

## SPECIAL ARTICLE

# Cost Effectiveness of Lung-Volume–Reduction Surgery for Patients with Severe Emphysema

National Emphysema Treatment Trial Research Group\*

## ABSTRACT

**BACKGROUND**

The National Emphysema Treatment Trial, a randomized clinical trial comparing lung-volume–reduction surgery with medical therapy for severe emphysema, included a prospective economic analysis.

**METHODS**

After pulmonary rehabilitation, 1218 patients at 17 medical centers were randomly assigned to lung-volume–reduction surgery or continued medical treatment. Costs for the use of medical care, medications, transportation, and time spent receiving treatment were derived from Medicare claims and data from the trial. Cost effectiveness was calculated over the duration of the trial and was estimated for 10 years of follow-up with the use of modeling based on observed trends in survival, cost, and quality of life.

**RESULTS**

Interim analyses identified a group of patients with excess mortality and little chance of improved functional status after surgery. When these patients were excluded, the cost-effectiveness ratio for lung-volume–reduction surgery as compared with medical therapy was \$190,000 per quality-adjusted life-year gained at 3 years and \$53,000 per quality-adjusted life-year gained at 10 years. Subgroup analyses identified patients with predominantly upper-lobe emphysema and low exercise capacity after pulmonary rehabilitation who had lower mortality and better functional status than patients who received medical therapy. The cost-effectiveness ratio in this subgroup was \$98,000 per quality-adjusted life-year gained at 3 years and \$21,000 at 10 years. Bootstrap analysis revealed substantial uncertainty for the subgroup and 10-year estimates.

**CONCLUSIONS**

Given its cost and benefits over three years of follow-up, lung-volume–reduction surgery is costly relative to medical therapy. Although the predictions are subject to substantial uncertainty, the procedure may be cost effective if benefits can be maintained over time.

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**L**UNG-VOLUME-REDUCTION SURGERY IS a new treatment for patients with severe emphysema, the value of which is, as yet, uncertain.<sup>1-5</sup> Because the potential clinical and economic effects of lung-volume-reduction surgery are large, a federally sponsored, multicenter, randomized, controlled trial — the National Emphysema Treatment Trial (NETT) — was initiated to evaluate the effectiveness of lung-volume-reduction surgery. This trial included a prospective, economic analysis.

## METHODS

The design and methods of the NETT and the cost-effectiveness component of the trial have been described previously.<sup>6,7</sup> The trial design and economic analysis are briefly summarized below.

### CLINICAL TRIAL

The NETT is a multicenter, randomized, controlled trial comparing lung-volume-reduction surgery with medical therapy for patients with severe emphysema. Between January 1998 and July 2002, 17 centers randomly assigned 1218 patients with severe emphysema to either lung-volume-reduction surgery or medical therapy.<sup>8</sup> All patients provided written informed consent, and the study was approved by the institutional review board at each center.

Before randomization, all patients underwent pulmonary rehabilitation. The primary outcome measures were overall mortality and maximal exercise capacity (on bicycle ergometry) two years after randomization. Secondary outcomes included results on the six-minute walk test<sup>9</sup> and lung-function tests and general health-related quality of life as measured on the Quality of Well-Being scale.<sup>10</sup> These outcomes were assessed at screening, after pulmonary rehabilitation (base line), at 6 months, at 12 months, and yearly thereafter.

### COST-EFFECTIVENESS ANALYSIS

We conducted a cost-effectiveness analysis prospectively with the use of a societal perspective to determine the cost per quality-adjusted life-year gained with lung-volume-reduction surgery plus medical therapy as compared with medical therapy alone for patients with severe emphysema.<sup>11</sup> For the cost analysis, we estimated the value of the following resources: medical goods and services, transportation to and from health care facilities, time spent by

family and friends in caring for the patient, and time spent by the patient in receiving treatment. A detailed description of the cost-effectiveness analysis is presented in Supplementary Appendix 1 (available with the full text of this article at <http://www.nejm.org>).

