

Economic evaluation of a tertiary prevention program for occupational skin diseases in Germany

Running Head: Economic evaluation of skin diseases prevention

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ABSTRACT

Background: Occupational skin diseases (OSD) are the most common work-related diseases in Germany and responsible for large individual and financial burdens. Therefore, a tertiary individual prevention programme (TIP) is offered to patients with severe OSD who are at increased risk of abandoning their profession.

Objectives: To define cost-of-illness (COI) of OSD in Germany and to economically evaluate the TIP from a societal perspective.

Methods: In this study, data of patients taking part in the TIP (11/2005-12/2009) were collected. Sociodemographic and medical data, costs, disease severity (Osnabrueck Hand Eczema Severity Index) and quality of life (Dermatology Life Quality Index) were assessed. COI and cost-effectiveness analysis were performed with a simulated control group.

Results: In the analysis, 1041 patients were included. Intervention costs per persons were €15009 with decreasing COI over time. Incremental cost-effectiveness ratio (ICER) revealed expenses per patient of €8942 for a reduction in severity level and €9093 for an improvement in QoL in the base case. Considering costs for retraining, the breakeven point is reached if the TIP prevents retraining in approximately 64% of participants.

Conclusions: The decreased COI in this long-term evaluation indicates that the TIP is cost-effective in patients with severe OSD.

KEYWORDS: cost of illness, cost of intervention, cost-effectiveness, hand eczema, work-related skin disease

1. INTRODUCTION

Estimates indicate that environmental factors, which include working environment, account for 70%-90% of all chronic diseases worldwide.¹ Work-related and occupational diseases arise from work activities and cause an enormous burden of disease and associated costs.² It is assumed that the true burden is strongly underestimated, as there is a shortage of data on work-related and occupational diseases.² However, morbidity and mortality of these diseases do not only affect the employee, since loss of productivity and its resulting economic burden is borne by society at large.³

According to the annual report of the German Statutory Accident Insurance, skin diseases are the most common occupational disease group in Germany. In 2017, 27695 new suspected cases of occupational skin diseases (OSD) were reported. This is a significant proportion of 36.7% of all suspected occupational diseases within that year.⁴ High risk professions for OSD are: hairdressers, bakers, confectioners, butchers, cooks, other professions in food industry, cleaning staff, miners, as well as personal hygiene and healthcare workers.⁵

OSD are associated with a marked reduction in quality of life (QoL) indicating a high personal burden of disease.⁶⁻⁸ Additionally, there is an immense financial impact. Although healthcare costs for OSD in Germany have hitherto only been investigated in a small sample of 151 individuals, resulting annual healthcare costs are high for both Statutory Accident Insurance and society with €6731 and €8799 per patient, respectively.^{9,10} This societal burden is particularly high in Germany, compared to results from other western countries.^{11,12}

Therefore, with the support of the Statutory Accident Insurance a multi-step approach has been established for the prevention and treatment of OSD in Germany consisting of various interventions depending on the stage and severity of the disease.¹³ For individuals with severe OSD insufficiently treated by secondary prevention measures, a tertiary individual prevention program (TIP) is provided which aims to reduce the severity of OSD, to improve QoL and to enable affected persons to remain in their profession.¹⁴ The program is divided into a three-week interdisciplinary inpatient rehabilitation period which includes treatment, education and counselling offered by five centres across Germany and a subsequent three-week period off work, in which supervision and treatment is continued by a local dermatologist. Afterwards, the

patients ideally return to their workplaces with ongoing continuous dermatological supervision and treatment.¹⁵

From November 2003 until December 2009, consecutive TIP participants were recruited in the five participating centres and followed up until 2013 within the framework of the “Medical-Occupational rehabilitation procedure skin – Optimizing and quality assurance of inpatient-management” (ROQ-study).¹⁴ Publications on the ROQ-study revealed the effectiveness of TIP in reducing the severity of the disease and improving QoL of patients as well as ability to work,¹⁵ also in the long-term.^{16,17} The present study aims i) to define the cost-of-illness (COI) of OSD in Germany and ii) to economically evaluate the TIP.

