Appendix S1.

MATERIALS AND METHODS

Study population and design

This study was performed alongside a 2-armed randomized controlled trial with 12 months follow-up. The study population was recruited from 3 academic hospitals, 1 academic centre for dentistry, 2 general hospitals and 2 nursing homes from different regions of the Netherlands. Departments were included as a whole and could participate if most workers within the department handled irritants during work (e.g. water, soap, food, gloves). Workers at the departments could participate in the study if they fulfilled the following inclusion criteria: (*i*) being employed at one of the participating hospitals; (*ii*) being able to complete Dutch questionnaires; (*iii*) aged between 18 and 64 years; and (*iv*) working for at least 8 h a week. Exclusion criterion was: not handling irritants during work. This was determined by means of the baseline questionnaire that contained several questions about exposure to irritants during work. The study protocol was approved by the medical ethics committee of the VU University Medical Center in Amsterdam (9).

Randomization, stratification and blinding

Randomization took place at the level of departments to avoid contamination between healthcare workers within departments. To establish equal groups at the department level we used pre-stratification based on the risk of hand eczema (HE) and whether the workers had contact with patients. Department managers were informed about the randomization outcome and study design. Workers in the participating departments were not informed about this, but received information about the goal of the study (i.e. the prevention of HE in healthcare workers) via a letter and a leaflet.

Due to the design of the implementation strategy, it was impossible to blind researchers, specialized nurses (who guided the implementation strategy) and department managers for the randomization outcome. Detailed information about the randomization, stratification and blinding is described elsewhere (9).

Intervention group: multifaceted implementation strategy

The intervention group received the multifaceted implementation strategy. This strategy contained several components. First, workers received a leaflet containing recommendations for the prevention of HE. These recommendations were derived from the guideline "Contact Dermatitis" of the NVAB (8). Secondly, a participatory working group was formed at every intervention department. Department managers selected members for these working groups based on their representativeness, their influence on colleagues and their motivation. Working group members identified problems with adherence to the NVAB guideline, came up with solutions for these problems, and implemented these solutions at the department. Each working group met 3 times during the intervention period (total duration approximately 4.5 h) and these meetings were guided by a specialized nurse. During the first meeting, the working group members received role model training (2 h), in which they learned how to motivate and stimulate their colleagues to use the recommendations of the NVAB guideline, and to put this into practice within their department. After the first meeting, the working group members and the specialized nurse performed observations at the department to identify problems with adherence to the NVAB guideline. The principal researcher (EWCM) subsequently wrote a report, in which information from these observations was combined with the workers' current HE problems as well as their behaviour related to the prevention of HE. This report was the starting point for meeting 2 in which the most important problems were chosen and an implementation plan was made to implement the solutions solving these problems. In the third meeting, this implementation plan was evaluated. The last component of the strategy was education and reminders. The specialized nurse gave a 20-min education session at the department on the risk of HE, the prevention of HE and how to use the preventive measures. After the education session, workers received a bag containing one moisturizer, a pair of cotton under gloves and two disinfectants. If necessary, the nurse held more sessions at a department to increase the reach of the education. Afterwards, role models placed posters with key messages (the reminders) at relevant places at the department.

Control group

Workers in the control group received the same information leaflet as those in the intervention group. This leaflet was considered to be a minimal implementation strategy.

Data collection

Baseline questionnaires were sent to all workers at the participating departments. Workers who completed the baseline questionnaire also received questionnaires at the 3, 6, 9 and 12 months follow-up. A maximum of 3 reminders was sent to enhance the response. Data collection took place between April 2011 and June 2013.

Baseline characteristics

We assessed the following variables at baseline: age (years), sex (male/female), number of working hours per week, number of working years in present job, having patient-related tasks (yes/no), education level (low/middle/high), co-worker support, decision authority, having an atopic predisposition and skin exposure to irritants in leisure time due to hobbies or care-related tasks outside work. A detailed description of these characteristics can be found elsewhere (11).