### *Life Expectancy and Health-State Preferences*

The number of quality-adjusted life-years is derived by the adjustment of survival data for health-state preferences, also known as “utilities.”<sup>12</sup> Weights for these utilities were obtained from the self-administered version of the Quality of Well-Being questionnaire, a comprehensive measure of health-related quality of life covering acute and chronic symptoms, self-care, mobility, physical activity and functioning, and social activity. Scores for each patient are converted to utility weights, on a scale ranging from 0 (death) to 1.0 (optimal quality of life). The Quality of Well-Being scale has been used in a variety of clinical studies for medical and surgical conditions, including chronic obstructive pulmonary disease,<sup>13</sup> the acquired immunodeficiency syndrome, cystic fibrosis,<sup>14</sup> diabetes, atrial fibrillation, lung transplantation,<sup>15</sup> arthritis,<sup>16</sup> and cancer.<sup>17</sup>

### *Measurement of Resource Utilization*

Information on the utilization of medical care was based on Medicare claims for study participants that were provided by the Centers for Medicare and Medicaid Services. Medicare reimbursed providers for trial-related medical care for study participants, including the screening evaluation, pulmonary rehabilitation before randomization, the surgical procedure itself, and trial-related follow-up visits after surgery. Other Medicare services included inpatient care; outpatient care provided by physicians; ambulatory laboratory, diagnostic, and radiology services; home health services; supplementary oxygen for home use; up to 100 days of care at a skilled nursing facility; and hospice care. The use of medications for emphysema on an outpatient basis (not covered by Medicare) was recorded at follow-up visits. Doses of medications were based on the usual doses for adults that are recorded in the manufacturer’s package insert.<sup>18</sup>

Several methods were used to estimate emphysema-related utilization of nonmedical goods and services. Travel distances to care facilities were estimated with the use of software that calculated the distances traveled from the ZIP Code of the patient’s residence to NETT-affiliated facilities.<sup>19</sup> Enrollees

gave estimates of the weekly average number of hours of care provided to them by unpaid caregivers (family and friends). The time spent by patients in seeking medical care was estimated on the basis of Medicare records for ambulatory care and hospitalizations.

#### *Valuation of Resources Used*

The value of medical care was estimated on the basis of Medicare reimbursements for covered services, with adjustment to 2002 dollars according to the medical care component of the Consumer Price Index.<sup>20</sup> Costs for medications related to respiratory disease were determined on the basis of the average wholesale price for 2002, discounted by 15 percent in order to adjust for typical retail-acquisition costs, with a \$2.50 dispensing fee added for each 30-day period.<sup>21</sup> The lowest price for available generic versions of medications was used. Costs for transportation to and from health care facilities were determined by multiplying the travel distances by the federal government's reimbursement rate per mile.<sup>19,22</sup> The value of time spent by family and friends in caring for patients was calculated on the basis of the average wage for workers 20 to 64 years of age, as reported by the Bureau of Labor Statistics.<sup>23</sup> The value of the time patients spent receiving treatment was calculated on the basis of the average wage for workers 65 years of age or older.<sup>23</sup> In accordance with guidelines for conducting cost-effectiveness studies,<sup>11</sup> costs and benefits accruing after year 1 were discounted at an annual rate of 3 percent.

#### **STATISTICAL ANALYSIS**

All analyses were conducted according to the intention-to-treat principle. Patients who were still alive at the time of a given visit but who did not complete a questionnaire were assigned a value for the Quality of Well-Being score that was half of the lowest score among all patients who completed a questionnaire at the corresponding visit.<sup>24</sup> In secondary analyses of patients who did not complete questionnaires, we used the mean and median values for the patient's treatment group. All analyses exclude patients who did not use Medicare as their primary insurer and those who were enrolled in Medicare+Choice plans, since no health care claims were available for these patients. The average total costs and the mean numbers of quality-adjusted life-years gained and associated 95 percent confidence intervals were determined for each treatment group with

the use of the nonparametric Kaplan–Meier sample-average estimator.<sup>25</sup> This estimator sums over intervals of follow-up either the mean costs (for the calculation of total costs) or the mean utility weights (for the calculation of the number of quality-adjusted life-years) for patients who are alive at the beginning of the interval, weighted according to the Kaplan–Meier estimate of the probability of surviving until the beginning of the interval. All reported P values are based on two-sided tests.

Cost effectiveness was calculated as the ratio of the difference in costs between the surgery group and the medical-therapy group divided by the difference in quality-adjusted life-years gained between the two groups. Cost-effectiveness ratios were computed for the trial period (3 years of follow-up) and then projected for 5 and 10 years after randomization. To estimate long-term survival for the medical-therapy group, a log-logistic model was fitted, with the use of data from patients who survived for at least one year after randomization. Regression analysis was used to determine the relation between survival and treatment-group assignment in order to derive estimates of the parameters for the model. The relative hazard of death in the surgery group as compared with the medical-therapy group was set at observed levels for year 3 and then, in separate models, was assumed to change to 1.0 (no survival benefit) by 3 years, 5 years, and 10 years. Projected costs and Quality of Well-Being scores were based on trend lines fitted to monthly values for the surgery and medical-therapy groups during the third year of follow-up.