2. METHODS

2.1 Data sources and management

The economical evaluation was based on data from the ROQ-study.¹⁴ The study population consisted of consecutive TIP patients recruited in the five participating centres between November 2005 and December 2009. Cost data were collected over a four-year period from a societal perspective at the following time points:

- (T1) at inpatient admission for the TIP (information on the 12 months before TIP)
- (T2) at discharge (information on the inpatient rehabilitation)
- (T3) before return to work, three weeks after discharge (information on the time since discharge)
- (T4) four weeks after return to work (information on the time since return to work)
- (T5) one year after discharge (measurement of sustainability)
- (T6) three years after discharge (measurement of sustainability)

In health economic evaluations, different types of costs are considered. On the one hand, there are direct costs that include costs for pharmaceuticals, non-pharmaceutical treatment and diagnostics. On the other hand, indirect costs arise from productivity losses due to a particular disease. In addition, benefit parameters are relevant for economic evaluations.

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To determine resource consumption, associated costs and the duration of inability to work, questionnaires of time points T1, T2, T5 and T6 were relevant. Those questionnaires, except the one at T2, were structured comparably with regard to their content and recall period, ie one year before survey. Altogether, the four questionnaires cover the entire period before, during, and after the TIP. In each of these time points, one questionnaire for physicians and one for patients was used for data collection. The physicians' questionnaires requested the following information about TIP patients: sociodemographic data, occupation, medical history, prior treatment, disease severity, current therapy. The patients' questionnaires assessed QoL. The assessed parameters on benefit, resource consumption and costs as well as the evaluation procedures are described in detail below.

All participants with available questionnaires who were employed at T1, T5 and T6 were included in the analysis. We cleared and aligned free text information. Additionally, we coded drugs, harmonised information on dosages and classification to categories of active substances, i.e. glucocorticosteroids, antihistamines and other systemic drugs. Subsequently, we performed plausibility checks.

2.2 Direct costs of illness

We calculated costs for pharmaceuticals with prices from the German statutory health insurance. Due to a lack of data, it was not possible to use costs from the Statutory Accident Insurance. For all other services, the medical fee schedule for physicians of the Statutory Accident Insurance (UV-GOÄ) regulates prices for medical treatment of occupational diseases in Germany. Cost calculations for non-pharmaceutical treatment comply with these regulations.

2.2.1 Pharmaceuticals

The relevant therapeutic agents were classified into topical and systemic drugs. To identify the defined daily doses (DDD) of pharmaceuticals, active substances of drugs have been determined according to Lauer Taxe.¹⁸ The anatomical-therapeutic-chemical classification of daily doses (ATC) from 2012¹⁹ gave information on particular drugs' DDD and the German medication order from 2013²⁰ information on prices.

For topical drugs, we calculated average costs per application for each steroid class and active substance (Table 1). The application on hands was assumed to amount to 2g per day on average according to the

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manual for ATC classification and DDD determination.²¹ Types and dosages of systemic drugs were requested in the questionnaires. To determine costs for the stated duration of treatment with topical and systemic drugs, we multiplied the dosages with the recommended frequency of usage according to the manufacturer. To determine the quantity of topical and systemic drugs for the stated duration of treatment, we multiplied the frequency per week reported in the questionnaire with the number of weeks and the number of DDDs.

*** Please insert Table 1 here ***

2.2.2 Non-pharmaceutical treatments

Non-pharmaceutical treatments included tap water iontophoresis and ultraviolet radiation (UV) therapies. For some of these services, frequencies were not specified in the questionnaires. To include these services into the calculations, we computed a weighted average of standard options if frequencies were not specified in the questionnaires (Table 2).

If the date of beginning for tap water iontophoresis was missing, we assumed midyear (1st of July) as therapy start. Whenever physicians reported the duration of a therapy shorter than one week, we assumed one week of therapy duration. Treatment frequencies were assumed to be three sessions per week, if the answer “regular interval with $\geq 3x$ per week” was given, and one session per week, if “irregular interval with $< 3x$ per week” was reported.

For UV therapy, the questionnaires assessed data on utilisation of different forms and durations of therapy. The frequency of UV therapies was set at three sessions per week for the total duration of therapy, which corresponds to the average value for UV therapy in hand eczema.

2.2.3 Diagnostics

Diagnostic procedures included allergy diagnostics, laboratory diagnostics and other diagnostic procedures.

Whenever information about the date was available within the first questionnaire, only diagnostics within the 12 months prior to T1 were taken into account. For diagnostic procedures without date specification, all indicated services were considered. The questionnaires did not obtain the frequency of some diagnostic procedures. For these procedures, we computed a mixed price estimation following German clinical standards (Table 2).

