Chapter 6

Economic evaluation of an integrated care program for patients with hand eczema

Submitted as:
van Gils RF, Bosmans JE, Boot CRL, Rustemeyer T, van Mechelen W, van der Valk PGM, Anema JR. Economic evaluation of an integrated care program for patients with hand eczema.

Abstract

Objective

To evaluate the cost-effectiveness of integrated, multidisciplinary care compared with usual care for patients with moderate to severe, chronic hand eczema after 52 weeks follow-up.

Design

This study is an economic evaluation alongside a randomized controlled trial.

Methods

Patients who visited the department of dermatology at one of the participating hospitals for their hand eczema were randomized to integrated care (IC) or usual care (UC). IC was provided by a multidisciplinary team and integrated clinical and occupational care to optimize treatment of hand eczema aimed at improving the patient's quality of life and social functioning. Effect outcomes were clinical assessment of hand eczema using the Hand Eczema Severity Index (HECSI) (primary outcome), disease specific quality of life, work performance and quality-adjusted life-years using the EQ-5D (QALYs). Health care utilization was measured from a societal perspective. Linear mixed models were used to assess differences between the two groups in improvement on the HECSI score. Multiple imputation was used to impute missing cost and effect data. Bootstrapping with 5000 replications was used to estimate the uncertainty surrounding the cost differences and the cost-effectiveness ratios. Cost-effectiveness planes and cost-effectiveness acceptability curves were also estimated.

Results

The mean difference in improvement on the HECSI between both groups after 52 weeks was 8.7 (SE 5.3, 95% CI -1.8 to 18.9), which was not statistically significant (p=0.105). No statistically significant differences between the groups were found on the secondary outcome measures. Mean total costs in the integrated care group (€3613; SD 798) were significantly higher (difference €2037, 95% C.I. €483; €3812) than in the usual care group (€1576, SD 430). The ICER for improvement in HECSI score was -247. Of the bootstrapped cost-effect pairs, 94% were located in the north-east quadrant. Based on the findings of this study, integrated care was not considered cost-effective in comparison with usual care. The probability that integrated care was cost-effective is 90% at a ceiling ratio of 1500 € per point improvement in HECSI score extra.

Conclusion

Integrated care was not (cost)-effective after 12 months follow-up, in contrast to our findings after 6 months. Future studies evaluating the cost effectiveness of integrated care should evaluate a program with longer duration in order to have sustained effects on clinical outcomes and should include presenteeism due to hand eczema as indirect costs. Decision makers should decide whether the clinical benefits of integrated care on the short term outweigh the higher costs compared to usual care.

Introduction

Hand eczema is a common disease with a prevalence ranging from 25 to 66 cases per 1000 patient years and incidence rates from 4 to 7% among full-time workers [1,2]. It accounts for 90% of all occupational skin diseases, and is in the top three of registered work-related disorders[3,4]. Hand eczema is a disease with an unfavourable prognosis. Less than 50% of the patients has recovered after 5 years[5]. The physical and emotional burden of hand eczema is high for individuals[4]. Moreover, hand eczema has a large impact on society as a whole, because it is associated with high costs related to medical consumption, and productivity losses[6]. Sixty percent of all patients with hand eczema visit their general practitioner each year and 20% visits a medical specialist[4]. In the Netherlands, annual costs of medical care, absenteeism and disability pensions due to occupational skin disease in employees were estimated at €98 million[7].

Usual care for hand eczema mainly focuses on achieving short-term improvement of clinical signs. However, considering the unfavourable prognosis of hand eczema, interventions for hand eczema should not only aim at improving quality of life and clinical signs of hand eczema in the short term, but also at reducing productivity losses to lower the economic burden in the long term. We developed an integrated care program that aimed to improve both short and long term outcomes of hand eczema by paying attention to both personal and external factors, for example at the workplace.

The integrated care program is an intensive treatment provided by a multidisciplinary team consisting of a dermatologist, a specialized nurse and, if indicated, a clinical occupational physician. The costs of integrated care were expected to be higher than the costs of usual care. Therefore, it was important to know whether the additional resources needed to implement the intervention, weighed up against the clinical and financial benefits. Economic evaluations provide this information by comparing costs and effects of two or more interventions. This information can be used by policy makers to decide whether the intervention should be covered by health insurance. In an earlier publication we showed that integrated care is effective in improving clinical symptoms of hand eczema after 6 months. The main objective of this study was to evaluate the cost-effectiveness of the integrated care program compared with usual care after one year of follow-up for patients with moderate to severe, chronic hand eczema.