The nonparametric bootstrap method with 2000 replications was used to derive a 95 percent confidence interval for the incremental cost-effectiveness ratio at three years of follow-up.<sup>26</sup> To describe the uncertainty in the estimates of cost effectiveness at 10 years, we constructed cost-effectiveness–acceptability curves with the bootstrap method applied to projected survival and estimates of cost and quality-adjusted life-years gained for each group of patients.<sup>27</sup>

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## RESULTS

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#### **STUDY PATIENTS**

Interim analysis of the NETT cohort identified a subgroup of 140 patients with a high risk of death and little chance of improved function after surgery.<sup>24</sup> Patients in this subgroup became ineligible for enrollment as of May 2001 and are thus exclud-

ed from the cost-effectiveness analysis. Twelve additional participants were excluded from the cost-effectiveness analysis (seven in the surgery group and five in the medical-therapy group) — three patients because they were not enrolled in Medicare, eight because they were enrolled in Medicare+Choice plans at the time of randomization, and one because the patient's Medicare claims could not be located. The mean ( $\pm$ SD) Quality of Well-Being score before randomization was  $0.58\pm 0.12$  in the surgery group and  $0.57\pm 0.11$  in the medical-therapy group.

#### USE AND COSTS OF RESOURCES

During the first six months of follow-up, the mean number of inpatient hospital days was significantly

higher in the surgery group than in the medical-therapy group (23.3 days vs. 3.0 days,  $P<0.001$ ), as was the percentage of patients with more than 25 hospital days (26 percent vs. 3 percent,  $P<0.001$ ). During the first year, the mean numbers of hospital days and days of ambulatory care per person and the total number of nursing-home admissions were significantly greater in the surgery group than in the medical-therapy group (Table 1). In contrast, during the second year, the mean numbers of hospital days and emergency-room visits per person were significantly lower in the surgery group than in the medical-therapy group ( $P=0.005$  and  $P=0.04$ , respectively). During the third year, there were no significant differences between the two groups in the use of resources (Table 1). Use of bronchodila-

**Table 1. Measures of Health Care Utilization According to Time after Randomization.\***

Variable	Surgery Group		Medical-Therapy Group		P Value
	No. of Patients	Mean No. (95% CI)	No. of Patients	Mean No. (95% CI)	
<b>0–12 Mo after randomization</b>	531		535		
Hospital days		24.9 (22.3–27.6)		4.9 (4.0–5.8)	<0.001
Days of ambulatory care		10.3 (9.5–11.2)		8.6 (7.8–9.4)	0.005
Emergency-room visits		0.6 (0.5–0.7)		0.8 (0.6–0.9)	0.11
Hospice days		1.2 (0.0–2.7)		1.0 (0.0–2.3)	0.27
Nursing-home admissions		0.1 (0.0–0.3)		0.0 (0.0–0.1)	0.005
Claims for supplemental oxygen		6.7 (6.2–7.3)		7.2 (6.6–7.7)	0.19
<b>13–24 Mo after randomization</b>	407		424		
Hospital days		3.2 (2.3–4.1)		6.1 (4.5–7.6)	0.005
Days of ambulatory care		5.0 (4.4–5.6)		4.9 (4.2–5.5)	0.49
Emergency-room visits		0.5 (0.4–0.6)		0.7 (0.6–0.8)	0.04
Hospice days		1.7 (0.0–3.6)		2.2 (0.0–4.6)	0.15
Nursing-home admissions		<0.1 (0.0–0.1)		<0.1 (0.0–0.1)	0.49
Claims for supplemental oxygen		5.8 (5.2–6.4)		6.5 (5.9–7.1)	0.09
<b>25–36 Mo after randomization</b>	277		278		
Hospital days		4.0 (2.3–5.8)		5.2 (3.8–6.7)	0.08
Days of ambulatory care		4.5 (3.8–5.2)		4.4 (3.5–5.2)	0.43
Emergency-room visits		0.5 (0.4–0.6)		0.7 (0.5–0.8)	0.10
Hospice days		2.5 (0.3–5.2)		3.6 (0.9–6.2)	0.12
Nursing-home admissions		<0.1 (0.0–0.1)		<0.1 (0.0–0.1)	0.10
Claims for supplemental oxygen		5.9 (5.1–6.6)		5.6 (4.8–6.3)	0.39

\* P values were derived by two-sided t-tests for equality of means. CI denotes confidence interval.