*** Please insert Table 2 here ***

2.2.4 Additional direct costs

The additional direct costs included patient expenses related to OSD and costs of retraining measures. The questionnaires obtained information on the annual expenditure of patients, segregated in seven cost intervals, ie ranging from €0 to € >1200. We applied the mean values of the intervals as costs for the analysis. Patients with severe OSD who are unable to continue their occupation, notwithstanding participating in TIP, may receive retrain measures. We assumed costs of these retrain measures based on the mean costs for retrain measures of the specific years provided by the German Employers' Liability Insurance Association for Health Service and Welfare Work (BGW), discounted for the corresponding period. These costs include the following employment benefits for participation in work life: contributions in kind, transitional payments, other cash benefits, social security benefits, travel expenses, budgetary support for benefits and other additional benefits.

2.3 Costs of intervention

For the direct costs of intervention, an inpatient daily rate of €270 was stated by the Statutory Accident Insurance. To estimate the direct costs of intervention, we multiplied this rate with the number of inpatient days.

We determined the indirect costs by multiplying the days with incapacity for work by the nationwide average gross salary per capita of €167.75 per day. Here, one week was regarded as seven days. The days missed at work during inpatient rehabilitation and working leave subsequent to the inpatient rehabilitation as well as the resulting indirect costs were assigned to the TIP. The days missed at work one year before, one and three years after the TIP were assigned to annul COI.

2.4 Benefit parameters

We defined the patients' QoL and the disease severity as benefit parameters for the economic evaluation. The influence of the disease on QoL was assessed by a dermatology-specific instrument, the Dermatology Life Quality Index (DLQI) with a total score ranging from 0 to 30 (higher scores denote larger effects on patients' lives) and allowing to categorise QoL into five levels.^{22,23}

Disease severity was determined by dermatologists at all time points using the Osnabrueck Hand Eczema Severity Index (OHSI). The OHSI score ranges from 0 to 18 (higher values indicating higher disease severity) and is structured in four severity levels.^{24,25}

2.5 Statistical analysis

We analysed sociodemographic data of included participants with descriptive statistics and performed a sensitivity analysis taking participants into account who were not employed at all times of data collection. The cost-of-illness and cost-effectiveness analyses performed are described in the following. For both analyses, we conducted a pre-post comparison. Hereby, we compared TIP participants with a simulated extrapolated historical cohort to estimate the incremental costs. All statistical analyses were carried out with SPSS version 23 (IBM, Armonk, New York).

2.5.1 Cost-of-illness analysis

In order to enable a comparison of resource consumption and resulting costs between the periods of one year (T1 and T5) and the period of 2 years (T6), we converted the parameters assessed at T6 for a period of 2 years into annual values for the second and the third year after TIP. The COI analysis was conducted by using a pre-post design comparing annual costs arising within the period before and after the intervention. If normal distribution was not given, log transformation was performed. In order to verify the results, we carried out additional non-parametric tests.

2.5.2 Cost-effectiveness analysis

In the first part of the cost-effectiveness analysis, we calculated the incremental cost-effectiveness ratio (ICER). The ICER can be considered as the associated costs of gaining an additional unit of effectiveness.²⁶ In the following analyses, the ICER indicates the incremental costs per patient between T1 and T6 for an improvement in disease severity (OHSI) and QoL (DLQI). For the calculation of the ICER, we compared the TIP participants with the simulated control group. In cost-effectiveness analysis, costs and benefits were discounted with 3% per year to take social opportunity costs into account. A sensitivity analysis examined the effects of discount rates of 0% and 5%.

One important goal of the TIP is the workability maintenance. Therefore, in the second part of cost-effectiveness analysis, we defined the ability to remain in the profession and thus circumvent a retraining as benefit parameter. If this maintenance was not achieved, we included costs of retrain measures

additionally in the cost-effectiveness analysis. For the simulated control group, we performed a scenario analysis. Here, we assumed the TIP to reduce the need of retrain measures by 50% in the base case and varied the proportion of prevented retraining between 25% and 75% in sensitivity analyses. Finally, we determined the break-even point of the TIP, that is, the proportion of retraining measures at which TIP becomes cost-neutral compared to standard outpatient treatment.

