ORIGINAL ARTICLE

Cost-effectiveness and Quality of Specialized and Routine Care in a German Cohort of Patients with Chronic Pruritus

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Chronic pruritus is a prevalent interdisciplinary symptom with a strong influence on health-related quality of life. Patients need extensive diagnostics and long-term treatment. This retrospective and prospective cohort study compared routine and university-based specialized care in terms of cost-effectiveness and patient benefit. Direct medical and non-medical costs and patient-reported outcomes (PRO; pruritus intensity, quality of life, treatment needs and benefits) were assessed. Data analyses were conducted using descriptive methods and non-parametric statistical tests. A total of 300 adult patients (54.3% female) participated in the study. Six months after the treatment start in a specialized German pruritus care unit, the total costs were significantly reduced (mean total costs 686 € vs 433 € per patient per half year (total cohort); $p < 0.001$; mean out-of-pocket costs 198 € vs 124 € per half year (total cohort), $p < 0.001$). Pruritus intensity (numerical rating scale 5.3 vs 3.7, $p < 0.001$), quality of life (Dermatology Life Quality Index 8.9 vs 5.7, $p < 0.001$) and patient benefit (Patient Benefit Index Pruritus 1.2 vs 2.1, $p < 0.001$) improved significantly (total cohort). The results of this study show, that treatment of chronic pruritus patients in a specialized itch centre leads to an improvement in patient benefit and reduces the economic burden at the same time.

Key words: cost-benefit analysis; cost of illness; patient-reported outcome measures; pruritus; quality of healthcare.

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SIGNIFICANCE

Chronic pruritus is a burdensome symptom that affects 16.8% of the German working population and requires specialized, often cost-intensive diagnostics and treatment. Cost-effectiveness analyses are necessary to provide high-quality care and to reduce economic burden. This is the first retrospective and prospective cohort study that compares treatment quality and cost of a specialized university-based German itch centre with that of routine care. The results show that the treatment of patients with chronic pruritus in a specialized university itch centre improves the quality of care and patient penefits and, at the same time, reduces the economic burden.

Chronic pruritus (CP; duration at least 6 weeks) affects approximately 16.8% of the German working population (1). Patients experience a physical and mental burden of disease, as quality of life, sleep and social interaction are highly affected (3). CP is associated with many comorbidities (e.g. neurological, psychiatric, internal) and requires extensive diagnostics and long-term, specialized treatment (2).

According to the classification of the International Forum for the Study of Itch (IFSI), patients with CP can be divided into 3 groups: CP on diseased skin (IFSI I), CP on non-diseased skin (IFSI II) and CP with chronic scratch lesions (IFSI III) (2). Patients with chronic prurigo, especially prurigo nodularis (PN), make up a large proportion of IFSI III (2).

In the context of diagnosis and treatment monitoring of CP, pruritus-specific, validated patient-reported outcome (PRO) measures are required to assess pruritus intensity, health-related quality of life (HRQoL), anxiety, depression, sleep and treatment needs and benefits.

The patient-individual diagnostic workup of CP is often complex and includes the assessment of pruritus underlying and accompanying disorders, laboratory tests and medical imaging (e.g. X-ray, ultrasound, magnetic resonance imaging (MRI), computed tomography (CT)); therapies often consist of costly off-label medication (2).

In Germany, patients with CP are treated in inpatient and outpatient settings by general practitioners and specialists (4). Diagnosis and treatment often remain unsuccessful in routine care, as therapeutic setbacks and, often, long treatment spans are described (5). Complex diagnostics and cost-intensive therapies, which are insufficiently represented in the German Diagnosis-Related Groups (G-DRG) system, mean high financial expenditure for treating physicians (6). Resident physicians' budgets are limited and their time quota is exhausted rapidly, which makes patients feel inadequately treated and informed (6).

Specialized interdisciplinary care units, often attached to university hospitals, may improve patient treatment benefit by delivering sufficient diagnostics and treatment. This might cause additional cost to the health insurance and increase future health expenses (7). Therefore, cost-effectiveness analyses are essential to investigate costly specialized treatment and to improve quality of routine and specialized care of patients with CP (8).