**Table 2. Mean Direct Medical Costs and Total Health Care–Related Costs According to Time after Randomization.\***

Variable	Surgery Group		Medical-Therapy Group		P Value
	No. of Patients	Mean Cost (95% CI)	No. of Patients	Mean Cost (95% CI)	
		\$		\$	
<b>0–12 Mo after randomization</b>	531		535		
Direct medical costs		61,145 (56,069–66,220)		15,738 (14,006–17,470)	<0.001
Total costs		71,515 (65,921–77,109)		23,371 (21,056–25,686)	<0.001
<b>13–24 Mo after randomization</b>	407		424		
Direct medical costs		9,474 (8,260–10,688)		15,648 (12,934–18,362)	<0.001
Total costs		13,222 (11,479–14,964)		21,319 (18,004–24,635)	<0.001
<b>25–36 Mo after randomization</b>	277		278		
Direct medical costs		10,199 (8,161–12,236)		12,303 (9,977–14,629)	0.18
Total costs		14,215 (11,529–16,901)		17,870 (14,785–20,954)	0.08

\* Costs are reported in 2002 dollars. Direct medical costs include Medicare reimbursements and pharmacy costs. Total costs include direct medical costs plus the value of the time spent by caregivers, the value of the time spent by the patient, and travel costs. After year 1, costs were discounted by 3 percent per year. P values were derived by two-sided t-tests for equality of means. CI denotes confidence interval.

tors did not differ between the groups during any period (data not shown).

The total costs were substantially higher for patients in the surgery group than for patients in the medical-therapy group during the first 12 months after randomization, largely because of costs incurred during surgery and during the 6 months after surgery (total at 6 months, \$62,753 vs. \$12,932;  $P < 0.001$ ). During the second year, the total costs and the costs of medical care were significantly lower for patients in the surgery group; the total costs were not significantly different in the two groups during the third year (Table 2). The mean total medical cost per patient during follow-up months 7 through 36 was nearly \$10,000 lower in the surgery group than in the medical-therapy group (\$36,199 vs. \$49,628,  $P < 0.001$ ), largely because patients in the surgery group had fewer hospital days during that period.

The mean total costs per person at three years were \$98,952 in the surgery group and \$62,560 in the medical-therapy group ( $P < 0.001$ ). Per-person costs for direct medical care alone were \$80,818 in the surgery group and \$43,689 in the medical-therapy group over the three-year period ( $P < 0.001$ ) (Table 2). Nonmedical costs did not differ significantly between the two groups ( $P = 0.57$ ; data not shown).

#### QUALITY-ADJUSTED LIFE-YEARS

After three years of follow-up, the mean number of quality-adjusted life-years gained was higher in the surgery group than in the medical-therapy group (1.46 vs. 1.27,  $P < 0.001$ ) (Table 3). The mean number of quality-adjusted life-years gained was also significantly higher in the surgery group at 12 and 24 months of follow-up (data not shown). Alternative methods of imputing missing Quality of Well-Being scores did not substantively change the results.

#### COST-EFFECTIVENESS RATIOS

With the exclusion of the previously described subgroup of high-risk patients, the estimated cost-effectiveness ratio for lung-volume–reduction surgery as compared with medical therapy during the three years after the initiation of treatment was \$190,000 per quality-adjusted life-year gained (Table 3). When costs for direct medical care alone were considered (as they would be from the perspective of the health insurer), the cost-effectiveness ratio for surgery as compared with medical therapy was \$193,000 per quality-adjusted life-year gained.