2.6 Ethics

The study was carried out in accordance with the Code of Ethics of the Declaration of Helsinki and was approved by the respective institution's ethics committees of the participating study centres. The primary approval was obtained from the ethics committee of the University of Osnabrück. Participants provided written informed consent before participating in the study.

3. RESULTS

During the observation period, 1788 TIP patients gave their written informed consent and were recruited for the ROQ study in the five participating centres. Information assessed at all relevant survey dates was available from 1379 TIP participants. Of these, 1041 were included in the analyses as they were employed at all times of survey. The average observation period was 1113 days. Gender was distributed evenly with 525 (50.4%) women. Age ranged from 17 to 67 years, with a mean age of 44 years (± 11.1) at the start of the study. Before the onset of the OSD, most patients worked in the metal industry (30.6%) or in health and elderly care (30.5%) (Table 3).

*** Please insert Table 3 here ***

3.1 Costs of illness

Mean annual direct medical costs per person (comprising diagnostics and treatment) increased from €382.6 (± 551.7) in the year before the TIP to €455.2 (± 648.5) in the subsequent year and decreased to €202.4 (± 416.5) in the second and third year after the TIP. This cost reduction was mainly induced by a decrease in costs for UV therapy, topical drugs and diagnostic procedures. Annual out-of-pocket payments declined from €111.2 (± 169.6) in the year before the TIP to €79.8 (± 152.1) one year after and increased

again to €86.76 ($\pm$ 155.5) in the second year and to €93.7 ($\pm$ 155.5) in the third year after the TIP (Table 4).

Indirect costs due to incapacity to work caused the highest proportion in COI. In the year before the TIP, the mean annual number of days absent from work was 29.0 ($\pm$ 53.9). They decreased to 13.0 ($\pm$ 42.2) in the first and to 8.2 ($\pm$ 31.2) on average in the second and third year after the TIP. The proportion of persons without days absent from work increased from 44% in the year before the TIP to 78% in the first year after the TIP and 77% in the second and third year after the TIP; therefore, the distribution of indirect costs is highly skewed. The resulting indirect costs decreased from €4864.6, with a median of €1174.3 (interquartile range €0 to €5032.50) in the year before the TIP to €2180.8 with a median of €0 (interquartile range €0 - €0) one year after the TIP. Indirect costs were €1 376.4 with a median of €0 (Interquartile range €0 - €0) on average two and three years after the TIP (Table 4).

The mean total COI per person were €5358.4 with a median of €1877.2 (interquartile range €359.4 to €5574.25) in the year before the TIP, 90.8% of them were indirect costs. Costs decreased to €2715.7 with a median of €436.0 (interquartile range €70.8 to €1749.73) in the first year after the TIP with 80.3% indirect costs. Costs decreased to €1791.7 with a median of €355.8 (interquartile range €109.5 to €1187.8) in the second year after the TIP with 82.4% indirect costs and to €1672.5 with a median of €190.1 (interquartile range €60 to €994.2) in the third year after the TIP with 82.3% indirect costs. For the whole cohort of TIP participants, COI amounted to €5.6 million for the year before the TIP, €2.8 million for the year after the TIP and €1.7 million for the third year after the TIP.

*** Please insert Table 4 here ***

3.2 Cost of intervention

The intervention costs are comprised of direct intervention costs as well as indirect costs. The inpatient therapy lasted 22 days on average and caused direct costs of €5996.3 ($\pm$ 1262.8) per person (Table 5). The length of stay differed between patients who have resumed work after T3 (n = 969) and patients who were unable to do so (n = 72). The latter remained 2.3 days longer in hospital on average. This deviation was attributed to a few outliers.

The indirect costs of intervention result from work incapacity days during inpatient treatment and subsequent work leave (Table 5). The 22 days of incapacity to work during inpatient treatment caused average indirect costs of €3725.5 per patient. Additionally, TIP participants who have resumed work after T3 had on average 32 days of absence. For participants unable to do so we have assumed this mean value as days of absence. Thus, the loss of productivity for subsequent work leave amounted to €5288 per person. The duration from the beginning of the TIP until the return to work was 54 days on average. Resulting costs were €9013 per person. In total, the number of missed days at workplace amounted to 55934 with associated costs of approx. €9.4 million.