The aim of the current study was to analyse the cost-effectiveness of treatment of chronic itch patients at a specialized university-based German itch centre in comparison with routine care.

MATERIALS AND METHODS

Data collection

Patients with CP were recruited when attending the competence centre for chronic pruritus (Kompetenzzentrum Chronischer Pruritus (KCP)) in Münster, North Rhine-Westphalia, Germany, for the first time (T0). Inclusion criteria were: age ≥18 years and the ability to give and declare consent. Data collection was carried out using paper-based methods in personal interviews and on mobile devices that were routinely used at the centre (9, 10).

At T0 and 6 months after the first consultation (T1), direct medical and non-medical costs and PRO data were calculated from the patients' and medical records. The patients were assigned to the pruritus groups according to the IFSI classification, in order to enable subgroup comparisons.

Patient-reported outcomes

Pruritus intensity was measured with a numerical rating scale (NRS) (0–10; NRS-24 h: mean intensity of the last 24 h). The minimal clinically important difference (MCID, smallest PRO change that can be detected by the patient) for the NRS-Itch is defined as a change of 2–2.5 points (11). HRQoL was analysed using the Dermatological Life Quality Index (recommended MCID 4 points) (12) and the pruritus-specific ItchyQoL (13) (DLQI: 0–30, ItchyQol: 0–110). Patients' needs and benefits were assessed with the Patient Benefit Index for pruritus (PBI-P: 0–4), which consists of 27 treatment goals of 5 different need dimensions. The "cut off value" for a patient relevant benefit is determined as ≥1 (14).

Costs

Direct medical costs include all monetary services that are provided in the context of diagnosis and treatment of a disease (inpatient and outpatient costs including medical consultations, services, medication, etc.) (15). These costs were assessed according to G-DRG (16) and the German system for reimbursement of outpatient care ("EBM – *Einheitlicher Bewertungsmaßstab*", Uniform Value Scale, quarter 1/2017, respectively, GOÄ, "*Gebührenordnung für Ärzte*", fees for physicians, 1 January 2002) guidelines as well as to the valid reimbursement medication price in the German Drug Directory (as referenced in the "*LauerTaxe*") (reference: LAUER-TAXE® - Apotheke - Produkte - cgm.com).

Direct non-medical costs occur as a by-product of the use of medical resources (e.g. costs for transportation to the physician, costs for skin care, special food or clothing, family care costs) (15). In order to record these as precisely as possible, patients were asked to keep receipts or bank statements and to bring them to the personal interview. If these were not available, patients were asked to estimate these costs as accurately as possible.

Cost-effectiveness was calculated from the perspective of the total compulsory health insurance cost, using the formula:

$$Pre - Post\ Comparison = \frac{Cost\ T1 - Cost\ T0}{Benefit\ T1 - Benefit\ T0}.$$

Statistical analysis

Statistical analyses were performed in SPSS Statistics for Windows (version 25.0 (IBM Corp., Armonk, N.Y., USA) using descriptive analyses.

Prior simulations showed that the data were not normally distributed. Therefore, non-parametric tests were used for analysis of significance. The Wilcoxon signed-rank test was used for post hoc analyses (comparison of cost-effectiveness and quality of specialized and routine care within each IFSI group). For intergroup comparisons (comparisons between IFSI group I–III) the Kruskal–Wallis test was used. If the Kruskal–Wallis test showed significant results between the 3 groups, the Mann–Whitney *U* test was added as a more specific test to investigate 2 groups more precisely.

Ethics statement

The study was approved by the Medical Ethics Committee of the University Medical Center Münster, Germany (2015-262-f-S). All patients gave written informed consent.

RESULTS

At T0, 300 adult patients with CP were recruited (mean age 57 years, 54.3% female, mean pruritus duration 92.0 ± 123.0 months). Of these, 85% ($n=255$) had presented themselves to outpatient clinics 6 months beforehand. Out of all the patients, 246 (82%) attended the follow-up examination (T1). Most patients belonged to IFSI group II (CP on non-diseased skin) (see **Table I**). The most common underlying diseases for chronic pruritus were dermatoses (50.3%; $n=151$), followed by multifactorial (22.3%, $n=67$), neurological (10.7%, $n=32$), systemic (8%, $n=24$), psychological/psychosomatic (0.7%, $n=2$) and other causes (8%, $n=24$).

