Cost-effectiveness of an 8% Capsaicin Patch in the Treatment of Brachioradial Pruritus and Notalgia Paraesthetica, Two Forms of Neuropathic Pruritus

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In a range of diseases with a similar pathogenesis, such as post-herpetic neuralgia, peripheral neuropathic pain and atopic dermatitis, the cutaneous application of capsaicin is one of the therapeutic mainstays (6–9). Capsaicin reduces intraepidermal nerve fibre density (4, 5). The aetiology is attributed mostly to the damage of peripheral nerves, with a reduction in intraepidermal nerve fibre density (2, 3).

MATERIALS AND METHODS

Study design

Routine data were analysed for 44 BRP and NP patients 6 months retrospectively to the first application of the capsaicin patch (T1) and 6 months prospectively (T2) at the Center for Chronic Pruritus, Münster, Germany. A paper-based standardized interview on sociodemographic criteria, different patient-reported outcomes and cost variables was complemented by data from the medical records.

Inclusion criteria were: written informed consent, a confirmed diagnosis of BRP and NP; compulsory health insurance; and age ≥ 18 years. The treatment decision was made according to clinical routine. Ethical approval was gained from the ethics commission of the State Medical Association Westfalen-Lippe, Münster, Germany (2015-262-fS). The patients completed an informed consent form.
**Patient-reported outcomes**

Pruritus intensity was measured using the following validated scales: a 0–10 visual analogue scale (VAS); a 0–3 verbal rating scale (VRS); and a 0–10 numerical rating scale (NRS) (13–17). Considerations of the minimum clinically important difference (MCID) suggest that a reduction of at least 2.0 points (VAS and NRS) is required for a change in pruritus symptoms to be perceived by the patient (18). As NP and BRP can induce pain sensations a low VAS (0–10) was also examined.

Anxiety and depression are common symptoms in patients with chronic pruritus (CP) and were measured using the Hospital Anxiety and Depression Scale (HADS; 0–21) (13). Patients’ quality of life (QoL) was analysed with the Dermatological Life Quality Index (DLQI). A score of 0–30 can be calculated, indicating “no”, “little”, “moderate”, “strong” or “very strong” impairment (19, 20). An improvement of at least 4 points has been shown to be the MCID (21).

The Patient Benefit Index (PBI) provides a validated method for the assessment of patient-relevant treatment benefit, related to the individual importance of 27 treatment needs in the form of a global score of 0–4. The patient is thought to have a relevant benefit from the respective therapy in case of a PBI ≥ 1 (“cut-off-value”). The higher the value of the PBI, the higher the therapeutic benefit is thought to be (22).

**Cost definition and calculation**

Costs were classified into direct cost, first to the German compulsory health insurance and secondly to the patient, and indirect cost through loss of productivity.

Direct costs to the compulsory health insurance were the cost for inpatient treatment, outpatient medication, consultation and diagnostics. These costs were assessed according to the Diagnosis Related Groups (DRG) and Einheitlicher Bewertungsmaßstab, Uniform Value Scale (EBM) catalogues valuable in 2014, according to information on “standard service volumes” by the appropriate Association of Statutory Health Insurance Physicians, and according to valid medication prices in Germany, as referenced in the Lauer-Taxe (German medical information system) or in pharmacies.

Direct costs to the patient included travel expenses or the time taken for skin care. The time taken for skin care, as well as the loss of productivity due to loss of working time (indirect cost), were estimated from the mean gross income according to the human capital approach (23, 24).

Almost all cost questionnaires were completed. One patient had missing values for the calculation of outpatient treatment cost and travel expenses at T2. Due to the fact that this patient did not differ from the other study patients according to clinical and economic outcomes, missing values were replaced by a group mean at T2.

The cost-effectiveness analysis was performed with a pre-post comparison of the cost-effectiveness relation at T1 and T2, which is calculated by the division of the change in benefit by the change in cost in order to determine the incremental cost-effectiveness ratio (23, 25, 26).

**Statistical analysis**

Data input was executed by means of double entries by experienced data managers. All data were described using standard statistical parameters (frequencies for categorical data, mean value, standard deviation for continuous data) using IBM SPSS Statistics Version 22.0. The paired Wilcoxon signed-rank test was applied for significance testing. A result of p ≤ 0.05 was seen as statistically significant.

**RESULTS**

Three-quarters of patients were female (n = 33) and one-quarter male (n = 11), with a mean age of 61.3 ± 10.0 years. A high proportion, 57.5% (n = 23), were retired and only 24.5% (n = 10) of patients were economically active. BRP was diagnosed in 24 patients, NP in 19 patients, and one patient had both diagnoses. The mean disease duration at baseline was 16.9 ± 23.9 months, with a maximum duration of 92.0 months.