Projected at all 1041 persons, the costs amount to an average of €15009 per person and total costs of approx. €15.7 million (Table 5). If only including persons who resumed work, the average intervention costs are €15010 ($\pm$ 4168) per person and total costs for all participants are approx. €14.5 million. However, costs of persons who have not yet resumed work is about €1000 higher than for persons who have already resumed work at that time.

*** Please insert Table 5 here ***

3.3 Quality of life and disease severity

The DLQI questionnaire, assessing QoL, was completed at T1 by 972, at T5 by 995 and at T6 by 1015 persons. Considering persons completing questionnaires at all time points ($n = 913$), DLQI improved from an average of 9.93 to 5.18 and 4.88, with median dropping from 9.0 to 3.0 ($P < .05$). Between T1 and T5, QoL improved for 583 persons (63.9%), remained the same for 221 persons (24.2%), and worsened for 109 persons (11.9%). Between T1 and T6, QoL improved for 597 persons (65.4%), remained the same for 221 persons (24.2%), and worsened for 95 persons (10.4%).

Disease severity, measured by OHSI, was assessed at each time point for all participants ($n = 1041$) and showed a steady average improvement from 6.3 at T1 to 3.3 at T5 and 2.9 at T6 (both $P < .05$), with medians decreasing from 6 to 3 at T5 and to 2 at T6.

3.4 Profession and retraining

Of the 1041 participants, 67 (6.4%) underwent retraining at the expense of the Statutory Accident Insurance and changed their profession. Of those, 51 (48.7%) were female. People who have undergone retraining were significantly younger with an age of 26.5 years (± 9.1) on average compared to the remainder with 44.7 years (± 10.2) ($P < .05$). Occupational groups with the highest proportion of retraining were: hairdressers with 29 persons (43.3%), health/elderly care with 18 persons (26.8%) and the metal industry with 13 persons (19.4%). There was no significant difference in length of inpatient stay during TIP or days with incapacity to work between participants with retraining and those without.

With a discount rate of 3%, retraining costs were €50302 on average. Costs ranged between €47483 and €55316 per person, depending on the year and time (T5 or T6) of retraining beginning. Total costs of retraining were about €3.37 million. In sensitivity analysis, varying the discount rate between 0% and 5%, the retraining costs were between €3.22 million and €3.62 million.

3.5 Cost-effectiveness

With a 3% discount rate, total costs per participant (direct costs, indirect costs and TIP costs), excluding the time before TIP, were €20869 ($\pm €14607$). Of which €5713 ($\pm €27091$) are incremental costs of TIP. The calculation of the ICER resulted in expenses for a patient with a reduction of at least one severity level in OHSI of €8942. The deterministic sensitivity analysis with 0% and 5% discount rates resulted in variations between €7761 and €9517, depending on the chosen discount rate. For an improvement in the disease-specific QoL of at least one level measured by the DLQI, the average costs per patient were €9039 varying between €7822 and €9842 in sensitivity analysis.

In the second part of the cost-effectiveness analysis, retraining measure and associated costs were additionally included. The scenario analysis revealed incremental total costs for TIP of €2475 per person for three years in the base case scenario assuming a 50% reduction of the need for retraining measures. In the worst-case scenario, with 25% reduced retraining, the TIP intervention led to additional costs of €4633 per patient. In contrast, the best-case scenario, with a 75% reduction, resulted in cost savings of €4000 per patient over a period of three years. In this analysis, there is a possibility for the TIP intervention to be cost neutral, leading neither to incremental costs nor to cost savings. This break-even point will be reached if the need for retraining measures is prevented in approximately 64% of TIP participants.

The sensitivity analysis including all TIP participants with available questionnaires at all relevant survey dates (n = 1379) showed significant higher COI when compared to COI who were additionally employed at all relevant survey dates (e. g. €6367 p. p. vs. €5358 p. p. within the year before the TIP and €2277 p. p. vs. €1672 p. p. within the third year after intervention) (data not shown). In contrast, the cost-effectiveness showed results that are more favourable for TIP participants with available questionnaires at all relevant survey dates (DLQI: €8519 p. p. vs. €9039 p. p.; OHSI: €8385 p. p. vs. €8942 p. p.). Concerning the break-even point, results for both cohorts were with 62% and 64% of prevented retraining measures due to the TIP quite similar.