Systemic therapies comprised antihistamines, corticosteroids, gabapentinoids, opioid antagonists and immunosuppressants; topical therapies included corticosteroids, calcineurin inhibitors, anti-infectives (antiseptics, antimycotics, antiparasitics) and emollients. The prescription of systemic antihistamines, systemic corticosteroids, topical corticosteroids, as well as topical emollients and combination treatment was significantly reduced after the first presentation in favour of a more focused prescription, due to expert treatment ($p<0.005$; see Table I).

Patient-reported outcomes

Pruritus intensity and HRQoL improved significantly according to the NRS and the DLQI/ItchyQol at T1 ($p<0.001$), while the patient benefit increased signifi-

Table I. Sociodemographic data, pruritus characteristics and therapies before (T0) and after (T1) the treatment in a specialized pruritus care unit

Sociodemographic data	T0 (n = 300 patients, 100%)	T1 (n = 246 patients, 82%)
Male patients, n (%)	137 (45.7)	137 (55.7)
Female patients, n (%)	163 (54.3)	109 (44.3)
Age, years, mean±SD (median)	57.4±17.3 (59.0)	58.7±16.8 (60.0)
Pruritus manifestation	T0 (n = 300 patients, 100%)	T1 (n = 246 patients, 82%)
Generalized pruritus, n (%)	218 (72.7)	177 (72.0)
Localized pruritus, n (%)	82 (27.3)	69 (28.0)
Classification of Itch (IFSI)	T0 (n = 300 patients, 100%)	T1 (n = 246 patients, 82%)
Pruritus on diseased skin (IFSI group I), n (%)	106 (35.3)	85 (34.6)
Pruritus on non-diseased skin (IFSI group II), n (%)	122 (40.7)	105 (42.7)
Chronic scratch lesions (IFSI group III), n (%)	72 (24.0)	56 (22.8)
Treatment modalities	T0 (n = 300 patients, 100%)	T1 (n = 246 patients, 82%)
Outpatient treatment, n (%)	255 (85.0)	212 (86.2)
Inpatient treatment, n (%)	35 (11.3)	28 (11.4)
Duration of inpatient treatment, days, mean±SD	14.2±12.5	7.3±6.2
Systemic treatment	T0 (n = 298 patients, 99.3%)	T1 (n = 245 patients, 81.6%); p-values
Antihistamines n (%)	179 (60.1)	88 (35.9); <0.001***
Corticosteroids n (%)	29 (9.7)	4 (1.6); 0.003**
Anticonvulsants	25 (8.4)	28 (11.4); 0.157
Immunosuppressants	6 (2.0)	9 (3.7); 0.564
Naloxone/naltrexone	3 (1.0)	3 (1.2); 0.564
Topical treatment	T0 (n = 298 patients, 99.3%)	T1 (n = 245 patients, 81.6%); p-values
Topical corticosteroids	139 (46.6)	74 (30.2); 0.001**
Topical immunomodulators	25 (8.4)	19 (7.8); 0.705
Topical capsaicin	7 (2.4)	5 (2.0); 0.564
Topical emollients	91 (30.5)	43 (17.6); <0.001***
Topical anti-infectives	34 (11.4)	15 (6.1); 0.480
Combination treatment	49 (16.4)	10 (4.1); <0.001***

For systemic and topical treatment, the corresponding p-values are shown to enable post-hoc comparisons (Wilcoxon signed-rank test).
*p<0.05; **p<0.01; ***p<0.001; topical anti-infectives: topical antibiotics, antiseptics, antimycotics, antiparasitics, combination treatment: pharmacy-mixed creams that combine at least two active ingredient classes, e.g. topical corticosteroids and anti-infectives.
SD: standard deviation; IFSI: International Forum for the Study of Itch.

cantly (PBI, p<0.001; see **Fig. 1**). Significant differences were found between the IFSI groups (see Table SI): patients with diseased skin (IFSI I & IFSI III) reported a higher pruritus intensity (NRS-mean 24 h, p<0.005) and a more impaired HRQoL (DLQI: p<0.01; ItchyQol: p<0.001) at T0 than patients with non-diseased skin (IFSI II), whereas no significant differences were found at T1. At T0 and T1, the highest impairment in HRQoL, as measured with the ItchyQol, was found in patients with chronic scratch lesions (IFSI III, p<0.001).