Methods

We carried out a randomized controlled trial with an economic evaluation alongside to compare integrated care with usual care for patients with moderate to severe, chronic hand eczema. The study was conducted at three University Medical Centers in the Netherlands (Amsterdam, Groningen and Nijmegen) between July 2008 and December 2010. The

follow-up period was one year. The Medical Ethical Committees of all participating hospitals approved the study protocol. Patients gave written informed consent. Details of the study have been published elsewhere[8].

Study population

The population in this study comprised patients aged 16 years and older with moderate to severe, chronic (>3 months) hand eczema who visited a dermatologist at one of the participating hospitals. The degree of hand eczema was determined by the dermatologist using the Photographic Guide[9]. Patients with mild hand eczema who were on sick leave from work because of their eczema, or who scored at least 4 points on a Visual Analogue Scale (VAS) for perceived burden of disease in the last three months before baseline were also eligible for inclusion. We excluded patients who had generalized eczema where hand eczema was not the main disease, used topical pharmacotherapy or phototherapy other than the ones used in the study, used systemic treatment affecting hand eczema, or were unable to complete questionnaires in Dutch.

Randomisation and blinding

Randomisation was performed at the patient level. Patients were assigned to either the integrated care group or the control group. Pre-stratification was performed for hospital (Amsterdam, Nijmegen and Groningen) and risk profession (yes/no). This led to a total of six strata. Block randomisation (with blocks of four) was applied to ensure equal group sizes. Within each stratum, a research assistant prepared sequentially numbered sealed envelopes containing allocation to either the intervention or control group.

Patients, health care professionals and researchers were not blinded for treatment allocation because of the nature of the intervention. A research assistant entered all data in the computer by research code. Therefore, the analyses of the data by the researcher were blind.

Usual care

Patients allocated to the usual care (UC) group underwent standard allergological evaluation (intra-cutaneous tests and / or epicutaneous test with the European baseline series and additional series) by their own dermatologist. The patient's own dermatologist was responsible for further usual medical care, such as pharmacotherapy, and provision of standard written information and advices.

Integrated care

Patients allocated to the intervention group received integrated care (IC) by a multidisciplinary team. Like the usual care group, they also underwent standard clinical and allergological evaluation by the dermatologist. A specialized nurse / physician assistant was responsible

for counselling the patient to improve compliance to topical treatment, to hand washing and care procedures, and to the use of protection measures such as protective gloves in general and the use of cotton gloves underneath them. Topical treatment was standardized and consisted of dermatocorticosteroids and emollients, if needed supplemented with calcineurin-inhibitors.

If the hand eczema was work-related or when there was a risk of work absenteeism due to hand eczema, the clinical occupational physician was added to the multidisciplinary team. If indicated, materials derived from the workplace were tested and workplace visits were organised. The clinical occupational physician also gave advice about prevention of hand eczema at work and about changing work procedures to prevent hand eczema. If needed, provision of adapted work was organized in communication with the employer's supervisor.

Clinical outcome measures

The primary outcome measure was the difference in clinical severity of hand eczema measured with the Hand Eczema Severity Index (HECSI, range 0-360)[10] between both groups after 4, 12, 26 and 52 weeks of follow-up compared to baseline. Clinical scoring of the HECSI was performed by an independent, specifically trained clinical investigator, who was blinded for the allocated treatment. Secondary outcome measures included disease-specific quality of life, measured using the Skindex[11], patients' global assessment using Visual Analogue Scales (VAS) for itching, pain and fatigue, and generic quality of life using the EuroQol (EQ-5D)[12]. Work performance was expressed as a percentage, where actual work performance in the last 4 weeks was divided by regular work performance in the last 2 years and multiplied by 100. Quality Adjusted Life Years (QALYs) were calculated based on the EQ-5D. To estimate the utility of health states described by the patients, the Dutch EQ-5D tariff was used[13]. QALYs were calculated by multiplying the utility with the amount of time a patient spent in a particular health state thereby linearly interpolating the transitions between health states.

Costs

Cost data were collected from a societal perspective over 12 months. All costs were adjusted to the year 2010 using consumer price indices if necessary. The year 2010 was chosen because most data were collected in this year. Health care utilization was measured using cost calendars which were completed on a monthly basis and comprised visits to primary and secondary healthcare providers, and use of medication. Dutch standard costs were used to value the utilisation of care[14]. Medication was valued using prices of the Royal Dutch Society for Pharmacy [15]. Costs of implementation of the integrated care program were calculated for each patient by multiplying the cost price of a consult with a specific health care professional with the number of visits to that professional for each patient. Afterwards,

the costs of visits to specific professionals were added to calculate the total intervention costs.

Sick leave due to hand eczema was also reported on the cost calendars. Cost of productivity losses were calculated using the Friction Cost Approach (FCA, main analysis). The cumulative number of days of sick leave was converted into work-hour equivalents based on a Dutch average of 1540 work-hours per year. The FCA assumes that costs are limited to the friction period (i.e. the time it takes to find a replacement). A friction period of 161 calendar days was used.