4. DISCUSSION

The ROQ study shows that the TIP is effective in reduction of disease severity (measured with OHSI), improvement of QoL (measured with DLQI) and returning to work or rather remaining employed in patients with severe OSD.^{16,17,27} At the 12-months follow-up, 87.4% of participants were still in active workforce.¹⁷ After three years, 82.7% of the participants were still working, 75% of them in the same occupation field as one year before the TIP.^{15,17} In the present study, these previous findings were confirmed in a subset of 1041 ROQ study participants who were employed and available at all follow-ups.

At the same time, as disease severity and QoL improved, annual COI per patient decreased from €5 358 in the year before the TIP to €1 531 three years after the TIP. Most of the cost reduction was attributable to indirect costs (95%). COI during the year before the TIP were lower than findings from a subgroup of 151 patients from one single centre resulting in €8799.¹⁰ These variations can be explained partly by the consideration of outpatient consultation in the analysis from Diepgen et al. We did not include these services because the number of consultations in the years after the TIP was not specified. Another reason may be differences in monetary valuation of days on sick leave leading to a higher share of indirect costs in our calculations (91% vs. 70%). In line with these findings, a study from Denmark also shows that indirect costs account for the largest share of COI in patients with OSD.¹¹ These observations emphasise the importance of best possible care for OSD patients with the aim of maintaining employment - also from an economic perspective. In contrast, the proportion of indirect costs was much lower in Italy (44%), but the indirect costs were assessed for employed persons only, i.e. 39% of study participants whereas direct

costs were assessed for all participants.²⁷ However, a comparison of studies from Germany also reveals differences in the amount and distribution of costs. If the payer is the statutory health insurance, the COI (€2514 vs. €10153) and the share of indirect costs is significantly lower (18% vs. 51%) compared to the statutory accident insurance.^{9,28} In this study, the payer's perspective is the perspective of the Statutory Accident Insurance, whose primary objective is to maintain the ability to work, by all means available. In contrast to health insurance, which only covers disability to work for a limited period, accident insurance is obliged to cover all losses in earnings until the person is able to work again. Here, the human capital cost approach was preferred to the friction cost approach, as it does not deal with the indirect costs for society and the employer, but with those of the accident insurance. This perspective and the obligation of the accident insurance leads to these high indirect costs (about 90%) compared to other studies. Regarding medical services (leading to direct medical costs) contrasting trends for the different types of services were observed. For systemic drugs and tap water iontophoresis, the annual costs after the TIP were significantly higher for each of the three years observed when compared to the year before the TIP. Possibly, these treatments were initiated or recommended during the TIP or started if the disease was still severe even after the TIP. In contrast, costs for diagnostic procedures and topical drugs were lower in the years after the TIP. This is probably related to the overall decrease of disease severity resulting in a lower need for topical drugs and the extensive diagnostic procedures performed during the TIP rendering more diagnostics unnecessary in the subsequent years.

The cost-effectiveness analysis revealed costs for improvement in disease severity and QoL of €8942 and €9093 per person, respectively. Incremental costs of TIP per participant, taking retraining into account, were estimated with €2475 in the best-case and €4633 in the worst-case scenario for three years. The best-case scenario would even lead to cost savings of €4000 per person.

The cost of the TIP can be offset by productivity gains if participating in the TIP avoids the need for retraining in about 64% of patients. If the participating in the TIP results in a higher rate of retraining prevented, the program can be even cost saving. However, the extent to which retraining measures can be prevented is highly dependent on the age on occupation field of the TIP participants, since persons at younger ages and in particular, hairdressers were more likely to undergo retraining.

4.1 Interpretation of findings

There are only few other economic evaluations of prevention programs for (occupational) skin diseases combining the effectiveness and the costs of prevention programs. Comparison is difficult because the interventions and international healthcare settings are very different. Van der Meer et al have investigated the cost-effectiveness of a multifaceted implementation strategy for the prevention of hand eczema among healthcare workers in the Netherlands. In conclusion, they could not recommend the intervention to be cost-effective, as the effects were non-significant after 12-months follow-up.²⁹ Van Gils et al economically evaluated an integrative care program for patients with hand dermatitis in the Netherlands, as well. This was significantly effective compared to usual care after six months, but not at 12-months follow-up. Therefore, the authors' endorsement of the integrated care program is strongly limited.³⁰ Another study from Denmark, evaluating the effectiveness of a nurse-led counselling program for hand eczema, showed small but significant positive effects of the intervention at 26-weeks follow-up. However, the effects were smaller than anticipated and no cost-effectiveness analysis was performed.³¹ In contrast, the positive effects of the TIP seem comparably strong and long-lasting. The cost-effectiveness of the TIP certainly depends on the number of prevented cost-intensive retraining measures, leading to a wide uncertainty ranging from significant costs to savings by the TIP. However, we assume that the costs of the worst-case scenario would also be justified in order to achieve such strong improvements for the participants.