**Cost of illness**

At T1, 15.9% (n = 7) of patients had needed an inpatient pruritus treatment within the past 6 months, at T2 only one patient had needed such treatment. Outpatient visits to the doctor accounted for 6.3 ± 5.2 (T1) and 4.7 ± 2.5 visits (T2) (p > 0.05). Taking into account the entire study population, mean inpatient and outpatient treatment cost for diagnostics and consultations were reduced by €227.23 per patient (p.p.) (Table I).

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**Table I. Cost to the compulsory health insurance and to the patient (direct cost) 6 months before (T1) and 6 months after (T2) start of treatment with the capsaicin patch (n = 44)**

<table>
<thead>
<tr>
<th>Cost/patient/6 months, €</th>
<th>T1 (Mean (95% CI))</th>
<th>T2 (Mean (95% CI))</th>
<th>Diff. T2–T1</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health insurance cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient treatment</td>
<td>316.90 (114.75–572.99)</td>
<td>104.59 (0.00–313.76)</td>
<td>-212.31</td>
<td>0.236</td>
</tr>
<tr>
<td>Outpatient treatment</td>
<td>81.25 (69.86–94.06)</td>
<td>66.33 (56.15–77.33)</td>
<td>-14.92</td>
<td>0.050</td>
</tr>
<tr>
<td>Systemic medication</td>
<td>352.34 (205.79–558.19)</td>
<td>277.74 (168.98–408.72)</td>
<td>-74.60</td>
<td>0.157</td>
</tr>
<tr>
<td>Topical medication</td>
<td>56.23 (34.18–85.53)</td>
<td>45.01 (25.30–70.75)</td>
<td>-11.22</td>
<td>0.232</td>
</tr>
<tr>
<td>Cost to the health insurance without capsaicin patch</td>
<td>806.72 (547.65–1,106.38)</td>
<td>493.67 (289.10–789.16)</td>
<td>-313.05</td>
<td>0.003</td>
</tr>
<tr>
<td>Cost for the capsaicin patch</td>
<td>0.00</td>
<td>767.02</td>
<td>+767.02</td>
<td></td>
</tr>
<tr>
<td>Total cost to the health insurance</td>
<td>806.72 (563.34–1,091.78)</td>
<td>1,260.69 (992.21–1,613.82)</td>
<td>+453.97</td>
<td>0.005</td>
</tr>
<tr>
<td>Patient cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Travel expenses</td>
<td>208.22 (92.82–401.73)</td>
<td>168.89 (107.45–256.61)</td>
<td>-39.33</td>
<td>0.514</td>
</tr>
<tr>
<td>Other expenses</td>
<td>254.39 (163.19–361.47)</td>
<td>162.95 (108.00–224.58)</td>
<td>-91.44</td>
<td>0.034</td>
</tr>
<tr>
<td>Cost for loss of time for home skin care</td>
<td>2,036.70 (1,394.99–2,731.40)</td>
<td>1,726.41 (1,175.86–2,290.89)</td>
<td>-310.29</td>
<td>0.234</td>
</tr>
<tr>
<td>Total cost to the patient</td>
<td>2,499.31 (1,834.95–3,270.59)</td>
<td>2,058.25 (1,495.30–2,675.74)</td>
<td>-441.06</td>
<td>0.103</td>
</tr>
<tr>
<td>Total cost without capsaicin patch</td>
<td>3,306.03 (2,527.30–4,156.20)</td>
<td>2,058.25 (1,495.30–2,675.74)</td>
<td>-1291.78</td>
<td>0.044</td>
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<td>0.044</td>
</tr>
</tbody>
</table>

CI: confidence interval for mean (bootstrap results).
Nearly all patients (98%, n = 43) received a systemic pruritus medication, 61.4% a topical medication (n = 27) prior to T1. After the first patch application, only 77.3% of patients (n = 34) still needed systemic medication and 50.0% (n = 22) needed topical treatments (Table II). The total cost of medication decreased by €85.82 p.p. at T1 (n = 27). A single capsaicin patch costs €341.22. As the number of individual patch applications differed (Table III), the mean cost of the capsaicin patch was €767.02 p.p. within 6 months (Table I).

To summarize, total costs to the compulsory health insurance were €806.72 at T1 and €1,260.69 at T2 (p ≤ 0.01). Neglecting the cost of the capsaicin patch, costs were reduced by €313.05 (Table I).

Cost to the patients for travel expenses and skin care or special food decreased after introduction of the patch treatment. Time lost in skin care was reduced from T1 (2.5 ± 2.9 h per week) to T2 (2.1 ± 2.3 h per week), resulting in a total cost to the patient reduced by €441.06 (Table I).