Costs of production losses were calculated by multiplying the number of sick leave hours by the estimated productivity loss of a worker per hour of sick leave, based on age and gender[14]. In a sensitivity analysis, costs of productivity losses were calculated using the Human Capital Approach.

Sample size

The sample size calculation was based on a pilot study carried out in the Radboud University Medical Centre. In this pilot study, the Hand Eczema Area and Severity score (HEAS) was used. Because the HEAS and the HECSI differ only on minor aspects, we assumed that the results of the pilot study were applicable to the current study. In the pilot study, a reduction in HEAS of 50% was observed during the first six months after the intervention. During the next six months the reduction in HEAS was hypothesized to be 40%. The standard deviation (on a logarithmic scale) of the HEAS was 1.2 and the correlation between measurements from 1 to 6 months apart was 0.5. The correlation did not depend on the length of the interval. Based on these findings, a two-sided type I error of 5% and a power of 80%, 85 evaluable patients with at least three follow-up assessments were required per treatment group. Taking into account a drop-out rate of 15%, 200 patients needed to be included.

Statistical analyses

All analyses were performed at the patient level according to the intention-to-treat principle. To assess whether protocol deviations caused bias, we compared the results of the intention-to-treat analyses with those of per-protocol analyses. Student T-tests and Chi square tests were performed to test for differences in baseline characteristics of patients between the IC group and the UC group. A non- response analysis was done using student T-tests and Chi square tests comparing baseline differences between patients with and without complete effect measurements and between patients who completed at least 9 monthly cost measurements (i.e. 75%) and patients who did not. The primary independent variable in the effect analyses was the treatment to which the patient was allocated. The primary dependent variable long-term effect was the clinical severity score HECSI. Linear mixed models were used to assess differences between the two groups in improvement

in the HECSI score. A mixed model allows for clustering of patients within hospitals and of measurements within patients. To assess the effect over time, time was specified as a fixed factor with levels 0 (baseline), 4, 12, 26 and 52 weeks. The main effect was the difference in improvement from baseline after 52 weeks between both groups.

Linear mixed models were also applied to assess differences between the groups in improvement in the secondary outcomes (Skindex and patient's global assessment measures) after 52 weeks.

First, an unadjusted linear mixed model analysis was performed. Second, in an adjusted analysis confounding and effect modification were assessed. The potential confounders or effect modifiers were predefined and were all measured at baseline: personal characteristics (age and gender); job characteristics (working in a risk profession), medical history (a history of atopic eczema and the presence of allergens) and HECSI score at baseline. Age was checked on linearity and HECSI score was dichotomized into low and high baseline score using the median in both groups; all other factors were dichotomous. Univariate tests for confounding and effect modification were performed for all outcome measures. Covariates were considered confounders if the ß of the intervention variable changed more than 10% by adding the covariate to the mixed model. Effect modification was tested by performing the mixed model analyses separately for subgroups. For continuous variables (age, HECSI baseline), subcategories were defined based on the median score. When the results for the subgroups showed significantly different effects for one subgroup, the covariate was considered an effect modifier. For all effect modifiers, subgroup analyses are presented. We considered p-values lower than 0.05 as statistically significant. The data were analysed with SPSS statistical software, version 17.0.

For the economic evaluation, multiple imputation based on the Multivariate Imputation by Chained Equations (MICE) procedure was used to impute missing cost and effect data[16]. An imputation model containing important demographic and prognostic variables was specified to estimate five complete data sets. Effects and costs from the five complete data sets were pooled using Rubin's rules [17]. Costs generally have a highly skewed distribution. Therefore, bootstrapping with 5000 replications was used to estimate "approximate bootstrap confidence" (ABC) intervals around cost differences[18].

For the cost-effectiveness analyses, incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in total costs between the IC and UC by the difference in effects. Incremental cost-utility ratios (ICURs) were calculated by dividing the incremental costs by the difference in QALYs between the groups.

Bootstrapping with 5000 replications was also used to estimate the uncertainty surrounding the ICERs and ICURs. Bootstrapped cost-effect pairs were used to plot cost-effectiveness planes and to estimate cost-effectiveness acceptability curves. Cost-effectiveness acceptability curves show the probability that a new treatment is cost-effective in

comparison with usual care for a range of different ceiling ratios, which is the maximum amount of money a decision maker is willing to pay to gain one extra unit of effect[19]. The statistical software program "R" was used to estimate the cost-effectiveness planes and cost-effectiveness acceptability curves.

