Regionalization of Treatment for Subarachnoid Hemorrhage
A Cost-Utility Analysis

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Background—Previous studies have shown that for the treatment of subarachnoid hemorrhage (SAH), outcomes are improved but costs are higher at hospitals with a high volume of admissions for SAH. Whether regionalization of care for SAH is cost-effective is unknown.

Methods and Results—In a cost-utility analysis, health outcomes for patients with SAH were modeled for 2 scenarios: 1 representing the current practice in California in which most patients with SAH are treated at the closest hospital and 1 representing the regionalization of care in which patients at hospitals with <20 SAH admissions annually (low volume) would be transferred to hospitals with ≥20 SAH admissions annually (high volume). Using a Markov model, we compared net quality-adjusted life-years (QALYs) and cost per QALY. Inputs were chosen from the literature and derived from a cohort study in California. Transferring a patient with SAH from a low- to a high-volume hospital would result in a gain of 1.60 QALYs at a cost of $10 548/QALY. For transfer to result in only borderline cost-effectiveness ($50 000/QALY), differences in case fatality rates between low- and high-volume hospitals would have to be one fifth as large (2.2%) or risk of death during transfer would have to be 5 times greater (9.8%) than estimated in the base case.

Conclusions—Transfer of patients with SAH from low- to high-volume hospitals appears to be cost-effective, and regionalization of care may be justified. However, current estimates of the impact of hospital volume on outcome require confirmation in more detailed cohort studies. (Circulation. 2004;109:2207-2212.)

Key Words: cost-benefit analysis ■ quality of health care ■ hemorrhage, subarachnoid
calculated for each hypothetical patient entered into the decision tree (Figure 1).

To model the elevated risk of death resulting from disability over the lifetime of an average patient after admission for SAH and discharge, we used Markov models.\textsuperscript{9,10} Our models trace a hypothetical cohort of patients until all are dead, placing them into 1 of 3 health states: well, disabled, or dead. The number of patients in each health state was recorded in yearly increments, and the total number of person-years of time spent in each health state was tallied to calculate QALYs.

We modeled all direct medical costs associated with patient transfer, SAH hospitalization, and long-term disability. We took the societal perspective in which all costs are included regardless of who pays. A discount rate of 3\% was used in calculating costs and benefits.\textsuperscript{11}

Model inputs were derived from the literature and from a large cohort study (Table 1). The following hierarchy of evidence was used: the most recent meta-analysis; randomized, placebo-controlled clinical trials; prospective cohort studies; case-control and case-series data; and estimations based on consultation with experts in the field. Input ranges for sensitivity analyses were derived from 95\% CIs from experimental data when available; conservatively large CIs were estimated for other inputs.

**Risks**

The following inputs were derived from a cohort study of care for SAH in California from 1990 to 1998\textsuperscript{7}: mean age of patients admitted with SAH to hospitals in California and differences between low- and high-volume hospitals in mortality risk, risk of disability, mean hospital charges, and time to treatment. Methods of the cohort study are detailed elsewhere.\textsuperscript{7}

Briefly, discharge abstracts from the Office of Statewide Health Planning and Development for all patients with ICD-9 codes for SAH admitted to nonfederal hospitals in the state of California from 1990 to 1998 were retrieved. Only admissions through the emergency department were analyzed. The outcome of disability was defined as discharge to a rehabilitation hospital or nursing home because prediagnosis disability is unusual and discharge to one of those institutions has been shown to correlate with Rankin Scale score.\textsuperscript{12} Multivariable analysis adjusted for age, sex, ethnicity, year of treatment, payment source, and admission acuity.\textsuperscript{7}

For the present analysis, risks and charges were calculated for low-volume hospitals, and then ORs and ratios of geometric means from a multivariable analysis were used to determine the adjusted risks and charges for high-volume hospitals. Variables in the previous publication that were calculated in quartiles were recalculated using a dichotomous definition of high-volume. To evaluate the independent contribution of offering endovascular services at high-volume hospitals, we included a separate term in the multivariable model for hospitals using endovascular treatment in \textsuperscript{\geq}5\% of cases of SAH. Projected rates of disability, death, and costs were then calculated for high-volume hospitals with endovascular services by including this coefficient when projecting from low-volume hospitals.

The time to treatment variable was defined as the number of days between admission and either surgical clipping or coil embolization.\textsuperscript{13} If the procedure was performed on the day of admission, the coefficient when projecting from low-volume hospitals.