The cost-effectiveness ratio for surgery as compared with medical therapy at 10 years was \$53,000 per quality-adjusted life-year gained. Under the as-

**Table 3. Total Health Care–Related Costs, Quality-Adjusted Life-Years Gained, and Estimated Cost-Effectiveness Ratios at Three Years.\***

Variable	Surgery Group		Medical-Therapy Group		P Value	Incremental Cost-Effectiveness Ratio for Surgery (\$)
	No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)		
All patients	531		535			190,000
Total costs (\$)		98,952 (91,694–106,210)		62,560 (56,572–68,547)	<0.001	
Quality-adjusted life-years gained		1.46 (1.46–1.47)		1.27 (1.27–1.28)	<0.001	
Patients with predominantly upper-lobe emphysema and low exercise capacity	137		148			98,000
Total costs (\$)		110,815 (93,404–128,226)		61,804 (50,248–73,359)	<0.001	
Quality-adjusted life-years gained		1.54 (1.53–1.55)		1.04 (1.03–1.05)	<0.001	
Patients with predominantly upper-lobe emphysema and high exercise capacity	204		212			240,000
Total costs (\$)		84,331 (73,699–94,962)		55,858 (47,161–64,555)	<0.001	
Quality-adjusted life-years gained		1.54 (1.54–1.55)		1.42 (1.42–1.43)	<0.001	
Patients with non–upper-lobe emphysema and low exercise capacity	82		65			330,000
Total costs (\$)		111,986 (93,944–130,027)		65,655 (52,075–79,236)	<0.001	
Quality-adjusted life-years gained		1.25 (1.23–1.26)		1.10 (1.09–1.12)	<0.001	

\* Upper-lobe predominance of emphysema was defined according to the results on computed tomography. Exercise capacity was defined as the maximal workload on bicycle ergometry. Low exercise capacity was defined as a workload of 25 W or less for women and 40 W or less for men; a workload above these thresholds was considered to represent high exercise capacity. P values were derived by two-sided t-tests for equality of means. The results for the overall cohort exclude 140 patients previously found to be at high risk for death, 3 patients who were not enrolled in Medicare, 8 patients who were enrolled in Medicare+Choice plans, and 1 patient whose claims records were missing. Total costs include direct medical costs (Medicare reimbursements and pharmacy costs) plus the value of the time spent by caregivers, the value of the time spent by the patient, and travel costs. After year 1, costs were discounted by 3 percent per year. The incremental cost-effectiveness ratio is the cost per additional quality-adjusted life-year gained with lung-volume–reduction surgery. The subgroup of patients with non–upper-lobe emphysema and high exercise capacity is not included, because in this subgroup, surgery was associated with higher total costs and fewer quality-adjusted life-years gained than was medical therapy. CI denotes confidence interval.

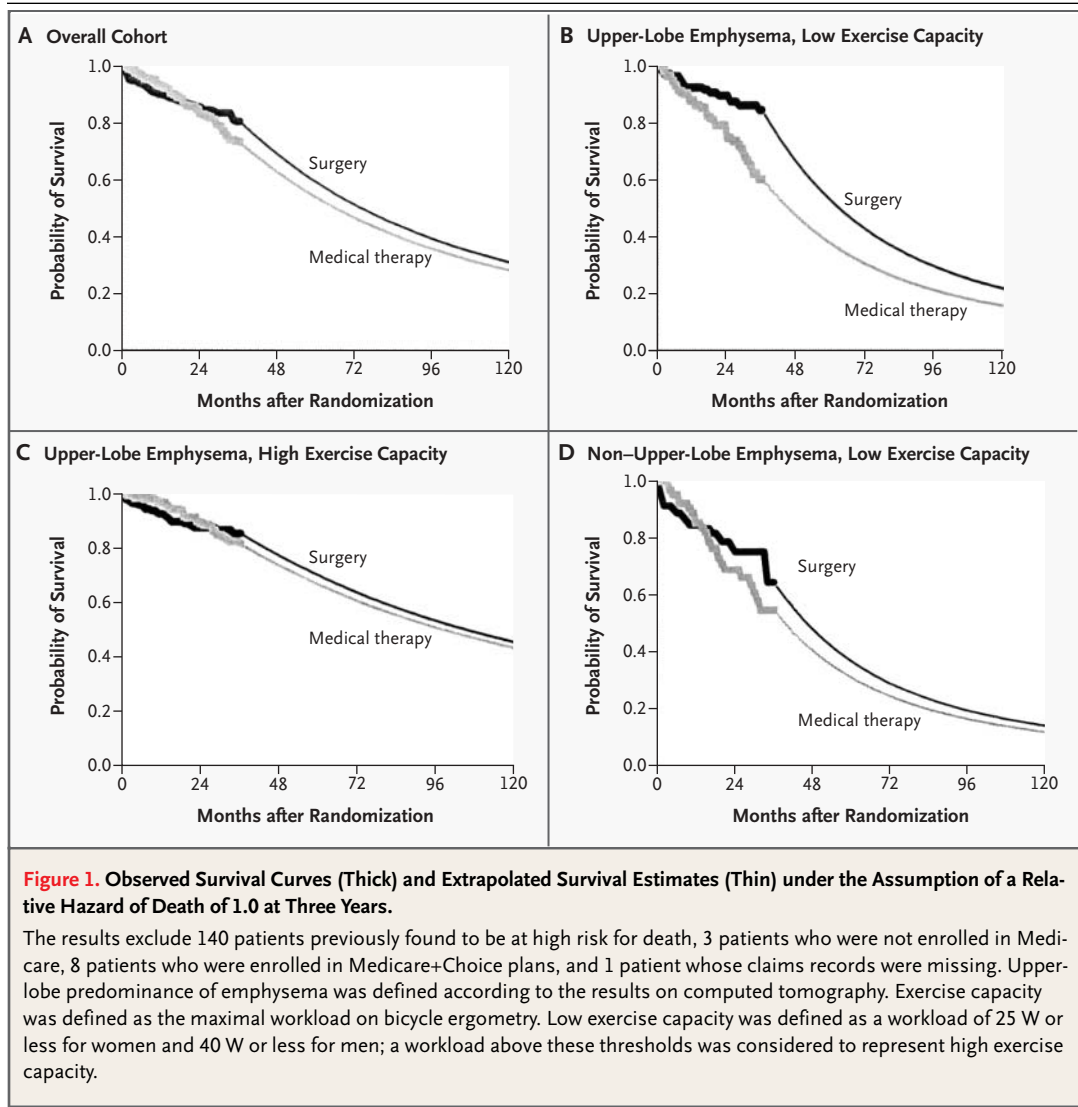
sumption that the survival benefit from surgery lasted 3 years, the projected absolute difference in survival was less than 3 percent at 10 years (Fig. 1A). Increasing the assumed duration of the relative survival benefit from surgery (up to 10 years) changed the incremental cost-effectiveness ratio at 10 years by less than 2 percent.