Cost of illness

Six months after the treatment start in the specialized care unit total costs were significantly reduced compared with previous routine care (433.42 vs 686.4 € per patient per half year (phy) (p<0.001). The main cost drivers at both assessment periods were costs of inpatient and outpatient treatment (composed of costs of physician visit; diagnostics including blood test, allergy and food intolerance test, MRI, CT; systemic and topical medication, lymphatic drainage, ultraviolet (UV) therapy, physiotherapy). These costs were significantly reduced, by approximately 212 € (inpatient treatment, p<0.05) and 134 € (outpatient treatment, p<0.001), following specialized care treatment start. Cost for topical therapy were reduced by more than 50% (outpatient treatment, total cohort; $p \leq 0.001$); and patients' out-of-pocket costs by almost 40% (total cohort; p<0.001, see **Table II**).

At T0 and T1, patients with diseased skin (IFSI I, III) reported significantly higher costs (especially out-of-pocket costs) than patients with pruritus on non-diseased

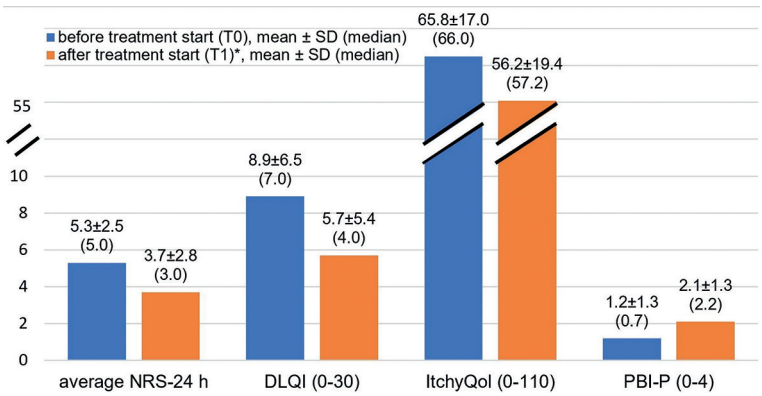

Fig. 1. Patient-reported outcomes (PRO) before and after treatment start in a specialized pruritus care unit (all $p \leq 0.001$; Wilcoxon signed-rank test). *p (post-hoc difference T1–T0) <0.001; NRS: numerical rating scale; DLQI: Dermatology Life Quality Index; PBI-P: Patient Benefit Index for Pruritus; SD: standard deviation.

Table II. Costs to the compulsory health insurance and to the patient (direct costs) 6 months prior to (T0) and 6 months after (T1) treatment start in a specialized itch centre (n = 300)

	T0	T1		
Costs/patient/6 months (€)	Mean (95% CI)	Mean (95% CI)	Diff. T1–T0	*p*-value
Health insurance costs				
Inpatient treatment	315.6 (166.4–464.8)	103.3 (43.3–163.3)	–212.3	0.021*
Outpatient treatment	333.9 (262.5–405.3)	200.0(153.3–246.7)	–133.9	< 0.001***
Outpatient physician visit	41.5 (38.0–44.9)	17.6 (13.8–21.4)	–23.9	< 0.001***
Outpatient diagnostics	81.5 (58.3–104.6)	46.3 (29.4–63.2)	–35.2	< 0.001***
Systemic medication	114.9 (67.3–162.6)	87.4 (58.4–116.5)	–27.5	0.003**
Topical medication	85.8 (53.9–117.6)	40.5 (29.5–51.5)	–45.3	< 0.001***
Other therapies	16.1 (10.4–21.9)	5.2 (2.1–8.4)	–10.9	0.002**
Total costs to the health insurance	548.9 (420.0–677.9)	322.6 (230.8–414.4)	–226.3	< 0.001***
Out-of-pocket costs	197.7 (158.6–236,7)	123.5 (93.1–154.0)	–74.2	< 0.001***
Total costs	686.4 (543.4–829.3)	433.4 (315.2–551.7)	–253.0	< 0.001***