Results

Participants

Between July 2008 and December 2009, 196 patients who visited a dermatologist because of hand eczema at one of the participating hospitals and who signed informed consent, were randomized: 101 to the integrated care group (IC) and 95 to the usual care group (UC). Figure 1 shows the flow of patients through the study. The number of participants with a history of atopic eczema was significantly higher in the integrated care group (Table 1). Other baseline characteristics are also presented in Table 1 and did not differ between the groups. Data on the HECSI were complete for 170 (87%) patients after 52 weeks. Nine patients did not comply with the intervention for various reasons: no time (n=4), no perceived improvement (n=3) or perceived recovery (n=2). Of all participants, 129 completed at least 9 cost calendars (65.8%).

Figure 1. Flow of patients through the study

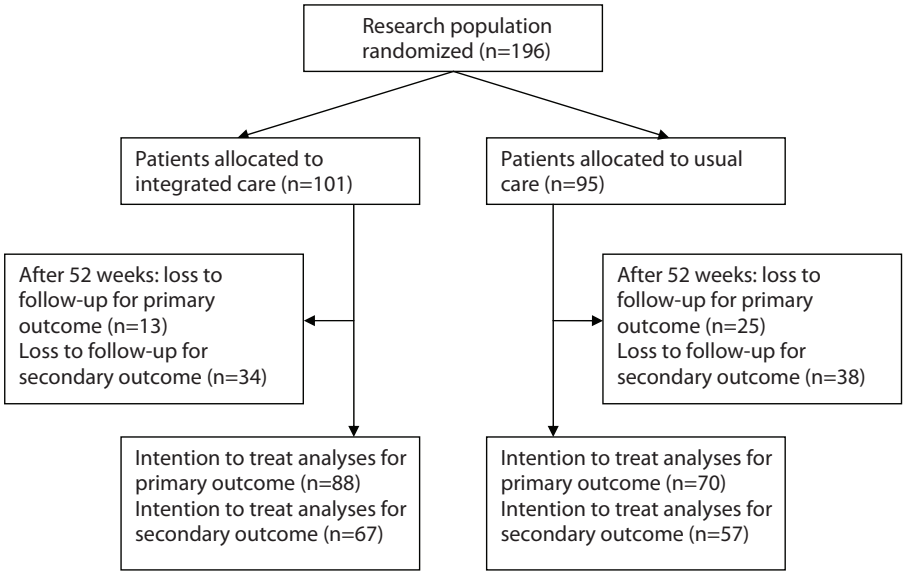


Table 1. Baseline characteristics and prognostic factors of outcome measures.

Variable	Integrated care (n=101)	Usual care (n=95)
Men	46 (46)	48 (52)
Women	55 (54)	47 (48)
Age (years) Mean (SD)	43.4 (13.8)	43.0 (13.9)
Risk profession	50 (50)	38 (40)
History of atopic eczema	34 (34)	18 (19)
Presence of allergens	65 (64)	66 (69)
Level of education - Low - Intermediate - High	 35 (35) 35 (35) 31 (30)	 30 (32) 38 (40) 27 (28)
HECSI Mean (SD)	43.9 (33.7)	36.5 (33.9)
Quality of life Mean (SD)	38.7 (15.9)	36.4 (15.5)
Patient's global assessment Mean (SD) Pain Itching Fatigue	 4.4 (2.7) 4.2 (2.4) 4.5 (2.9)	 4.5 (2.4) 4.1 (2.6) 3.9 (2.7)

Values are expressed as number of patients (percentages) unless stated otherwise.

Implementation of the intervention program

The average number of visits of patients in the intervention group to the specialized nurse was 3.9 and 1.2 to the dermatologist. In total, 29 patients had an indication to consult the clinical occupational physician (COP) of whom 18 patients (69%) visited the COP at least once.

Effects on primary outcome measure: HECSI

Patients in IC improved from 43.9 points at baseline (range 2 – 146) to 19.3 points after 52 weeks (range 0 – 98) on the HECSI. In UC, the average improvement was from 36.5 points at baseline (range 3 – 174) to 20.6 after 52 weeks (range 0 – 123). This means an improvement on HECSI of 24.6 points in IC and 15.9 points in UC. Figure 2 presents the graph of the fixed predicted values for the two groups. The mean difference in improvement on the HECSI between both groups after 52 weeks was 8.7 (SE 5.3, 95% CI -1.8 to 18.9), which was not statistically significant (p=0.105) (see Table 2). No prognostic variables were found to be confounders or effect modifiers.