#### SECONDARY COST-EFFECTIVENESS ANALYSIS BASED ON PREOPERATIVE PREDICTORS OF OUTCOME

Post hoc analyses in the clinical study, including the 1078 patients remaining after the exclusion of the 140 high-risk patients, suggested differential relative benefits from lung-volume–reduction surgery in four subgroups of patients defined according to combinations of two base-line characteristics—the presence or absence of upper-lobe predom-

inance in the distribution of emphysema on computed tomography and low or high maximal exercise capacity after pulmonary rehabilitation (low capacity being defined as a workload of  $\leq 25$  W for women and  $\leq 40$  W for men and high capacity as a workload above these thresholds).<sup>8</sup> In the subgroup of patients who had emphysema without upper-lobe predominance and who had high exercise capacity, patients assigned to lung-volume–reduction surgery had significantly higher mortality than patients assigned to medical therapy, had reduced quality-adjusted survival, and had higher costs.

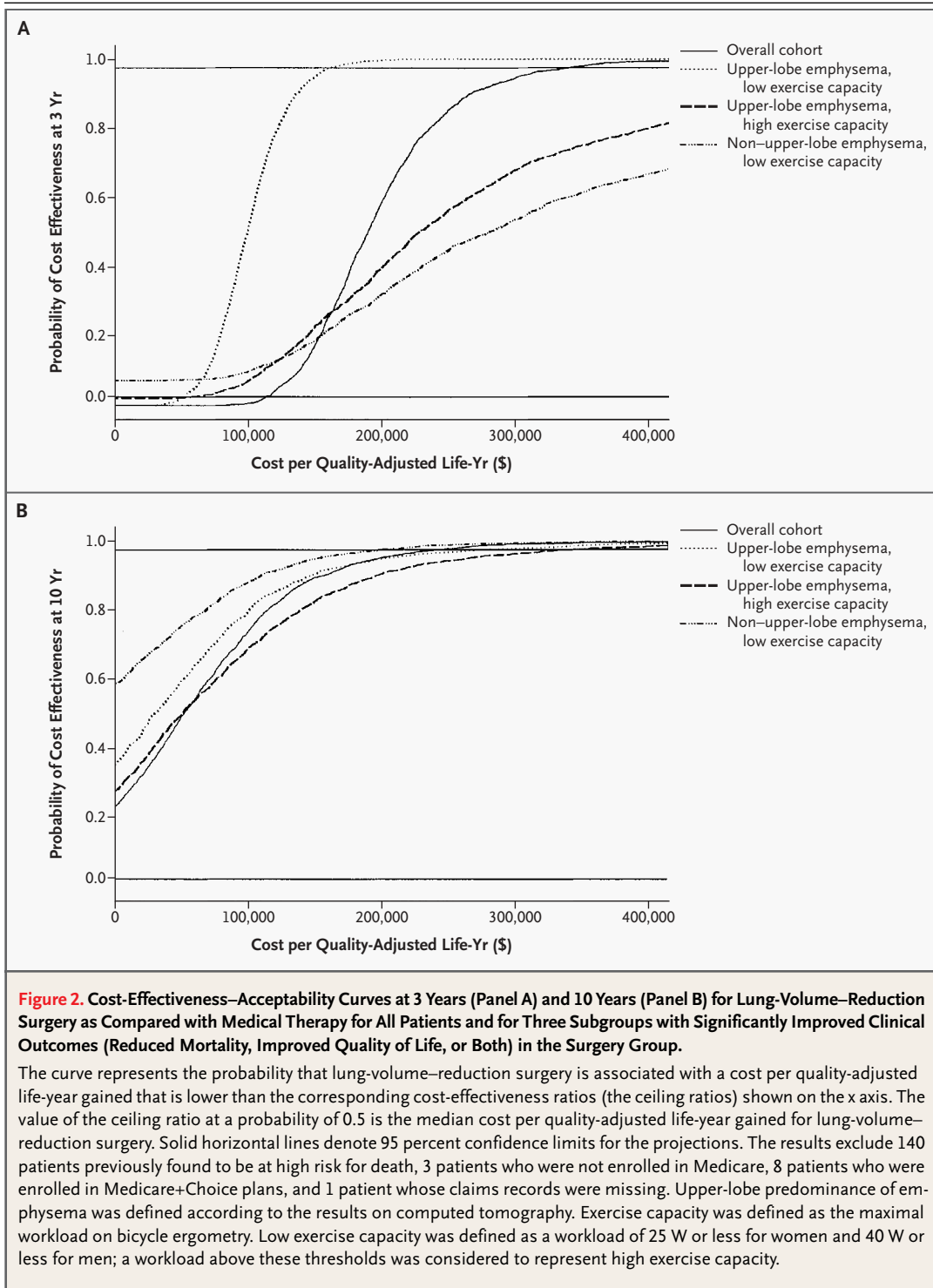
Of the remaining three subgroups, patients with predominantly upper-lobe emphysema and low exercise capacity had the most favorable cost-effectiveness ratio for surgery at three years (\$98,000 per quality-adjusted life-year gained) (Table 3). Although the average total health-related costs were higher



in this subgroup than in the cohort as a whole, the relative improvement in quality-adjusted survival in the surgery group as compared with the medical-therapy group was greater in this subgroup, resulting in improved cost effectiveness. The estimated cost-effectiveness ratio over the three-year follow-up period was much less favorable in the two remaining subgroups of patients — those with predominantly upper-lobe emphysema who had high exercise capacity (\$240,000 per quality-adjusted life-year gained) and those with non-upper-lobe emphysema who had low exercise capacity (\$330,000 per quality-adjusted life-year gained) (Table 3).