Other therapies: physical therapy, ultraviolet (UV) therapy, lymphatic drainage.
Outpatient diagnostics: blood test, allergy test, food intolerance tests, magnetic resonance imaging, computed tomography; systemic medication: antihistamines, corticosteroids, anticonvulsants, opioid antagonists (naloxone/naltrexone), immunosuppressants; topical medication: corticosteroids, immunomodulators, anti-infectives, antiseptics, antimycotics, antiparasitics, emollients, combination products; other therapies: lymphatic drainage, light therapy, physiotherapy, combination therapies.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ (Wilcoxon signed-rank test). 95% CI: 95% confidence interval for mean (bootstrap results).

skin (IFSI II) ($p < 0.05$) (see **Table III**), while IFSI I patients had the highest costs for topical treatment of all ($p < 0.001$).

The highest out-of-pocket costs were found for IFSI I ($p < 0.05$) at T0, and for IFSI III at T1 ($p < 0.05$). Costs for inpatient treatment, physician visits and systemic medication did not differ significantly between the groups (see Table III).

Table III. Costs to the compulsory health insurance and to the patient (direct costs) 6 months prior to (T0) and 6 months after (T1) treatment start in a specialized itch centre, in €, separated by pruritus groups of International Forum for the Study of Itch (IFSI); *p*-value for significance tests between the groups (Kruskal–Wallis test)

	T0		T1	
	Mean (95% CI)	*p*-value	Mean (95% CI)	*p*-value
Inpatient treatment				
IFSI I	150.6 (11.3–289.9)		127.6 (–10.2–265.4)	
IFSI II	327.5 (45.4–609.6)		54.6 (1.2–108.0)	
FSI III	538.4 (191.6–885.2)	0.09	150.1 (30.5–269.7)	0.29
Outpatient treatment				
Physician visit				
IFSI I	39.8 (35.0–44.7)		19.6 (12.3–26.9)	
IFSI II	42.9 (36.5–49.4)		14.6 (8.5–20.7)	
IFSI III	41.4 (34.8–47.9)	0.89	19.7 (13.6–25.8)	0.10
Diagnostics				
IFSI I	62.8 (38.4–87.1)		58.7(25.9–91.4)	
IFSI II	94.6 (54.8–134.4)		32.2 (8.1–56.2)	
IFSI III	82.9 (55.1–110.6)	0.07	46.1 (20.3–71.9)	0.01*
Systemic medication				
IFSI I	101.3 (37.1–165.4)		90.4 (32.9–147.8)	
IFSI II	110.7 (37.3–184.1)		73.3 (41.6–105.0)	
IFSI III	114.1 (55.0–173.3)	0.13	108.3 (33.7–182.9)	0.90
Topical medication				
IFSI I	119.3 (55.3–183.2)		57.0 (37.5–76.5)	
IFSI II	53.7 (23.5–83.9)		27.2 (9.8–44.5)	
IFSI III	81.6 (49.7–113.4)	< 0.001***	38.0 (18.8–57.1)	< 0.001***
Other therapies				
IFSI I	19.9 (9.9–30.0)		4.0 (–0.5–8.5)	
IFSI II	7.4 (1.7–13.1)		5.9 (0.5–11.2)	
IFSI III	24.4 (13.1–35.7)	0.01*	5.5 (–0.8–11.9)	0.88
Patient costs				
IFSI I	224.7 (160.6–288.8)		139.3 (86.9–191.7)	
IFSI II	173.5 (119.5–227.6)		84.5 (51.6–117.4)	
IFSI III	208.7 (147.1–270.4)	0.04*	165.5 (79.7–251.3)	0.02*

Other therapies: physical therapy, ultraviolet (UV) therapy, lymphatic drainage.
SD: standard deviation.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ (differences between the groups).

Cost-effectiveness analysis

Significant differences in cost-effectiveness between the IFSI groups could be found only for the differences in NRS-mean 24 h ($p < 0.01$). Patients with CP on diseased skin had a better cost-effectiveness (mean ± SD; median –66.1 ± 585.7; 0.0; Δ€/ΔNRS/phy than patients with pruritus with non-diseased skin (mean ± SD; median: 97.3 ± 276.9; 26.7; Δ€/ΔNRS/phy) and chronic scratch lesions (mean ± SD; median: –30.8 ± 681.7; –5.8; Δ€/ΔNRS/phy).