Figure 2. Model based means of the primary outcome measure HECSI

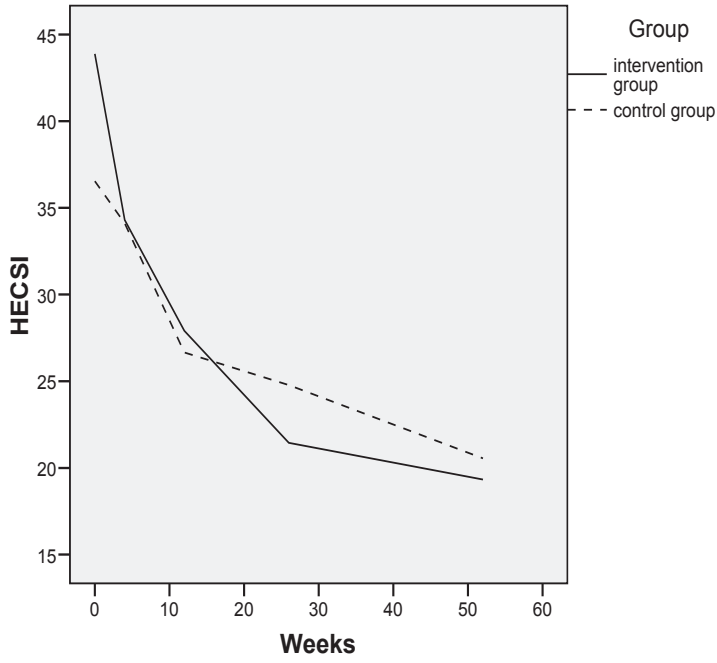


Table 2. Effects from the mixed model analyses, pooled mean costs and differences in mean total effects and costs over 12 months of follow-up

Pooled effects	**Mean total effects (SD)**		**Mean effect difference (95% CI)**
	Integrated care (N=101)	**Usual care (N=95)**	
HECSI	24.6 (34.0)	15.9 (35.9)	8.7 (-1.8; 18.9)
QALY	0.85 (0.14)	0.89 (0.11)	-0.04 (-0.08; -0.00)
Pooled costs	**Mean total costs (SD)**		**Mean cost difference (95% CI)**
Total direct	957 (80.3)	480 (67.6)	475 (245.1; 693.9)
Total indirect	2656 (772.0)	1097 (409.0)	1559 (86.2; 3283.9)
Total societal	3613 (798.2)	1577 (429.5)	2036 (483.4; 812.2)

Effects on secondary outcome measures

Table 3 presents the results of the effectiveness of integrated care on disease-specific quality of life and patient's global assessment. A large improvement was observed on all outcomes in both groups. However, no statistically significant differences in improvement were found between both groups. An increase in work performance of 8.7% was observed in the intervention group, compared to 0.5% in the usual care group. This difference of 8.2% was not statistically significant (C.I. -3.5; 19.9, p=0.17). There was a statistically significant

difference in QALYs at 12 months of follow-up between the groups of 0.04 QALYs in favour of the usual care group.

Table 3. Differences (Mean (S.E.)) in Quality of life and patient's global assessment at baseline and after 52 weeks.

	Group	Baseline	52 weeks	p Value
Skindex				
- Symptoms	IC	59.8 (1.73)	42.0 (2.61)	0.93
	UC	60.1 (1.88)	41.8 (2.73)	
- Emotion	IC	31.6 (1.94)	20.0 (2.21)	0.58
	UC	29.0 (2.10)	19.3 (2.33)	
- Function	IC	24.3 (1.88)	16.7 (1.92)	0.80
	UC	21.2 (2.03)	11.9 (2.02)	
- Total	IC	38.6 (1.58)	24.0 (1.95)	0.89
	UC	36.8 (1.72)	21.8 (2.05)	
Global assessment				
- Itching	IC	5.4 (0.27)	2.7 (0.28)	0.63
	UC	5.7 (0.30)	3.0 (0.31)	
- Pain	IC	4.4 (0.28)	2.4 (0.29)	0.60
	UC	4.5 (0.30)	2.4 (0.32)	
- Fatigue	IC	4.5 (0.29)	3.0 (0.30)	0.87
	UC	3.9 (0.31)	3.0 (0.32)	

IC, integrated care; UC, usual care.

Costs

Table 2 shows the cost estimates for the two groups and the differences between groups. Mean integrated care costs per patient in the IC group of were €324. Productivity losses (indirect costs) were the largest contributor to total costs in both groups. Indirect costs were statistically significantly higher in the intervention group (€2656) compared with the control group (€1097; difference €1561, 95% C.I. €86; €3284). Total costs were €3613 (SD 798) in the integrated care group and €1576 (SD 430) in the usual care group. The difference between the groups was statistically significant (€2037, 95% C.I. €483; €3812).

Cost-effectiveness and cost-utility analyses

The main analysis (Table 4) showed that the ICER for improvement on HECSI was -247 (mean difference in total costs (€2038) divided by the mean difference in HECSI (-8.3 points) for the total group). This means that an additional €247 needs to be invested in integrated care for one point more improvement on the HECSI compared with usual care. The cost-effectiveness plane for the HECSI is shown in Figure 3a. This figure shows that 94% of the bootstrapped cost-effect pairs are located in the north-east quadrant, which confirms that integrated care was more effective and more expensive than usual care. The cost-effectiveness acceptability curve presented in Figure 3b indicates that if society is willing to pay €1500 for one point improvement extra on the HECSI, the probability that integrated care is cost-effective is 90%.