Effect measures

Hand eczema. The Nordic Occupational Skin Questionnaire – 2002 (NOSQ-2002) was used to measure the 3-month self-reported prevalence of HE (13, 14). Questions D1 ("Have you ever had hand eczema?"), D2 ("Have you ever had eczema on your wrists or forearms?") and D5 ("When did you last have eczema on your hands, wrists and forearms?" (Answers: "I have it just now"; "Not just now, but within the past 3 months"; "Between 3 – 12 months ago"; "More than 12 months ago") were combined to create a dichotomous measure. We defined the presence of HE in the past 3 months as answering "yes" to question D1 or D2, 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". HE prevalence was measured at baseline and at 3, 6, 9 and 12 months of follow-up.

Compliance measure. A partly modified version of the NOSQ-2002 was used to assess compliance with the NVAB guideline (13, 14). The questionnaire had to be modified in order for the questions to be in accordance with the work characteristics of the healthcare workers (i.e. work environment) (10). To determine compliance with the NVAB guideline, a sum score was created, ranging from 0 to 5, in which a respondent received 1 point for each of the following behaviours: (*i*) performing wet work for less than 2 h a day; (*ii*) washing the hands 20 times a

day or less; (*iii*) not using body lotion; (*iv*) not wearing jewellery during work; and (*v*) using a moisturizer at least 6 times a day. Higher scores indicate better HE prevention behaviour. The cut-off points mentioned above were based on the aforementioned guideline "Contact Dermatitis" from the NVAB (8). This measure was assessed at baseline, and at 6 and 12 months follow-up.

Costs

Healthcare, absenteeism and presenteeism were assessed at baseline, and after 3, 6, 9 and 12 months using questionnaires. All costs were converted to 2012 € using consumer price indices (15). Discounting of costs and effects was not necessary, because neither cost nor effect data were collected beyond 12 months (16).

Healthcare costs. Workers who indicated that they had (symptoms related to) HE during the previous 3 months were asked to complete a questionnaire assessing their utilization of primary healthcare (e.g. general practitioner, allied health professionals, complementary medicine), secondary healthcare (e.g. medical specialists) and both prescribed and over-the-counter medications. Use of primary and secondary healthcare services was valued using Dutch standard costs (17). If these were not available, prices according to professional organizations were used. Medication use was valued using unit prices obtained from the Dutch Royal Society of Pharmacy (18).

Absenteeism costs. Sickness absence was measured using a slightly modified question of the PROductivity and DISease Questionnaire (PRODISQ) (19), asking participants to report their total number of sick leave days due to HE during the previous 3 months. Labour costs associated with 1 h of sick leave were calculated using Dutch age- and sex-specific price weights (17). For the societal perspective, we estimated absenteeism costs by means of the Friction Cost Approach (FCA), with a friction period of 23 weeks and an elasticity of 0.8 (20). For the employer's perspective, the Human Capital Approach (HCA) was used, in which costs are not truncated to the friction period and no elasticity factor is applied.

Presenteeism costs. A slightly modified version of the PRODISQ was used to assess productivity losses at work due to HE (i.e. presenteeism) (19). The questions from the PRODISQ measured the following: the number of days participants went to work while having HE during the previous 3 months; the quality of their work at those days measured on a 11-point scale (0: worst quality; 10: same quality as usual); and the amount of work that was performed on those days measured on a 11-point scale (0: could not do anything; 10: could do the same as usual). The number of days lost due to presenteeism ($P_{prodisq}$) during the previous 3 months was calculated using the following formula: $P_{prodisq}$=number of working days with HE * (1 – ((quality of work*amount of work)/100))).

Presenteeism costs were subsequently calculated by multiplying the participants' total number of days of work lost due to presenteeism during follow-up by their labour costs (based on sex and age) per day (17).

Intervention costs. To estimate intervention costs, a bottom-up micro-costing approach was used. This means that detailed data were collected regarding the quantity of resources consumed as well as their unit prices (21). Intervention costs included all costs related to the implementation of the multifaceted implementation strategy, i.e. costs for intervention materials, training of the specialized nurses, education sessions, participatory working groups sessions (including the observations related to the intervention) and the role model training (including the reminders). Costs of intervention materials were based on invoices. The number and duration of training sessions for the specialized nurses, participatory working group sessions and role model training sessions were registered by the principal researcher and/or research assistant. We estimated that 2×20-min education sessions were delivered per intervention department, that working group members invested 4 h of their time for implementing the solutions, and that the workplace observations lasted, on average, 40 min per worker. Labour costs of specialized nurses and working group members/role models were calculated by multiplying their total time investments by their gross hourly salaries including overhead costs. Capital costs were estimated using cost data collected from financial department staff.