DISCUSSION

To our knowledge, this is the first cost-effectiveness analysis from a societal perspective in pruritus research in Europe. Compared with other prevalent diseases with high economic impact, such as chronic low back pain (CLBP), the mean duration of CP (current study 7.7 ± 10.3 years; other studies related to CP approximately 3–6 years (3, 17)) seems to be longer (duration of 92% of all episodes of CLBP: 6 months or less (18)) and intensity values (NRS) prior to and after interventions appear to be slightly higher for CP (3,19) . In terms of HRQoL, patients with CP are often even more affected than patients with other chronic inflammatory skin diseases, such as psoriasis or atopic dermatitis (3).

Moreover, treatment benefit (assessed with PBI) seems to be lower in CP than in other pruritic skin diseases (20). Whereas a score of 2.1 ± 1.3 was calculated for patients CP in specialized university care in the current study (T1), patients with psoriasis tend to achieve highest PBI values (e.g. 3.0 ± 1.0 (20)), followed by patients with atopic dermatitis (e.g. PBI = 2.3 ± 0.8 (20)). This reflects the high need for improved care of patients with CP, as they often do not receive sufficient antipruritic therapies (21). Recently, it has been shown that 77% of patients

who received outpatient care only did not benefit from an improvement in pruritus, but still experienced pruritus frequently or permanently (21). Moreover, despite a notable improvement in all PRO after the treatment start in a specialized pruritus care unit, patients remain affected by pruritus and require care.

Despite the severe impairment of patients with CP and the extensive diagnostics and expensive long-term treatments, including over-the-counter (OTC) medication (22), the economic burden to the compulsory health insurance and to the patient, has been analysed in only a few studies.

The analysis of a nationally representative survey assessing patterns of utilization of outpatient care in the USA shows that expenditures in the USA for pruritus account for 90 billion US dollar ($) per year (23). Recently, annual median total costs of $1,067 (~880 €) for patients with CP were presented, of which $286 (~236 €) were direct costs, $662 (~546 €) opportunity costs, and $118 (~97 €) OTC costs (24). In the current study, direct costs are almost 5 times higher than in the US study, which could be due to unconsidered costs for diagnostics, which account for a quarter of the total costs of outpatient treatment in the current study. Especially in CP, diagnostics are costly and time-consuming owing to a patient-individual systematic diagnostic work-up, laboratory analyses, imaging tests and interdisciplinary cooperation (25).

Compared with the costs of CLBP (78–380 € per capita per year (26–28)), the economic burden of CP might be much higher (686 € respectively (resp.) 433 € per patient per half-year), though only direct medical and non-medical costs were focused. When treating psoriasis, total direct costs range up to 5,164 € per patient per year (29). Therefore the costs for CP are also expected to increase in the future, as new immunomodulating therapies, such as dupilumab and nemolizumab, are in the pipeline, especially for PN (30). In addition, outpatient systemic therapies have already been among the main cost drivers in the current study conducted before the advent of biologic agents in CP. Costs for inpatient stays are also usually one of the main cost drivers in pruritic dermatological diseases other than PN (31) (e.g. psoriasis (29), chronic hand eczema (32), and atopic dermatitis (33)).

Unfortunately, the duration of skin improvement after inpatient treatment is short, and a high need for outpatient biologic prescription is reported after the discharge of patients with psoriasis without decreased follow-up costs (34). This might also apply to CP due to similar inpatient treatment (UV therapy, intensified local therapy), short hospitalization periods and an increasing pressure of economizing (4).

For severely affected patients, those with multiple comorbidities who require extensive diagnostic procedures, inpatient treatment will remain an important pillar of therapy in the future. For less affected patients, the increase and strengthening of specialized outpatient care may reduce the need and costs of inpatient treatment. The alarming shift from inpatient and outpatient settings towards costly emergency room treatment of patients with CP (23) could be prevented by easier access to specialized outpatient pruritus care. As proposed by Ständer et al. (6), specialized centres should receive an additional compensation to enable provision of better care and manage increasing economic regulations as cost pressures increase.