Table 4. Results of cost-effectiveness analyses (difference = intervention minus control)

		Sample size		Cost difference (95% C.I.)	Effect difference (95% C.I.)	ICER	Distribution CE-plane			
		IC	UC				%NE	%SE	%SW	%NW
Main analysis	HECSI	101	95	2037 (483; 3812)	-8.3 (-18.6; 2.1)	-247	93.8	0.4	0.1	5.7
	QALY	101	95	2037 (483; 3812)	-0.04 (-0.08; -0.0)	-49566	1.9	0.1	0.4	97.6
HCA	HECSI	101	95	1708 (-611; 3571)	-8.3 (-18.6; 2.1)	-207	90.1	4.3	0.6	4.9
	QALY	101	95	1708 (-611; 3571)	-0.04 (-0.08; 0.0)	-41557	1.5	0.3	4.7	93.4
P.P.	HECSI	80	95	1978 (431; 3837)	-10.2 (-20.1; 0.6)	-195	96.0	0.7	0.1	3.2
	QALY	80	95	1978 (431; 3837)	-0.04 (-0.08; 0.0)	-50498	2.7	0.1	0.6	96.6

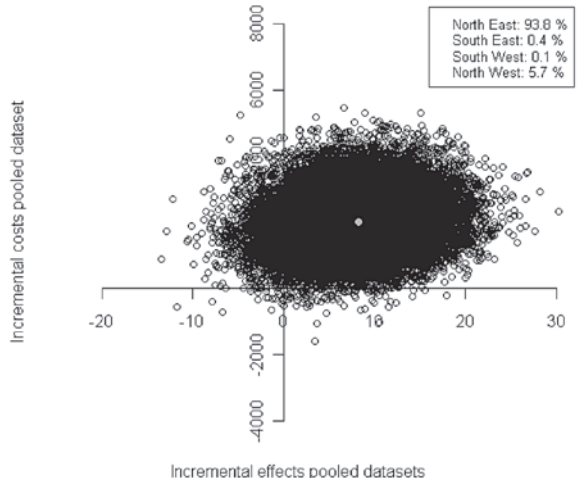
*Human capital approach: no friction period was used for work absenteeism

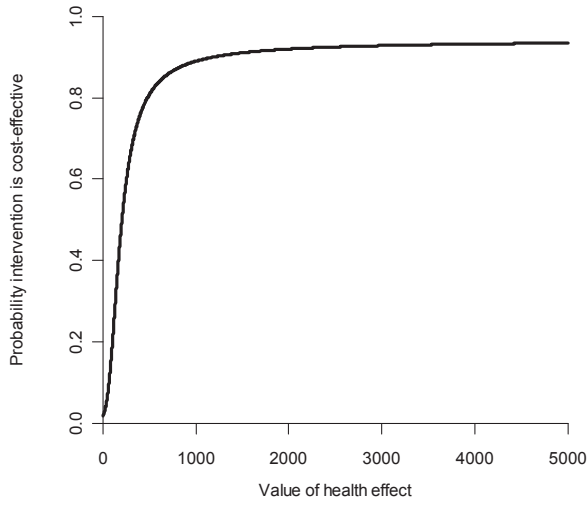
**Per protocol: patients who visited the specialized nurse at least 75% and visited the clinical occupational physician when indicated.

The maximum probability integrated care is cost-effective in comparison with usual care is at a ceiling ratio of 94%. The per-protocol analysis and the sensitivity analysis using the Human Capital Approach show comparable results on the cost-effectiveness of integrated care in comparison with usual care for improvement on HECSI.

The difference in QALYs at 12 months of follow-up between the group was 0.04 QALYs in favour of the usual care group. In combination with the higher costs of integrated care in comparison with the control group, this means that integrated care is never considered cost-effective in comparison with usual care, regardless of the willingness to pay per additional QALY.

Figure 3a and b. Cost-effectiveness plane and cost-effectiveness acceptability curve for the difference in HECSI after 52 weeks





Discussion

Integrated care (IC) was superior to usual care with an improvement on HECSI of 24.6 points in IC and 15.9 points in UC after 12 months of follow-up. This difference in improvement was not statistically significant anymore after 12 months of follow-up in contrast to the difference between IC and UC after 6 months of follow-up [20]. The cost-effectiveness acceptability curve shows that the probability of integrated care being cost-effective in comparison with usual care was approximately 90% for ceiling ratios larger than €1500 for improvement on the HECSI. For QALYs gained, integrated care was not cost-effective in comparison with usual care for any possible ceiling ratio. Based on the long term results of this study, integrated care was not considered cost-effective in comparison with usual care.