When the subgroup of patients with significantly higher mortality and costs was excluded from the

analysis and the most conservative estimates of the survival benefit from surgery were used (Fig. 1B, 1C, and 1D), the projected cost-effectiveness ratios over 10 years of follow-up were \$21,000 per quality-adjusted life-year gained among patients with predominantly upper-lobe emphysema who had low exercise capacity and \$54,000 per quality-adjusted life-year gained among patients with predominantly upper-lobe emphysema who had high exercise capacity. Among patients with non-upper-lobe emphysema and low exercise capacity, surgery was associated with lower costs than medical therapy and a higher number of quality-adjusted life-years gained. The cost-effectiveness-acceptability curves (Fig. 2A and 2B) reveal substantial uncertainty in



these estimates, especially for the group with predominantly upper-lobe emphysema and high exercise capacity and the group with non-upper-lobe emphysema and low exercise capacity.

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#### DISCUSSION

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Many experts propose that the cost effectiveness of lung-volume-reduction surgery should be considered in relation to the outcomes and costs for other medical and surgical procedures.<sup>28-30</sup> Over the observation period in our study, the cost-effectiveness ratio for surgery as compared with medical therapy was relatively unfavorable because of the costs of the surgical procedure and the number of adverse clinical outcomes, very long periods of hospitalization, and a greater number of nursing-home admissions during the first few months after surgery.

