. Good method to assess prevalence of hand eczema. Limitations • No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed) • No exclusion of non-occupational hand eczema Comparability • Relatively narrow outcome definition

- Time frame: probably combined incidence at any weekly follow-up -> comparatively many cases expected

Scoring system for the severity of OIHD: no score assessed

Quality of bioengineering methods (Pinnagoda 1990): 'Baseline TEWL measurement was made on the skin overlying the dorsal 3rd metacarpophalangeal (MCP) joint of both hands with an Evaporimeter (Servomed, Vallingby, Sweden). We chose the 3rd MCP joint because of the ease of identifying the exact spot for repeat measurements. We conducted a pilot measurement on mid-dorsal hand, 1st, 3rd, 5th dorsal MCP joints, mid-ventral forearms and mid-dorsal forearms on the 1st 30 volunteers. All showed fairly consistent recordings. We found the 3rd dorsal MCP joints to have the highest TEWL recordings and that these were fairly consistently reproducible. The method of TEWL measurement was as follows. The machinist rested in the examination room for 10 to 15 min. The TEWL on the dorsal 3rd MCP joint of each hand was then measured. TEWL values on the left hand followed by those on the right hand were recorded. The procedure was repeated once. 2 recordings of TEWL values for each hand were thus obtained; the average was recorded.' (p. 177)

Strengths

- Information is given on instrument (Evaporimeter, Servomed, Vallingby, Sweden) and the test room (temperatures, humidity)
- TEWL measurements were taken in a standardized environment (draft-free, air-conditioned)
- Measurements were always taken from the same skin area
- Method is well-described

Notes	Groups were comparable at baseline.
	No dropouts
	Study funding sources not described. ('A research grant was obtained.' p. 176)
	Possible conflicts of interest not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: 'Machinists were randomly assigned.' (p. 177). No further information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants were not blinded to the intervention because original samples of the products were supplied. Possible influence on proportion of OIHD.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	No information provided on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Low risk	No influence of blinding is expected for the objective measurement of TEWL. Corneometry was not measured.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Low risk	No dropouts reported in either group.

Goh 1994 *(Continued)*

Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	All outcomes reported. No protocol available.
Other bias	Unclear risk	**Design:** participants were recruited consecutively (when they started work) over a period of 3 years, in which the work conditions and exposures might have been changed -> unclear bias
		More than one intervention group. This was accounted for in meta-analysis. The control group was not double-counted within one meta-analysis.
		Baseline imbalances: baseline imbalance regarding turning vs grinding section: controls - 14 vs 9; barrier cream - 8 vs 9; emollient cream - 4 vs 10 -> unclear bias
		Blocked randomisation in unblinded trials: no block randomisation reported
		Differential diagnostic activity: no different diagnostic activities across study arms

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Halkier-Sørensen 1993

Methods	Individually randomised controlled trial Cross-over design, 2 arms
	Duration: 2x2 weeks
	2 follow-ups (at 2 and 4 weeks or at time of dropout)
Participants	**Final number completing the 2x2 weeks**: N = 70 initially healthy cleaners and kitchen workers
	Number of participants randomised: N = 111 (N = 56 started with moisturiser; N = 55 started with no treatment)
	Lost to follow-up: N = 41
	Mean age in years (groups I, II, III): 41 (range 19 to 67)
	Mean duration of employment (groups I, II, III): 10 (range 1 to 35) years
	Sex: 110 out of 111 included participants were female.
	Setting: field study, Denmark
Interventions	Comparison of the effectiveness of:
	• a moisturiser Locobase (Ferndale Laboratories, USA); • versus no treatment
	in a 2x2 weeks cross-over design. Application requirements were not described. Locobase, manufactured by Ferndale Laboratories, USA, is a wound and skin emulsion formulation intended for topical application. No details were given about the composition of the cream.
Outcomes	The study investigators reported the results after grouping all participants in 4 groups according to their ability to complete the 4 week study. Finally, only results of groups I and II were reported.

Halkier-Sørensen 1993 *(Continued)*

Comparisons of intervention vs no treatment were only reported for corneometry, TEWL, and sum score in groups I and II

- Group I, N = 70, completed both periods Locobase (L) and Control (C).
- Group II, N = 23, completed L, but dropped out of in period C after developing severe dryness of the skin.
- Group III, N = 12, violated the protocol or declined to continue the study because they developed or feared to develop hand dermatitis during period C.
- Group IV, N = 6, turned up only once, did not find Locobase acceptable or went on vacation.
1. Proportion of skin changes (dryness only, dryness and scaling) and OIHD (dry eczema)
2. Biometric methods: corneometry values, TEWL (only figures and P values)
3. Subjective opinion
4. Mild adverse effects
5. A sum score was assessed, but not reported separately for incident cases of OIHD. This outcome does therefore not fit the review's outcomes (not extracted).

Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD): the degree of certainty could not be assessed because no diagnostic criteria for OIHD were described.

Scoring system for the severity of OIHD

- Clinical signs and symptoms assessed: Itching, dryness, scaling, fissuring, erythema, vesiculation
- Localisation of eczema assessed: fingers, hands, wrists, arms
- Severity rating: 1 = mild, 2 = moderate, 3 = severe
- Sum Score: multiplication of the severity ratings of all symptoms and sites (highest possible score: 8 (sites) x 7 (symptoms) x 3 (rating for severity) = 168

Strengths

- Contains different symptoms and severity rankings

Limitations

- Score not validated for inter- or intra-observer reliability
- Contains a parameter (itching) which is self-reported by the participant
- Extent of affected area is not assessed for each site

Quality of bioengineering methods (Pinnagoda 1990): 'Skin surface temperature (digital thermometer, Ellab type TRD, probe diameter 12 mm), transepidermal water loss (TEWL) (Evaporimeter EPI, Stockholm, Servomed, Sweden), and electrical capacitance (Corneometer CM420, Schwarzhaupt, W. Germany) were measured on both the right and left side and on the volar and dorsal aspect of the distal part of the 3rd finger, middle of the hands, and on the forearms (12 measurement points). The results are presented as overall mean values (the mean values for all measurements on all sites). All probes were hand-held. The measurements were performed in a separate room with minor draught and protection shields. The mean room temperature was 23°C (20-26°C) and the mean relative humidity (RH) 34% (25-42%).' (p. 267).

Strengths

- Information is given on instruments and the test room (temperatures, humidity)
- Measurements were taken in a standardized environment (minor draught and protection shields)
- Measurements were always taken from the same skin areas
- Method is well-described

| Notes | The study investigators did not report the results according to the groups randomised, but regrouped all participants in 4 groups according their ability to complete the 4 week study period.