All-cause mortality rates, specific for age and sex, were derived from US mortality figures from 1990 to 1995.\textsuperscript{14} These figures are provided for ages grouped by decade and for those \textsuperscript{\geq}85 years of age. We used geometric interpolation and, for ages \textsuperscript{\geq}85 years, geometric extrapolation to estimate mortality rates specific to year of age.\textsuperscript{15} The relative risk of mortality for disabled patients was derived from a study of patients with major disability after traumatic brain injury,\textsuperscript{16} which is similar to risks found in patients with stroke.\textsuperscript{17}

Death of critically ill patients during transport has been shown to be rare.\textsuperscript{18–20} However, there are increased risks associated with transferring a patient as a result of medical instability;\textsuperscript{21} significant changes in physiology and vital signs have been documented during interhospital transport.\textsuperscript{22} Observational studies have not dissociated the increased risk of death resulting from transfer from the increased risk of death associated with the poor prognosis of transferred patients. Using available evidence,\textsuperscript{18–21,23–27} we conservatively approximated that the risk of death associated with interhospital transfer was 2\%. For the regionalization policy, we assumed that

![Decision tree model](http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.104.159158/-/DC1/DC1.png)
patients would be transferred from low-volume hospitals within 24 hours of arrival.

**Costs**
Hospital charges for admission for SAH at low- and high-volume hospitals, which may include profits and uncollectible overbilling, were converted to costs by use of cost-to-charge ratios specific to aneurysm repair published by the US Health Care Financing Administration for 1999 to 2000. For cost of transfer, we assumed that patients would be transferred by helicopter and estimated cost from charges for emergency medical services transfer of critically ill trauma patients. Costs of caring for the disabled were estimated from a study of moderately or severely disabled stroke patients.

**Utility**
QALYs were used to measure benefits. Death was given a utility of 0, and disability-free survival given a utility of 1. Because there are no studies of the disutility of disability after SAH, disability was given a utility of 0.25 on the basis of the study by Gage and colleagues of outcomes after brain injury. In that study, an average utility for moderate and major strokes was derived by use of time tradeoff and standard gamble methods for permanent disability states after stroke for 83 patients with atrial fibrillation.

**Sensitivity Analysis**
Sensitivity analyses were performed to determine the robustness of the findings and to identify key variables for future research. We varied each input individually through a broad range of reasonable values to determine whether conclusions would change at the extremes. Because interventions with cost-utility ratios of <$100 000/QALY or <$50 000/QALY are both considered cost-effective, values for model inputs resulting in these cost-utility ratios were determined. All analyses were performed with Stata Version 7.0 or Microsoft Excel 2000.

**Results**
In the base case (Table 1), we modeled outcomes for a 59-year-old woman with SAH arriving at a hospital with 20 admissions per year for SAH. If the patient was not transferred, expected QALYs were 5.64 per patient, and cost per patient was $100 457. If the patient was transferred to a high-volume hospital, expected QALYs were 7.23 per patient, and cost was $117 284 per patient. Thus, regionalization resulted in a net gain of 1.60 QALYs per patient at a cost of $10 548/QALY. If the patient was transferred to a high-volume hospital that offered endovascular treatment in 5% of cases, regionalization resulted in a net gain of 2.04 QALYs and a cost of $4553 per patient, for a net cost of $2232/QALY.

Sensitivity analyses were performed by determining model results through a reasonable range of each input variable (Table 2). With higher cut points to define high volume, the cost-utility ratio decreased. If the definition of high volume was set at ≥50 admissions for SAH per year, the regional-