Statistical analyses

Analyses were performed according to the intention-to-treat principle. Descriptive statistics were used to compare baseline characteristics between the intervention and control group. Missing data were multiply imputed. The imputation model included sex, age, working days per week, having an atopic predisposition, skin exposure in leisure time, co-worker support, and baseline and follow-up cost and effect measure values (i.e. 3, 6, 9 and 12 months). Imputations were performed per study group (intervention/control) using predictive mean matching and fully conditional specification in IBM SPSS (v20, Chicago, IL, USA). In total, 20 complete datasets were needed to reach a loss of efficiency below 5% (22, 23). Datasets were analysed separately, as specified below. Pooled estimates were subsequently calculated using Rubin's rules (24). Cost-effectiveness analyses and ROI analyses were performed using Stata (V12, Stata Corp, College Station, TX, USA). We considered $p < 0.05$ as statistically significant.

CEAs. CEAs were conducted using HE and the compliance measure as outcome measures from both the societal and employer's perspective. In the societal perspective, all costs and consequences related to the intervention were incorporated, whereas only those relevant to Dutch employers were included in the employer's perspective (i.e. presenteeism, absenteeism and intervention costs).

Effectiveness at 12-month follow-up was analysed using linear multilevel analyses, adjusted for baseline values. A 2-level structure was used for all outcome measures (i.e. worker, department). Cost differences between study groups were calculated for total as well as disaggregated costs. Differences in costs were estimated using linear multilevel analyses with 2 levels (i.e. worker, department). To estimate 95% CIs around cost differences bias-corrected (BC) bootstrapping with 5000 replications was used. Bootstrap replications were stratified for departments, to account for the clustering of data (25). Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the adjusted differences in costs by those in effects. Bootstrapped incremental cost-effect pairs (CE-pairs) were plotted on cost-effectiveness planes (CE-planes) (26). To provide a summary measure of the joint uncertainty of costs and effects, cost-effectiveness acceptability curves (CEACs) were constructed that show the probability of the intervention being cost-effective in comparison with usual care for a range of ceiling ratios (i.e. the maximum amount of money decision-makers are willing to pay per unit of effect) (27).

ROI analysis

The ROI analysis was performed solely from the employer's perspective. Within these analyses, costs were defined as intervention costs, and benefits as the difference in monetized outcome measures (i.e. absenteeism and presenteeism costs)

between the control and intervention group during follow-up, with positive benefits indicating reduced spending. Three ROI-metrics were calculated: (*i*) net benefits (NB); (*ii*) benefit cost ratio (BCR); and (*iii*) return-on-investment (ROI) (28–30).

NB=Benefits – Costs

BCR=Benefits/Costs

ROI=((Benefits – Costs)/Costs)*100

The NB indicates the amount of money gained after costs are recovered (i.e. net-loss or net-savings). The BCR indicates the amount of money returned per € invested. The ROI indicates the percentage of profit per € invested. To quantify uncertainty, bootstrapped 95% CIs around the NB, BCR and ROI were estimated using the percentile method based on bootstrapping with 5,000 replications. Again, bootstrap replications were stratified for departments (25). Subsequently, the probability of the intervention resulting in a positive financial return to the employer was estimated by determining what proportion of bootstrapped ROI estimates was positive (i.e. NB > 0, BCR > 1 and ROI > 0%) (28–30).

Sensitivity analyses

Three sensitivity analyses were performed to assess the robustness of the results. In the first sensitivity analysis (SA1), The World Health Organization Health and Work Performance Questionnaire (WHO-HPQ) was used for estimating presenteeism costs (31, 32). In contrast to the slightly modified version of the PRODISQ, the WHO-HPQ measures productivity losses in general, instead of productivity losses due to HE specifically. In the second sensitivity analysis (SA2), absenteeism costs were valued using the HCA instead of the FCA for the societal perspective. In the third sensitivity analysis (SA3), presenteeism costs were excluded, because no overall consensus exists about whether to include presenteeism costs in economic evaluations.