Therefore not included in meta-analysis. |
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Halkier-Sørensen 1993 *(Continued)*

Study funding sources: 'The study was supported by the Danish Insurance Association, Copenhagen, L. P. Hansen's fund,
Odense, and Danfoss A/S, Nordborg, Denmark.' (p. 270)

Possible conflicts of interest not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: 'They were randomised into 2 groups' (p. 267). No further information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants were not blinded due to study design.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Blinding of outcome assessors was probably not done. Quote: 'Clinical examination and skin physiological measurements were performed on entry...' (p. 267).
Blinding of outcome assessment (detection bias) TEWL and corneometry	Unclear risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	High risk	N = 23 dropped out in period C after developing severe dryness of the skin, N = 12 violated the protocol or declined to continue the study because they developed or feared to develop hand dermatitis, N = 6 turned up only once, did not find Locobase acceptable, or went on vacation.
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	Dropout analysis did not address this outcome conclusively.
Selective reporting (reporting bias)	High risk	Results were not reported according to the original randomisation, but according to the ability of the participants to complete the study period. This was an attempt to deal with the high risk of attrition bias. Consequently, the results were not reported in a way appropriate for an RCT.
Other bias	High risk	In-study use of moisturiser was twice as high in participants who dropped out in the no-treatment period (N = 23) compared to the participants who completed both parts of the study (2.3 g/person/day versus 1.2 g/person/day). **Design:** cross-over -> unclear bias **Baseline imbalances:** pre-study use of moisturiser differed significantly between the groups despite randomisation (96% versus 82%, P < 0.01). -> high risk **Blocked randomisation in unblinded trials:** no block randomisation reported. **Differential diagnostic activity:** not applicable because study arms were not evaluated separately.

Kütting 2010

Methods	Cluster-randomised controlled trial; 18 clusters (enterprises)
	Parallel design, 4 arms
	Duration: 12 months
	2 follow-ups at 6 and 12 months
Participants	**Final number evaluable after 12 months**: N = 800 initially healthy metal workers exposed to cutting fluids (group 1: N = 217 in 6 enterprises; group 2: N = 209 in 5 enterprises; group 3: N = 213 in 4 enterprises; control: N = 161 in 3 enterprises)
	Number of participants randomised: N = 1020 (group 1: N = 263; group 2: N = 253; group 3: N = 258; control: N = 246)
	Lost to follow-up: N = 220 (21.6%) withdrawal/exclusion at 2nd follow-up (group 1: N = 46; group 2: N = 44; group 3: N = 45; control: N = 85)
	Median age (all included participants): group 1: 40; group 2: 40; group 3: 44,5; control: 42
	Sex: male
	Inclusion criteria
	• Male
	• Age >= 18 y
	• Regular exposure to cutting fluids
	• Working contract for one further year at minimum
	• Fitness for work at randomisation
	• Willingness to comply
	Exclusion criteria:
	• Manifest hand eczema
	• Intake of immunosuppressive drugs or topical application of corticosteroids or of other immunosuppressive agents on the hands
	Setting: German factories mainly of small or medium-size
Interventions	Comparison of the effectiveness of skin protection and/or skin care creams vs no recommendation in a 4-armed trial
	• Group 1: 'skin protection programme as generally recommended (i.e. use of skin protection and skin care)' (p. 363). Timing not explicitly stated, but obviously skin protection (barrier cream) before or during work and skin care (moisturiser) after work.
	• Group 2: 'use of skin protection creams before or during working hours but complete avoidance of postexposure skin care' (p. 363)
	• Group 3: 'use of skin care products solely after work' (p. 363)
	• Group 4: 'The control group did not receive any recommendations concerning the use of skin protection or skin care.' (p. 363) (Only 31.4% used neither skin protection nor skin care after 6 months, 25.5% after 12 months. However, the participants were **not** instructed to avoid these measures.)
	Pragmatic approach: 'All participants used the skin care and protection products provided by the employer.' (p. 363).
Outcomes	1. Proportion of OIHD: Dermatological history (hand eczema) in the last 6 months as reported by the participant in a standardised personal interview. This was also reported for the first 6 months, but not extracted for this review.

Kütting 2010 *(Continued)*

2. Severity was rated in a skin score, but not reported separately for incident cases of OIHD. This outcome does therefore not fit the review's outcomes (not extracted).

Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD)

Strengths

- Standardised interview

Limitations

- Self-reporting of hand eczema underestimates the true prevalence of hand eczema. Especially mild changes are often not reported.
- No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed)
- No exclusion of non-occupational hand eczema

Comparability

- Relatively narrow outcome definition
- Time frame: period prevalence: last 6 months -> comparatively many cases expected

Scoring system for the severity of OIHD: percentage change of skin score as primary outcome and relative change from baseline as secondary outcome: 'A quantitative skin score was used. In brief, the score comprised all morphological criteria and physiological abnormalities (e.g. dryness) characteristic of hand eczema. Extent, intensity and anatomical site of each type of skin lesion were also recorded.' (pp. 363-4).

'All three physicians underwent standardized training before using the score. Moreover, during the study period digital photographs of the hands of randomly chosen participants were regularly evaluated and results discussed in order to maintain similarity of visual assessments between observers.' (p. 366).

Strengths

- Dermatologist were trained in using the score before start of study
- Good to excellent inter- and intra-observer reliability
- Quantification of minimal skin lesions

Quality of bioengineering methods (Pinnagoda 1990): not relevant

Notes	Primary intervention: no inclusion of workers with manifest hand eczema (despite high baseline values on their very sensitive score). This was confirmed through correspondence with H Drexler.	
	Study funding sources: 'The study was funded by the German Statutory Accident Insurance (DGUV) and the Franz-Koelsch-Stiftung e.V.' (p. 369).	
	Possible conflicts of interest: none declared	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: 'Randomization was performed on the basis of the 19 included enterprises, assigning each enterprise randomly to one of four study arms.' (p. 363) Apparently, an undescribed method was applied to ensure approximately equal size of the groups despite varying numbers of workers per enterprise.
Allocation concealment (selection bias)	Unclear risk	It cannot be excluded that allocation was biased by the results of the baseline screening. Potential confounders differed significantly at baseline. Even though the study investigators do not report significant associations with their

Kütting 2010 *(Continued)*

outcomes, they did not test the association with review outcome 'proportion of OIHD'. Baseline skin condition was better in the control group, thus allowing less improvement after 1 year compared to other groups.

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding reported; possible to influence proportion of OIHD.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Blinding of participants (= outcome assessors) was probably not done. This would be likely to influence reporting of OIHD, but clear information on blinding is lacking.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Unclear risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Unclear risk	78.4% of recruited participants were available at last follow-up (1 year), no analysis of dropouts. Attrition in control was 2x as high as in other groups. 'High risk' judgement was therefore considered but discarded because dropout reasons are unknown.
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	Skin score was presented in various ways: percentage change of skin score as primary outcome, categorized percentage change as secondary outcome; further outcomes including absolute change of skin score were reported. This is questionable, but at least the study investigators did not omit their less significant calculations. No protocol available
Other bias	High risk	**Design:** no correction for cluster randomisation -> no bias, but over-precise results and limited comparability. More than one intervention group. This was accounted for in meta-analysis. The control group was not double-counted within one meta-analysis. **Baseline imbalances:** significant differences of potential confounders and dyshidrotic eczema, but not of other dermatological disorders. It remains unclear whether this was due to lack of allocation concealment or happened by chance and was worsened by the cluster design -> high risk of bias **Blocked randomisation in unblinded trials:** no block randomisation reported. **Differential diagnostic activity:** no different diagnostic activities across study arms.