The prescription of most drugs, except for antihistamines, is off-label for pruritus, which could lead to uncertainty among outpatient clinics (5). Consequently, topical therapies and OTC medication are recommended predominantly, resulting in high out-of-pocket costs (6) that were more than 3 times as high as in the US comparative study (24). In the current study, patients with CP had higher annual out-of-pocket costs than patients with mild and moderate atopic dermatitis, as described by Launois et al. (35). However, out-of-pocket costs in patients with psoriasis and atopic dermatitis that were comparable and higher than in the current study, are reported as well (29, 34, 35, 36, 37).

The current data show that patients with diseased skin (IFSI I and III) are significantly more burdened than patients with CP on non-diseased skin (significantly higher pruritus intensity and impairment of HRQoL). Patients in the IFSI III group report a significantly higher pruritus intensity than IFSI I and II before treatment start, which correlates with other results (3, 38, 39). Regarding ItchyQol, IFSI III patients show significantly higher score values than IFSI I and II patients at both times of examination, which matches other data (3). It has been reported that 50% of IFSI III patients have psychiatric comorbidities and are more stressed psychologically than other patients (40). Patients with PN are severely affected, experience the highest pruritus intensities, a highly negatively affected quality of life and mental health and increased systemic diseases in comparison with patients with other inflammatory skin disorders (17).

The current data show statistically higher costs of diagnostics, topical medication, and patient expenses for patients with CP on diseased skin, closely followed by patients with chronic scratch lesions. The high financial burden on the patients themselves is underlined by the fact that patients with chronic scratch lesions, especially, rated the therapeutic need of having lower out-of-pocket treatment costs as more important than did the other groups (38).

In particular, the treatment of high-need patients (patients with chronic scratch lesions, such as PN) requires more attention.

Study limitations

Other cost analyses determine a high impact of indirect costs (costs of lost productivity, absenteeism, inability

to work, presenteeism, reduced functionality in terms of quantity and quality while working, early retirement) as they account for more than 80% of total costs (26). Thus, the economic burden of pruritus may be even higher, as they were not considered in this cost-effectiveness analysis.

Moreover, the current results may have been influenced by some bias that due to the chosen methodology: (*i*) as some patients had to estimate their direct non-medical costs, if receipts or bank statements were not available, recall bias cannot be ruled out, which might have affected the actual costs in both directions (under- and over-estimation of costs); (*ii*) patients were included and prospectively observed in the study who had been diagnosed and treated in different outpatient settings previously (primary/secondary care services). One should bear in mind that the observed reduction in costs and improvement in cost-effectiveness might result from less diagnostics (which might have been done prior to the first presentation in the specialized centre) and more targeted therapies (since less effective therapies may have already been tried previously). Furthermore, it is possible that a more focused and rational treatment plan, which is predominantly worked out in a specialized centre, may also determine cost-reductions.

The generalizability of cost of illness analyses is limited, because cost calculations depend on the different national health systems in which they are conducted. The cost calculation in the current study is, for example, based on German Diagnosis Related Groups (G-DRG) and the German system for reimbursement of outpatient care ("EBM - *Einheitlicher Bewertungsmaßstab*", Uniform Value Scale, quarter 1/2017 respectively GOÄ, "*Gebührenordnung für Ärzte*", fees for physicians, dated 1 January 2002) guidelines. Therefore, the cost of illness analysis is of only limited significance for other countries, on the one hand. On the other hand, the data could very well mirror cost-effectiveness and quality of specialized care of itch centres throughout Germany. The study's single-centre design and the pre-post comparison, however, impairs the generalization of results. For further evaluation, prospective long-term, multicentre cost of illness analyses are required.

Conclusion

This study shows that the treatment of patients with CP in a specialized university itch centre improves the quality of care and patient benefits and, at the same time, reduces the economic burden. Further research concerning the medical (e.g. the development of new effective antipruritic therapies) and (socio-)economic point of view (e.g. effectiveness of interventions and the economic burden of CP) is imperative to improve the outcomes and care of patients with CP.

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