Strengths and limitations

The most important strength of this study is the unique integrated care approach, in which many factors that may cause or maintain hand eczema are addressed by a multidisciplinary team. This approach was evaluated in a well designed, pragmatic randomized controlled trial with an economic evaluation alongside. To the best of our knowledge this is the first economic evaluation in the field of dermatology. The primary outcome measure was assessed using an objective, reliable and simple scoring method by a blinded assessor. Due to the broad inclusion criteria, the cost-effectiveness of integrated care was evaluated in a wide variety of patients with different degrees of hand eczema who visited different hospitals with varying expertise. Thus, the external validity of the study results is high.

However, the study also had some methodological limitations. First of all, the amount of missing data was relatively high for cost data. Sixty-five participants returned all cost calendars and 129 returned nine or more calendars. In total, approximately 33% of all cost data had to be imputed. We used multiple imputation to impute missing data which is considered the most appropriate technique to impute missing cost data because it takes into account the uncertainty about the missing data[14]. Non response analysis for participants who had returned nine or more calendars showed a comparable ICER, implying bias is unlikely.

Second, the power of the economic evaluation was insufficient which is reflected in the wide confidence intervals for cost differences. This is a common problem in economic evaluations alongside RCTs, in which sample sizes are usually based on detecting relevant differences in clinical effects. Because the distribution of cost data typically is heavily skewed, large study populations are needed[21].

Third, the significantly higher indirect costs in the intervention group were due to patients in the intervention group being longer on sick leave than patients in the control group. This may be a side-effect of the intervention, because patients in the intervention group were advised by the multidisciplinary team to call in sick, when their hand eczema was

aggravating. However, results show that the actual work performance as a percentage of regular work performance increased with 8.2% more in the intervention group than in the control group. Thus, the participants in the intervention group were more often on sick leave, but when at work, they performed better although not statistically significantly so.
Although we used work performance as a proxy for presenteeism, costs due to presenteeism (productivity loss as a result of reduced productivity when an employee is at work) were not measured in this study. However, according to a review of Schultz et al.[22], 70% of all costs in allergies including hand eczema can be attributed to presenteeism. Based on the more positive results for work performance in the intervention group in comparison with the control group, we expect that inclusion of presenteeism costs will lead to a larger increase in indirect costs in the usual care group more than in the intervention group. This means that the cost-effectiveness of integrated care may have been underestimated by not including presenteeism cost in this study.

Interpretation of results

To our knowledge, no other cost-effectiveness studies have been carried out to evaluate an integrated care intervention for patients with hand eczema. An economic evaluation by Lambeek et al.[23], showed that a comparable integrated care approach was cost-effective for patients with chronic low back pain. They found that an investment of €4.10 in the integrated care program resulted in a reduction in sick leave of one day compared with usual care.
Although the interventions were based on the same principles, there are some important differences which may explain the different results. Most importantly, Lambeek et al. used duration until return to work as primary outcome measure versus a clinical score in our study. However, the improvement in clinical symptom scores found in this study was not accompanied by a reduction in sick leave, which was the most important cost driver. Besides, only a small number of patients in our study were on sick leave compared to all patients in the LBP study where sick leave was an inclusion criterion. Since the monetary gains of improvement on clinical outcomes and general participation as described in the ICF[24] are negligible compared to the monetary gains of less sick leave, and since sick leave was not an inclusion criterion in our study, it was difficult for our study to get a positive cost benefit ratio. Inclusion restricted to patients with work-related hand eczema, might have lead to more positive results.

Implications for research and practice

Economic evaluations are important for decision makers to decide whether or not to implement an intervention on a wider scale. Recommendations for future economic evaluations in the field of dermatology include the following. Firstly, presenteeism should

be included in the measurements since it is estimated to be responsible for 70% of total costs of allergies including hand eczema[22]. Secondly, the effects of the integrated care program on clinical scores diminished during long term follow-up. To maintain these effects, the integrated care program should cover a longer period than the 3 month period in this trial. The relatively short duration of the integrated care program may also explain that no effect on quality of life could be demonstrated. It is important to improve the (psychological) burden of disease of chronic hand eczema, because it's burden is comparable to other diseases[4] such as rheumatoid arthritis or multiple sclerosis.

Conclusion

Integrated care was not (cost)effective after 12 months follow-up, in contrast to our findings after 6 months. Future studies evaluating the cost effectiveness of integrated care should evaluate a program with longer duration in order to have sustained effects on clinical outcomes and should include presenteeism due to hand eczema as indirect costs. Decision makers should decide whether the clinical benefits of integrated care on the short term outweigh the higher costs compared to usual care.