Löffler 2006

Methods	Cluster-randomised controlled trial; 14 clusters (nursing schools) Parallel groups, 2 arms **Duration**: 3 years

Löffler 2006 *(Continued)*

2 follow-ups at 1.5 and 3 years

Participants	**Final number evaluable after 3 years**: N = 250 initially healthy 1st-year nurse apprentices (intervention: N = 121; control N = 129)
	Number of participants randomised: N = 521 (numbers of participants allocated to groups were not reported)
	Lost to follow-up: N = 196 (37.6%; dropout per group was not reported)
	Excluded from review due to OIHD at beginning of study: only the number of healthy participants who were evaluable were provided (N = 250). This included participants who had OIHD at least at 1 follow-up before they dropped out.
	Mean age in years (all included participants): intervention: 20.9 (SD 4.9); control: 23.6 (SD 7.7)
	Sex: 13% male (intervention), 12% male (control)
	Mean duration of employment: 0 years, baseline examination was before beginning of the nurse training
	Inclusion criteria: not described **Exclusion criteria**: not described
	Setting: field study in 14 nursing schools (general nurses, paediatric and geriatric nurses, midwifes), Central Germany
Interventions	Comparison of the effectiveness of a: • training program, versus • no intervention The intervention group received regular training (educational lecture with practical parts), and skin care cream (Asche Basis Creme). The lectures took place 3 times in the first year, 2 times in the second and third year. The nurse apprentices were encouraged to use alcoholic hand disinfection instead of hand washing or scrubbing. The effect of applying skin care cream was assessed by the use of a fluorescence technique with the Dermalux-system as part of the training. Participants in the control group also received the skin care cream.
Outcomes	1. Proportion of OIHD (abnormal morphology = irritant skin changes during apprenticeship) defined as the occurrence of at least 1 morphology category at 1.5 or 3 years, or both 2. Frequency of treatment discontinuation due to adverse effects: study investigators state that dropouts were not due to skin problems **Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD):** Irritant Skin changes were recorded using the operational definitions of Uter 1998b. Strengths • Clinical examination by physician. Good method to assess prevalence of hand eczema. • Differentiation between mild changes and hand eczema ('moderate' or 'severe') Limitations • No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed) • No exclusion of non-occupational hand eczema Comparability • Broad outcome definition -> comparatively many cases expected • Time frame: combined incidence at 1.5 years, 3 years (or both). No information on hand eczema in between.

Löffler 2006 *(Continued)*

> **Scoring system for the severity of OIHD:** no scores assessed
> **Quality of bioengineering methods** (Pinnagoda 1990): not relevant

Notes	Demographic data and dropout rates were only available for the entire study population of 521 nurse trainees.
	Study funding sources: 'This work was generously supported by a grant from Asche Chiesi GmbH, Hamburg, Germany.' (p. 207)
	Possible conflicts of interest: not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: 'Randomly divided' (p. 203); details not described
Allocation concealment (selection bias)	Unclear risk	Method not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants unclear, possible influence on proportion of OIHD.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Evaluation of skin changes was performed by 2 blinded physicians.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Unclear risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Low risk	Quote: 'The dropout rate was 37.6% which was not due to skin problems, but due to their absence because of illness at the date of evaluation.' (p. 204) Quote: 'For follow up of dropouts, we performed a telephone interview with the trainee or (if he could not be reached) with his teacher. The aim of this interview was to evaluate, whether or not skin changes were responsible for the dropout.' (p. 204) Low bias because the study investigators convincingly explain that they ensured no dropout was related to hand eczema
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Low risk	**Design:** no correction for cluster randomisation -> no bias, but over-precise results and limited comparability. **Baseline imbalances:** no imbalances **Blocked randomisation in unblinded trials:** no block randomisation reported

	Differential diagnostic activity: no different diagnostic activities across study arms

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Meer 2015

Methods	Cluster-randomised controlled trial; 48 clusters (hospital departments)
	Parallel design with different recruitment dates, 2 arms
	Duration: 12 months
	4 follow-ups at 3, 6, 9, and 12 months
Participants	**Final number evaluable after 12 months**: N = 981 initially healthy hospital employees handling irritants during work (intervention: N = 559; control: N = 422)
	After correction for ICC = 0.005: N = 893 initially healthy hospital employees handling irritants during work (intervention: N = 509; control: N = 384)
	Number of participants randomised: N = 1649 (intervention: N = 876; control: N = 773)
	Excluded from review due to OIHD at beginning of study: N = 144 (intervention: N = 64; control: N = 80)
	Lost to follow-up: N = 524 (intervention: N = 253; control: N = 271) out of the 1505 initially healthy participants
	Mean age in years (all included participants): intervention: 40.07 years, SD 11.5; controls: 40.8 years, SD 11.3
	Sex: 78.4% female (intervention), 78.3% female (control)
	Inclusion criteria
	• Being employed at one of the participating hospitals
	• Being able to fill out Dutch questionnaires
	• Being aged between 18 and 64 years
	• Working for at least 8 hr weekly
	Exclusion criteria: not handling irritants during work
	Setting: field study in 48 hospital departments (different cities in the Netherlands)
Interventions	Comparison of the effectiveness of:
	• a multifaceted implementation strategy, versus
	• leaflet only
	The multifaceted implementation strategy included participatory working groups, role modes, educational programme including reminders, and a leaflet. The main recommendations were:
	'1. When there is no visible contamination of the hands, use an alcohol-based hand disinfectant instead of water and soap to disinfect the hands* 2. Wear gloves when performing wet work 3. Wear cotton undergloves when you wear gloves for longer than 10 min 4. Use a moisturizer on a daily basis to nurse the skin and do not use a body lotion 5. Do not wear jewellery at work 6. Perform as little wet work as possible

Meer 2015 *(Continued)*

* This means that the use of disinfectant should be increased and the use of water and soap should be decreased.' (p. 3)

All workers who were present at the educational session received a bag with one moisturiser, a pair of cotton undergloves, and two disinfectants (no product names or details reported). The intervention went on for 4 months. The comparison group received only the leaflet.

Outcomes	1. Proportion of OIHD (hand eczema in the past 3 months) as measured with the Nordic Occupational Skin Questionnaire – 2002 (NOSQ 2002): Defined as answering 'yes' to question D1 (ever had HE) or D2 (ever had eczema on wrists or forearms), and choosing one of the following answer categories for question D5: 'I have it just now' or 'Not just now, but within the past 3 months'. Assessed at 3, 6, 9, and 12 months
	2. A healthy skin score was assessed, but not reported separately for incident cases of OIHD. This outcome does therefore not fit the review's outcomes (not extracted).
	Study investigators did not evaluate healthy skin score separately for participants **in incident cases** (as defined as review outcome).
	Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD)
	Strengths
	• The questions used to assess the prevalence of hand eczema belong to a validated questionnaire (NOSQ 2002).
	• Questions cover 3-months-period
	Limitations
	• Self-reporting of hand eczema underestimates the true prevalence of hand eczema. Especially mild changes are often not reported.
	• No differentiation between hand eczema and eczema on the forearms
	• No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed)
	• No exclusion of non-occupational hand eczema
	Comparability
	• Relatively narrow outcome definition
	• Time frame: period prevalence (last 3 months) -> comparatively many cases expected
	Scoring system for the severity of OIHD: 'Workers assessed the health of the skin on their hands by means of the following question: 'How would you judge the health of your hands/forearms at the moment on a scale from 0 to 10?' (0, unhealthy skin; 10, healthy skin). This question was based on question D12 of the NOSQ-2002.' (p. 4)
	Strengths
	• Standardised questions that belong to a validated questionnaire (NOSQ 2002)
	Limitations
	• Self-reporting is less accurate than clinical examination by a physician
	• Very subjective, no objective parameter
	Quality of bioengineering methods (Pinnagoda 1990): not relevant
Notes	Demographic data and only reported for the study population including those with hand eczema at baseline.
	Contingency table and dropouts were calculated based on the raw data received from the study investigators.