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**TABLE 1. Model Inputs**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Best Estimate</th>
<th>Source</th>
<th>Range Tested</th>
<th>Results at Low and High Points in Range, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59</td>
<td>Cohort study (mean)</td>
<td>30–70</td>
<td>Low: 3569, High: 22 895</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Male/mixed group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-volume definition, admissions/y</td>
<td>≥20</td>
<td>Cohort study (optimal definition)</td>
<td>≥3, ≥50</td>
<td>Low: 17 103, High: Dominant*</td>
</tr>
<tr>
<td><strong>Risks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background mortality</td>
<td>US age/sex specific</td>
<td>Actual rates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival difference for HVHs vs LVHs, %</td>
<td>10.1</td>
<td>Cohort study</td>
<td>0–20</td>
<td>Ineffective* 5274</td>
</tr>
<tr>
<td>Disability difference for HVHs vs LVHs, %</td>
<td>2.2</td>
<td>Cohort study</td>
<td>0–20</td>
<td>Dominant*</td>
</tr>
<tr>
<td>Risk of death during transfer, %</td>
<td>2.0</td>
<td>Case-control (used as basis for expert opinion)</td>
<td>0–10</td>
<td>8478, 54 424</td>
</tr>
<tr>
<td>RR of mortality resulting from disability after SAH</td>
<td>3.73</td>
<td>Cohort study</td>
<td>2.74–5.07</td>
<td>Low: 10 236, High: 10 880</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference between HVHs vs LVHs, $</td>
<td>$19 783†</td>
<td>Cohort study</td>
<td>15 000–50 000</td>
<td>Low: 7649, High: 28 983</td>
</tr>
<tr>
<td>Disability, annually, $</td>
<td>$20 000</td>
<td>Estimate</td>
<td>13 000–30 000</td>
<td>Low: 11 542, High: 9128</td>
</tr>
<tr>
<td>Transfer, $</td>
<td>$2214</td>
<td>Cost-effectiveness analysis</td>
<td>2000–8000</td>
<td>Low: 10 434, High: 14 091</td>
</tr>
<tr>
<td>Discount rate, %</td>
<td>3.00</td>
<td>Standard</td>
<td>0–5‡</td>
<td>Low: 6815, High: 13 338</td>
</tr>
<tr>
<td><strong>Utilities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well</td>
<td>1</td>
<td>Definition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>Definition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent disability</td>
<td>0.25</td>
<td>Extrapolation</td>
<td>0–0.5</td>
<td>Low: 10 202, High: 10 954</td>
</tr>
</tbody>
</table>

HVHs indicates high-volume hospitals; LVHs, low-volume hospitals. Input ranges are derived from the literature and normal, unless noted.

*For definition of high-volume of ≥50 admissions annually, 2.64 QALYs gained and $5044 saved; for 0 survival difference between HVHs and LVHs, 0.02 QALYs lost and $16 827 spent; for 0 difference in disability risk, 4.00 QALYs gained and $4955 saved.
†Cost of LVH is $47 517 per patient. Cost of HVH was varied to calculate sensitivities.
‡Log-normal distribution.
§Estimated range.
Regionalization policy resulted in cost savings and a gain in QALYs (Figure 2). When the absolute difference in mortality between high- and low-volume hospitals was ≤0.15% (compared with 10.1% in the base case), regionalization was ineffective. Borderline cost-effectiveness ($50,000/QALY) occurred when the risk of death in transfer was 5-fold higher than the base case (Figure 3) or cost of transfer was 30 times the base case. A difference in mortality between low- and high-volume hospitals of <2.2% (Figure 4) or a difference in cost between low- and high-volume hospitals of >$84,480 also resulted in a cost-effectiveness ratio of >$50,000/QALY.

Discussion

Regionalization of treatment for patients with SAH involves a tradeoff between an initial period of greater instability during patient transfer and a potential reduction in the risk of death or disability from SAH in the subsequent hospitalization.7 From inputs derived from the literature and a recent cohort study in California, we found that transfer of patients with SAH from low- to high-volume hospitals was cost-effective. A gain of 1.60 QALYs per patient would result, at a cost of $10,548/QALY. Transfer remained cost-effective over a broad range of model inputs. If a patient was transferred to a high-volume hospital that offered endovascular therapy, the benefit of transfer was greater, with a net cost of $2232/QALY. We were unable to evaluate the independent impact of neurointensivists on outcomes, but prior studies suggest that their presence at high-volume hospitals may account for some of the benefit.31,32

Although we relied heavily on estimates from a large cohort study of SAH treatment in California,7 it is likely that our conclusions would have been the same if we had used data from other published cohort studies. The differences in in-hospital mortality between high- and low-volume hospitals have been measured variably, but each study has found a significant reduction in mortality at high-volume hospitals compatible with absolute differences greater than the 2.2% threshold we found for borderline cost-effectiveness.3–6 Thus, transfer to high-volume hospitals would be expected to be cost-effective if model inputs from these other studies were used.