4.2 Strengths and limitations

The ROQ study is one of the largest and most comprehensively documented intervention studies for patients with OSD. Here, we present the first economic evaluation of the TIP in Germany and one of only few economic evaluations of OSD interventions. The large sample size of 1788 participants, the low drop-out rate even at three-year follow-up, and the results of drop-out analyses indicate very good validity and reliability of findings.¹⁶ The main objective, remaining in workforce, was achieved for the vast majority of the study population. Notably, this effect was maintained over the whole observational period with only small reductions in the effectiveness over time. This is remarkable considering that a three-year follow-up is a relatively long and profound observation period compared to similar studies.

The main limitation of the present study is the lack of a control group. Including a control group was not possible for two reasons. First, ethical responsibilities require to offer measures if they have already been

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proven to be effective in reducing patients' burden.^{13,17,32} Second, all workers are insured by Statutory Accident Insurance, which is obliged by German law to offer prevention by all appropriate means.^{13,17} Therefore, TIP could not be denied to any applicant. Thus, results have to be treated with care, as we cannot be sure to which extent the effects can be assigned to TIP and to which extent to improvement over time, not necessarily being attributable to the intervention. Such an improvement could also be caused by change of professions or shift to activities with lower exposure within the same occupational field. Additionally, costs of non-participation could either be over- or underestimated. To adjust for this, we performed a sensitivity analysis, taking different scenarios for the control group into account.

For the cost calculation, the quantities and frequencies were not assessed for all resources. Missing data on the corresponding resources were estimated based on DDDs and expert opinions. Additionally, drug costs borne by the Statutory Accident Insurance were not available. Therefore, the costs of drugs used for treatment of OSD were obtained from an analysis of statutory health insurance data.²⁰

As the study was not designed for economic evaluation, QoL was not measured with an instrument from which QALYs can be derived. It was not possible to transform the EuroQol (EQ-5D)³³ out of the DLQI.³⁴ Therefore, we decided on calculating two types of ICER: one for the improvement of QoL with DLQI as measurement and one for diseases severity with OHSI as measurement.

In conclusion, OSD intervention studies frequently show only small or no long-term effects of the respective interventions. The ROQ study demonstrated several significant positive effects of the TIP in short-, middle- and long-term observations. Even though it is very difficult to estimate the true costs of the TIP, the results of the ROQ study indicate that the TIP is effective in significantly reducing the patients' burden and the cost-of-illness underlining its importance in prevention of OSD.

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TABLES

TABLE 1 Costs per defined daily doses (DDD) of topical drugs

Topical drug	Costs per DDD [†] (€)
Mainly class I, II steroids (>50%)	0.88
Mainly class III, IV steroids (>50%)	0.99
Steroids, unclarified class	0.93
Tacrolimus	5.90
Pimecrolimus	5.24

[†] For application on hands.

TABLE 2 Costs of medical services and diagnostic tests

Medical service	Price (€)	Estimated frequency	Mixed price (€)
Tap water iontophoresis			
≥ 3 per week	6.08	3 p. w.	18.24 p. w.
< 3 per week	6.08	1 p. w.	6.08 p. w.
UV therapy			
<i>Bath-PUVA/Cream-PUVA</i>	14.56	3 p. w.	43.68 p. w.
<i>Other UV therapy</i>	6.28	3 p. w.	18.84 p. w.
Allergy diagnostics			
<i>Patch test</i> [†]	3.47	-	-
<i>Prick test</i>	4.51	4 p. p.	22.16 p. p.
<i>Intracutaneous test</i> [†]	5.54	-	-
<i>Provocation test</i>	13.27	2 p. p.	26.54 p. p.
<i>Rub test</i>	3.72	4 p. p.	14.88 p. p.
<i>Scratch test</i>	3.72	4 p. p.	14.88 p. p.
<i>Scarification test</i>	3.72	4 p. p.	14.88 p. p.
Laboratory diagnostics			
<i>Mycological test</i>	16.54	3 p. p.	49.62 p. p.
<i>IgE analyses</i>	29.42	1 or 8 p. p.	98.07 p. p.
<i>Bacteriological test</i>	15.22	3 p. p.	45.66 p. p.
Other diagnostics			
<i>Alkali resistance test</i>	13.95	1 p. p.	13.95 p. p.
<i>Skin biopsy</i>	21.85	1 p. p.	21.85 p. p.

