In a pooled analysis of 3 randomized trials in patients with space-occupying hemispheric infarction, surgical decompression within 48 hours of stroke onset reduced case fatality and increased the probability of a favorable functional outcome at 1 and 3 years. However, the reduction in mortality also came at the expense of an increased risk of moderately severe or severe disability, and the majority of survivors had global cognitive impairment. Because severely disabled patients often stay in rehabilitation centers or nursing homes, the costs of this treatment may be high.

We compared costs and cost-effectiveness of surgical decompression for space-occupying hemispheric infarction with that of best medical treatment, on the basis of data derived from the randomized Hemicraniectomy After Middle Cerebral Artery Infarction With Life-Threatening Edema Trial (HAMLET). Data on medical consumption were derived from case record files, hospital charts, and general practitioners. We calculated costs per quality-adjusted life year (QALY). Uncertainty was assessed with bootstrapping. A Markov model was constructed to estimate costs and health outcomes after 3 years.

**Background and Purpose**—Surgical decompression reduces mortality and increases the probability of a favorable functional outcome after space-occupying hemispheric infarction. Its cost-effectiveness is uncertain.

**Methods**—We assessed clinical outcomes, costs, and cost-effectiveness for the first 3 years in patients who were randomized to surgical decompression or best medical treatment within 48 hours after symptom onset in the Hemicraniectomy After Middle Cerebral Artery Infarction With Life-Threatening Edema Trial (HAMLET). Data on medical consumption were derived from case record files, hospital charts, and general practitioners. We calculated costs per quality-adjusted life year (QALY). Uncertainty was assessed with bootstrapping. A Markov model was constructed to estimate costs and health outcomes after 3 years.

**Results**—Of 39 patients enrolled within 48 hours, 21 were randomized to surgical decompression. After 3 years, 5 surgical (24%) and 14 medical patients (78%) had died. In the first 3 years after enrollment, operated patients had more QALY’s than medically treated patients (mean difference, 1.0 QALY [95% confidence interval, 0.6–1.4]), but at higher costs (mean difference, €127 000 [95% confidence interval, 73 100–181 000]), indicating incremental costs of €127 000 per QALY gained. Ninety-eight percent of incremental cost-effectiveness ratios replicated by bootstrapping were >€80 000 per QALY gained. Markov modeling suggested costs of ≈€60 000 per QALY gained for a patient’s lifetime.

**Conclusions**—Surgical decompression for space-occupying infarction results in an increase in QALYs, but at very high costs.

**Clinical Trial Registration**—URL: http://www.controlled-trials.com. Unique identifier: ISRCTN94237756.

**Key Words:** cost-effectiveness analysis ▪ decompression, surgical ▪ hemicraniectomy ▪ malignant infarction ▪ space-occupying infarction

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Table. Use of Resources and Cumulative Costs in the First 3 Years

<table>
<thead>
<tr>
<th>Resource</th>
<th>Use of Resources (Mean±SD)</th>
<th>Cumulative Costs (Mean±SD)</th>
<th>Mean Difference in Costs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgical Decompression</td>
<td>Best Medical Treatment</td>
<td>Surgical Decompression</td>
</tr>
<tr>
<td>Inpatient days</td>
<td></td>
<td></td>
<td>€4600</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>6.4±8.0</td>
<td>1.0±3.1</td>
<td>€14000±17400</td>
</tr>
<tr>
<td>High-care unit</td>
<td>7.2±8.1</td>
<td>3.6±10.4</td>
<td>€4200±4600</td>
</tr>
<tr>
<td>Stroke unit (academic)</td>
<td>8.4±9.9</td>
<td>1.7±3.1</td>
<td>€4800±5700</td>
</tr>
<tr>
<td>Stroke unit (general)</td>
<td>23.1±39.8</td>
<td>4.3±12.1</td>
<td>€10000±17300</td>
</tr>
<tr>
<td>Rehabilitation center</td>
<td>125±136</td>
<td>29±62</td>
<td>€51700±72600</td>
</tr>
<tr>
<td>Nursing home</td>
<td>187±357</td>
<td>0</td>
<td>€53400±95700</td>
</tr>
<tr>
<td>Consultations/visits</td>
<td></td>
<td></td>
<td>€144000±109000</td>
</tr>
<tr>
<td>Outpatient department</td>
<td>5.8±7.6</td>
<td>0.3±0.8</td>
<td>€747±928</td>
</tr>
<tr>
<td>General practitioner</td>
<td>11.1±15.9</td>
<td>0.3±1.3</td>
<td>€320±461</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>€144000±109000</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.