Meer 2015 *(Continued)*

Study funding sources: 'This study was supported by a grant from the Netherlands Organization for Health Research and Development (ZONMW).'

Possible conflicts of interest: none declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: 'Based on the sequence of inclusion, randomisation was performed in strata of two by an independent researcher.' (Meer 2011, p. 3)
Allocation concealment (selection bias)	Unclear risk	Not described. Randomisation took place before baseline measurements by an independent researcher and was stratified by cluster-based criteria. The study investigators excluded 17 out of 1666 baseline responders after randomisation.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: 'Workers were not informed about the design of the study and outcome of randomisation.' (pp. 2-3) No blinding of personnel and department managers is expected to introduce only a low risk.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	OIHD was self-reported and participants were blinded.
Blinding of outcome assessment (detection bias) TEWL and corneometry	Unclear risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Unclear risk	Only superficial analysis of dropouts, reasons for dropout unknown. Quote: 'Another limitation was that there was a non-response rate of >30% at the final follow-up measurement. However, the differences between the baseline values of the non-responders and the baseline values of the total population were minimal.' (p. 11)
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Low risk	Primary study outcome predefined in strategy and reported; secondary study outcomes predefined in strategy.
Other bias	Unclear risk	**Design:** no correction for cluster randomisation -> no bias, but over-precise results and limited comparability. **Baseline imbalances (whole study population including participants with HE at baseline)** • In the intervention group 7.3% had HE at baseline compared to 10.3% in control group. • In the intervention group, 69.4% performed patient related tasks compared to 81.2% in control group. • In the intervention group, 57.4% had high education compared to 51.7% in control group. • -> probably no strong impact on HE **Blocked randomisation in unblinded trials:** no block randomisation reported

Differential diagnostic activity: study investigators speculate that participants of the intervention group are more aware of HE and were therefore more likely to report them: 'The educational session given during the intervention period might have increased awareness among the participants in the intervention group concerning their hand eczema symptoms. They may have evaluated their symptoms — which might have already been present at baseline — differently after the educational session. This might have led to an increase in hand eczema reports at follow-up as compared with the control group that may be independent of a change in clinical status.' (p. 10)

Perrenoud 2001a

Methods	Individually randomised controlled trial Cross-over design, 2 arms **Duration**: 2 x 2 weeks Follow-ups: day 12, day 15, day 26, day 29
Participants	**Final number evaluable after 2x2 weeks**: N = 16 initially healthy 2nd year apprentice hairdressers (numbers allocated to groups not reported) **Number of participants randomised:** N = 21 (numbers allocated to groups not reported) **Lost to follow-up:** N = 5 (numbers allocated to groups not reported) **Sex:** 20 female out of 21 included participants **Median age (all included participants):** 18 (range 16 to 30) **Atopy**: 1 had a probable and 3 had a possible atopic disposition **Inclusion criteria**: at least 5 times shampooing per day without gloves **Exclusion criteria**: hand dermatitis **Setting**: field study with apprentices from the main regional occupational training centre, Geneva, Switzerland
Interventions	Comparison of the effectiveness of: • a barrier cream Excipial protect, and • its vehicle The participants were randomised to start either with barrier cream (Excipial protect) or with its vehicle. Excipial protect contains aluminium hydroxychloride and glycerine. Glycerine promotes water retention in the skin and the aluminium salt reduces excess sweating. The vehicle was designed specifically for skin care for occupational users. The first cream was applied 5 days a week for 2 weeks with a washout period of 2 days followed by another 2-week treatment period with the second cream.
Outcomes	1. Proportion of irritant skin changes and OIHD (but as scores for dryness, redness, breaks in the skin; no quantitative data reported) 2. Biometric: corneometry; chromometry and TEWL; no quantitative values given, only figures and P values (test and comparison not described sufficiently) 3. Subjective opinion 4. Mild adverse effects 5. Frequency of treatment discontinuation due to adverse effects: The study investigators stated that the dropouts were 'for reasons not related to the study.' 6. A clinical scores was applied, but without reporting any quantitative data. This outcome does therefore not fit the review's outcomes (not extracted).

Perrenoud 2001a *(Continued)*

Participants were assessed at the beginning at day 12, day 15, day 26, and day 29. The primary outcome measures were the proportion of irritant skin changes (score defined by study investigators). The secondary outcome measures were the amount of skin barrier impairment (TEWL), skin hydration (corneometry), and skin colour (chromometry) in the groups. A further secondary outcome measure was the subjective opinion of the participants concerning different features of the creams (ease of use, consistency, oiliness, protective effect, tolerance, general aspects).

Diagnostic criteria for OIHD (degree of certainty for the diagnosis of OIHD): not relevant

Scoring system for the severity of OIHD: three scores were assessed: Dryness, redness, breaks in the skin. Scale of 0 to 3 (0 = none, 1 = mild, 2 = strong, 3 = maximum).

Strengths

- Clinical examination

Limitations

- Only a very limited number of symptoms were documented, many other symptoms of hand eczema are missing (e.g. vesicles, hyperkeratosis).
- No exclusion of endogenous/atopic hand eczema or allergic contact dermatitis of the hands (no patch test performed)
- No exclusion of non-occupational hand eczema

Quality of bioengineering methods (Pinnagoda 1990)

'The biometric measurements were taken on the back of the dominant hand. The following instruments

- The Evaporimeter EP2 (ServoMed, Kinna, Sweden) was used to measure the transepidermal water loss (TEWL). The measurement represents the average over a 15 s period following a 30 s stabilization period.
- The Corneometer 820 PC (Courage and Khazaka, Köln, Germany) measured skin capacitance as a reflection of moisture. 3 measurements were taken and the average was calculated.' (p. 135)

Strengths

- Information is given on instruments and the test room (temperatures, relative humidity)
- Measurements were taken in a standardized environment (temperature, relative humidity)
- Measurements always on the same days of the week
- Method is well-described

Limitations

- Measurements were taken on the back of the dominant hand. Rather vague information. Does not ensure that always the same area was measured.

Notes	Not included in meta-analysis because no quantitative data reported.
	Study funding sources: not described
	Possible conflicts of interest: not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: 'The subjects were randomly assigned.' No further information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.

Perrenoud 2001a *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	The participants were blinded: They received 3x 50 g tubes with identical markings at the beginning of the study and another 3 tubes after 2 weeks. Comment: Probably done
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Quote: 'Double-blind' (p. 135). Participants, and outcome assessors were blinded. Comment: Probably done
Blinding of outcome assessment (detection bias) TEWL and corneometry	Low risk	No influence of blinding is expected for these objective measurements.
Incomplete outcome data (attrition bias) Hand-eczema-related outcomes	Unclear risk	5 out of 21 apprentices dropped out during only 4 weeks. The study investigators stated that the dropouts were 'for reasons not related to the study. Their withdrawal did not effect the balance between the 2 groups to which they had been assigned' (p. 134). No further details provided. Dropout reasons unknown although it is doubtful they were truly unrelated to the study or outcome.
Incomplete outcome data (attrition bias) Consumer satisfaction	Unclear risk	The study did not address this outcome.
Selective reporting (reporting bias)	Unclear risk	Results concerning primary outcome measure was only summarised briefly. Quote: 'Clinical scores were generally very low... under either cream' (p. 136), but not reported separately for verum and vehicle.
Other bias	Unclear risk	Application frequency of barrier cream and vehicle unclear. **Design:** cross-over -> no impact because no quantitative data for proportion of HE provided **Baseline imbalances:** comparability of groups at baseline unclear, no details given. **Blocked randomisation in unblinded trials:** no block randomisation reported **Differential diagnostic activity:** no different diagnostic activities across study arms

g: gram
HE: hand eczema
ITT: intention-to-treat
N: number
OIHD: occupational irritant hand dermatitis
RCT: randomised controlled trial
SD: standard deviation
TEWL: transepidermal water loss