Abbreviations: p. p., per person; p. w., per week per patient.

[†] If the frequencies were queried in the questionnaire, they were not estimated, but calculated on the basis of the stated frequencies.

TABLE 3 Descriptive statistics of the study participants at T1 (N = 1041)

Variable	N (%)	Mean (SD)	Range
Gender			
<i>Men</i>	516 (49,6)	-	-
<i>Women</i>	525 (50.4)	-	-
Age [<i>years</i>]	-	43.52 (11.1)	17-67
Occupation			
<i>Metal industry</i>	319 (30.6)	-	-
<i>Health/elderly care</i>	318 (30.5)	-	-
<i>Hairdressing</i>	90 (8.6)	-	-
<i>Construction industry</i>	91 (8.7)	-	-
<i>Others</i>	223 (21.6)	-	-
Quality of Life			
<i>DLQI (N = 972)</i>	-	9.99 (6.5)	0-29
<i>OHSI</i>	-	6.34 (3.5)	0-18

Abbreviations: T1, time point 1 (at admission to the TIP); N, number of participants; SD, standard deviation; DLQI, Dermatology Life Quality Index; OHSI, Osnabrueck Hand Eczema Severity Index.

TABLE 4 Average annual costs of illness per person with 0% discount rate (N = 1041)

Type of costs		1 year before the TIP (T1)	1 st year after the TIP (T5)	2 ⁿ year after the TIP (average of T5 and T6)	3 rd year after the TIP (T6)
		M in € (SD)	M in € (SD)	M in € (SD)	M in € (SD)
direct medical	Diagnostics	47.24 (62.33)	5.13 (26.11)	4.95 (19.42)	4.77 (25.72)
	Topical drugs	85.23 (112.95)	56.80 (109.66)	53.51 (84.62)	50.23 (96.86)
	Systemic drugs	40.43 (274.86)	48.03 (180.83)	48.43 (167.12)	48.83 (261.33)
	Tap water iontophoresis	19.79 (106.55)	79.32 (221.83)	61.59 (159.82)	43.86 (169.99)
	UV therapy	189.98 (434.02)	265.89 (551.34)	160.28 (315.26)	54.66 (224.78)
Out-of-pocket costs		111.18 (169.60)	79.80 (152.10)	86.76 (126.36)	93.72 (155.52)
Indirect costs		4864.59 (9043.37)	2180.75 (7071.89)	1376.43 (5233.72) [†]	1376.43 (5233.72) [†]
Total costs		5358.45 (9097.60)	2715.71 (7157.72)	1791.74 (5 300.32)	1672.48 (5 300.06)

Abbreviations: TIP, tertiary prevention program; M, mean; €, Euro; SD, standard deviation.

[†] Indirect costs of 2 years and 3 years after TIP are averaged over both years and therefore extrapolated equally.

TABLE 5 Costs of intervention (TIP) per person with 3% discount rate (N = 1041)

		TIP		Work leave following TIP[†]		Work leave (TIP + following TIP)		
	Days	Direct costs (€)	Indirect costs (€)	Days	Indirect costs (€)	Days	Indirect costs (€)	Direct + indirect costs (€)
Mean	22.2	5996.28	3725.47	31.5	5287.98	53.7	9013.44	15009.73
SD	4.7	1262.80	784.5	20.6	3614.34	21.6	3614.34	4168.47
Min	14	3780.00	2348.50	1	167.75	21.0	3522.75	8477.00
Median	21	5670.00	3522.75	26	4361.50	48.0	8052.00	13722.00
Max	63	17010.00	10568.25	244	40931.00	267.0	44789.25	52349.25

Abbreviations: TIP, tertiary individual prevention program; Min, minimum; Max, maximum; SD, standard deviation.

[†] From discharge until return to work.