*Number (percentage) of patients.

functional outcome at 3 years, and case fatality and quality of life (SF-36) at 1 and 3 years.

To generate health state utility values at 1 and 3 years, the SF-6D score was derived from the SF-36. A baseline utility value of 0.2, indicating severe stroke, was estimated. With linear interpolation for the periods between utility measurements, we calculated quality-adjusted life-years (QALYs) by determining the area under the curve for each patient.

We calculated absolute risk reductions for poor outcome and mean differences between the 2 treatments in QALYs and costs for the first 3 years, including 95% confidence intervals (CIs). Incremental costs were divided by incremental QALYs, providing the incremental cost-effectiveness ratio of €80000 per QALY gained. Uncertainty was assessed with bootstrapping, generating 2000 replications of the ratio.

We developed a Markov model to estimate health outcomes and costs during a patient’s remaining lifetime. The model’s 7 health states, estimations of life expectancy by age- and sex-specific death rates, hazard ratios for mortality, and annual costs were based on mRS scores at 3 years (online-only Data Supplement).

Results

Of 64 patients included in HAMLET, 39 were included within 48 hours, of whom 21 were randomized to surgical decompression. There were no cross-overs. For baseline characteristics, online-only Data Supplement.

After 1 year, 16 operated (76%) and 14 medically treated patients (78%) had a poor outcome (absolute risk reduction, 2%; 95% CI, −25 to 28). Four operated (19%) and 14 medically treated patients (78%) had died (absolute risk reduction, 59%; 95% CI, 33%–84%). After 3 years, these results were essentially the same (online-only Data Supplement).

In the first 3 years, operated patients had 1.0 more QALYs than medically treated patients (95% CI, 0.6–1.4; Figure 1; online-only Data Supplement), but against higher costs (mean difference, €127000; 95% CI, 73100–181000; Table), indicating incremental costs of €127000 per QALY gained. In the sensitivity analysis, 98% of the estimates was above a threshold of €80000 per QALY gained (Figure 2; online-only Data Supplement).

Long-term modeling suggested an estimated lifetime incremental cost-effectiveness ratio of €60000 per QALY (€247000/4.2 QALY; online-only Data Supplement).

Discussion

This study shows that in patients with space-occupying hemispheric infarction, surgical decompression leads to an increase in QALYs. However, this increase comes at the expense of a large increase in costs, with €127000 per QALY gained in the first 3 years and an estimated €60000 per QALY gained during the lifetime.

Although there is no generally accepted cost-effectiveness threshold, and consensus across countries is lacking, from a societal perspective, an upper limit of €80000 per QALY gained is usually considered high. Our sensitivity analyses showed that with this threshold it is unlikely that surgical decompression would be cost-effective.
decompression can be considered cost effective. Admissions in rehabilitation centers and chronic nursing homes are the most important cost drivers. These are unlikely to be modifiable.

This economic evaluation has limitations. First, although the cost-effectiveness analysis for the first 3 years after stroke was based on data from a randomized trial, the analyses for the period thereafter are based on assumptions. Therefore, the analysis for the first 3 years can be considered robust, but the analysis for lifetime should be interpreted with caution. Second, data on the use of medication and on consultation of paramedics were not included. These data had not been prospectively collected and retrospective collection seemed unreliable. Third, in HAMLET, ≈75% of operated patients had an mRS>3 at 1 year, whereas in 2 other trials this was ≈50%. Therefore, long-term stays in nursing homes may have been less frequent in these other trials. However, our sensitivity analyses showed costs >€80,000 per QALY gained in 98% of the cases with various mRS scores at 1 and 3 years.

Conclusions
Surgical decompression for space-occupying infarction results in health-gain against very high costs.

Disclosures
Hemicraniectomy After Middle Cerebral Artery Infarction With Life-Threatening Edema Trial (HAMLET) and Dr van der Worp were supported by the Dutch Heart Foundation (grants 2002B138 and 2010T075). The authors report no conflicts of interest.

References
Cost-Effectiveness of Surgical Decompression for Space-Occupying Hemispheric Infarction
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