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Amphoux 1975	Double-blind CCT: inclusion of workers with hand dermatitis (intervention group: 21.0%, control group 21.4%), no separate data for healthy workers available. No inclusion of dropouts and withdrawals in the analysis.
Arbogast 2004	RCT: only workers with compromised skin were included. Outcome: secondary prevention of OIHD.
Bauer 2002	CCT: quality criteria for quasi-RCT not fulfilled. No blinding of participants, clinicians and outcome assessors.
Berndt 2000	RCT: only workers with compromised skin were included. Outcome: secondary prevention of OIHD.
Bolam 1971	Not randomised, but groups were similar. Housewives.
Bregnhøj 2012	Not randomised. No primary intervention (8 out of 397 apprentices showed HD at inclusion).
Brown 2007	Qualitative study, intervention implementation research, no quantitative data available.
Davis 2005	RCT: no field study, laboratory experiment.
Dobson 1979	RCT: effect of industrial hand cleansers on TEWL was evaluated. This type of intervention was not considered in this review. No data on OIHD, only outcome is TEWL.
Frosch 2003	RCT: no separate data for healthy dental technicians available. Only 5 laboratories were randomised to 4 products; only partial cross-over-design (2 out of 4 products were tested in the same laboratory).
Glantz 1976	Probably not randomised. Under field conditions it was only investigated whether or not the protective ointment had a negative influence on the handling of dental instruments. The protective effects were only measured in a laboratory experiment.
Held 2001	CCT: inclusion of apprentices with hand dermatitis (intervention group 25%, control group 20%), no separate data for healthy apprentices available. No blinding of participants and clinicians, blinding of outcome assessors unclear.
Held 2002	RCT: inclusion of workers with hand dermatitis (intervention group 25%, control group 30% with two or more of the following symptoms: redness, vesicles, papules, itching, scaling, dryness, fissuring, rough and thickened, or suppurate skin changes), no separate data for healthy workers available.
McCormick 2000	RCT: only workers with compromised skin were included. Outcome: secondary prevention of OIHD.
Mody 2003	RCT: the objectives were to investigate the impact of an alcohol-based hand rub on knowledge, compliance, and hand colonisation of healthcare workers. The prevention of OIHD was not addressed.
Perrenoud 2001b	RCT in an intensive care unit: unclear if only healthy participants were included, only preliminary data available. No quantitative data on OIHD available.
Schwanitz 2003	CCT: inclusion of apprentices with hand dermatitis (intervention group 13.7%, control group 27.8%), no separate data for healthy apprentices available. No blinding of participants, clinicians, and outcome assessors. No information on loss to follow-up.
Sell 2005	CCT: inclusion of workers with hand dermatitis (12%), data on healthy workers were provided, but study could not be included because of violation of quality criteria (no blinding of participants, clinicians, and outcome assessors).

Study	Reason for exclusion
Winker 2009	RCT: Primary and secondary intervention mixed. Winker answered to our emails, but did not provide the requested data for initially healthy participants (primary prevention). He stated that the number of cases (HE) would be too small to detect significant differences between groups. This is probably true, but may introduce reporting bias to our review. Their study included 456 participants without and 27 with HE at baseline. At last follow-up, 24 participants had eczema.
Winnefeld 2000	RCT: Comparison of a non-medicated soap vs an alcohol-based hand rinse: This type of intervention was not considered in this review. Primary outcome proportion of OIHD was not assessed. Only 8 days of duration.

CCT: controlled clinical trial
HE: hand eczema
RCT: randomised controlled trial
OIHD: occupational irritant hand dermatitis
TEWL: transepidermal water loss

Characteristics of studies awaiting assessment *[ordered by study ID]*

Visscher 2014

Methods	Randomised controlled trial Parallel design, 2 arms **Duration**: 4 weeks 3 follow-ups at 1, 2, and 4 weeks
Participants	**Number of participants randomised:** N = 63 intensive care HCWs (over 60% with knuckle dryness and erythema scores of 2 at baseline) **Setting**: hospital
Interventions	'The objective was to determine the effects on hand skin condition of • a pseudoceramide test cream, designed for moisture barrier repair and substantivity, • relative to the hospital provided lotion.' 'Application was 33 daily.'
Outcomes	'The primary outcome was skin condition measured as 1. expert visual scoring of dryness and erythema, 2. digital imaging and analysis, 3. stratum corneum integrity (TEWL), and 4. skin hydration (capacitance) after 1, 2, and 4 weeks.'
Notes	Conference publication, only abstract available. 'There was significant irritant dermatitis at baseline as over 60% of HCWs had knuckle dryness and erythema scores of 2.' This trial will only be eligible if the data on OIHD is available in a dichotomised form and separately provided for HCWs without OIHD at baseline.

Characteristics of ongoing studies *[ordered by study ID]*

Madan 2016

Trial name or title	A behavioural change package to prevent hand dermatitis in nurses working in the national health service (the SCIN trial)
Methods	Cluster-randomised controlled trial (35 sites)
	Parallel design, 4 arms
	Duration: 12 months
Participants	Nurses working in the National Health Service (NHS) who are particularly at risk
	Focus on two groups of staff:
	• student nurses who are about to start their first clinical placements, and who are at increased risk of hand dermatitis because of a past history of atopic disease or hand eczema: **Inclusion criteria**: student nurses who are due to start their first clinical placement and have a history of atopic disease or hand eczema **Exclusion criteria:** mental health nursing students;
	• nurses working in ICUs, who are at increased risk of hand dermatitis because of the nature of their work **Inclusion and exclusion criteria:** not specified in the protocol
	Sample size: 'Field workers will be encouraged to recruit as many eligible student nurses and ICU nurses as possible, with the aim of recruiting at least 40 student nurses and 40 nurses from the ICUs at each site.'
	Setting: '12 NHS acute hospital trusts/health boards which provide OH care to both student and ICU nurses, 18 NHS trusts which provide OH care to ICU nurses and 5 university OH departments which provide OH care to student nurses'
Interventions	Comparison of the effectiveness of:
	• a bespoke, web-based behavioural change intervention to improve hand care, coupled with provision of hand moisturisers ('intervention-plus': 'The BCP will be supported by provision of facilities to encourage adherence. These will include personal supplies of moisturising cream for at-risk student nurses, and provision of (1) optimal equipment for cleaning hands, and (2) moisturising cream dispensers on ICUs.'), vs:
	• standard care ('intervention-light': 'Nurses at intervention-light sites will be managed according to what would currently be regarded as best practice, with provision of an advice leaflet about optimal hand care entitled 'Dermatitis: occupational aspects of management. Evidence-based guidance for employees' (also provided to the intervention-plus group) and encouragement to contact their OH department early if hand dermatitis occurs. However, they will not receive the BCP or active reinforcement of its messages. Nor will they routinely be offered supplies of moisturising cream over and above what is already standard practice at their site.')
Outcomes	1. Proportion of objectively assessed hand dermatitis after 1 year
	2. Impacts on participants' beliefs and behaviour regarding hand care (as a measure of adherence)
	3. Days off sick over a 1-year follow-up period
	4. Use of hand moisturisers
	5. Cost-effectiveness of the intervention compared with normal care
Starting date	'At the time of submission, the main trial has been underway since September 2014, with final recruitment planned for March 2016.'
Contact information	ira.madan@kcl.ac.uk
Notes	Inclusion and exclusion criteria might be refined. It is unclear whether or not nurses with hand dermatitis present at baseline will be included.