From 1990 to 1998, a total of 9683 patients were admitted with SAH through the emergency departments of hospitals in California.7 Of these patients, only 4.8% were transferred to high-volume hospitals.7 Implementation of a regionalization policy for SAH in California would involve fundamental changes in current practice patterns and in the distribution of specialized resources. Our

### Table 2. Threshold Levels for Model Inputs for Varying Costs of Policy of Transferring Patients

<table>
<thead>
<tr>
<th></th>
<th>$10,548/QALY (Base Case)</th>
<th>$50,000/QALY</th>
<th>$100,000/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference in survival at HVHs vs LVHs, %</td>
<td>10.1</td>
<td>2.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Difference in cost at HVHs vs LVHs, $</td>
<td>19,783</td>
<td>84,480</td>
<td>166,510</td>
</tr>
<tr>
<td>Risk of death in transfer, %</td>
<td>2.0</td>
<td>9.8</td>
<td>10.9</td>
</tr>
<tr>
<td>Cost of transfer, $</td>
<td>2214</td>
<td>66,911</td>
<td>148,941</td>
</tr>
<tr>
<td>Disability utility</td>
<td>0.25</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
</tbody>
</table>

*Cost of low-volume hospital (LVH) is $47,517 per patient. Cost of high-volume hospital (HVH) was varied to determine threshold levels.

Figure 2. Cost-utility ratios for various definitions of high-volume hospitals (annual admissions for SAH). Cost-utility ratios were calculated with Markov models with changing inputs for each definition based on data from discharge abstracts for SAH admissions in 1990 to 1998 from California’s Office of Statewide Health Planning and Development. Expected cost-utility ratio is demonstrated for range of cut points differentiating high- and low-volume hospitals. Definitions of high volume at greater annual admissions for SAH are generally more cost-effective. However, all cut points are associated with favorable cost-utility ratios. Negative values for net cost per QALY ($/QALY), such as those associated with volumes >44, represent cut points at which transfer would be cost saving.

Figure 3. Univariate sensitivity analysis evaluating net cost per QALY ($/QALY) vs estimation of risk of death during transfer. Base-case assumption of 2% increased risk of death associated with transfer is labeled. Also labeled are risks at which transfer is no longer cost-effective by standard criteria of $50,000/QALY or $100,000/QALY (9.8% and 10.9%, respectively).
Low-volume hospitals (black) have high-volume hospitals based on admissions for SAH from 1990 through 1998. Low-volume hospitals (black) have <20 annual admissions for SAH; high-volume hospitals (white) have ≥20 annual admissions.

Analysis suggests that the efforts required to make such changes would likely be rewarded with improvements in outcome at a cost that is modest by current standards.

Our analysis has several limitations. Data from only nonrandomized observational studies are available for important inputs: risk of death associated with transfer and the difference in mortality between low- and high-volume hospitals. Although the observational studies controlled for differences in measured patient characteristics, undetected biases may have affected results. The model found that transfer was cost-effective even with an absolute difference in mortality of only 2.2% compared with 10.1% in the base case, but risk differences in those treated at high- and low-volume hospitals could account for some of the difference in outcomes, and a prospective cohort study could provide important confirmation. The risks of transportation in SAH may be significantly greater than in other critical medical illnesses because time to treatment is an important predictor of outcome after aneurysmal bleeding. However, we found that aneurysms were treated more rapidly at high-volume centers (mean, 3.0 days after presentation) compared with low-volume centers (mean, 3.8 days; \(P=0.01\)), and this may partially mitigate any delay from patient transportation.

A policy of regionalization could be difficult to implement because of the distances between transferring and receiving hospitals. However, low- and high-volume hospitals are distributed fairly evenly across California (Figure 5), with a regional high-volume center already present in most areas of the state. Although the northernmost area of California does not have a regional center, one of the several hospitals serving that community could be designated a regional center, and its volume would subsequently increase. Gradual implementation of the policy in the existing network of California hospitals could allow redistribution of patients and resources. Of course, any such policy would need to be flexible because transfer for a particular patient may be inappropriate for a variety of reasons.

The Brain Attack Coalition has published guidelines for primary stroke centers and is creating guidelines for comprehensive stroke centers. The goal of this effort is to improve quality of care for patients with stroke by recognizing centers that provide the best care. Our analysis suggests that treatment volume may be an important predictor of quality of care for SAH. Even if the volume of SAH cases treated is the only criterion for defining comprehensive stroke centers, transfer to such centers may be cost-effective.

This analysis suggests that transferring patients with SAH who arrive at low-volume hospitals to high-volume hospitals is probably cost-effective. Further studies should include more detailed prospective cohort analysis delineating the differences in outcomes between low- and high-volume hospitals and the risks associated with transfer.

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