References

1. Diepgen TL, Coenraads PJ: **The epidemiology of occupational contact dermatitis.** *Int Arch Occup Environ Health* 1999, **72:**496-506.
2. Koch P: **Occupational contact dermatitis. Recognition and management.** *Am J Clin Dermatol* 2001, **2**:353-365.
3. Meding B, Wrangsjo K, Jarvholm B: **Fifteen-year follow-up of hand eczema: persistence and consequences.** *Br J Dermatol* 2005, **152**:975-980.
4. Verhoeven EW, Kraaimaat FW, van de Kerkhof PC, van WC, Duller P, van d, V, van den Hoogen HJ, Bor JH, Schers HJ, Evers AW: **Psychosocial well-being of patients with skin diseases in general practice.** *J Eur Acad Dermatol Venereol* 2007, **21:**662-668.
5. Driessen LHHM, Coenraads PJ, Groothoff WJ, Nater JP: **A group of patients with eczema after 5 years. (In Dutch: Een groep eczeempatiënten- 5 jaar later.)**. *Tijdschr Soc Geneesk* 1982.
6. Cvetkovski RS, Rothman KJ, Olsen J, Mathiesen B, Iversen L, Johansen JD, Agner T: **Relation between diagnoses on severity, sick leave and loss of job among patients with occupational hand eczema.** *Br J Dermatol* 2005, **152**:93-98.
7. Koningsveld EAP, Zwinkels WS, Mossink JCM, Thie XMAbspoel M: *Maatschappelijke kosten van arbeidsomstandigheden van werknemers in 2001. Rapport aan Ministerie van Sociale Zaken en Werkgelegenheid.* 2003.
8. van Gils RF, van der Valk PGM, Bruynzeel D, Coenraads PJ, Boot CRL, van MW, Anema JR: **Integrated, multidisciplinary care for hand eczema: design of a randomized controlled trial and cost-effectiveness study.** *BMC Public Health* 2009, **9**:438.
9. Coenraads PJ, Van Der WH, Thestrup-Pedersen K, Ruzicka T, Dreno B, De La LC, Viala M, Querner S, Brown T, Zultak M: **Construction and validation of a photographic guide for assessing severity of chronic hand dermatitis.** *Br J Dermatol* 2005, **152:**296-301.
10. Held E, Skoet R, Johansen JD, Agner T: **The hand eczema severity index (HECSI): a scoring system for clinical assessment of hand eczema. A study of inter- and intraobserver reliability.** *Br J Dermatol* 2005, **152**:302-307.
11. Chren MM, Lasek RJ, Quinn LM, Mostow EN, Zyzanski SJ: **Skindex, a quality-of-life measure for patients with skin disease: reliability, validity, and responsiveness.** *J Invest Dermatol* 1996, **107**:707-713.
12. Brooks R: **EuroQol: the current state of play.** *Health Policy* 1996, **37:**53-72.
13. Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. **Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff.** Ned Tijdschr Geneeskd 149(28), 1574-1578. 2005.
14. Oostenbrink JB, Koopmanschap MARutten FF: *Handbook for cost studies, methods and guidelines for economic evaluation in health care.* 2006.
15. **Z-index. G-Standaard. The Hague, The Netherlands: Z-index**. 2006.
16. van Buuren SOudshoorn CG: *Multivariate Imputation by Chained Equations.* Leiden, TNO; 2005.
17. Rubin DB: *Multiple imputation for nonresponse in surveys.* New York; 1993.
18. Efron B, Tibshirani RJ: *An introduction to the bootstrap.* New York: 1993.
19. Fenwick E, O'Brien BJ, Briggs A: **Cost-effectiveness acceptability curves—facts, fallacies and frequently asked questions.** *Health Econ* 2004, **13**:405-415.
20. van Gils RF, Boot CRL, Knol DL, Rustemeyer T, van Mechelen W, van der Valk PGM, Anema JR. **The effectiveness of integrated care for patients with hand eczema: results of a randomized, controlled trial.** *Contact Dermatitis:* **66**: 197–204

21. Briggs A: **Economic evaluation and clinical trials: size matters**. *BMJ* 2000, **321**:1362-1363.

22. Schultz AB, Chen CY, Edington DW: **The cost and impact of health conditions on presenteeism to employers: a review of the literature.** *Pharmacoeconomics* 2009, **27**:365-378.

23. Lambeek LC, Bosmans JE, Van Royen BJ, van Tulder MW, van Mechelen MW, Anema JR: **Effect of integrated care for sick listed patients with chronic low back pain: economic evaluation alongside a randomised controlled trial**. *BMJ* 2010, **341**:c6414.

24. World Health Organization: *International Classification of Functioning, Disability and Health*. 2001.