The effect of lung-volume-reduction surgery on the national health care budget is uncertain, but it could be substantial. Fewer patients were enrolled in the trial than expected, and about 32 percent of those who began to undergo screening were ultimately determined to be eligible. Nevertheless, if 1 percent of the estimated 2 million persons with emphysema were potentially eligible for lung-volume-reduction surgery, national health expenditures for this procedure (excluding those for initial screening and the costs of pulmonary rehabilitation) might range from \$100 million to \$300 million per year, depending on patients' interest in the procedure and their suitability for it after pulmonary rehabilitation.

A longer-term view is preferable for cost-effectiveness analyses.<sup>31</sup> Our 10-year estimates required mathematical modeling based on extrapolation of the 3-year trial data. These models are based on assumptions that may not be realized. The 10-year estimates suggest that the cost effectiveness of lung-volume-reduction surgery may approach recognized thresholds if the moderate benefits observed during the trial are sustained.<sup>32</sup> We arrived at the relatively favorable results for long-term cost effectiveness using the most conservative estimates for survival (an absolute benefit of <3 percent for surgery), cost, and quality of life at 10 years. Nevertheless, the estimates of long-term cost effectiveness are characterized by substantial uncertainty. We caution that extended follow-up of patients enrolled in the NETT is necessary in order to derive more precise estimates of the long-term cost effectiveness of lung-volume-reduction surgery.

Post hoc subgroup analyses were conducted to identify characteristics of persons who are more likely to have favorable clinical and survival outcomes after surgery. Among patients with predominantly upper-lobe emphysema who had low exercise capacity, lung-volume-reduction surgery was associated with significant improvements in survival and functional outcomes as compared with medical therapy. The cost-effectiveness ratio for lung-volume-reduction surgery for patients who met both of these criteria was more favorable than that for patients who met only one of the criteria and was superior to that for the entire cohort. The very high level of uncertainty regarding the cost effectiveness of lung-volume-reduction surgery in the subgroups that met only one of the two clinical criteria precludes the drawing of any conclusion regarding the cost effectiveness of the procedure for such patients.

Cost-effectiveness ratios for other types of surgery as compared with medical therapy include (in 2002 dollars) \$8,300 to \$64,000 per quality-adjusted life-year gained for coronary-artery bypass surgery,<sup>33-35</sup> \$130,000 to \$220,000 per quality-adjusted life-year gained for lung transplantation,<sup>36,37</sup> \$65,000 per quality-adjusted life-year gained for heart transplantation,<sup>38</sup> and \$47,000 per quality-adjusted life-year gained for the implantation of a cardioverter-defibrillator in a survivor of cardiac arrest with a low cardiac ejection fraction.<sup>35,39</sup>

Our analysis has limitations. Medical and non-medical costs that patients incurred as part of their screening and pulmonary rehabilitation before randomization and administrative costs associated with the maintenance of a center that performs lung-volume-reduction surgery were not included. Although screening and pulmonary rehabilitation increase the cost of treatment, they do not influence the incremental analysis because they are applied equally to both groups. Medicare copayments and deductibles paid by patients for NETT-related services were not included in the analysis. The amounts of these payments varied from center to center and from service to service and thus were extremely difficult to quantify. Clinical trials also necessarily involve more intensive monitoring of patients than does typical clinical practice.<sup>40</sup>

Optimal use of limited health care resources depends on accurate economic information and systematic analysis of new forms of medical technology. Joint sponsorship by the Centers for Medicare

and Medicaid Services permitted parallel collection of Medicare claims for trial participants, thus maximizing the accuracy of the economic data. Modeling is necessary in cost-effectiveness analyses in order to help decision makers consider the long-term effects of the adoption of new medical techniques. The per-patient cost of the adoption of lung-volume-reduction surgery will be high in the short run. The effect of the use of such surgery on national health care expenditures will depend on the fraction of the estimated 2 million people with emphysema who meet the criteria for eligibility and are willing to undergo the procedure, which at present is un-

known. The extent of experience of the participating clinical centers also influenced the economic outcomes in this trial. Health care payers should consider clinical experience as well as the criteria for selection of patients when establishing reimbursement policies for lung-volume-reduction surgery.

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#### APPENDIX

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