Summarizing the costs to the compulsory health insurance and to the patient, these were nearly equal before and after the introduction of the capsaicin patch treatment. Without the cost of the capsaicin patch, costs were significantly lower at T2 (€2,551.92) than at T1 (€3,306.03).

Indirect cost for loss of labour time could be calculated for 2 patients at T1 (10 days and 14 days of unemployability, respectively) and for 1 patient at T2. The last patient had 183 days of unemployability. Therefore, indirect costs were €137,45 ± €646.38 at T1 and €1,048.09 ± €6,952.25 at T2.

### Treatment benefits

According to all scales, except the VRS, pruritus and pain were significantly reduced from T1 to T2. Patients also presented a significantly higher rating of QoL according to the DLQI (Table IV). The anxiety and depression ratings on the HADS scales did not show significant differences.

The patient-relevant benefit increased after treatment with the capsaicin patch. At T1 65.5% (19 out of 29 patients) had a relevant therapeutic benefit (PBI ≥ 1), and at T2 83.3% (20 out of 24 patients).

### Cost-effectiveness

The introduction of the capsaicin patch treatment increased the cost to the compulsory health insurance by €453.97 per patient per 6 months. Cost-effectiveness was calculated using the formula (Fig. 1), taking the perspective of the compulsory health insurance.

The costs to reach a 1-unit improvement, as well as a patient-relevant improvement in the respective benefit outcomes, are shown in Table V.

### DISCUSSION

This cost-effectiveness analysis is, to our knowledge, the first in pruritus research, and compares the cost and benefit of a new and highly effective, but cost-intensive 8% capsaicin patch treatment for BRP and NP.

Taking into account all cost changes 6 months after the introduction of the capsaicin patch, total costs remained almost the same (€3,306.03 p.p. at T1, €3,318.94 p.p. at T2).
T2). Where cost to the patient in the form of travel expenses or loss of time due to home skin-care diminished by €441.06, the total cost to the compulsory health insurance increased significantly, by €453.97 p.p. (Table I). This is mainly due to the high costs of the capsaicin patch itself (€341.22 per patch). In our collective 41% of patients needed more than one patch at T1, as the pruritus area had to be covered completely by the patch. In addition, repeated treatments had to be carried out because of a certain duration of the epidermal nerve fibre alteration, which is subject to actual research. A further application after 3 months was needed in 34.1% of patients, and in only 18.2% again after 6 months. Together with similar findings in pain research (27), it might be supposed, that the treatment repetitions, and therefore treatment cost, will further decline in a longer time horizon with the alteration of epidermal nerve fibres.

Similarly, further medical costs also declined continuously. Within 6 months, there was an almost 40% reduction in medical costs for concomitant treatments and diagnostics. Nevertheless, this cost reduction did not outweigh the additional costs for the patch, as Schweitzer et al. (28) also concluded in another study on pain patients. Many of the systemic treatments cannot be withdrawn abruptly, but need to be tapered off over a period of some weeks. In our study, 77.3% of all patients still had to continue their prior systemic medication for some time after the first patch application.

Therefore, if the study horizon was extended, continuous cost reductions for concomitant medication, as well as for the patch applications themselves, might outweigh the initial high product costs of the capsaicin patch. This aspect should be addressed in further studies.

On the benefit side, the capsaicin patch treatment led to an improvement in different patient-reported outcomes. The pruritus was significantly reduced on different scales (VAS, NRS). The reduction ranged from 1.0 points (NRS past 24 h) to 2.4 points (VAS past 12 h). Other studies report slightly greater reductions in pruritus in patients with CP, ranging from 2.8 to 3.7 points for gabapentin (NRS), paroxetine, fluvoxamine or pimecrolimus and hydrocortisone cream (VAS) (15, 29–31). As the reference period for the pruritus evaluation was not always indicated, these data cannot be directly compared.

The patch also helped to reduce pain sensations, which are frequent in NP and BRP. In pain research a 30% reduction is established as the minimum required effect. In our study the whole collective achieved a 47% pain reduction with patch treatment, which appears to be even higher than in pain patients (31). Our study has a comparably long time interval of 6 months due to the economic perspective. The reported studies had time intervals of up to 12 weeks maximum, due to which a comparison of the pain reduction is not fully reliable (32).