Madan 2016 *(Continued)*

Study funding sources: The SCIN Trial is funded by the National Institute of Health Research, Health Technology Assessment (HTA) programme grant: NIHR grant number 11/94/01. The trial is sponsored by the National Institute for Health Research (NIHR) Biomedical Research Centre based as Guy's and St Thomas' NHS Foundation Trust and the UKCRC-registered King's Clinical Trials Unit at King's College London.

Possible conflicts of interest: 'There are no competing interests to declare by any of the authors.'

Soltanipoor 2016

Trial name or title	The healthy hands project: Effectiveness of a skincare programme for the prevention of contact dermatitis in healthcare workers
Methods	Cluster-randomised controlled trial Parallel design, 2 arms **Duration**: 18 months Questionnaire every 6 months
Participants	**Number of participants randomised:** healthcare workers (N unknown, 34 wards) **Setting**: University Medical Center
Interventions	'The experimental intervention will comprise provision of hand creams in dispensers at the wards, with regular training and feedback, including reports of the electronically monitored consumption. Both the experimental and control groups will receive basic education on skin protection (as care as usual).'
Outcomes	'The primary outcome is the change in Hand Eczema Severity Index from baseline to 12 months. The secondary outcomes are the natural moisturizing factor levels in the stratum corneum as a bio-marker of skin barrier damage, and the total consumption of creams per ward.'
Starting date	Probably 2016
Contact information	Not known
Notes	Conference publication, only abstract available Unknown whether purely primary prevention

DATA AND ANALYSES

Comparison 1. Barrier creams versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of OIHD	4	999	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.72, 1.06]

Analysis 1.1.   Comparison 1 Barrier creams versus no treatment, Outcome 1 Proportion of OIHD.

Study or subgroup	Skin protec-tion creams	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Brüning 2008	18/46	14/46		11.34%	1.29[0.73,2.27]
Duca 1994	99/248	117/249		64.55%	0.85[0.69,1.04]
Goh 1994	11/17	17/23		19.15%	0.88[0.57,1.34]
Kütting 2010	8/209	12/161		4.96%	0.51[0.22,1.23]
Total (95% CI)	**520**	**479**		**100%**	**0.87[0.72,1.06]**
Total events: 136 (Skin protection creams), 160 (Control)					
Heterogeneity: Tau²=0; Chi²=3.3, df=3(P=0.35); I²=9.07%					
Test for overall effect: Z=1.35(P=0.18)					

Favours barrier creams   0.1 0.2   0.5   1   2   5   10   Favours control

Comparison 2.   Moisturisers versus no treatment

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Proportion of OIHD	3	507	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.46, 1.09]

Analysis 2.1.   Comparison 2 Moisturisers versus no treatment, Outcome 1 Proportion of OIHD.

Study or subgroup	Skin care creams	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Brüning 2008	15/50	14/46		43.55%	0.99[0.54,1.81]
Goh 1994	5/14	17/23		30.54%	0.48[0.23,1.02]
Kütting 2010	10/213	12/161		25.91%	0.63[0.28,1.42]
Total (95% CI)	**277**	**230**		**100%**	**0.71[0.46,1.09]**
Total events: 30 (Skin care creams), 43 (Control)					
Heterogeneity: Tau²=0.02; Chi²=2.23, df=2(P=0.33); I²=10.29%					
Test for overall effect: Z=1.58(P=0.11)					

Favours moisturisers   0.01   0.1   1   10   100   Favours control

Comparison 3.   Barrier creams and moisturisers vs no treatment

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Proportion of OIHD	2	474	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.33, 1.42]

Analysis 3.1.   Comparison 3 Barrier creams and moisturisers vs no treatment, Outcome 1 Proportion of OIHD.

Study or subgroup	Skin care and protection	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Brüning 2008	14/50	14/46		59.79%	0.92[0.49,1.72]
Kütting 2010	7/217	12/161		40.21%	0.43[0.17,1.07]
Total (95% CI)	**267**	**207**		**100%**	**0.68[0.33,1.42]**
Total events: 21 (Skin care and protection), 26 (Control)					
Heterogeneity: Tau²=0.13; Chi²=1.84, df=1(P=0.17); I²=45.75%					
Test for overall effect: Z=1.03(P=0.3)					

Favours intervention 0.01 0.1 1 10 100 Favours control

Comparison 4.   Skin protection education versus no or minimal intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of OIHD	3	1355	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.54, 1.08]

Analysis 4.1.   Comparison 4 Skin protection education versus no or minimal intervention, Outcome 1 Proportion of OIHD.

Study or subgroup	Education	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Flyvholm 2005	15/59	56/153		27.62%	0.69[0.43,1.13]
Löffler 2006	69/121	112/129		52.06%	0.66[0.55,0.78]
Meer 2015	25/509	15/384		20.32%	1.26[0.67,2.35]
Total (95% CI)	**689**	**666**		**100%**	**0.76[0.54,1.08]**
Total events: 109 (Education), 183 (Control)					
Heterogeneity: Tau²=0.05; Chi²=4.44, df=2(P=0.11); I²=54.96%					
Test for overall effect: Z=1.54(P=0.12)					

Favours education 0.01 0.1 1 10 100 Favours control

ADDITIONAL TABLES

Table 1.   Sensitivity analysis for comparison 1

Excluded trials	Rationale for exclusion	Number of included trials	Number of included participants	RR (95% CI)	P	I²
-	-	4	999	0.87 (0.72 - 1.06)	0.18	9%
Kütting 2010	cluster design without	3	629	0.89 (0.75 - 1.06)	0.18	0%

Table 1.   Sensitivity analysis for comparison 1 *(Continued)*

	correction					
Brüning 2008	split-body design without paired analysis	3	907	0.84 (0.70 - 1.00)	0.05	0%
Brüning 2008 Duca 1994	PO1 was not manifest hand dermatitis	2	410	0.75 (0.43 - 1.29)	0.30	35%

Table 2.   Median skin hydration and TEWL in Brüning 2008

Study arm	N	Skin hydration[1] baseline	Skin hydration[1] last follow-up	TEWL[2] baseline	TEWL[2] last follow-up
Barrier cream + moisturiser	50	24.73	27.18	17.65	14.9
Moisturiser	50	24.42	26.43	16.93	14.4
Barrier cream	46	25.15	28.5	16	13.68
Control[3]	46	25.73	27.35	16	14.5

1 Skin hydration measured by corneometry
2 Skin barrier function measured as TEWL (transepidermal water loss, $g/m^2/h$)
3 Differences of interventions compared to the control were not significant at baseline or last follow-up (no P values reported)

Table 3.   Median skin hydration and TEWL in Perrenoud 2001

Study arm	Skin hydration[1] after 11 days control	Skin hydration[1] after 11 days barrier cream	TEWL[2] after 11 days control	TEWL[2] after 11 days barrier cream
Control before barrier cream	67	60	10	14
Barrier cream before control	74	64	13	12
Mean of both study arms[3]	70.5	62	11.5	13

1 Skin hydration measured by corneometry (units), figures extracted from diagram
2 Skin barrier function measured as TEWL (transepidermal water loss, $g/m^2/h$), figures extracted from diagram
3 Differences of barrier cream compared to control group were significant for skin hydration (P < 0.01) and not significant for TEWL (no P values reported)

Table 4.   Sensitivity analysis for comparison 2

Excluded trials	Rationale for exclusion	Number of	Number of	RR (95% CI)	P	I[2]

Table 4. Sensitivity analysis for comparison 2 *(Continued)*

		included trials	included participants			
-	-	3	507	0.71 (0.46 - 1.09)	0.11	10%
Kütting 2010	cluster design without correction	2	133	0.71 (0.36 - 1.43)	0.34	53%
Brüning 2008	PO1 was not manifest hand dermatitis; split-body design	2	411	0.55 (0.31 - 0.94)	0.03	0%

Table 5. Mean skin hydration and TEWL in Halkier-Sørensen 1993

Study arm	N	Skin hydration[1] after 2 weeks control	Skin hydration[1] after 2 weeks moisturiser	TEWL[2] after 2 weeks control	TEWL[2] after 2 weeks moisturiser
Control before moisturiser group I[3]	70	72	80	39	42
Moisturiser before control group I	70	72	83	40	41
Control before moisturiser group II[4]	0	-	-	-	-
Moisturiser before control group II	23	66	86	41	37
Mean of both study arms and both groups[5]	-	71.2	82.1	39.7	40.9

1 Skin hydration measured by corneometry (capacitance), figures extracted from diagram
2 Skin barrier function measured as TEWL (transepidermal water loss, $g/m^2/h$), figures extracted from diagram
3 Group 1: participants who completed both periods
4 Group 2: participants who completed the moisturiser period but dropped out of period C after an average of 6 days (1-10 days) because they developed severe dryness of the skin
5 Differences of moisturiser compared to control were not significant for skin hydration or TEWL (no P values reported)

Table 6. Sensitivity analysis for comparison 3

Excluded trials	Rationale for exclusion	Number of included trials	Number of included participants	RR (95% CI)	P	I[2]
-	-	2	474	0.68 (0.33 - 1.42)	0.30	46%
Kütting 2010	cluster design without correction	1	96	0.92 (0.49 - 1.72)	0.79	-
Brüning 2008	PO1 was not manifest	1	378	0.43 (0.17 - 1.07)	0.07	-

Table 6. Sensitivity analysis for comparison 3 *(Continued)*

	hand dermatitis;
	split-body design

Table 7. Sensitivity analysis for comparison 4

Excluded trials	Rationale for exclusion	Number of included trials	Number of included participants	RR (95% CI)	P	I²
-	-	3	1355	0.76 (0.54 - 1.08)	0.12	55%
Flyvholm 2005	cluster design without correction	2	1143	0.86 (0.43 - 1.70)	0.66	78%
Löffler 2006	cluster design without correction; PO1 was not manifest hand dermatitis	2	1105	0.90 (0.51 - 1.61)	0.73	54%
Flyvholm 2005 Löffler 2006	cluster design without correction	1	893	1.26 (0.67 - 2.35)	0.47	-

A P P E N D I C E S

Appendix 1. Cochrane Skin Group Specialised Register search strategy

(((dermat* or eczema or dermatos*) and (occupation* or irritant* or contact) and (hand* or finger* or palm*))) AND (INREGISTER) [REFERENCE] [STANDARD]

Appendix 2. CENTRAL (Cochrane Library) search strategy

#1 ((dermat* or eczema) and (occupation* or irritant* or contact) and (hand* or finger* or palm*)):ti,ab,kw
#2 MeSH descriptor: [Hand Dermatoses] this term only
#3 MeSH descriptor: [Dermatitis, Occupational] this term only
#4 MeSH descriptor: [Dermatitis, Allergic Contact] this term only
#5 MeSH descriptor: [Dermatitis, Contact] this term only
#6 MeSH descriptor: [Dermatitis, Irritant] this term only
#7 {or #3-#6}
#8 (hand* or finger* or palm*):ti,ab,kw
#9 MeSH descriptor: [Hand] explode all trees
#10 #8 or #9
#11 #7 and #10
#12 #1 or #2 or #11

Appendix 3. MEDLINE (Ovid) search strategy

1. ((dermat$ or eczema) and (occupation$ or irritant$ or contact) and (hand$ or finger$ or palm$)).ti,ab.
2. Hand Dermatoses/
3. Dermatitis, Occupational/

4. Dermatitis, Allergic Contact/
5. Dermatitis, Contact/
6. Dermatitis, Irritant/
7. or/3-6
8. (hand$ or finger$ or palm$).mp.
9. exp Hand/
10. 8 or 9
11. 7 and 10
12. 1 or 2 or 11
13. randomised controlled trial.pt.
14. controlled clinical trial.pt.
15. randomized.ab.
16. placebo.ab.
17. clinical trials as topic.sh.
18. randomly.ab.
19. trial.ti.
20. 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp animals/ not humans.sh.
22. 20 not 21
23. 12 and 22

[Lines 13-22: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 4. Embase (Ovid) search strategy

1. ((dermat$ or eczema) and (occupation$ or irritant$ or contact) and (hand$ or finger$ or palm$)).ti,ab.
2. hand eczema/
3. occupational eczema/
4. contact dermatitis/
5. exp occupational skin disease/
6. skin allergy/
7. irritant dermatitis/
8. or/3-7
9. exp hand/
10. (hand$ or finger$ or palm$).mp.
11. 9 or 10
12. 8 and 11
13. 1 or 2 or 12
14. crossover procedure.sh.
15. double-blind procedure.sh.
16. single-blind procedure.sh.
17. (crossover$ or cross over$).tw.
18. placebo$.tw.
19. (doubl$ adj blind$).tw.
20. allocat$.tw.
21. trial.ti.
22. randomised controlled trial.sh.
23. random$.tw.
24. or/14-23
25. exp animal/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
26. human/ or normal human/
27. 25 and 26
28. 25 not 27
29. 24 not 28
30. 13 and 29

W H A T ' S   N E W

Date	Event	Description
17 January 2018	New search has been performed	We included five new studies and were able to perform meta-analyses of four different prevention strategies (up to four studies per intervention). We identified three ongoing studies. We re-assessed risk of bias for the four studies included in the first review version, in accordance with the methods outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*. For one study (Goh 1994), we selected a different study outcome as matching the primary review outcome. We chose to use risk ratio, instead of odds ratio, as the measure of treatment effect.
17 January 2018	New citation required and conclusions have changed	We included five new studies and performed meta-analyses of two additional prevention strategies. We reassessed risk of bias for the four studies included in the first review version. We chose to use risk ratio, instead of odds ratio, as the measure of treatment effect. We used GRADE methodology to assess evidence quality and draw conclusions about our certainty in the review findings.

H I S T O R Y

Protocol first published: Issue 4, 2003
Review first published: Issue 6, 2010

Date	Event	Description
7 October 2008	Amended	Converted to new review format.