Before the start of treatment at T1, the mean DLQI was 7.4 points, which indicates a moderate effect on QoL and is comparable to other CP or dermatological patients (33–36). With patch therapy, QoL could be improved significantly, by 2.8 points, thus the score suggests only a small impairment in QoL. Other dermatological studies report similar reductions in the DLQI (31, 37, 38), which is why we assume that our patients also perceived the QoL improvement, even though the proposed MCID of 4 points (21) has not been reached. A 4-point DLQI improvement would therefore cost €644.52, which is low compared with US$2,250–27,136 for a 5-point DLQI improvement in psoriasis patients, as shown by cost-effectiveness studies for biologic treatments (26).

Regarding the increase in patient-relevant benefit by the patch treatment, approximately one-third of patients additionally presented a PBI ≥1 (T1 65.5%, T2 83.3%). Thus, the mean PBI increased from 1.5 to 2.1 points. This result was not significant, probably due to a reduced sample size as a result of missing values of up to 34% at T1 (n=15 missing) and 45% at T2 (n=20 missing).

It has to be kept in mind, that the capsaicin patch treatment was recently introduced as a therapeutic alternative to BP and NRP, resulting from scientific research.

### Table V. Benefit difference after the introduction of the capsaicin patch treatment from T1 (first patch application) to T2 (T1 + 6 months) and cost-effectiveness (n=44)

<table>
<thead>
<tr>
<th>Benefit difference</th>
<th>T2–T1 Mean</th>
<th>Cost per 1 unit incremental benefit per patient €</th>
<th>Cost per patient for achieving the MCID €</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI [0–30]a</td>
<td>–2.8</td>
<td>161.13</td>
<td>644.52 (4 points)</td>
</tr>
<tr>
<td>HADS–Anxiety [0–21]a</td>
<td>–0.5</td>
<td>907.94</td>
<td>n.a.</td>
</tr>
<tr>
<td>HADS–Depression [0–21]a</td>
<td>–0.9</td>
<td>504.41</td>
<td>n.a.</td>
</tr>
<tr>
<td>Pruritus VAS past 24 h [0–10]a</td>
<td>–1.2</td>
<td>378.31</td>
<td>756.62 (2 points)</td>
</tr>
<tr>
<td>Pruritus VAS past 12 h [0–10]a</td>
<td>–2.4</td>
<td>189.15</td>
<td>378.30 (2 points)</td>
</tr>
<tr>
<td>Pruritus VAS maximum past 4 weeks [0–10]a</td>
<td>–1.4</td>
<td>324.26</td>
<td>648.52 (2 points)</td>
</tr>
<tr>
<td>Pruritus VAS mean past 4 weeks [0–10]a</td>
<td>–1.7</td>
<td>267.04</td>
<td>534.08 (2 points)</td>
</tr>
<tr>
<td>Pain VAS past 12 h [0–10]a</td>
<td>–1.6</td>
<td>283.73</td>
<td>n.a.</td>
</tr>
<tr>
<td>Pruritus VRS [0–3]a</td>
<td>–0.3</td>
<td>1,513.23</td>
<td>n.a.</td>
</tr>
<tr>
<td>Pruritus NRS [0–10]a</td>
<td>–1.0</td>
<td>453.97</td>
<td>907.94 (2 points)</td>
</tr>
<tr>
<td>PBI–Score [0–4]a</td>
<td>0.6</td>
<td>756.62</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

aBest achievable value to worst value. bWorst value to best achievable value. cCost to reach a 1-unit improvement of the respective outcome. dCost to reach a patient-relevant improvement of the respective outcome.

DLQI: Dermatological Life Quality Index; HADS: Hospital Anxiety and Depression Scale; VAS: visual analogue scale; VRS: verbal rating scale; NRS: numerical rating scale.
on the origin of the disease. In addition, the 2 diseases are very rare and their treatment is mostly carried out in university centres specialised in the treatment of CP. The small patient number and the monocentric character of the study impair generalization of our results, especially as cost calculations are always country-specific.

In conclusion, according to the present data, the introduction of the 8% capsaicin patch treatment led to an overall improvement, not only of pruritus and pain, but also of QoL. Important therapeutic aims appeared to be fulfilled better through the novel treatment than through other standard therapies used within the previous 6 months. Although, at first glance, the patch treatment presented high costs to the health insurance companies, other medical and patient-related costs could be reduced, so that total costs did not increase within a short time of only 6 months. Moreover, all cost categories, especially to the health insurance companies, might be subject to further cost reductions in the long run, as the patch treatment regimen will change to longer patch application intervals, and co-medication will be further reduced. Therefore, the capsaicin patch treatment can be seen as a promising treatment for NP and BRP, 2 forms of neuropathic pruritus, which has the potential to be even more cost-effective in the long-term. Further studies including control groups with other treatment options should be promoted in the future. In addition, research concerning the MCID of different scales is of vital importance regarding future discussions on the cost-effectiveness of pruritus treatments.

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