C O N T R I B U T I O N S   O F   A U T H O R S

AB was the contact person with the editorial base. AB and HR co-ordinated contributions from the authors. HR worked on the methods section.
AB and HR obtained data on ongoing and unpublished studies. HR, PE, AB, and HCW independently screened papers against eligibility criteria. HR, JL, DD, MLS, and AB extracted data for the review. HR, DD, AB, and MLS appraised the risk of bias of the included trials. HR sought additional information about papers, entered data into Review Manager, and analysed and interpreted the data. SMJ assessed the diagnostic criteria for the outcomes of the included studies and worked on the final draft of the review. AB, HR, and HCW judged the quality of the evidence. AB and HR wrote the final draft of the review.

CB worked with AB on the previous published version of the review, provided data extraction templates, advised on the update, and provided critical appraisal of the draft review.

HR responded to the comments of the referees. HCW gave advice concerning the revisions and the final draft of the review.
AB is the guarantor of the update.

Disclaimer

D E C L A R A T I O N S   O F   I N T E R E S T

Andrea Bauer: "I have received lecture fees from manufacturers of skin care and protection products (Spirig, Astellas, GSK, and La Roche-Posay). I was the chief investigator (lead author) of an excluded study (Bauer 2002)."

Henriette Rönsch: none known.

Peter Elsner: "I was the co-author of an excluded study (Bauer 2002)."

Daan Dittmar: none known.

Cathy Bennett: "I am the proprietor of Systematic Research Ltd., and received a consultancy fee for my work on this review."

Marie-Louise A Schuttelaar: none known.

Judit Lukács: none known.

Swen Malte John: "I have received lecture fees from Galderma, Admirall, and Biogen-Idec."

Hywel C Williams: "I have helped a team led by Dr Ira Madan in London to design and deliver a national clinical trial to prevent occupational irritant hand dermatitis in nurses, which is due to start recruiting in late 2014. The study will probably report in 2017 or 2018, and at some point will be eligible for inclusion in this systematic review future update. The trial tests the behavioural package alongside supply of emollients at work. I was the co-author of an excluded study (Bauer 2002)."

SOURCES OF SUPPORT

Internal sources

- TU Dresden, Germany.

  The TU Dresden provided computer workplaces and access to literature.
- Cochrane Skin Group, UK.

  The CSG provided financial support and accompanied the entire review process.

External sources

- The National Institute for Health Research (NIHR), UK.

  The NIHR, UK, is the largest single funder of the Cochrane Skin Group.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The protocol was completed in 2003, therefore predating the Cochrane 'Risk of bias' tool. This update was conducted applying the current version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), which required some substantial amendments and modifications. The applied methods were described more clearly in order to comply with the *Handbook* (Higgins 2011):

- Assessment of risk of bias in included studies was done according to Higgins 2011. The protocol referred to Juni 2001.
- Unit of analysis issues were addressed more clearly according to Higgins 2011. They were not mentioned in the protocol.
- We clarified how heterogeneity was assessed in the Assessment of heterogeneity section of the review. This was not mentioned in the protocol.
- We clarified in the Assessment of reporting biases section that we planned to create funnel plots but that they could not be applied due to the small number and methodological heterogeneity of included trials. Reporting bias was not addressed in the protocol.
- Data synthesis: the protocol did not define how to deal with multiple outcome data. When this became apparent during data extraction we decided to extract data from the last available time point of each study. Apart from timing, multiple outcome data were not an issue in the included studies.
- We have defined our key outcomes (primary outcomes 1 and 2) and presented them in one 'Summary of findings' table for each preventive intervention. The protocol did not address key outcomes.
- GRADE methods and 'Summary of findings' tables were applied in this update. These tools were not available when the protocol was completed.

Several changes from the protocol were predefined in the proposal (the title registration form) of this update and were adopted in the update:

- Terminology: in the protocol different terms for OIHD were used, which was leading to confusion. In the proposal of the update only OIHD was used, except when referring to the terminology applied in study reports.
- We clarified the inclusion criteria and have stated more clearly throughout the review that we include only primary prevention studies and not studies where participants had existing OIHD, unless the participant population was mixed and disaggregated data was presented for those participants who were healthy with no OIHD at the start of the study.
- The protocol allowed for the inclusion of quasi-RCTs. We only considered RCTs for this update.

- The protocol listed five categories of interventions. Before starting the update, the comparison of behavioural and psychological interventions versus no intervention was added to the types of interventions to be reviewed. However, these are elements of the existing category 'skin protection education', not a separate category. Accordingly, the Types of interventions section of this review still lists only the five categories that were specified in the protocol.
- We defined the outcomes under investigation more clearly and numerated them differently (compare Primary outcomes; Secondary outcomes).
  - The protocol had only one primary outcome: 'Proportion of participants developing any signs and symptoms of hand dermatitis (incident cases) as rated by the investigators (physician/nurse) or the participants.' We amended the definition.
  - We added a second primary outcome (concerning adverse effects).
  - We added a more precise definition of the secondary outcome concerning clinical course of signs and symptoms of hand dermatitis.
  - We modified the secondary outcome concerning adverse effects, to cover only less severe adverse effects that are not addressed as a primary outcome.

The following changes from the protocol were also necessary.

- We did not identify any eligible trials in the predefined comparison of complex interventions using barrier creams, moisturisers, and protective gloves versus no intervention. Instead, we analysed the effects of the combination of barrier creams and moisturisers versus no intervention.
- The protocol did not clarify which meta-analyses were planned. In this update, meta-analyses were only undertaken for the main outcome, OIHD, because there were not sufficient comparable data for the meta-analysis of other outcome
- The protocol predefined sensitivity analyses for investigating the impact of lower-quality studies and the potential impact of missing data. In order to avoid excessive subjective judgment, we clarified that we would only investigate the following methodological weaknesses in sensitivity analyses: cluster design without correction, split-body or cross-over design, and reporting only minor signs and symptoms of OIHD (as opposed to manifest OIHD). All but one study had missing data due to attrition. Dropout rates were sometimes considerably higher than cases of OIHD so that applying worst- or best-case scenarios would have introduced a large bias. Data needed for other types of ITT assumptions were not available. We therefore did not perform any ITT calculations and missing data was dealt with descriptively.
- No standardised mean difference could be calculated for continuous outcomes because the studies did not report sufficient data. These results were reported descriptively in the review.
- We planned to do subgroup analyses (at less than, and greater than 30 years of age; sex; atopy; occupation). In this review, we did not analyse subgroups of trials because we could not perform meta-analysis for most outcomes, or too few trials were included per comparison. We did not analyse subgroups of participants either, because such data were not available. Subgroups were assessed descriptively only.
- Search methods: we did not correspond with authors and pharmaceutical companies to identify unpublished or ongoing trials, or grey literature. Instead we expanded the number of trials registers we searched in line with current Cochrane Skin methods.
- We stated in the protocol that we would calculate odds ratios (ORs) as the measure of the treatment effect. However, we chose to report relative risk (RR) instead for the meta-analyses in this and future review versions because odds ratios are more difficult to understand and often misinterpreted as risk ratios (Higgins 2011). This decision was made without considering any results which would have occurred by using odds ratios.
- Split-body designs were eligible for this update.
- For this update, other review authors than predefined in the protocol performed the study selection and extraction.

I N D E X   T E R M S

Medical Subject Headings (MeSH)

*Patient Education as Topic; Dermatitis, Irritant [*prevention & control]; Dermatitis, Occupational [*prevention & control]; Emollients [*administration & dosage]; Excipients [administration & dosage]; Gloves, Protective; Hand Dermatoses [*prevention & control]; Organic Chemicals [administration & dosage]; Randomized Controlled Trials as Topic; Risk Reduction Behavior

MeSH check words

Humans